EMERGING TRENDS OF BIOMEDICAL APPLICATIONS IN HEALTHCARE

Dr. Prerana Gupta
Dr. Ruby Varghese
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ALEXIS PRESS

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CHAPTER 1

DESIGN AND IMPLEMENTATION OF MENTAL HEALTH MONITORING AND COUNSELING SYSTEM WITH PATIENT HEALTH QUESTIONNAIRE MODULE-9 (PHQ9)

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ABSTRACT:

Individuals' physical and mental well-being determine their personality, which has a significant impact on their lives in a variety of sectors, including their personal, professional, and social lives. The current study discusses a mental health monitoring and counseling system that monitors the mental health of a user continuously by keeping track of daily activities performed and providing counseling to the user. Some existing systems provide mental health monitoring systems but no system provides counseling. Current research is focused on the mental health monitoring and counseling system which consisting a portable body which is installed with multiple wheels and a thermal imaging unit assembled on the body for capturing images of a user having mental health issues, a processing unit connected with the imaging unit for determining facial expression and identity of the user, a communication module integrated with a microcontroller installed on the body for fetching the which are data stored in a user-platform, a touch-responsive display unit assembled on the body for displaying personalized questionnaire for the user, a headband fabricated with the asset of sensors worn by the user for detecting variations in brain activity of the user while responding to the questionnaire and a projection unit mounted on the portable body for providing audio-visual graphic to the user for counseling the user to improve the mental health condition of the user. This system monitors the mental health of a user and accordingly provides counseling to the user on a regular basis to improve the user's mental health including depression and anxiety. This study will help in the proper treatment and reduction of anxiety and depression faced by individuals.

KEYWORDS:

Anxiety, Counseling System, Depression, Mental Health, Psychiatrist.

1. INTRODUCTION

Mental disease is a comprehensive expression that refers to a multiplicity of conditions that might manifest themselves in symptoms that impacts a person's perceptions, thinking, emotions, or behavior. Somebody suffering from a "mental illness" may find it difficult to deal with the

responsibilities of a job, relationships, and other obligations [1], [2]. It is unclear what the link between mental and stress illness is, but it is recognized that stress may exacerbate an episode of mental illness when it occurs. The majority of individuals can manage their "mental illnesses" with medicine, counseling, or a combination of the two [3]–[5]. People are concerned about an individual's physical well-being by checking to see whether he or she has any illness or physiological condition. However, mental health is rarely seen as a crucial aspect impacting a person's life and is sometimes overlooked, or the individual is blamed for failing to execute or complete everyday chores with determination and passion. This leads to questions about a person's commitment, conduct, enthusiasm, and way of life, rather than determining the cause of the person's demotivation [6], [7].

Depression and other mental diseases are stigmatized in society, leaving the sufferer unhappy and alone. Indeed, records and statistical data from the previous several decades demonstrate a rise in the number of persons suffering from depression and other mental illnesses [8]–[10]. People with mild mental illnesses are often found to be unhappy as a result of social pressure and the unsupportive behavior of their loved ones, which leads to a worsening of their mental illnesses and sadness. People suffering from depression are often observed committing suicide owing to a lack of support and suitable counseling or treatment since many people avoid seeing a psychiatrist in the event of mild mental illness due to social pressures and fear. Various free counseling sessions or consultations with psychiatrists have been made available on a public platform by governments in many countries to assist those suffering from anxiety or depression. People, on the other hand, avoid attending such sessions or consultations out of fear of being judged by society as well as the dread of being physically or emotionally isolated [11]–[13].

Usually, several methods exist that assist in providing relief to a user suffering from a mental condition such as depression or anxiety by using various treatments. These systems, on the other hand, do not concentrate on delivering daily and regular support to the user depending on the user's daily routine to help battle depression or anxiety. To address the aforementioned disadvantages, a system that monitors a user's mental health and provides counseling to the user regularly based on the user's day-to-day activities is needed to help in improving the user's mental health.

2. LITERATURE REVIEW

Enrique Garcia-Ceja et al. [14] stated that multimodal sensing, as well as machine learning, are being used to track mental wellness. In their study machine learning approaches were used to predict the user contextual information like mood, location, as well as a physical activity using continuous sensor data. The author's survey research works in "mental health monitoring systems" (MHMS) machine learning and using sensor data, as well as concentrated on studies on mental diseases and ailments such as bipolar disorder, depression, anxiety as well as stress. The authors examined mental state monitoring with a particular emphasis on those that employ sensors to collect "behavioral data and machine learning" to interpret it and also identify the major problems of the mental state monitoring system. According to the research reviewed, the use of multimodal sensing technologies in conjunction with "machine learning" methodologies represents a significant development in the provision of "mental health care technology tools for treatment".

Mélodie Vidal et al. [1] stated the technology to track the eye for monitoring the mental health of an individual. As tiny and inconspicuous on-body sensors become accessible, "pervasive

healthcare" is a promising subject of study. Despite significant advancements in the area, existing systems have limitations in terms of the illnesses they can identify, notably in the case of mental disorders. "Wearable eye tracking" is proposed as a novel tool for mental health monitoring in this paper. The authors provided two reviews: one on the state-of-the-art "wearable eye tracking" technology, and another on experimental psychology and clinical studies on the relationship between eye movements and cognition. Both studies suggest that wearable eye tracking has a lot of promise for "mental health monitoring" in everyday life. Further study on unobtrusive sensor equipment and innovative methods for the automated examination of long-term eye movement data is needed as a result of this discovery.

Vidhi Mody and Vrushti Mody [15] discussed the Artificial Intelligence-based Mental Health Monitoring System. According to the author mental health is a major public health problem across the globe, and it should be prioritized in the healthcare profession. However, it seems that progress in this area is moving at a snail's pace. AI approaches have recently gotten a lot of interest in a variety of fields, including mental health. This study evaluated the algorithms and parameters utilized in different systems for mental health monitoring, such as virtual counseling, precision treatment, and diagnostic systems. Finally, the authors proposed a system that incorporates the components discussed above and is designed to deliver tailored mental health treatment.

Several methods make it possible to deliver relief to a user suffering from a mental condition such as depression or anxiety by using various treatments. These systems, on the other hand, do not concentrate on delivering daily and frequent help to the user. To overcome the aforementioned limitations, a system that monitors a user's mental health and provides counseling to the user regularly based on the user's day-to-day activities is required to help in the improvement of the user's mental health.

Research Question:

1. How this present system has overcome the disadvantages of the existing system?
2. How this system is capable of determining a user's present mood and healing the user in case of disturbing mood by providing counseling to the user?

3. METHODOLOGY

3.1. Design:

The present research relates to a mental health monitoring and counseling system that is capable of fetching the daily life activities of a user along with assessing the mood of the user regularly for monitoring the mental health status of the user and accordingly provides counseling to the user based on a PHQ9 ("Patient Health Questionnaire module-9") module for effectively improving the user's mental health condition including anxiety and depression in a user-interactive manner without any requirement of a psychiatrist. Also, this system is capable of fetching all the information related to a user for finding out the root problems of the user that are suffering from anxiety or depression in day-to-day life and tries to resolve it by inspiring the user day by day, and the complete design of the system is shown in Figure 1.

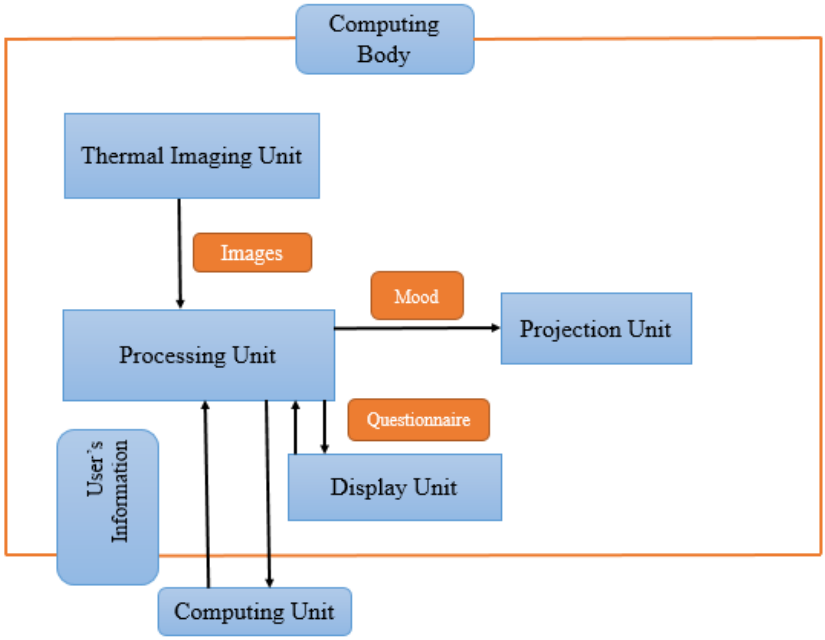

Figure 1: Illustrating the Design of the Mental Health Monitoring and Counseling System.

3.2. Instruments:

The whole system consists of a portable body that has kiosk-like arrangements as well as equipped with multiple wheels which move in any direction. This setup arranged with an Artificial Intelligence (AI) based thermal imaging is linked with a microcontroller. The processing unit is used to examine the captured images of the user by detecting the facial expressions of the user through facial recognition protocol and it is also used to store the identity of the user. The microcontroller is used to integrate with a communication module which is connected to the processing unit for establishing a wireless connection between a user's platforms also it fetches all the relevant data stored in the user platform to analyze recent and past incidents.

Touch responsive display connected with a user interface in such a way that the user is capable of accessing the display unit as well as the computing unit for taking questionnaires related to the mental health of the user. The PHQ9 module is based on the clinical psychological questions that are selected by examining the facial expression or mood of the user through machine learning protocols. The user's head is connected to the system through a communication module such that the headband includes a set of sensors for detecting variations in the brain activity of the user while responding to the questionnaire.

FBG (Fiber Bragg Grating) and EEG (electroencephalography) sensors are fabricated on the headband which is linked to the microcontroller**.** The FBG sensor is made by laterally exposing the core of solitary mode fiber to periodic patterns of intense laser light. The EEG sensor consists of electrodes that non-invasively detect the brainwaves of the user by positioning the electrodes on the scalp of the user and sending them to the microcontroller in the form of an electrical signal. The projectionunit is connected to the user platform in such a way that the

microcontroller generates a command to activate the projection unit for projecting audio-visual graphics based upon the determined dissimilarity in brain activity of the user. The projection unitincludes a projector that works by using light diffraction phenomena to create an image. Thissystem isarranged with a battery for supplying a constant direct current (DC). The battery used in this system is a Lithium-ion battery which is a rechargeable unit that demands a power supply after getting drained.

3.3. Data Collection and Analysis:

This proposed system includes a portable body structure having a “kiosk-like” arrangement as well as equipped with several wheels which move in every direction which helps the system or body to be moved from one place to another place based on the necessity of a user. The body includes an artificial intelligence-based thermal imaging unit in connection with a microcontroller, where the microcontroller is pre-programmed to manage system operation and it is provided with artificial intelligence and machine learning capabilities for managing system tasks. All protocols, as well as commands essential to the system's operation, should be stored in a database connected to the microcontroller. The thermal imaging unit collects various photographs of the user in a standing or sitting position in front of the body to seek treatment for mental health issues and transmits them to a processing unit linked with the imaging unit. The user's captured photographs are analyzed by the processing unit, which uses a facial recognition protocol built into the microcontroller to recognize the user's facial expressions. The processing unit additionally records the user's identity based on the user picture to generate a particular user profile which is based on the user's identity and stores the relevant user data inside the profile. The processing unit analyses the user's mood and saves the determined mood in the user's profile for identifying the user's mental health status after determining the user's facial expressions.

The microcontroller is connected to the processing unit by a communication module for creating a wireless connection between a user's platforms placed in a user's computing unit. The communication module may include, but is not limited to, Wi-Fi (Wireless Fidelity) or Bluetooth, while the user's computing unit may include, but is not limited to the user's smartphone or computer, which is accessed by the user daily and stores all data related to the user's day-to-day activities. While monitoring the user's mental health status, the microcontroller collects all relevant data stored in the user platform to analyze recent and past incidents related to the user for determining the likely reason for the user's likes poor mood, anxiety, or sadness. This system is connected to any server or social media-based platform for retrieving data about the user's photographs, work schedules, videos, and other live updates that the microcontroller may access. The body or system is equipped with a touch-responsive display unit with a user interface that allows the user to access both the display unit and the computer unit to complete questionnaires on the user's mental health. The touch interactive display unit is connected to the microcontroller and presents a tailored questionnaire that includes PHQ9 which is based on the clinical psychological questions that are picked using machine learning methods that analyze the user's facial expression. The user answers the questionnaire presented on the display unit by inputting responses to the questionnaire on the display unit, and the processing unit analyses the responses to the questionnaire to evaluate the schedule of displaying the questionnaire routinely using artificial intelligence and machine learning protocols. The processing unit assesses the user's answers to the questionnaires to compare the corresponding user's profile to other profiles kept in a database and allows the user's profile to be compared to other user profiles as well as faults to be detected. The processing unit uses data cluster protocols to evaluate the imaging

unit's output about the user's mood and the display unit's replies to the questionnaire to determine the likely source of the user's mental health difficulties.

The user is needed to wear a headband over his or her head while taking the questionnaire, which is linked to the computing body through the communication module and contains a set of sensors for detecting differences in the user's brain activity while answering the questionnaire. An FBG and EEG sensor are constructed on the headband and work with the microprocessor. The FBG exposure causes a permanent rise in the refractive index of the fiber's core, resulting in a fixed index modulation that can be used to detect the user's pulse rate and communicate it to the microcontroller as an electrical output. The EEG microcontroller analyses the received signal for pulse rate and fluctuations in neurological response signals to determine the user's brain activity while answering questions on the questionnaire. The microcontroller creates a command to activate the projection unit for projecting audio-visual images depending on the calculated variation in brain activity of the user, and the projection unit is connected to the user platform. The projection unit consists of a projector that creates an image by using light diffraction phenomena, where the light wave interference pattern is recorded to create a hologram as the lasers produce pure, coherent light that accurately records the light wave interference patterns and recreates a 3D ("Three dimensional") image from the recorded patterns. The microcontroller is connected to the actuated projection unit which projects audio-visual graphics related to the user's existing memory fetched from the platform to induce feel-good type changes in brain activity to recover the user if the user is anxious or feeling low at the time at which taking the questionnaire. The microcontroller generates a command for the projection unit for displaying any motivational video for counseling the user regarding the determining issues. The audio-visual graphics are based on behavioral activation treatment, which helps users improve their mental health. The processing unit analyses the user's routine responses to track mental health improvements, and the communication module notifies the computing unit accessed by the user's guardians if the user's current mental health condition, as determined by the processing unit, corresponds to a suicidal tendency. This avoids any negative incidence with the user, such as suicide or injury to the user, and the complete workflow diagram is shown in Figure 2.

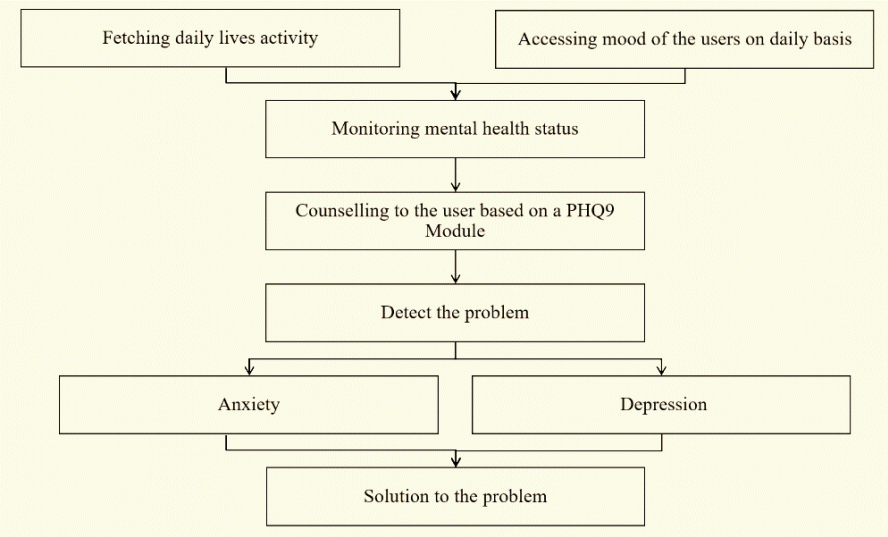

Figure 2: Illustrating the Work Flow Diagram of the Mental Health Monitoring and Counseling System.

4. RESULTS AND DISCUSSION

Suppose that, if any exam, meeting, or incident is approaching due to which the user is facing mental issues then the system fetches some happy memory or memory which depicts the user making efforts or showing some positive response towards the situation. If no memory could be fetched related to the state of the user, the projection unit then displays motivational videos to let the user make positive efforts toward a situation. Consequently, the proposed system can monitor the mental health of the user by analyzing the user's everyday life activities as well as providing counseling to the user comfortably to recover the user from any grievances, anxiety, or depression experienced by the user. Therefore improving the user's mental health conditions including anxiety or depression without the need for the user to consult with a psychiatrist or other medical professional, is the key point of this research.

This mental health monitoring and counseling system may be connected with the musical unit with the microcontroller to provide musical therapy to the users. There are several advantages to using this system, including the fact that it saves the user's time and money, that it may be used in connection with a mental health monitoring system, and that it gives a better solution for the user (patient). It is simple to use, which implies that no advanced knowledge is required; thus, this system may be managed by any person or anybody with just a rudimentary understanding of how to use this system, such as a child. Psychological well-being is a state of mind in which a person sees his or her potential, can cope with daily challenges, can work well, and is capable of contributing positively to society. There are a variety of variables that lead to mental health difficulties, as seen in Figure 3.

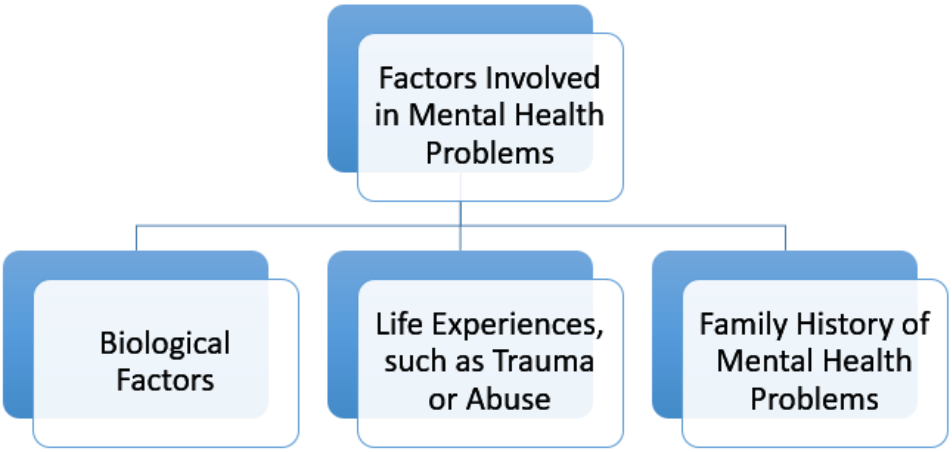

Figure 3: Illustrating the Main Factors which are involved in Mental Health Problems.

4.1. The Most Common Types of Mental Illness:

4.1.1. Anxiety Disorders:

When faced with particular objects or events, people suffering from these illnesses feel tremendous fear or worry. The majority of people with anxiety disorders will want to avoid being exposed to whatever it is that makes them nervous. A mental health condition is defined as

anxiety, worry, or fear that is strong enough to interfere with one's daily activities. Counseling or medicine, such as antidepressants, are used to treat depression.

4.1.2. Depression and Bipolar Disorder:

People suffering from these illnesses have major fluctuations in their mood, which are often characterized by either mania, which is characterized by excessive energy and exhilaration, or sadness. Unhappiness might be caused by a combination of biological, psychological, and social causes. These factors, according to recent research, may cause changes in brain function, such as altered activation of certain neural networks. The cornerstone of treatment is usually talking therapy, medication, or a combination of the two. This therapy, according to recent research, may help to restore depression-related brain abnormalities. Treatment options include both therapy and medication.

4.1.3. Schizophrenia is a Mental Illness:

Psychological problems that are often seen To identify whether schizophrenia is a single condition or a collection of connected disorders, mental health authorities are currently investigating the issue. It is a very difficult issue to diagnose. Signs and symptoms of schizophrenia often manifest themselves between the ages of 16 and 30. According to the National Institute of Mental Health, this is a dependable source. The person will have fragmented ideas, and they may also have difficulty processing new information as a result of this condition. Schizophrenia manifests itself in both bad and good ways. Treatment is frequently ongoing and consists of a mix of drugs, counseling, and specialized care coordination.

While the majority of online tools are designed for those with mild to moderate anxiety or depression, they are a crucial element of new ‘stepped' health models in which consumers may pick from a tailored variety of alternatives, which typically includes self-directed treatment. Now Anxiety and Depression is currently the most common mental disorder and most peoples are suffered from these problems so, this research helps to detect the problems and identify and based on detected problems, gives the proper solution.

5. CONCLUSION

Mental health is a serious public health concern that affects people all over the world, and it should get significant attention from those in the healthcare industry. The pace of progress in this field, on the other hand, seems to be somewhat slow in comparison. People are now taking this issue seriously, and everyone understands that the best way to resolve this issue is via therapy. Patients' concerns are detected by this system ("Mental Health Monitoring and Counseling"), which then conducts counseling based on a questionnaire and gives appropriate solutions. This is a significant development in the progress of delivering mental health care technology tools for treatment. From the above study, it is concluded that when the user's mental health is monitored by analyzing their day-to-day activities, then this proposed system provides counseling to help them heal from any anxiety, grievances, or depression, they may be experiencing conveniently, thus improving the user's mental health conditions such as anxiety or depression, without the need of psychiatrist for the users. It also seeks to develop a system that may give real-time help or support to a user at any time of day to avoid any possibility of suicidal thoughts from entering the user's head as a result of the user's inability to get sufficient emotional support. In the future, this system can have other modifications that are within the possibility of the present research.

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CHAPTER 2

AN ANALYSIS OF RECENT ADVANCES AND FUTURE OF TRADITIONAL TREATMENT FOR TYPE-2 DIABETES MELLITUS

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ABSTRACT:

According to epidemiological research, Diabetes Mellitus (DM) will develop as a pandemic globally, followed by endocrine and metabolic disorders. The majority of diabetics have Type-2 diabetes mellitus (T2DM), which causes insulin secretion and insulin resistance issues. Numerous traditional diabetic medications have been discovered as a result of extensive studies. To manage and cure diabetes and its consequences, extracts, and substances derived from diverse natural sources, notably flora, have been crucial tools. Researchers have discovered that among patients with DM, the severity of "coronavirus disease 2019 (COVID-19"), triggered by infection of "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)", has risen as a result of the pandemic. The increased understanding of Natural Products (NPs) for their diverse regulatory effects on different signal pathways and targets would substantially aid in the development of anti-T2DM medicines. As a result, the current study will assist the reader in comprehending the significance of different kinds of herbal and NPs formulations that have been used historically to treat DM.

KEYWORDS:

Blood Sugar, Diabetes Mellitus, Glucose Levels, Medicinal Plants, Side Effects, Sugar Levels, Type-2 DM (T2DM).

1. INTRODUCTION

Diabetes mellitus (DM) is a complicated chronic systemic illness characterized by metabolic problems such as hyperinsulinemia, hyperglycemia, and hypertriglyceridemia. Diabetes has become increasingly common, and the majority of patients has climbed to even more than 422 million, with a projected growth to 592 million by 2035. Presently, the worldwide incidence amongst adults is 8.5 percent, with rates growing faster in low- and middle-income nations [1]. Diabetes is divided into two types: Type-2 DM (T2DM)and type 1 DM (T1DM), with Type-2 DM accounting for roughly 95 percent of cases [2]. T1DM is characterized by absolute insulin shortage accompanied by pancreatic cell death, though T2DM is primarily caused by insulin secretion shortfall and insulin resistance (IR) [3]. T2DM may harm several organs and create a variety of problems. Certain acute consequences are largely associated with increased morbidity in diabetics, whereas chronic problems are by far the most damaging impact of long-term high blood glucose levels. Diabetic neuropathy, diabetic nephropathy, and diabetic retinopathy may

all be caused by microvascular abnormalities. Cardiovascular and cerebrovascular disorders are also examples of macrovascular problems. T2DM may also induce dementia [4], sexual dysfunction [5], and depression [6].

For patients, their families, and the healthcare structure, T2DM has developed into an expensive chronic illness. Lifestyle adjustments and Weight reduction may partially reduce hyperglycemia to control T2DM [7], [8]. Nonetheless, certain anti-diabetic medications are essential to maintain glycemic control. Nevertheless, numerous unpleasant side effects such as heart failure, osteoporosis, fluid retention, and hypoglycemia have been reported after the use of oral antidiabetic medications [9]–[12], limiting their clinical uses. To treat hyperglycemia, hyperinsulinemia, and hypertriglyceridemia, novel anti-diabetic options with low adverse effects must be developed. Natural products (NPs), including herbal formulations and extracts, have been utilized for hundreds of years to treat human illnesses using a unique system of ideas and treatments [16], and are now being progressively employed to treat T2DM. The processes and effects of NPs have gotten a lot of attention in recent years [9], [12]–[15].

1.1.Diabetes mellitus diagnosis:

Diabetes may be diagnosed by monitoring blood sugar levels. Fasting blood sugar levels in healthy men are 80 mg/dl, while postprandial levels may reach 160 mg/dl. Different laboratory tests for diabetes diagnosis include finger prick blood sugar testing, fasting blood sugar testing, glucose tolerance diagnostic testing, and glycohemoglobin [16], [17].

1.2.Herbal Treatment:

DM treatment without side effects remains the most difficult topic for medical practitioners. To avoid DM, 800 medicinal plants are employed, according to the World Ethnobotanical Organization. Only 450 medicinal plants have been clinically confirmed to have anti-diabetic effects, with 109 medicinal plants having a comprehensive mode of action. In ancient times, both doctors and laypeople employed traditional medicinal plants with active ingredients and qualities to cure ailments such as heart disease, cancer, and diabetes. Traditional botanicals have been used to treat diabetes for centuries in China and India. Various literature, such as Susruta Samhita and Charaka Samhita, is accessible that discusses the phytopharmacology aspects of diabetes and its harmful effects [18]. Sickness, faintness, malignant anemia, swelling, migraine, alcohol flush, diarrhea, and vomiting have all been reported as side effects of synthetic medications used to treat diabetes.

Herbal medications are a superior alternative to synthetic pharmaceuticals owing to fewer side effects and bad consequences. Herbals may be obtained without the doctor's prescription. These natural medicines are used to treat life-threatening diseases. These medications are also utilized when chemical treatments fail to treat an illness. These are natural and harmless medications, with no hazardous side effects. Herbal medications permanently heal people and treat ailments, but synthetic pharmaceuticals only temporarily cure people. Herbal formulations comprise natural herbs, fruits, and vegetable extracts that are effective in the treatment of a variety of disorders with no negative side effects. Chemical medications, on the other hand, are synthesized and have adverse effects. Herbal formulations are less expensive than allopathic treatments. Herbal compositions are environmentally friendly. Herbal remedies are created using natural substances, whereas allopathic medicines are created using natural ingredients that have been

chemically and/or chemically altered. All allopathic medications require a prescription; herbal versions are available without one [19], [20].

2. DISCUSSION

2.1.Traditional herbal anti-diabetic medications:

Medicinal herbs and plants are now being employed in extract form for their anti-diabetic properties. Several clinical research has proven that therapeutic plant extracts have antidiabetic potential and may restore pancreatic-cell function [21], [22].

2.1.1. Sativum Allium:

Garlic belongs to the Liliaceae family, which includes Allium sativum. Garlic ethanolic extract (10 ml/kg/day) usually has hypoglycemic action [23]. Garlic extract outperformed the anti-diabetic medication glibenclamide. In STZ-induced rats, extracts of petroleum, ethanol, and ethyl acetate ether were shown to have antidiabetic action. Garlic has a variety of therapeutic benefits, including antiplatelet, antimicrobial, blood pressure, and cholesterol reduction [24], [25].

2.1.2. Indica Azadirachta:

It is known as a neem in India and is a member of the Meliaceae family. It is sold in India and Myanmar [26], [27]. In large doses, ethanolic and aqueous extracts of Azadirachta indica reduce blood glucose levels. It may be supplemented with allopathic medications in Type-2 diabetic individuals whose diabetes cannot be controlled alone with allopathic drugs. Natural neem pills are used to treat a huge number of people worldwide. Its extract enhances blood circulation by expanding blood vessels and is beneficial in lowering blood glucose levels in the body [28], [29].

2.1.3. Papaya Carica:

It is known as papaya and is a member of the Caricaceae family. In alloxan-induced diabetic mice, seed and leaf extract lowers blood sugar levels, lowers lipid levels, and promotes wound healing [30]–[32].

2.1.4. Sativum Coriandrum:

It is often known as coriander and is a member of the Apiaceae family. It is commonly used as a spice in a variety of foods. 200 mg/kg seed extract regularly boosts the activity of Langerhans cells and reduces blood sugar in alloxan-induced diabetic mice, as well as insulin generation from pancreatic cells. Coriandrum sativum extract has blood sugar-reducing and insulin-synthesizing properties [33].

2.1.5. Eugenia Jamun:

It is a member of the Myretaceae family. Eugenia jambolana dry seeds and ripe fruits are included. Its active ingredients are malvidin 3-laminaribiosidea and ferulic acid. Diabetes patients were treated with a dried seed extract (200 mg/kg) [34]

2.1.6. Indica Mangifera:

It belongs to the Anacardiaceae family and is generally known as the mango. Although leaves extract (250 mg/kg) has an anti-diabetic effect, “oral administration of aqueous extract did not modify blood glucose levels in alloxan-induced diabetic rats” [35], [36].

2.1.7. Charantia Momordica:

It is a member of the Cucurbitaceae family and is commonly known as karela or bitter melon. Momordica charantia's active ingredients are momordic I and II, as well as cucurbitacin B. It is utilized in the management of diabetes. It is made up of lectin, which has insulin-like action. Lectin is a nonprotein that is associated with insulin receptors. By acting on peripheral tissues, this lectin lowers blood sugar levels. M. charantia fruit extract (200 mg/kg) has hypoglycemic action [37], [38].

2.1.8. Tinospora cardifolia:

It belongs to the Menispermaceae family and is often known as Guduchi. T. cardifolia's active ingredients include diterpene substances such as giloin, berberine, Syringen, tinosporic acid, and tinosporone. T. cardifolia root extract (50-200mg/kg) reduces urine and blood sugar levels in streptozotocin-induced diabetic rats after 6 weeks of oral dosing. It is primarily utilized to induce diabetes in the Indian Ayurvedic system of medicine. Extracts of roots help in losing weight. In general, soxhlet extraction, decoction, percolation, infusion, and maceration are used to remove plant components such as roots, stems, leaves, and fruits. Solvents such as ethanol, methanol, and petroleum ether are often utilized [39], [40].

2.2. Flavonoids:

Flavonoids may be found in abundance in herbs, vegetables, fruits, and other plant foods. Their behavior is influenced by the hydroxylated phenolic structure. Many flavonoids have anti-viral, anti-inflammatory, hepatoprotective, and cancer-fighting properties. In recent times, it has been demonstrated that several flavonoids have anti-diabetic characteristics as shown in Figure 1.

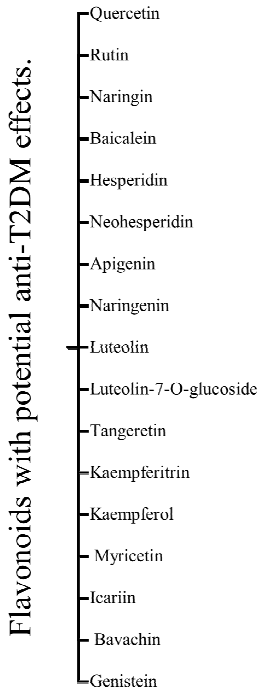

Figure 1: Illustrating the Names of NPs Containing Flavonoids Having Anti Type-2 Diabetes Mellitus Properties.

2.3. Polyphenols:

Polyphenols, also known as polyhydroxy-phenols, are abundant in vegetables, cereals, coffee, tea, and cocoa, and are useful in handling many illnesses owing to their anti-oxidant, anti-inflammation, metabolic regulatory, and anti-fibrotic effects. Antirhea borbonica polyphenols exhibit antioxidant and antiinflammatory actions on adipocytes, protecting them against obesity-associated metabolic diseases. As a consequence, antidiabetic activity is amongst the extensively explored biological characteristics of polyphenols. Several compounds that have their main ingredient as polyphenols and act as Anti-T2DM are illustrated in Figure 2.

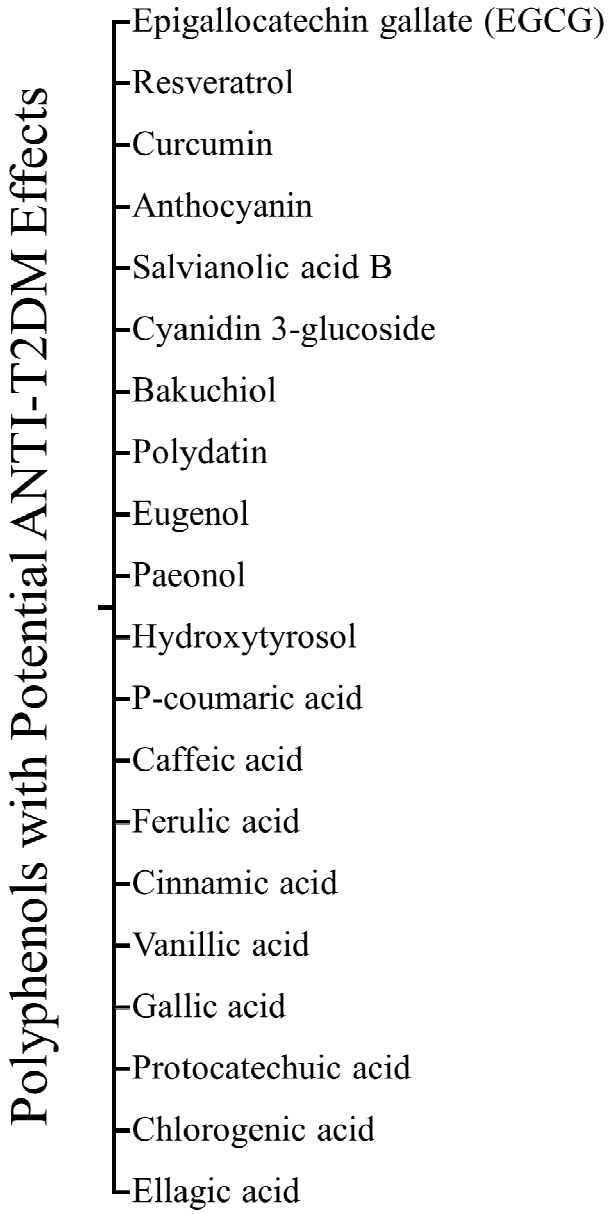

Figure 2: Illustrating the Names of NPs Containing Polyphenols Having Anti Type-2 Diabetes Mellitus Properties.

2.4. Terpenoids:

Traditional herbal medicines rely heavily on plant terpenoids. Several terpenoids have been identified as potential antidiabetic medicines, making terpenoids one of the most significant classes of natural compounds. Most of these are being developed into antidiabetic medicines and are now through different phases of pre-clinical and clinical testing. These substances can inhibit the enzymes that are in charge of normalizing glucose and insulin levels, glucose metabolism, and developing insulin resistance. By blocking several pathways connected to diabetes and its consequences, terpenes have the potential to be effective treatments for impaired wound healing nephropathy, neuropathy, and diabetic retinopathy. There have been very few attempts to comprehend the biological processes and clinical research regarding the use of triterpenes in the treatment of diabetes. A list of potential terpenoids is illustrated in Figure 3.

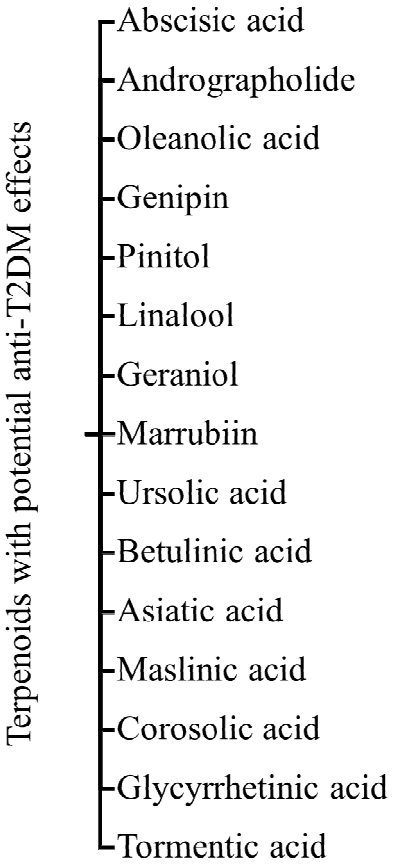

Figure 3: Illustrating the Names of NPs Containing Terpenoids Having Anti Type-2 Diabetes Mellitus Properties.

2.5. Quinones:

Quinones have been utilized to develop antimalarial, anticancer, and antibacterial medications. There are numerous types of quinones components in Rhei, and some of them have substantial anti-T2DM actions [41]. A few quinones that have the potential to treat DM are represented in Figure 4.

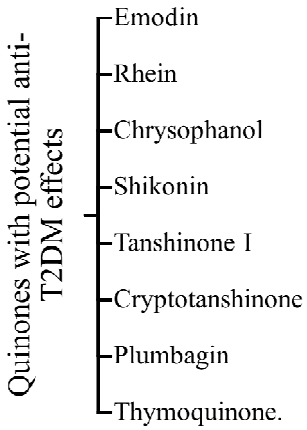

Figure 4: Illustrating the Names of NPs Containing Quinones Having Anti Type-2 Diabetes Mellitus Properties.

2.6. Alkaloids:

Antimalarial, antihyperglycemic, antiasthmatic, anticancer, and antibacterial properties are all possessed by alkaloids. Many of them have been used for drug development in traditional or contemporary medicine. Some of these are represented in Figure 5

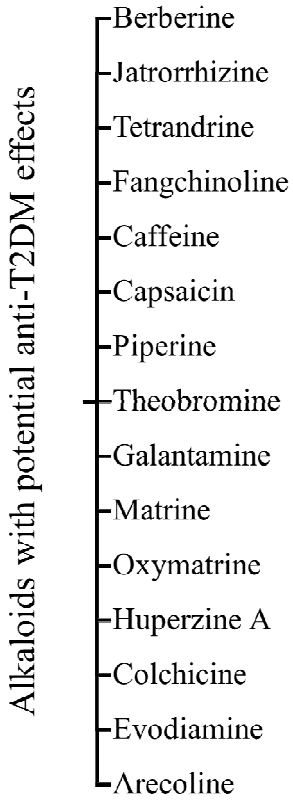

Figure 5: Illustrating the Names of NPs Containing Alkaloids Having Anti Type-2 Diabetes Mellitus Properties.

2.7. Saponins:

It is a family of triterpenoids or steroid glycoside components found in several plants with a variety of biological functions and is extensively employed in the cosmetic and pharmaceutical industries. A list of potential Saponins is illustrated in Figure 6. Ginsenoside Rg3, Rg1, and Re are found to be the potential therapeutic compounds for the treatment of DM.

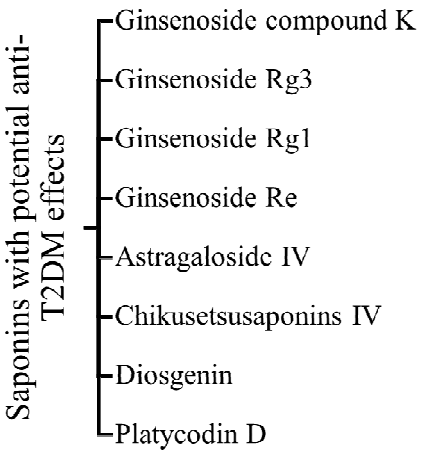

Figure 6: Illustrating the Names of NPs Containing Saponins Having Anti Type-2 Diabetes Mellitus Properties.

2.8. Other elements:

Aside from the NPs described above, a variety of amino acids, proteins, polysaccharides, and other active NPs have been shown to have anti-T2DM activity. Cinnamaldehyde, a natural flavoring and aroma ingredient in the kitchen, lowers glucolipids in diabetic mice by inhibiting IR, improving islet dysfunction, and boosting glycogen synthesis.

2.9. Herbal Medicine's Difficulties in India:

Even though herbs have medical benefit, there are a few drawbacks, such as the need for consistency, the fact that a fixed quantity of medicine is not administered to the patient, the dosages is not stringently provided on time, and variable quantities of the main substance are available because of production technique is not homogenized. Now the issue is "how to create these herbal treatments to overcome the aforementioned objections to compete with pharmaceutical medicines". It will entail an extensive study that will include the isolation and classification of active elements of medicinal plants. Furthermore, natural medications and even conventional medicine are not presently being used to heal many disorders. There is a need to research alternative medicinal treatments via plant kingdom investigations and the reasoning of their potential through comparative studies [42], [43].

2.10. Future of Diabetes Mellitus Herbal Treatments:

People utilize several herbal remedies, and many indigenous drugs are being brought into contemporary treatments regularly. In underdeveloped nations, especially in rural areas, over 80% of people depend on traditional medicinal treatments for their health care needs. Due to a significant increase in the taste of items derived from natural sources, there has been a

renaissance of interest in herbal medications in industrialized nations. As a result, there is a need to distinguish between herbal pharmaceuticals provided by a medical practitioner and herbal treatments readily available to the public for self-medication. Diabetes mellitus, which is on the rise, is a serious threat to human health all over the globe. Recently, new active medications produced from plants have been discovered to have anti-diabetic action that is more effective than oral hypoglycemic drugs utilized in established treatment. A substantial consideration is focused on the identification of plants that have anti-diabetic action and may be valuable to humans. It might potentially indicate the development of a novel oral medication for the treatment of T2DM [44]–[47].

3. CONCLUSION

Millions of people throughout the world suffer from diabetes, the most common endocrine disease. It belongs to a group of metabolic disorders that are characterized by hyperglycemia brought on by deviations in insulin production, action, or both. The increasing resistance, at-risk patient groups, and few commercially accessible diabetic medications with still-significant negative effects and problems such as unwanted hypoglycemic effects, are driving researchers to shift their focus to traditionally available medicines that have low side effects, a broad range of bioactivity, and do not require laborious pharmaceutical synthesis. This review article may help health practitioners, scientists, and academics build evidence-based alternative medicine to treat many types of diabetic problems utilizing herbal preparations. Extracts and substances obtained from the environment and natural sources play a critical part in the preparation of medicines and handling the hyperglycemic problems in diabetes mellitus.

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CHAPTER 3

AN INVESTIGATIONAL STUDY TO ADDRESS VARIOUS MENTAL HEALTH DISORDERS OF POPULATION

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ABSTRACT:

Mental health is very significant at every stage of human life, from infancy and adolescence to maturity. Although there is a lot of mental health stigma, people with mental health difficulties can get better, and several times patients make a full recovery. Mental health has three components such as psychological, social, and emotional, it affects feelings, thoughts, and actions. It also affects how individuals engage, handle stress, and make wise decisions. This study provides an overview of mental health issues and various solutions for them. Major medical disorders such as heart attacks can affect people, and lack of attention to mental health problems has a significant negative impact on those who are affected by them. It should move towards a society where people are fully aware of these problems and strive for a higher standard of living by getting their diseases treated despite the stigma attached to them.

KEYWORDS:

Disorders, Health, Mental Health, Psychological, Physical Health.

1. INTRODUCTION

The psychological, social, and emotional well-being of individuals is all components of their "mental health". As we negotiate life, it influences how individuals feel, think, as well as behave. Decision-making, interpersonal relationships, and stress reactions are also impacted. Every stage of life, including infancy, youth, and adulthood, including aging, requires attention to mental health. Sustaining excellent mental health is as crucial as keeping good physical condition. Your mental health may influence how you feel, as well as the quality of your thoughts, how well you handle stress, and how people interact with other people [1]–[3]. A human's capacity to make wise and logical judgments may also be impacted by mental health. Anyone may experience irritability, rage, depression, or moodiness if someone's mental health is neglected. In addition to causing physical symptoms like exhaustion, high blood pressure, chest discomfort, and ulcers, not taking time to meditate may also have those effects. The excellent thing is that you do not have to go on living in that manner. Anyone may make many dietary and behavioral adjustments to start enhancing overall mental health right immediately.

Mental health may affect daily living, interpersonal connections, as well as physical health. However, this link may also work the other way around. Personal traits, interpersonal ties, and

physical factors may all contribute to mental health problems. Keeping one's mental health in good shape may aid in maintaining the enjoyment of life. Finding a balance between one's responsibilities, commitments, and interests in life is necessary for developing psychological resilience. Even while how you feel may be influenced by your mental health, being mentally healthy entails much more than simply feeling good. "Mental health", according to the "World Health Organization" (WHO), is a state of happiness that enables you to reach your full possible, work effectively, manage life's stresses, and give back to your community. In many respects, having a healthy mental state means being able to appreciate life and manage your own emotions, both good and bad, constructively even in trying times. Various solutions that can help people with mental instability are shown in Figure 1.

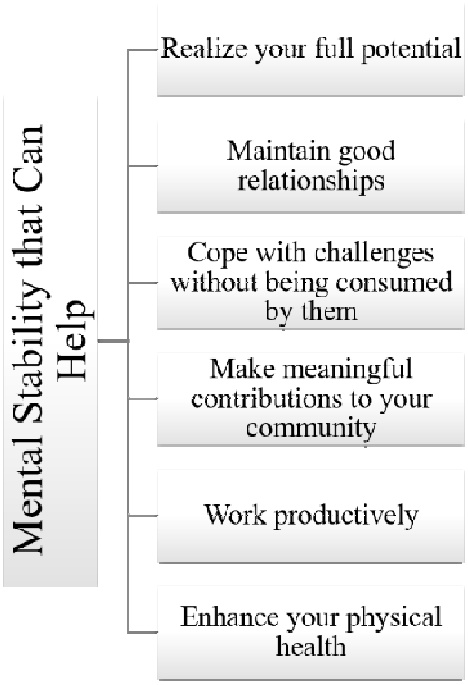

Figure 1: Illustrating the Various Solutions That Can Help People with Mental Instability.

1.1. Kinds of Disorders:

1.1.1. Anxiety Disorders:

Peoples with anxiety feel fear as well as uncertainty in response to certain circumstances or things, as well as exhibit bodily indications of concern or panic like racing heartbeat and sweating. When a person's reaction is appropriate for the condition, when they are incapable to regulate their response, or when their anxiety prevents them from doing daily tasks, it is known that they have an anxiety attack [4]. General panic disorder, anxiety symptoms, social anxiety symptoms, as well as particular phobias are a few examples of anxiety disorders.

1.1.2. Mood-Disorders:

These illnesses sometimes referred to as affective disorders, are characterized by prolonged episodes of exorbitant joy or sorrow [5], [6]. The most common mood disorders are cyclothymic disorder, bipolar disorder, and depression.

1.1.3. Psychotic Disorders:

Sensation, as well as thinking, are compromised as a consequence of these circumstances. The two utmost common symptoms of psychotic illnesses are "hallucinations", which are the perception of unreal sounds, such as auditory hallucinations, which are false set beliefs that the sick person holds all evidence to the contrary. Schizophrenia is such an instance of a psychotic disorder.

1.1.4. Eating Disorders:

Eating disorders are categorized by attitudes, intense feelings, as well as actions related to food and the body [7], [8]. "Anorexia nervosa", Bulimia nervosa, as well as impulsive feeding disorder are the three most common eating disorders.

1.1.5. Addiction Disorders and Impulse Control:

Pyromania Examples of conduct disorder include kleptomania and compulsive gambling, in which a person is incapable of restraining their urges or inclinations to act in ways that might harm them or other people. Two main factors that cause addiction are drugs and drinking. People with these illnesses often get so consumed with their addiction's goals that they begin to neglect their responsibilities and interpersonal relationships.

1.1.6. Personality Disorders:

Strong as well as inflexible personality traits that are disturbing to them and problems at work, in school, as well as their social relationships, are features of people with personality disorders. Furthermore, the person's thinking as well as behavior patterns are significantly unlike what society expects of them and are so unbending that they limit their capacity to accomplish basic activities [9]. Examples include mental disorders including paranoid disorder, obsessive-compulsive disorder, histrionic disorder, as well as schizoid disorder.

1.1.7. Obsessive Compulsive Disorder (OCD):

Patients with OCD engage in rituals or regular routines as a result of recurrent thoughts or worries [10], [11]. The words used to describe uncomfortable thoughts and behaviors are obsessions and compulsions. An example would be someone who has an irrational fear of bacteria and often washes their hands.

1.1.8. "Post-traumatic Stress Disorder" (PTSD):

When a traumatic occurrence such as a physical assault, or the untimely death of a loved one, PTSD may develop. People with PTSD usually display emotional numbness and have distressing memories and thoughts about the experience.

1.2. Symptoms and Signs of Mental Health:

Contingent on the problem, the environment, as well as other elements, there may be a wider range of symptoms and signs of mental illness [12]–[14]. Symptoms of mental illness may have an impact on actions, thoughts, and emotions. Examples of signs and symptoms as shown in Figure 2.

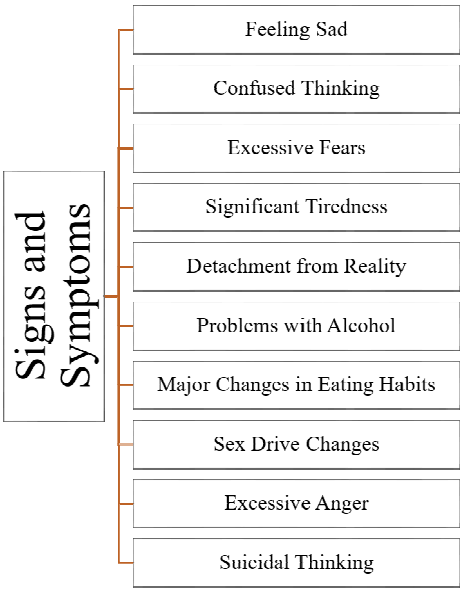

Figure 2: Illustrating the Symptoms and Signs of Mental Health Disorders.

Stress, despair, and worry are fewer of the ailments that may influence “Mental Health” and interfere with daily life. Although the phrase "mental health" is frequently used, many diseases that medical professionals classify as psychological disorders have physical causes. The words mental health and potential treatments for these types of diseases are defined in this research by the authors. Additionally, they describe the most common types of mental diseases, their early warning signs, and available treatments.

2. DISCUSSION

The idea that mental health just refers to the absence of mental disease necessity be urgently refuted. Gayathri Madhavi and N Satya Abhisht [15] stated the key concept of mental health and factors that advance several types of diseases. Several authors also stated that Good mental health is mostly a result of a healthy lifestyle, a secure home, and active community involvement. Given the severity of mental health conditions and the low level of awareness of the problem. The removal of stigmas and the promotion of something effective and beneficial may both be accomplished by raising awareness of mental health issues. Lack of education and awareness, self-diagnosis, and stigmatization all contribute to the increasing difficulties in treating mental health issues. It's crucial to understand that developing screening criteria is the only approach to detecting mental illness. The WHO defines “Mental Health” as a state of well-being characterized by self-awareness, the capacity to handle challenges of daily life, successful work, and community involvement. Among the prevalent mental health conditions mentioned in this research are depression as well as anxiety disorders.

Other prevalent mental health issues include phobias of certain objects or circumstances. “National Institute for Health and Care Excellence” (NICE) will provide separate guidance for those who struggle with social anxiety. Because they together impact more individuals than other mental health issues, these issues are referred to as common mental health issues. Some individuals may struggle with many mental health issues. Many Indians complain about the pressure to maintain a near-perfect online persona and to post pictures of their flawless life.

Because of the strain, some individuals have started to undergo a digital detox and take a vacation from their phones and other electronic gadgets (Figure 3).

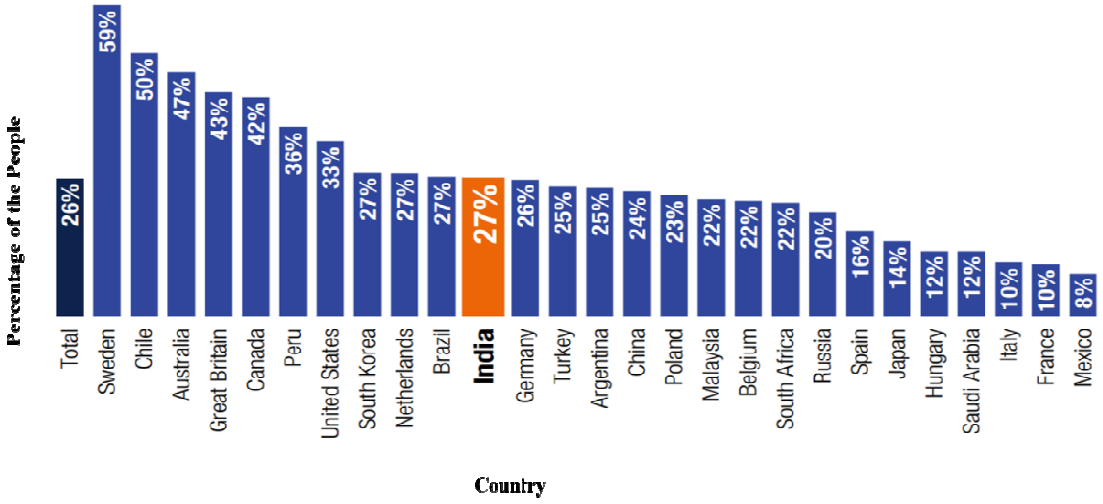

Figure 3: Representing of data Based on the Percentage of People who Agree with Mental Health Problems is a Major Issue [16]**.**

Having a mental disease mentions a diversity of disorders with symptoms that may affect a person's thinking, emotions, and perceptions. Somebody with a mental illness could find it challenging to manage their relationships, career, and other obligations. Despite the complicated link between stress and mental disease, stress may make a mental illness episode worse. The majority of people can manage their mental diseases with medication, treatment, or a mix of the two. This study includes some of the most common mental illnesses and challenges.

Every age, from infancy and adolescence to maturity, calls for the maintenance of mental health. Although the phrases are sometimes used synonymously, poor mental health and mental disease are distinct from one another. A person may be in poor mental health even if they do not have a mental disorder. There may be times when a person with a mental disorder is in exceptional physical, mental, and social health. Aspects of overall health include both physical and mental well-being. Our emotional and mental well-being, which affects our ideas, behaviors, including emotions, is essential to maintaining human existence. In duties like work, schooling, or care, being emotionally balanced may boost efficiency and effectiveness. It is crucial for the well-being of anyone's relationships and enables you to adjust to life events and overcome hardship. To ascertain the diagnosis and look for associated problems:

1. A psychological evaluation
2. A physical exam
3. Lab tests

2.1. Causes of the Mental Health:

Many factors might be at play in “mental health” difficulties. Several people are likely affected by a complicated web of conditions, even though a few persons may be more adversely impacted

by some things than others. Figure 4 illustrates several factors that might lead to a period of poor mental health. There are three main causes of mental illness:

Figure 4: Illustrating the Major Causes that are Responsible for the Mental Health.

2.1.1. Biological Factors:

One of the main due of mental disorders is biological factors. Abnormalities like this may be caused by people who are born with brain defects or by neurological connections that aren't working properly. Additional biological aspects include heredity-based genetics. Some illnesses run in families, which increases the likelihood that future generations would get the condition if the person's predecessors did. The primary cause of this is related to genetic defects, while other variables may also cause these ailments. Infections have been associated with mental disorder development, brain damage, and aggravation of symptoms in pre-existing conditions. Such disorders may be brought on by prenatal injury, which refers to the interruption of fetal brain development, or by any trauma that occurs during delivery or pregnancy. Particularly persistent drug misuse has been connected to anxiety, sadness, and paranoia.

2.1.2. Psychological factors:

Psychological factors include any kind of physical or mental adversity as well as sexual abuse. Loss of loved ones at a young age might cause this. This may also be caused by a poor capacity to interact with people or connect to social settings.

2.1.3. Environmental Variables:

People who are predisposed to certain illnesses might develop illnesses due to a variety of environmental or surrounding factors. They include things like demise, divorce, unhappy marriages, poor self-esteem, feelings of inadequacy, anger management problems, anxiety, or

loneliness. A person may find it difficult to adjust rapidly if their environment changes often. Disorders including eating disorders may also be caused by cultural and social demands.

2.2. Initiatives Taken For Resolving Mental Health Disorder:

Informing individuals is the first and most important step in moving beyond this mental health epidemic. The adoption of preventative measures will follow early identification of the issue and expanding access to treatment as world mental health increases. It is necessary to spread awareness through a variety of venues and methods:

2.2.1. Programs and Policies of the Government:

Using the authority granted to the government by the people. It has the best opportunity of influencing social change and mend fences. Additionally, the government is the single largest spender in the field of mental health. Its efforts to raise awareness may have a significant influence. This public health system may reach remote populations by putting awareness-raising activities and campaigns into place. Through initiatives like the "Swatch Mansikta Abhiyan", the general public should be encouraged to learn about mental health. They will be able to deal with mental health difficulties quickly and effectively as a result, leading stress-free lives. The program would also compel individuals to discuss their mental health and, if necessary, seek help from a therapist or psychiatrist. Those who lack access to the media or any other sort of educational tool must be made aware. Thus, the roots will get stronger. In addition to the "National and District Mental Health Programs" and the "National Rural Health Mission", the government is collaborating with nonprofit and private groups to disseminate awareness at even deeper levels. India could be able to obtain a greater degree of knowledge on such mental illnesses and eventually overcome all the stigmas surrounding it if this rate of adoption grows quickly.

2.2.2. School System:

By including such material in textbooks and as a requirement for graduation from high school, educators are required to teach students about mental health. Younger students who are exposed to such delicate subjects have a deeper knowledge and are better equipped to cope with others who are struggling with mental health concerns. By educating young brains about these concerns early on, prejudice will be eliminated and a greater feeling of power will result.

2.2.3. Social Media and the Internet:

The use of technologies and technology has taken over our world. The internet and social media are such effective tools for distributing information and have completely changed how people raise awareness. Internet trends are a fantastic method to engage people and encourage participation. It is possible to increase comprehension and awareness. By using these channels, we can connect with today's young, who are crucial to de-stigmatizing and bringing about positive change. Self-help websites are available on the Internet, and users may also call these toll-free lines or visit websites with chat rooms to get assistance. Internet support groups may be a fantastic method to conduct therapeutic sessions.

2.3. Spread Mental Health Awareness:

One strategy for keeping a good outlook is to find a balance between positive and negative feelings. Positive thinking does not preclude having unpleasant emotions like sadness or fury. To

traverse them, you must be able to cope with problematic situations. They could help you react to a situation. You do not, however, want these feelings to dictate how you live your life. For instance, it is useless to obsess over painful memories from the past or worry about the future. Know when to put down your news reading or viewing. Use social media to communicate with others and ask for assistance, but use caution. Do not engage in discussions, rumors, or unjust comparisons of your life to that of others. The act of expressing gratitude for your advantages is one way to cultivate appreciation. It's helpful to do this every day, whether you wish to enumerate your blessings or keep a running list in a notebook. These may be momentous occasions. It's important to allow yourself time to enjoy finishing your duty. Given the connection between your physical and mental well-being, look after yourself very carefully. One of the ways to take care of your physical health. Someone who is sleep-deprived may be more prone to annoyance and fury. It affects mood. Having sleep issues over time may raise your chances of developing depression.

It is essential to adhere to a regular sleeping schedule and get enough sleep each night to recharge. A healthy diet may improve your physical and mental health as well as lessen stress and worry. Certain mental diseases may get worse if there is a food shortage. For instance, there can be a connection between depression and low vitamin B12 levels. You can make sure you are receiving all the nutrients you need by eating a well-balanced diet. Humans need to establish solid, durable relationships with other individuals since they are social beings. Having solid social ties may help you shield yourself from the damaging impacts of stress. Additionally, having a variety of links is advantageous. You may find methods to become engaged in your neighborhood or community in addition to staying in touch with your family and friends. For instance, you may offer your services to a neighborhood organization or join a club focused on a hobby you like. Additionally, there are many types of meditation, including transcendental and mindfulness techniques. By using relaxation techniques, one may cause their body's natural relaxation reaction. Progressive muscular relaxation entails contracting and relaxing different muscle groups, sometimes while practicing deep breathing techniques or focusing on something uplifting. During guided imagery, you are told to concentrate on calming mental images, which may make you feel more at ease and focused. Biofeedback teaches you how to control body functions including breathing, heart rate, and muscular tension using electrical equipment. With self-hypnosis, the objective is to make oneself drowsy and trance-like in reaction to a particular suggestion or visual cue.

3. CONCLUSION

Complete mental health is mostly a result of a healthy lifestyle, a secure home, and active community involvement. Given the severity of mental health conditions and the low level of awareness of these conditions. Through the different ways listed above, efforts must be made and actions must be performed to raise awareness. Efforts will aid in the sector's quick growth, which will result in advancements and innovation for illness diagnosis as well as improved treatment strategies. Given that the majority of the prior methods for improving mental health have historically failed. The removal of stigmas and the promotion of something effective and beneficial may both be accomplished by raising awareness of mental health issues. Evidence-based government policies, engaged media, a well-organized educational system, and the use of new technology might all be helpful in the battle against mental diseases. Considering how difficult it is to comprehend and research mental health concerns. The government needs to launch clinical trials to test if it is possible to treat or cure major illnesses that are now incurable.

The time has come for these reforms and exceptional steps to be put in place to end the mental health epidemic.

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CHAPTER 4

A STUDY ON OLD AGE PREGNANCY IN WOMEN AND ITS SIDE EFFECTS ON WOMEN'S HEALTH

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ABSTRACT:

The mother's old age is linked to several pregnancy-related health issues and concerns. Being in danger causes tension and anxiety, which more and more pregnant women try to lessen by learning about the situation. For some women, the amount of information available might be overwhelming. To accommodate older pregnant women's unique requirements within obstetric services, healthcare providers need to be aware of their various emotions or experiences. Some genetic conditions, such as Down syndrome, are more common among babies born to older mothers. With age, there is a higher chance of miscarriage or stillbirth. This may be due to pre-existing medical disorders or chromosomal problems in the newborn. In this paper, the author talks about health-related various risks in old age pregnancy and its management or treatment of old age pregnancy. This study aims to evaluate the risks associated with pregnancy in individuals of advanced maternal age, in line with previous studies on pregnant women over 40 years of age. This paper intends to help people aware of the ill effects of old-age pregnancy.

KEYWORDS:

Advanced Maternal Age (AMA), Health, Pregnancy, Syndrome, Women.

1. INTRODUCTION

Both the mother and the unborn child undergo major physical and emotional changes throughout pregnancy. These advancements may have an effect on mother and child health as well as the quality of life for pregnant women, even in straightforward pregnancies. Undoubtedly, the welfare of women and their present awareness and expertise would have a big influence on society. To strengthen their self-care abilities and empowerment while practicing preventative health behaviors, pregnant women require health knowledge. Pregnancy causes various changes to the cardiovascular system [1]. When compared to a non-pregnant woman, the blood volume of a typical, healthy pregnant woman rises by about 50%. Additionally, due to the vascular permeability associated with severe preeclampsia, efforts to raise blood volume in these individuals have failed. The reduction in venous return to the heart or decrease in cardiac output that is related to pregnancy in a critical care setting is brought on by the supine posture.

Obviously, in the third trimester, when the uterus is larger, this impact is more noticeable. This condition is known as a supine hypotensive syndrome [2], [3].

1.1. A health-related problem faced by women in old age pregnancy:

The term "advanced maternal age" refers to women who are above 35 when they get pregnant. When one of the birth parents is 35 or older, pregnancy difficulties are more likely to happen. Higher miscarriage rates, genetic abnormalities, or specific pregnancy difficulties including high blood pressure or gestational diabetes are some of these problems. Pregnancy in women of advanced maternal age is handled similarly to a usual pregnancy [4], [5]. A people healthcare practitioner could advise prenatal testing and keep a closer eye on you. When you're over 35, your risk for chronic diseases rises, so it's even more crucial to be aware of your pregnancy symptoms and maintain good health. There are various problems old-age women are facing during pregnancy, which are shown in Figure 1.

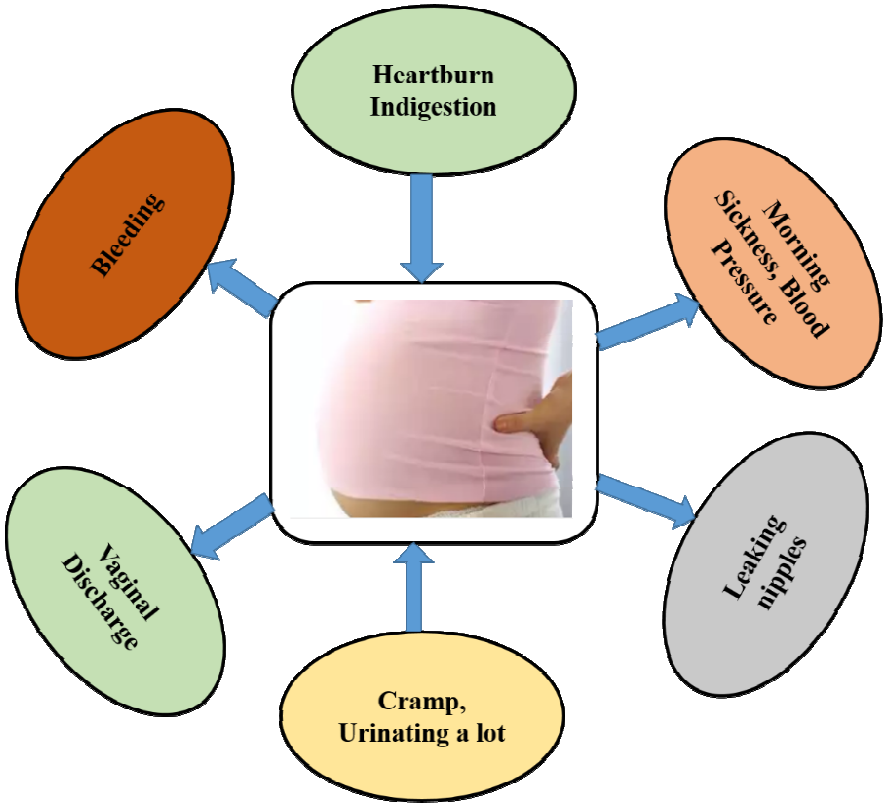

Figure 1: Illustrate the major problems faced by old age women during their pregnancy.

Despite these dangers, women can become pregnant and give birth to healthy children after the age of 35. A decline in egg quality is linked to advanced maternal age. This implies that your egg quality declines with age. Chromosomal abnormalities are more likely to occur in older eggs. In the first trimester, healthcare professionals scan for several of these chromosomal defects. The likelihood of getting the majority of chronic medical illnesses rises with age, which is another reason there are more issues beyond the age of 35. Simply said, as you get older, your body reacts to certain illnesses differently. Pregnancy and delivery may be impacted by some

persistent medical problems. For instance, the likelihood of having high blood pressure at 35 compared to 25 is higher even for non-pregnant people.

The risks of pregnancy in women over 35, particularly in prim parity, may be interpreted from two angles: first, from the standpoint of the real medical hazards, and second, from the viewpoint of the acceptability of the risks as defined by social discourse among various social groupings. Medical risks are associated with an aging reproductive system as well as the body, whereas social discourse dictates how and when women should have children and how older pregnant women are perceived as mothers [6]. Pregnant women and healthcare professionals are believed to have distinct understandings of the dangers: pregnant women evaluate the hazards subjectively, based on their personal experiences, whilst healthcare professionals analyze the risks in a manner that seems to be more objective.

Patients and healthcare professionals believe that "advanced maternal age" (AMA) is associated with worse pregnancy outcomes. This is mostly due to older women having a greater frequency of chronic medical issues. Even though there is no scientific justification for specialized treatment and no obvious medical issues, women of AMA are frequently treated as though they require the kind of care required for any high-risk pregnancy. High maternal expectations mixed with pre-existing and pregnancy-related illnesses, however, do make these women more dependent on intervention throughout pregnancy and delivery. Despite the assumption that there are more dangers associated with AMA, it has been said that these risks may be managed and that beneficial results can be anticipated [7].

The concerns connected to AMA, the connection between AMA and pregnancy outcomes, the proof of risks experienced by women of AMA, as well as the relationship between maternal age as well as stillbirth have all been the subject of recent reviews about pregnant women 35 years of age or older [8], [9]. Women's personal experiences with later childbearing and age-related pregnancy risks have received less attention in research. The current review article's goal is to give a summary of how past research has defined pregnant women over 35 and what the hazards of AMA during pregnancy are.

1.2. Recognize the Risk:

There is no escaping the biological clock. Therefore, being 35 has no particular significance. At a certain age, risks just become more debatable. You may need more time to become pregnant, and your egg supply is limited when you are born. As you get closer to your mid-to-late-30s, the quantity and quality of the eggs start to decrease. Furthermore, compared to when you were younger, it is more difficult for your eggs to fertilize as you age. Consider speaking with your doctor about whether you're over 35 and haven't been able to get pregnant for six months.

1. Multiple pregnancies are increasingly common, and your likelihood of having twins increases with age. This is due to the possibility of the simultaneous release of several eggs as a result of hormonal changes. Other assisted reproductive methods, such as in vitro fertilization, can be significant.

2. Gestational diabetes is now more likely to occur. Only expectant women are susceptible to this kind of diabetes. It is more common in older people.

3. People with gestational diabetes must strictly maintain their blood sugar levels through diet and exercise. Medicine is also necessary for some situations. Untreated

gestational diabetes might cause a baby's development to be above average. A birth injury is more common if the baby is larger.

4. Premature birth, high blood pressure during pregnancy, or issues for your unborn child are all risks that are increased by gestational diabetes.
5. An increased risk of developing high blood pressure is associated with pregnancy. According to a study, older adults appear to be more likely to experience elevated blood pressure during pregnancy. Your doctor will closely monitor both your blood pressure and your child's growth and development.
6. If you have high blood pressure when pregnant, you'll need to see your doctor more regularly. Users might also need to birth their kids before their due date to minimize complications. It is more probable to deliver a baby prematurely and have a child with a low birth weight. Complex medical problems are usually present in premature newborns, which raises the chance of a C-section. After age 35, the risk of difficulties during pregnancy that requires a C-section increase.
7. The likelihood of chromosomal abnormalities is higher. Babies born to older mothers are more likely to have particular genetic diseases, such as Down syndrome.
8. The likelihood of miscarriage is higher. Age increases the likelihood of miscarriage and stillbirth. This might be due to the baby's chromosomal problems or previous medical conditions.

A decline in egg quality is linked to advanced maternal age. This implies that your egg quality declines with age. Chromosomal abnormalities are more likely to occur in older eggs. In the first trimester, healthcare professionals scan for several of these chromosomal defects. The likelihood of getting the majority of chronic medical illnesses rises with age, which is another reason there are more issues beyond the age of 35. Simply said, as you get older, your body reacts to certain illnesses differently [10], [11]. Pregnancy and delivery may be impacted by some persistent medical problems. For instance, the likelihood of having high blood pressure at 35 is higher than it is at 25, even in non-pregnant people. The following health disorders are more prevalent in older women than younger ones and might pose issues before and during pregnancy:

1. The number of eggs that each woman is born with is fixed. Every time you ovulate, usually 14 days before your period, you release one egg. As a result, as you age, you produce fewer and fewer eggs, so those that you do have are more difficult to conceive with a man's sperm. You will find it more difficult to conceive as a result of all of this. If you are over 35 and have been trying to get pregnant for the past six months, let your doctor know
2. This occurs when your blood has an excessive amount of glucose, often known as blood sugar. People's body's organs, especially blood vessels, eyes, nerves, or kidneys, might suffer harm from high blood sugar levels. You have diabetes if it was present before becoming pregnant.
3. *Pregnancy diabetes:* This particular kind of diabetes can develop in some pregnant women.

4. *High blood pressure:* Blood pressure problems are sometimes referred to as hypertension occasionally. High blood pressure happens when the blood pushes too hard against the walls of your blood vessels.
5. *Preeclampsia:* This condition may manifest after the twentieth week of pregnancy or right after birth. It takes place when a pregnant woman exhibits indications of a malfunctioning liver, kidneys, and/or excessive blood pressure. Preeclampsia symptoms include protein in the urine, visual problems, and excruciating headaches. Preeclampsia risk increases with age compared to that of younger women.

This study is divided into several parts such as introduction, conclusion, literature review, discussion, and Conclusion. In the introductory part, the author talks about various health-related problems that old age pregnant women faced during their pregnancy period. In the literature review section, the author talks about the previous study on the same topic. In the discussion, section author talks about a possible solution to old-age pregnancy, and at the end, the author concludes the whole paper.

2. LITERATURE REVIEW

Zeinab Kamil Dhahi studied the satisfaction of pregnant females with primary health care. The study aimed to evaluate several aspects of expressed maternal pregnant women's satisfaction with the service received in 34 basic health facilities in the first and second areas of Basra city. A sample of 400 pregnant women was used, and the mothers received care as part of the investigation. When asked to identify steps to enhance treatment, 61.25% of the women said that ultrasonography was their top concern, and they urged that it be included in basic healthcare institutions. Following this, 41.25% voiced concerns about wait times and congestion, 33.75% advised hiring more dentists, 6.25% suggested hiring more physicians, 3.75% suggested hiring more female staff for the maternal health care unit, and 2.5% and 5% suggested moving the health center's maternal care section [12].

Itamar Glick et al. studied care for pregnant ladies who are older mothers. A risk factor for poor perinatal and maternal outcomes is when the mother is older than 35 at the time of pregnancy. However, it has grown increasingly typical for women to become pregnant later in their pregnancy during the past few decades. An increased risk of spontaneous miscarriage, early labor, stillbirth, chromosomal abnormalities, gestational diabetes mellitus, or cesarean delivery is only a few potential maternal problems associated with pregnancy at age 35 or older. Negative perinatal outcomes may include newborn intensive care unit hospitalization, autism spectrum disorder, underweight infants with intrauterine growth constraints, and more. An updated evaluation of the evidence and recommendations for the management of pregnancy with an advanced mother age are presented in this publication [13].

Caitlin Gerdts et al. studied mortality, physical health effects, or side effects of abortion and childbirth following an unintended pregnancy. The study gathered data on the effects of delivery or abortion on the women's self-reported physical conditions from women seeking abortions at 30 clinics across the country. All research participants' maternal mortality is also examined and reported. Findings confirm earlier research on the safety of induced abortion in comparison to stillbirth and indicate the substantial mortality and mortality risk associated with delivery following an unwanted pregnancy [14].

3. DISCUSSION

A database search on PubMed, Google Scholar, Research Gate, Science Direct, and other sites was used to conduct the current review study. Combining keywords like Advanced Maternal Age (AMA), Health, Pregnancy, Syndrome, and Women were used in the review technique. Title and abstract screening were used for the record's preliminary review. Additionally, non-extractable data, duplicate research, and inadequate information were grounds for excluding the Records. Figure 2 below provides more information on the methodology utilized to conduct the review study.

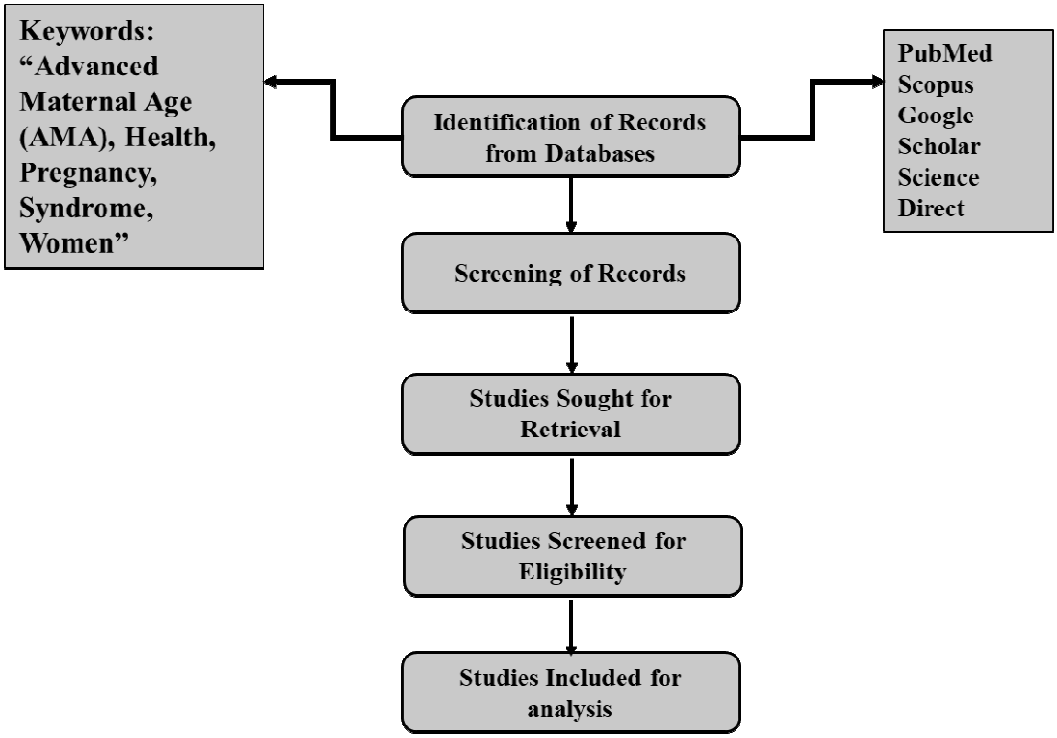

Figure 3: Illustrate the Design of the Methodology of the Current Review Work.

Today, many women put off starting families until later in life. The birth rate for women in their 30s in the United States is at its highest point in three decades. However, an older woman may be more vulnerable to miscarriage, birth deformities, or complications during pregnancy such as twins, gestational diabetes, high blood pressure, or challenging births. According to some research, while infants born to older mothers may have a higher probability of experiencing issues during pregnancy, those born to younger mothers may not. The risk is increased when women get prenatal care and give birth in a setting designed to treat high-risk pregnancies and newborns.

3.1. Chromosomal Abnormality Risks According to Mother Age:

With a mother's age, the likelihood of chromosomal abnormalities rises. Since many data only record live births and exclude chromosomally defective pregnancies that ended in abortion or spontaneous miscarriage, there may be a higher chance. The likelihood of having another child with Down syndrome increases typically after having one. The mother's age at birth determines

the risk of a second Down syndrome diagnosis after the age of 40. It's important to comprehend that moms under the age of 35 give birth to the majority of Down syndrome youngsters. This is because women under 35 have more children than women over 35. A genetic counselor or expert who can fully explain the results of chromosomal testing, including any potential risks of recurrence in later pregnancies and the types of tests available to find chromosome issues before a child is born, may be recommended to parents by the doctor.

3.2. Maternal Age and the Chance of Miscarriage

According to several research articles, elder moms had a greater risk of miscarriage and early pregnancy loss. A chromosomal defect in the fetus accounts for nearly half of the first-trimester losses when all women are taken into account. Miscarriage is also more common since these anomalies get worse as women get older. A novel test scans the mother's blood for cell-free fetal "Deoxyribonucleic Acid" (DNA) to screen for chromosomal abnormalities. The risks rise as a woman becomes older, even though 35 is regarded as an advanced maternal age. If you are a woman over the age of 30 or pregnant, speak with your doctor about your health. People should also discuss ways to maintain their health and the health of their unborn kids while they are pregnant.

3.3. Management and Treatment of old age Pregnancy:

Actually, no. The fact that you are an older mother does not usually make a difference in how you are treated by healthcare professionals. An expert in maternal-fetal medicine may be recommended by your doctor if genetic screening tests reveal your child may have a congenital disease. This person specializes in pregnancies with a greater risk. Other times, you could have earlier testing or more frequent prenatal appointments with your normal doctor. For instance, additional ultrasounds and fetal heart rate monitoring to make sure your baby is healthy, or an earlier glucose screening test to look for symptoms of gestational diabetes. To reduce your chance of getting preeclampsia if you also have other risk factors, your doctor may advise taking a baby aspirin every day for the majority of your pregnancy. Simply because your risk for some problems rises as you become older, your prenatal care is more crucial. Attending all visits and tests, eating a good diet, and maintaining a healthy weight during your pregnancy are therefore more crucial than ever.

Healthcare professionals may be better able to counsel patients about contraception by having a better understanding of the variables that affect contraceptive usage in women 35 and older. There are a few reasons that have been documented in various communities that discourage the use of contraception [15]. It has been demonstrated that a variety of circumstances, including pregnancy ambivalence, low socioeconomic status, the presence of a partner, views toward various procedures, the expense of contraception, as well as method satisfaction, might affect a woman's usage of a contraceptive method. When contraception is used, among other things, to manage a chronic medical condition or prevent probable obstetrical problems, additional findings may be specific to older women. These findings imply that life span perspectives should be included in contraceptive counseling and that older women should research contraceptive options and side effect profiles. The majority of respondents were concerned about how using contraception will affect their health [16], [17]. Several respondents chose hormonal therapy after getting assurance and counsel from their medical professionals because they understood it would treat their pre-existing medical problem or have other beneficial consequences on their

health. None noted additional significant health benefits of hormonal contraception, such as the reduction of risk of endometrial, ovarian, or osteoporosis.

The bulk of replies talked about people's poor experiences with “Intrauterine Contraception” (IUC), ignoring the fact that there are now newer “Instrumentation Unit Update Command Systems” (ICUs) available. Respondents were unable to explore potentially useful techniques due to misconceptions. These findings suggest that appropriate information regarding contraception must be distributed to women of all reproductive ages [18]. Information that is widely disseminated might improve contraceptive usage, especially for people who have limited access to the healthcare system. The benefits and drawbacks of periodic abstinence were not a particular question in the interview, although several participants indicated it as a technique they were now practicing or had previously used [19], [20]. The majority praised this technique for being chemical-free and natural. The debate in favor of it might suggest that women in their late reproductive years are looking for a method of contraception that doesn't involve ingesting or injecting steroids, doesn't interfere with sexual activity, and maintains normal menstruation even though some women unintentionally become pregnant while using it. There are various limitations to the findings of our research. First, participants' opinions regarding contraception were likely different from those of nonparticipants [21].

3.4. Advantages of being an Older Mother:

Even though it may be more difficult to conceive at your age, being an older mother has certain benefits for both you and your child. These consist of:

1. *Preschoolers who are healthier and speak more clearly:* Overall, preschoolers whose mothers are older are in better health. Compared to children born to younger moms, they had higher vaccination rates, fewer hospitalizations, and fewer accidental injuries. Additionally, they frequently exhibit stronger verbal and linguistic development.
2. *A rise in intelligence as you age:* When tested for thinking and verbal memory between the ages of 41 and 92, females who had birth after age 35 performed better. Furthermore, when they were older, a female who had used contraceptives for more than ten years had higher executive functioning abilities and better problem-solving abilities.
3. *Improved parenting abilities*: You likely possess greater patience now than you did in your youth. Older mothers are less likely to shout at or forcefully reprimand their kids. They are also more adept at establishing boundaries. Children of older moms often experience fewer emotional, social, or behavioral problems.

4. CONCLUSION

Understanding the factors that influence the choice and use of contraception among women 35 years of age and older who are at risk of unwanted pregnancy is crucial to enhance the use of contraception in this group. Women in this age group can gain from public health initiatives and medical treatment by evaluating their reproductive risks, all of their contraceptive options, and any potential side effects. It is important to evaluate how these treatments affect unwanted pregnancy rates in this age range in other areas of evidence-based medicine. This study found that complications such as preterm birth, gestational diabetes, intrauterine growth retardation, pregnancy-induced hypertension, instrumental delivery, and cesarean section are more common in older women than in younger ones. Older women should thus seek pre-pregnancy counseling,

and their doctors should let them know what to expect throughout pregnancy and what could happen. Age increases the likelihood of miscarriage or stillbirth. This could result from chromosomal problems in the newborn or pre-existing illnesses. This study aims to evaluate the risks of pregnancy among persons who are advanced in maternal age, in line with past studies on pregnant women over 40. This study will hopefully raise people's awareness of the negative repercussions of senior pregnancy in the future.

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CHAPTER 5

A COMPREHENSIVE APPROACH TO THREE-DIMENSIONAL VISUALIZATION TECHNOLOGY FOR EDUCATIONAL ANATOMY

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ABSTRACT:

A major component of the biological sciences and the training of medical practitioners, anatomy is crucial for performing a variety of therapeutic tasks. A rising number of educators, anatomists, and researchers are using three-dimensional (3D) visualization technologies to enhance the current curriculum and improve students' spatial comprehension of anatomy. This study emphasized how common and advantageous it was for medical students to use this technological table to teach gross anatomy. To improve the learning experience, recent medical developments have used 3D visualization techniques in the classroom, such as 3D printed anatomical models, Virtual Reality (VR), and Augmented Reality (AR). This study also looks at a variety of technologies for use in medical training, including conventional slide presentations, 3D printed anatomical models, augmented reality, and virtual reality. They also consider each technology's advantages and disadvantages. Anatomy may be taught through virtual dissections of cadavers, which might be particularly helpful in emergency circumstances like pandemics since it broadens clinical and anatomical knowledge.

KEYWORDS:

Anatomy, Education, Three dimensional (3D), Augmented Reality (AR), Virtual Reality (VR).

1. INTRODUCTION

When it comes to anatomy, having a clear picture of the big picture is crucial. They must also study how these systems relate to one another in space, not only how the body works. Static anatomical images, like those seen in anatomy textbooks and atlases, are helpful, but they can't show you how organs and tissues move in three dimensions. Students may struggle to mentally convert two-dimensional (2D) pictures into three-dimensional (3D) and grasp the dynamic nature of several parts of functional anatomy. In various liver sites, for instance, caudate-related structures may be identified [1].

To accurately identify anatomical components, students studying anatomy are required to rotate and manipulate objects from a variety of viewpoints. The capacity to cognitively manipulate objects in three-dimensional space is a definition of visual-spatial aptitude. Understanding anatomical structures is crucial for medical students and is also useful for surgical residents and practicing surgeons to have this skill. Since medical and dental students often encounter

anatomical data presented in several planes and locations, they must develop the capacity to cognitively manage 3D structures and accurately recognize them and associated structures [2].

Technology that can show digital three-dimensional images of anatomical characteristics is only one example of the many software packages that have been developed in response to the rising interest in technology-enhanced learning and its use in anatomy teaching. There are a variety of words used to characterize this innovation in the books. The term "3D pictures" will be utilized throughout this article to refer to scans from “Computed Tomography (CT)” and “Magnetic Resonance Imaging (MRI)” that are shown in three dimensions. This is reflected in studies that compare various 3D image formats to other techniques of teaching anatomies, like dissections, lectures, 2D pictures, live anatomy programs, plastination, and combinations of these and additional methods [3].

Aerospace, architecture, automotive, and education are just a few of the fields that have seen a rise in the use of 3D printing in recent years. With this innovation, a digitized file, like a (CT) scan or magnetic resonance imaging (MRI), may be transformed into a physical item that can be held and examined. When compared to 2D photos in a textbook, students may get a deeper knowledge of anatomical features through interacting with medical teaching using 3d printed models. Furthermore, using printed models in class projects has allowed teachers to express their unique creativity while simultaneously fostering students' critical thinking and teamwork abilities [4]. It is impossible to get a thorough understanding of anatomy and learn about anatomical defects and variations without using the cadaveric dissection method. By doing dissections, students get an appreciation for the human body as a three-dimensional (3D) structure and develop the ability to articulate anatomical relationships in detail. Thus, dissection offers not only students but also graduates and experts a significant benefit over two-dimensional representations in textbooks. Clinical training is enhanced by dissection, and surgeons benefit from the practice as they gain more proficiency with their instruments and fine-tune their manual dexterity by working on cadavers [5].

2. LITERATURE REVIEW

Katerina Bogomolova et al. conducted their study on the effects of stereopsis on 3D virtual reality anatomy education. Two authors picked research, culled data, and evaluated them separately. The tool for Evaluating the Efficacy of Research on Medical Education and the Bias Tool of the Cochrane Collaboration was used to evaluate the studies' research quality. For quantitative research, studies were categorized by instructional technique and control condition differences. Totaling 3934 citations, 67 were full-text reviewed. The meta-analysis includes 13 RCTs. Stereopsis is a defining feature of 3DVT that improves anatomical information acquisition in an interactive 3D environment, according to the author. Anatomical teaching and research must distinguish between stereoscopic and monoscopic 3DVT [6].

Iain D Keenan and Abdullah Ben Awadh stated in their study that introducing technology enhanced-learning (TEL) techniques aim to improve the medical student's understanding of clinically significant anatomy. The author explores the role of visualization and visual learning in anatomy for TEL techniques. The author will present visualization tools established at Newcastle University based on the results, of the School of Medical Education on how students learn anatomy. The author would describe possibilities for supplementary and independent usage of visual, 3D learning technology to enhance conventional ways of undergraduate anatomy instruction [7].

Zhenyu Wu et al. discussed in their study that improvements in technology and computer science have allowed for more refined methods of processing and analyzing medical images. Using techniques including image expansion, image corrosion, and the triangulation methodology based on surface contours, this research will examine the most effective approaches to Human anatomy-based segmentation of CT scans of the head and 3D reconstruction. The findings suggest that Anatomy-based CT image segmentation may enhance picture quality by obtaining the image's fundamental morphology and characteristics. The author stated that head CT image segmentation and human anatomy-based 3D reconstruction have excellent application results and may be used in treatment and diagnosis. The usefulness of animated and interacting 3D computer graphics was studied by Battulga et al. using a randomized controlled trial that centered on the perspective of medical students (3DCG). They discovered a there was a quite large gap between the 3DCG and textbook groups, with the former averaging a 4.26 on a 5-point Likert scale and the latter a 3.85 [8].

Yasser Alharbi et al. evaluated in the study investigate the usage of 3D-VR in training and education in the medical field has been advocated as a means to better serve students' educational needs to see how effective it was to use 3D-VR to teach medical students about human anatomy vs more traditional methods. To evaluate short- and long-term talent retention rates between 3D-VR and traditional models, as well as to evaluate students' experiences with 3D-VR as a tool for education and learning, a convergent mixed methods technique was utilized. Male students who used the 3D-VR group also performed better on tests of both immediate and permanent recall. Short-term recall scores for women's knowledge were higher for traditional methods than for 3D-VR. The author recommended using 3D-VR in anatomy classes. Various 3D-VR restrictions may impair teaching and learning. Before using 3D-VR in medical education and human anatomy classes, several issues must be resolved [9].

Using a multicenter quasi-experimental approach and rather low-quality data, Venail et al. investigated whether or not 3D computer software improved users' understanding of temporal bone structure. Students who took the 3D reconstruction instructional course outperformed the control group, which just got a presentation (89.92± 1.84 vs. 80.91± 2.18 on a scale from 0 to 100, $P < 0.001$). Before human anatomy classes at medical schools may benefit from 3D-VR technologies, several concerns must be addressed [10].

3. DISCUSSION

Recent years have seen a rise in the use of 3D printing across various fields, including the arts, architecture, manufacturing, and the academy. This innovation in imaging technology makes it possible to materialize a 3D picture from a digital file like a CT or MRI scan [4]. When compared to static 2D photographs in a textbook, medical students may get a more comprehensive knowledge of anatomical components when exposed to 3D-printed models. It's no secret that 3D printing has opened up a world of possibilities for both students and teachers[11].

By creating their 3D models, teachers and students alike may investigate abstract concepts. The building provides both real-world practice and a deeper dive into the process, therefore this activity is conducive to active learning.

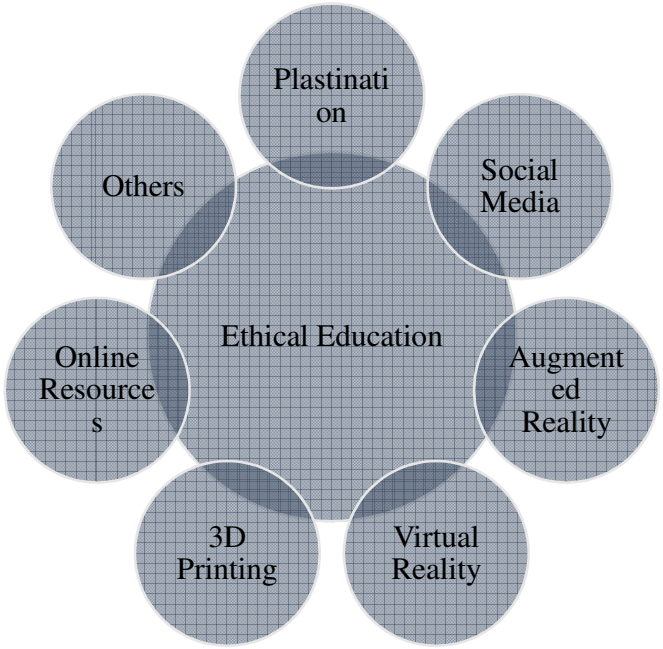

Figure 1: Displays that Anatomy education takes an interdisciplinary approach.

Since it is hard to compare them to conventional techniques in comparable and objective situations, most of the research examining the efficiency of these educational approaches or modalities has been subjective. Wilson et al. [12] conducted a meta-analysis and discovered that when conventional dissection was contrasted with various laboratory methodologies, such students' results were statistically similar across all assessment types (3D models, prosection, digital media, and hybrid techniques). The authors argued that teachers should choose a method of instruction based on its intended results rather than the method's features alone. The learning model has less influence on short-term memory retention than does prior anatomical knowledge, as revealed by the research of Lackey-Cornelison et al.[13] In addition to aiding students in learning human anatomy and physiology, cadaveric dissection may also help students grow in areas like collaboration, self-reflection, interprofessional and communication skills, and ethics. Finally, instead of debating whether or not human cadavers should be employed for anatomy education, the author should contend for their use as one of many simultaneous methodologies, as shown in Figure 1.

Figure 1 shows that prior knowledge of anatomy affects short-term memory more than the learning mode itself. Dissecting human corpses has many educational benefits beyond only teaching students about human anatomy and physiology, but it may also help students grow in areas such as self-awareness, critical thinking, empathy, and interpersonal and communicative competence. Recent years have seen an uptick in the usage of 3D-VR in medical education, specifically to visualize and display anatomical components in a simulated setting. When compared to more conventional approaches, this approach involves multimodal learning, which increases student participation, and so enhances knowledge retention, and may even entail using preserved bodies such as cadavers or plastinated models. The current study's qualitative results suggest that engaging in 3D-VR activities improves the interaction between educators and their students. Using 3D-VR to learn about human anatomy has been lauded by many students;

nevertheless, others felt that including the conventional cadaver model with 3D-VR will improve the educational process.

3.1.An Overview of the Many Different Methods Utilized in Three Dimensions for Learning Anatomy:

Four randomized controlled studies examined a computer-based 3D tool using a neuroanatomical model, with three indicating that 3D imaging and modeling on computers might lead to better anatomy instruction. Using functional positron emission tomography data, Ruisoto et al. created volumetric pictures with integrated 3D graphic models. Anatomical features were substantially more accurately recognized by the group given 3D representations that were shown 2D cross-sections of subcortical structures (42.1% vs. 25.4%, scale 0%-100%, $P< 0.01$) [14].

Contradictory findings have been found when comparing the efficacy of conventional and 3D approaches in the study of anatomy beyond only neuroanatomical. Two experiments using 3D ear models created on computers showed great promise [15]. A randomized controlled trial (RCT) was performed by Tan et al. to examine the usefulness of a 3D laryngeal model created on a computer. Important anatomical features from CAT scans and MRI scans were extracted for use in creating this model. After that, the model was transferred into Microsoft PowerPoint where it was given some visual, aural, and illustrative polish in the form of clinical vignettes and sound bites. In this research, the standard technique group scored 15.5 2.3 whereas the 3D group scored 15.7 ±2.0 [16].

Student's ability to learn, retain, and comprehend particular functions of anatomical structures may be hindered by their reliance on static 2D pictures from reference materials throughout the classroom and practical instruction. If the caudate lobe of the liver were relocated, for instance, a pupil may not identify it. In this approach, 3D-VR allows students to experiment with different manipulations of structures, which may aid in their grasp of anatomical ideas. By mentally manipulating the intended results in three dimensions, students may improve their visual-spatial abilities and hence their capacity to understand anatomical structures.

3.2.3D Printing as a Teaching Tool:

For a long time, educators have relied on tried-and-true practices including presenting material in a lecture format, using anatomical models, and studying actual human bodies (cadavers). Students that study anatomy via cadaver dissection have trouble retaining the information learned; a 2-week recall test shows that they have forgotten most of what they were taught. Cadaver dissection has fallen out of favor due to several factors, including ethical concerns, cost concerns, and difficulties in arranging necessary logistics. Cadaver labs are indeed a terrific tool for learning, but animal models are useful too. There are ethical, cultural, and economic considerations, in addition to the anatomical differences present in these models despite their genuine soft tissue texture and ability to correctly portray disease [17].

In the course of anatomical research, the use of 3D printing technology offers great promise. Models made with a 3D printer may be as flexible and have a delicate texture as actual organs, but this comes with a higher price and a longer manufacturing time. In the classroom or at home, these examples are invaluable. Li et al. [18] discovered that utilizing 3D printed models to teach anatomy was more successful than using 2D pictures in their research. According to data presented in a survey conducted by the National Association of Biology Teachers, students feel

less creative and produce fewer excellent visual aid items while utilizing traditional learning strategies. Students using 3D printing, on the other hand, are more invested in their work because they must spend more time on it [18].

3.3.Augmented Reality (AR in Education:

The Application of Augmented Reality in Undergraduate Science, Technology, Engineering, and Math (science, technology, engineering, and mathematics) classes have aided student learning and reduced teacher burden. In research conducted in first-year college physics laboratories, there were two groups that students might be placed in: those using augmented reality technology and those using a traditional laboratory manual. Students who utilized AR technology throughout the 5-week trial paid closer attention and made fewer mistakes than those who did not. The physics instructor said in an interview that he had far less work to do with AR technology being utilized in the classroom since pupils needed less assistance and grasped difficult physics topics more quickly [19].

One such upcoming technology is the area of augmented reality (AR), which has the potential to dramatically enhance the education of anatomy to students from grades [20]. The term "augmented reality" (AR) refers to a set of technologies that let people see and engage with digital representations overlaid over their real-world environments. Because the user is not submerged in a digital environment, they can include both digital input and real-world items in their augmented reality experience, which is a key distinction between AR and virtual reality. When used in the study of anatomy, the use of augmented reality (AR) in education has the potential to provide a very immersive and authentic atmosphere for learning that is conducive to the kind of complicated medical learning situations that anatomists often face.

Augmented reality (AR) can deliver an extremely realistic contextual learning experience when it comes to teaching human anatomy that is helpful in a variety of challenging medical learning situations The ability to visually disassemble and reassemble anatomical components for the in-depth study is a significant benefit of augmented reality (AR) for studying anatomy, especially when compared to practical models and cross-sections. The lack of tactile feedback4 is a potential drawback of augmented reality. Researchers discovered that, when compared to standard teaching approaches (like dissection, cross-sections, and 2D pictures),), 3D visualization tools were much more effective in helping students acquire spatial knowledge [21].

3.3.1. AR's Limitations in Education:

Research shows that students are more engaged in learning when they are exposed to novel technologies like augmented reality (AR) and that they prefer studying with graphics and audio to reading text from lab instructions. If students just had to recall information pertinent to AR technology, they may cut down on their time spent outside of class reading and studying. Despite these worries, the survey found that AR students were more aware of lab safety than students who relied only on lab instructions. Another disadvantage of AR technology is that if used for an extended length of time, it might cause simulator sickness in users. Eye strain, nausea, dizziness, and migraines are symptoms of simulator sickness. Hanna et al. described how research participants reported no such negative effects since their usage duration spanned from a few minutes to an hour [22].

3.4.Virtual Reality (VR) in Education:

Computer-based 3D models have grown more popular in recent years for use in teaching anatomy. Virtual reality (VR) is a medium through which 3D content may be seen and interacted with by its viewer's multimedia settings that have been created on a computer. Through its many immersion modes, it enables first-person, hands-on learning. In the 1960s, the entertainment industry was significantly responsible for the initial adoption of VR technology. Virtual reality (VR) can improve several sectors, from retail to media to corporate training to academic instruction [23].

Although both augmented reality and virtual reality are capable of rendering interactive 3D visuals, these two technologies are not interchangeable in many ways. Because an AR picture may be readily created by smart glasses, smartphones, or a headset, there is no need to wear a separate device while engaging in this technology. Because the computer generates an overlaid 3D picture, augmented reality enables virtual experiences to be combined with the actual environment. Virtual reality (VR) is a subset of augmented reality (AR) that replaces the actual environment with a digitally generated 3D picture seen via a headset. Virtual reality (VR) is gaining traction in the medical education sector, especially in the realms of anatomy instruction and surgical residency preparation [24]. The immersive nature of virtual reality (VR) allows for the rapid conceptualization of complex 3D anatomical linkages via simulation. Virtual reality (VR) has been compared to traditional anatomy education approaches including dissection, lectures, 2D visuals, and mixed learning in several studies.

In their study, Coyne et al. argued that the incorporation of VR into pharmacy curricula has been beneficial since it has helped students retain information from both classroom lectures and practical lab exercises. In pharmacy education, virtual reality (VR) has its roots in the use of patient case reports, 3D models, and simulation mannequins. The value of mannequins has grown in recent years, making them more prohibitive despite their usefulness in providing a realistic evaluation of students' performance in areas such as patient safety, ethical conduct, and patient care [25]. A shift from a receptive to an active learning environment is possible with virtual reality. The emphasis shifted from teaching and reading from slides to guiding and supporting pupils. There is less reliance on teachers and more opportunity for students to ask questions and figure out solutions on their own. When students can remember more information, even about boring topics, their motivation to actively participate in class grows. Incorporating challenging subjects, such as medication pharmacokinetics, generic and brand name memorization, and so on, into enjoyable games in VR has been shown to improve performance.

3.4.1. Virtual Reality Limitation in Education:

While virtual reality (VR) has the potential to improve the educational experience for both students and instructors, it is currently limited in its ability to substitute both specialized instruction and genuine human displays of emotion. Pottle et al. showed that VR-generated 3D graphics are merely another way of communicating, with limited applicability. Because it can only provide a physical depiction of the belly, the use of virtual reality as a training aid for abdominal palpation is not effective, for instance. Humans are still the finest examples of the intricacy of facial emotions and spoken language, which makes virtual reality a poor choice for certain tasks, such as breaking unfortunate news [26].

4. CONCLUSION

Recent years have seen an increase in medical training using 3D virtual reality, particularly to visualize and display anatomical components in a simulated setting. When compared to more conventional approaches like the use of cadavers or palatinate models, the multisensory learning involved here improves information retention. While some students had fruitful experiences studying human anatomy with the aid of 3D-VR, others felt that a combination of 3D-VR and the more conventional cadaver model would be most beneficial. AR and VR's immersive virtual environments enhance learning by stimulating students' imaginations, facilitating collaboration, and facilitating better communication. Combined, these three approaches not only help teachers spend less time on administrative tasks but also foster better student-teacher dialogue. For a long time now, schools have relied on students just listening to lectures and memorizing their material to pass their courses. More thoughtful questions are posed in class as a consequence of students' increased interest and involvement with the topic made possible by these interactive tools. Educators should investigate 3D printing, augmented reality, and virtual reality to enhance their teaching methods and student involvement.

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CHAPTER 6

OPPORTUNITIES AND THREATS OF TECHNOLOGICAL TRENDS ON HEALTHCARE SYSTEM: A COMPREHENSIVE REVIEW

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ABSTRACT:

The use of technology in people's lifestyles is increasing day by day, technology has made people's life easier. Healthcare plays an important role in human life, and technology and research created in this area are causing changes in the healthcare sector as well as other areas. The two objectives of this study are to examine the demands of health care and to set standards for selecting the best technology. The study looks at three recent technological trends in the literature. Within the parameters of the study, the ideas of edge computing, cloud computing, and fog computing were evaluated. The purpose of this study is to set standards and decide on the best appropriate technology for conducting health tests. The main objective of this study is to find out more about the effects of new technology trends on the health system. In the future, this paper will introduce people to new technology that could impact healthcare.

KEYWORDS:

Artificial Intelligence, Cloud Computing, Internet of Things, Healthcare, Technology.

1. INTRODUCTION

The importance of health in people's lives cannot be denied. The field of health has seen significant changes and advancements as a result of technological advancement. With these adjustments, technology has established itself as one of the essential components of the healthcare industry. Systems or applications that are ground-breaking in the field of health have been created. Changes that affected people's lives have taken place in this way. With the advent of technology, nevertheless, the health industry will inevitably adapt to these changes [1]. Classical and conventional data centers have been employed in the technology area for many years. The technical infrastructure is still being served by this occurrence. However, traditional data centers have given way to new technological infrastructure as a result of flaws and technological advancements [2], [3]. These days, it seems that edge computing, cloud computing, as well as fog computing have displaced traditional data centers. Following is a list of the primary reasons behind this desire for change.

1. A greater volume of data must be kept.
2. The requirement to exchange and transmit data held.
3. The need to evaluate previously recorded data.

This study aims to investigate the technologies that can be used for healthcare infrastructure and systems. The analysis will provide recommendations for the ideal infrastructure of the target, which will lead to a significant increase in health services. However, before deciding on the infrastructure that will best meet the demands, it is important to recognize supporting structures with technological advancements and weigh the benefits and drawbacks of each [4].This heading will cover cloud computing, fog computing, as well as edge computing topics. These three approaches' designs, benefits, and drawbacks will be discussed. These ideas must be clarified to choose the best service type in the sector of health.

1.1. Utilizing Cloud computing:

Internet-based IT services for PCs and other devices that provide shared, always-on computer resources are collectively referred to as cloud computing [5]–[8]. Research on cloud computing-based health services apps and services is also included in the study. The key findings from the analysis of the research in the literature are shown below.

1. Utilizing cloud computing may advance and enhance the healthcare industry and present significant prospects.
2. The security and privacy of patient data and data management are issues raised by the transmission of all data via the Internet. Studies in this area are still ongoing.
3. Healthcare decision support tools can employ cloud computing capability.
4. It is simpler to perform big data analyses in the healthcare industry thanks to cloud computing.
5. The need for data transmission necessitates high bandwidth needs.
6. The Internet of Things (IoT) is another popular topic in the literature, and a major issue with this technology is the lack of cloud computing.
7. Integration with the services it offers, such as “Platform as a Service” (PaaS), “Software as a Service” (SaaS), as well as “Infrastructure as a Service” (IaaS), is difficult with cloud computing (IaaS).
8. Using a distributed storage system to store files in the cloud.
9. Challenges with huge data analysis because of scattered files or data structure.

1.1.1. Computerized fog:

In contrast to architectures that allow information to be received and processed at a centralized computer, fog computing advocates doing smart device analysis locally before sending the results to the servers. Fog computing is a method for filtering, processing, and data storing that

involves creating a middle layer right before all data is stored in the cloud. According to estimates, there will be 5.63K IoT devices on the planet by 2020.

The estimations show that there is no doubt that IoT will continue to be a popular issue for a very long time. As IoT technology advances, it will also become more popular in the healthcare industry. The technological trend that will serve as the focus in the field of health must be in line with IoT technology. The suggested approach offers answers to IT issues in response to IoT issues in cloud computing. Sample fog computing architecture.

The key findings from the analysis of the literature-based studies on fog computing are shown below.

1. Low latency and fast reaction times make fog computing ideal for implementation in healthcare services.
2. It is compatible with IoT applications and services used in the healthcare industry.
3. Its local architecture, computing power, and storage capacity enable large data analysis.
4. It provides a scalable architecture that is superior to cloud computing.
5. Greater dispersed processing strength as a result of local processing strength.
6. Local operations result in a more secure and fault-tolerant architecture.

1.1.2. Edge Computing:

Due to their proximity to data processing and gathering, edge computing, as well as fog computing, are related. These two ideas are related to one another, yet they also significantly diverge from one another [9]–[11]. The location of the computation and processing power is the primary distinction between these two new technological trends. Processing is done through a local area network in SIS computing (LAN). Contrarily, edge computing relies on the incorporation of computers and processing capacity into real-world objects. Edge devices are used in fog computing through LAN. IoT technology is crucial to the development of edge computing, just like fog computing [12]. After reviewing the studies on edge count in the literature, the essential elements are listed below.

1. Wireless sensors are used in e-health care or telemedicine apps and services to collect comprehensive patient data. Edge computing can provide this demand in certain circumstances.
2. It is suited and fully compatible with IoT technology.
3. Price is more expensive than cloud computing.
4. It is appropriate to be chosen in low-latency applications.
5. It must match the devices it includes in terms of processing power or storage capacity.

With technological advancements, the healthcare sector is expanding into a new area of human well-being. Healthcare-related data obtained from many sources, such as medical imaging, electronic health records, wearables, pharmaceutical research, diagnostics, or medical devices, is what's driving these advancements. How to use these technological breakthroughs without

compromising the high level of patient care or the safety of patient data is the challenge that the healthcare sector today faces. By examining patents issued in these fields during the last five years, scientists get a deeper look at the newest developments in healthcare technology. Humans observe a few common patterns in the directions that healthcare providers are pursuing amid the fast transformation that is occurring. Figure 1 shows the Major Benefits of Emerging Healthcare Technologies.

Figure 1: Illustrate the Major Benefits of Emerging Healthcare Technologies.

The author examines a few of the cutting-edge technologies being used in healthcare in this article. These are including smart drug delivery systems, the Internet of Things (IoT), different Digital Health projects, and artificial intelligence (AI). In our past analyses of the patent landscape, we went into great depth about these technologies. Researchers examined the patterns over the previous five years and included tables and graphs with the most recent data for the same in this post.

1.2. Benefits of Emerging Technology in the Healthcare System:

The development of technology is frequently praised as humanity's greatest gift to itself. Technology influences every element of our life, and the healthcare sector is no exception. Figure 1 illustrates how the arrival of technology has changed the healthcare sector in various ways. This blog will discuss several subjects linked to how this modernizing wave has benefited the sector.

The following are the top 5 advantages of using technology in healthcare:

1. Patient medical records are easily accessible.
2. Decrease in medical mistakes

3. Improved patient care
4. Better education of the patient
5. Reduction of expenses.

1.2.1. Patient Medical Records are Easily Accessible.

The collecting of patient data is one of the most crucial aspects of the healthcare sector. Doctors need medical information to evaluate the patient's illness and condition to perhaps find a cure. Patient records produced a lot of paperwork in the past because everything was done on paper and ink. The acquisition of historical records proved challenging. However, with the development of digitalization, it is now possible to enter patient medical data into a cloud-based digital system. Patients, experts, and medical billers may now easily and quickly access information with just a single click from anywhere at any time.

“Electronic Medical Records” (EMRs), also called electronic health records, are these systems (EHRs). It is an electronic database that contains patient and population health data that has been digitally saved. The chief information officer or head of technology at Caregiver, Inc., Sameer Bhargava, stressed the critical efficiency that EHRs had given them. His team transferred eight million data from paper to an EHR system over eight months. When we switch to electronic records, Bhargava claims, our care ecosystem is elevated into a coherent process that can give a better network of services [13]. As a result, technology has made gathering medical data easier and made it possible for clinicians to quickly access patient information.

1.2.2. Decrease in Medical Mistakes:

Because they occur often and are an inherent aspect of human performance, medical mistakes are a growing societal issue. Medical mistakes are the third greatest cause of mortality in American hospitals and healthcare facilities, and about 98,000 people die each year as a result, according to official statistics from Starfield and the American Institute of Medicine (IOM). Fortunately, technological advancements have facilitated the development of solutions that have been demonstrated to reduce medical errors and boost lifesaving. The clinical Decision Support (CDS) system gives the medical practitioner patient-specific information as well as medical knowledge. To improve the healthcare provider's decision-making, this information is logically filtered and provided at the relevant moments. It is capable of offering guidelines, protocols, norms, and suggestions for care that are supported by evidence. According to research by the author, the “combined defense services” (CDS) system decreases significant medication mistakes by 55.00% and all pharmaceutical errors by 84.00%, underscoring the system's extraordinary ability to help medical professionals make diagnoses.

1.2.3. Improved Patient Care:

By utilizing technology, healthcare providers may increase patient engagement and collect data that helps them create hyper-targeted, tailored health and wellness regimens. Wearable fitness bands or other wirelessly connected gadgets, such as Fit Bits that may monitor blood pressure or Electrocardiographs, can provide patients and medical providers with personalized data (ECG). These devices might, among other things, show calorie counts, activity checks, blood pressure fluctuations, or appointments. Specialists are better able to keep an eye on patients' health,

particularly their adherence to treatment plans, etc. For elderly people and for individuals who live alone, this is essential since it guarantees that their families or concerned healthcare experts will be contacted as soon as any anomaly is identified. These technological advancements ensure that patients receive top-notch care as a consequence, raising everyone's access to or grade of care.

1.2.4. Better Education of the Patient:

Healthcare workers are embracing technology because it is essential to patient care and may help people be better educated and engaged. More than 75.00% of physicians, according to the findings of a recent poll of 200 U.S. doctors by Patient Point as well as the Digital Health Coalition, think that using technology for patient engagement or education may enhance the patient experience. 95.00% of respondents stated that they were presently educating and engaging patients utilizing engagement technology solutions [14].

Because of technology, individuals may now get personalized health education information based on their requirements and situations. One such safe online tool is the Patient Electronic Portal, which enables two-way electronic contact between patients and their healthcare providers from a computer or mobile device. According to research, this application has improved patients' adherence to their medications, self-awareness, and treatment of their ailments in addition to their compliance with preventative medical precautions.

1.2.5. Reduction of Expenses:

In clinics and hospitals in the US, medical mistakes cost USD 20 billion annually. A reduction in medical errors leads to immediate savings for patients and professionals. By using technology to reduce inaccurate diagnoses and prescriptions and converting a clinic from paper to a medical EMR, outpatient care costs can be reduced by 3%. According to estimates, each patient will save $5.16 per month as a result. A cloud EMR drastically minimizes the expense of other mistakes and the utilization of paper in clinical settings.

This study is divided into several sections such as introduction, literature review, discussion, and conclusion. In the introductory part, the author talks about cloud computing, computerized fog, and edge computing, and also discussed the major benefits of emerging health technologies. In the literature review section, the author discussed previous work on opportunities and threats affecting the healthcare system from technological trends. In the discussion part, the author talks about the importance of health systems based on traditional healthcare systems, IoT-based health systems, and real-time applications. And finally, the author concludes the whole study according to his observation in the conclusion section.

2. LITERATURE REVIEW

Shakir Khan et al. Studied medical technology's effects on rising healthcare costs. Long-term estimates of health spending, which must address the question of the relevance of previous trends to future periods, make the influence of medical technology on the increase in healthcare expenses a topic of important importance. This study's objective is to assess the potential ranges of technological change's contribution to the increase in healthcare expenses as well as potential future controllable variables. They calculated that, within an essentially plausible range of 38 to 62.00 % of expansion, the introduction and dissemination of new medical technology are responsible for around half of the rise in real per capita health care expenses [15].

Mohsen Vatandsoost and Sanaz Litkouhi studied facilities for healthcare in the future. They examine recent technological and medical developments in the healthcare industry, such as artificial 3D printing, robotic surgery, artificial intelligence (AI), and information technology (IT), and discuss how such developments may impact the Future healthcare facilities' architecture. Future hospitals won't need waiting rooms, thus they will need less space overall. Near the hospital, the majority of care will be provided. Every person may have a computer chip affixed to his body, ready to store and continuously monitor all of his medical information. Robots and artificial intelligence (AI) may eventually handle every task, from reception to detection. Robots will do nearly all surgeries, hence the physical layout of operation departments will require to alter. Future hospitals will need room for scanning and 3D printing since 3D printers can create practically anything, including medical equipment and human body parts [16].

Harold Thimbleby studied about use of technology in future healthcare. From anesthetics but also antibiotics to magnetic resonance imaging scanners and radiation, technological innovations have profoundly altered healthcare. Human factors will continue to be one of the major barriers to advancements in the healthcare sector, even while technologies (new drugs or treatments, new tools, increasing social media support for the healthcare system, etc.) will drive innovation [17].

3. DISCUSSION

Before conducting the full research for the studies, it is important to take note of previous studies that have been published in the literature. Giving a date range to technological ideas has allowed research to be reviewed to clearly show the influence of technological improvements on the health area. To provide a more comprehensive list of studies, the usage of “information or communication technologies” (ICTs) in the healthcare industry was examined at this stage. Cloud computing is the most well-known technology notion in our industry, so start there. The literature review demonstrates the enormous importance of cloud computing in the healthcare industry. In addition, cloud computing is still the preferred infrastructure.

With the development of technology, the Internet of Things became a prominent technology (IoT). The core of IoT is the development of a worldwide network infrastructure using data from physical devices. The objective is to link physical devices via this network. Although the now-used Internet of Things was first confined by RFID technology, it has evolved to varying degrees. These days, GPS, mobile platforms, and all other network-connected gadgets spring to mind when the concept of the Internet of Things (IoT) is addressed. The healthcare sector has not neglected this growth since, as was previously said, technical developments cannot be left indifferent to progress. The significance of big data has grown in recent years. Its importance is mostly due to the previously stated IoT technology. The big data problem in the realm of health is undeniable when taking into account data from patients, physicians, diagnostics, treatments, or hospitals. As a result, studies on the management of big data in the field of health have been published in the literature.

With technology advancements, several concepts are also applied in the healthcare industry. It is not within the scope of this document to discuss wireless body area networks (WBAN), wireless sensor networks (WSN), “machine-to-machine communication” (M2M), 3D printing, robotics, network technologies, social networking, or artificial intelligence difficulties. Some solutions are an alternative to cloud computing as well as a complement, and they fix the shortcomings of cloud computing. This research will examine the ideas of edge computing and fog computing. These concerns are the subject of several studies in the healthcare sector.

The focus of this study has been established as the cloud computing principles, which have gained popularity in this industry due to edge computing or fog computing in the area of health services. Technology trends' effects on healthcare systems have been studied. One of the newest technological advancements, edge computing, fog computing, as well as cloud computing is featured in the study. There are too many different types of health systems to discuss a single technology trend. As a result, health zones are divided into groups based on requirements. The study's findings have led to the following recommendations.

3.1. Conventional Healthcare Systems:

Modern conventional healthcare systems can be supported by cloud computing solutions. Systems for cloud computing are intrinsically less expensive than those for conventional data centers. The systems utilized for health services have extensive data flow. Therefore, this system has a huge bandwidth need. Patient records, or private patient information, are accessible in the healthcare system. The safety concern comes to mind while considering cloud storage for this data. It is claimed that studies on this topic have been published in the literature.

3.2. IoT-Based Health Systems:

One of the newest technological advancements in IoT. IoT research is also done in the area of health care. The logic of the Internet of Things is built in, and it collects data from all edge devices. The volume of data reaches huge proportions due to the data pouring from these gadgets. Edge computing is thought to be useful in these types of health applications. Therefore, data storage and processing requirements are expensive at all edge locations.

3.3. Health Systems Based on Real-Time Applications:

When real-time services are provided, using cloud computing in health systems may not be viewed as especially appropriate since it might cause bandwidth compression or time loss. Applications that run in real-time are crucial systems that require a quick reaction from the user. Fog computing or edge computing may be preferred in such systems depending on more specific requirements. This makes it feasible to transport data without relying on the internet or capacity.

3.4. Modern Healthcare Systems:

The problem raised in this area is to offer the best solution that addresses all health systems. Based on the required infrastructure, the intended solution must include edge, cloud, or fog computing. Cloud computing, edge computing, as well as traditional health apps, may all be used to interface with real-time applications. However, a comprehensive architecture or framework is required to address this demand. The use of cutting-edge technology in healthcare is widespread. For both diagnosis and treatment. The use of medical technology is the application of scientific knowledge to enhance healthcare equipment to make work more comfortable, efficient, and speedy. Technologists and biological engineers now work in contemporary hospitals to Engineers engage in ordinary daily activities, research, and technological advancement.

As a result, the close collaboration of these specialists has had a significant impact on contemporary medical facilities and led to the adoption of cutting-edge technologies throughout the healthcare industry. Biomedical engineers will contribute more to healthcare facilities in the future to make them more efficient and quality-based. The technical developments in diagnostics, surgery, and medication delivery, among other things, have made life more pleasant.

Disease prevention, diagnosis, and treatment have grown heavily reliant on advancements in modern medicine, surgery, and diagnostic and therapeutic tools. It is also true that the length of life has risen as a result of the accessibility of various diseases' treatments. The issues linked with the senior population must be addressed since several new illnesses have emerged and the number of elderly individuals has grown.

In emerging nations, health care is getting increasingly expensive and out of the grasp of the average citizen. Developing nations are uncritically following the healthcare paradigm used in affluent nations without taking socioeconomic factors or lifestyle preferences into account. Developing nations can't currently afford to have high-tech, five-star hospitals or interventions due to their restricted finances for expensive medical equipment. These amenities are only used by the wealthy, and their percentage is quite small. The infrastructure of basic healthcare must be strengthened in developing nations rather than opting for expensive medical centers. By ensuring that everyone has access to clean, contaminated-free water, three square meals per day, and a healthy living environment, they should focus on illness prevention. The most pressing needs in villages and slums of big cities are sanitation, with a focus on toilet facilities and wastewater disposal. It is not advisable to blindly adopt a novel, pricey therapy until or unless it is affordable and beneficial to the majority. Politicians and bureaucrats in charge of delivering healthcare to the populace lack confidence in their healthcare systems and seek treatment abroad in wealthy nations.

Future medical research would require a greater for better healthcare, a rigorous scientific approach and fresh ways of thinking are required. The full impact of technology should be considered rather than just one aspect. Health is influenced by a person's lifestyle, surroundings, cleanliness, diet, access to clean water, etc. Prevention is preferable to treatment. However, the current way of life has made prevention less important, and technology dependence is a bad trend. Modern living has made diseases more prevalent, which has generated significant revenue for the equipment and pharmaceutical industries. Any new medical technology must be able to deliver better health care and a higher quality of life without sacrificing the human touch.

4. CONCLUSION

In this study, emerging technological trends in healthcare applications or systems are looked at, and suggestions are given. Technology development has an impact on every aspect of our existence. But not all technical trends and ideas are useful or fit for all uses. Thus, cloud, edge, as well as fog computing technologies that can be applied in the healthcare system, are investigated, and recommendations are made as a consequence of the investigations. Valuable research has been offered to aid in the creation of new applications and systems in the healthcare industry. It was also acknowledged that a framework was needed to combine all of these technologies. In the big picture, there is little doubt that technology has impacted the healthcare industry. To streamline your operations or workflow and yet provide your patients with the finest care possible, you may now pick from several software packages and systems. Humans hope you found this information informative and beneficial for your career. “United Nations Organisation” (UNO) Clinic Management System is available to help you if you want to take your treatment plans to the next level. This study's major goal is to better understand how new technological trends are affecting the healthcare sector. This paper will inform readers about how new technologies may impact healthcare in the future.

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CHAPTER 7

CARDIOVASCULAR DISEASE PREDICTION USING RANDOM FOREST MACHINE LEARNING TECHNIQUES

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ABSTRACT:

The provision of health care is an essential function of human existence. The term heart disease refers to a broad class of infections that touch the heart as well as nerves. There is still untapped potential in the data set, so to increase accuracy, further hybrid techniques should be used. Create a predictive model to understand the diagnosis of heart disease with the help of a random forest classifier. The performance of clinical models is determined through the Random Forest Machine Learning techniques. This research aims to determine whether they are likely to be diagnosed with any heart disease based on the patient's medical characteristics such as gender, age, chest discomfort, fasting blood sugar levels, etc., and, also discussed the benefits of using random forest ML technique. Assessment of Cardiovascular Diseases (CVD) helped to make decisions about progression in high-probability patients, thereby reducing their risks. Research shows that developed random forest algorithms can predict heart disease in patients.

KEYWORDS:

Cardiovascular Disease, Disease Prediction, Health, Machine Learning, Random Forest.

1. INTRODUCTION

Cardiovascular disease (CVD) is a category of conditions that influence the heart or blood vessels. Coronary blood vessel diseases, such as myocardial infarction, and angina, are involved in cardiovascular disease [1]. Hypertensive heart disease, carditis, stroke, irregular heart rhythms, heart failure, rheumatic heart disease, Aortic aneurysms, cardiomyopathy, valvular heart disease, thromboembolic disease, congenital heart illness, venous thrombosis, peripheral artery disease are some more CVD [2]. The heart's blood arteries and lymphatic vessels are both a part of the cardiovascular system. The major goal is to maintain healthy blood circulation, which facilitates the delivery of nutrients to tissues and metabolic wastes to excretory and urogenital organs.Improved sensor machinery and industrial IoT (Internet of Things) devices combined with the application of Machine Learning (ML) techniques and artificial intelligence are driving a general trend toward digital health care [3], [4], [5]. ML is a set of mathematical algorithms, a subset of the larger field of Artificial Intelligence (AI), that has the potential to offer creative decision-support solutions to many problems in a big data environment, thus offering advancements beyond the rule-based engines that are widely used in many scientific fields [6]. As a result, explainable AI is a popular topic and important in all highly regulated businesses.

While other research teams have begun to define the idea of interpretive AI as related to several issue areas. Market analysts and medical professionals are aware of the cost-effectiveness of this and the new doors it provides for better care within the healthcare system. Recent research from the US's Brookhaven National Laboratory reveals that by utilizing machine learning techniques with patient electronic health information, Alzheimer's disease prevalence can be accurately predicted in the future Electronic Health Records (EHRs) [7]. Several decades ago, expert systems were first used to computerize the identification of Electrocardiogram (ECG) signals of cardiac arrhythmias. However, machine learning and artificial intelligence are still being actively researched in this area today. ML is a collection of scientific procedures, a subsection of the larger area of AI that has the prospective to offer creative decision-support explanations to various issues in the atmosphere of big data, thus contributing advancements outside the principle machines that are widely used in various scientific grounds [4]. As a result, understandable AI is a popular subject and important in totally highly structured businesses [7], [8].

CVDs are the main killers worldwide, accounting for 17.9 million deaths each year. Heart and blood vessel problems known as CVD include conditions such as “cerebrovascular diseases”, coronary heart sickness, rheumatic heart illness, and other illnesses. One of every five CVD deaths is caused by a heart attack or stroke, and more than four out of five CVD deaths occur before the age of 70 [8], [9]. The key behavioral possibility issues for cardiovascular disease and death contain a poor way of eating, laziness, smoking, and drinking. Due to behavioral possibility issues, persons might grow high blood pressure and blood sugar, blood lipid stages, obesity, and overweight. These intermediate risk variables can be assessed in main maintenance situations and show a complex possibility of complications such as stroke, heart failure, and heart attack. The most collective sign of a knock is sudden sickness in the arm, face, or leg, commonly one side body. Other symbols are as follows:

1. Arm, leg numbness, face, usually along one body side.
2. Perplexity, trouble comprehending or speaking.
3. A problem with single or together eyes seeing.
4. Walking difficulties, vertigo, and damage to stability.

Unknown causes of a strong headache, fainting, or unconsciousness are all possibilities. The smallness of breath, tiredness, improper heartbeats, pain in the chest, and dropping are all signs of rheumatic heart disease. Rheumatic fever symptoms include pain in the joints and swelling fever [7] vomiting, nausea, and stomach cramps. If left untreated, rheumatic fever can lead to rheumatic heart disease [8],. This research paper explained the prediction of cardiovascular disease using random forest machine learning methods. The literature from the previous study is discussed in the literature review section, and then the methodology is explained, based on the collection of data, and the results of the methodology are analyzed in the results and discussion section, and finally, the study findings are discussed in the conclusion.

2. LITERATURE REVIEW

According to Silvia Romiti et al. [8] major improvements in analysis and care, Cardiovascular disease (CVD) is still the major reason for mortality and morbidity around the globe. In their study, they carried out further usage of electronic health (E-Health), also known as digital health

essentially the Internet, of new communication and information technology to enhance healthcare. The findings of their study revealed the opportunity and duty to identify specific assisting tools for their clinical practices, clinicians should actively monitor the ongoing advances of AI approaches and use and use them following their demands.

According to Rachael Hagan et al. [7] putting a lot of work into developing algorithms that employ machine learning, a subsection of the larger subject of AI, to identify sickness in only the injured. The use of machine learning techniques in healthcare, particularly more especially, cardiovascular disease, has been the subject of substantial research. That study investigates the uncertainty associated with the classification of cardiovascular disease using Multi-Layer Perception Neural Networks (MLP), collective approaches, and Support Vector Machines (SVM). The author findings that the levels of uncertainty in models created for these two datasets using multilayer perceptron neural systems, support vector machines, and decision trees. Research indicated that expanding the analysis to include datasets from other pathophysiology's instructive.

Carlos Martin-Isla et al. [10] stated the image-based cardiac diagnosis with ML. Machine learning techniques that provide a list of clinical uses of each method are Support Vector Machines (SVMs), Random Forests (RF), Logistic Regression, Cluster Analysis, Artificial Neural Networks (ANNs), and Convolutional Neural Networks (ANNs). CNN). According to the authors, the future of cardiovascular treatment may well cover the path to precision medicine and heart diagnosis. AI in Cardiology has the potential to transform personalized disease monitoring and therapy, taking away existing single dimension that fits all methods obtained after extensive scientific trials.

The above research showed the application of several classifiers and their efficacy in the prediction of CVD, thus laying the groundwork for the identification of the optimal classifier. The present effort, however, was conducted after an assessment of the ability of simple random forests to produce a model for accurate CVD prediction.

Research Questions:

1. How the random forest machine learning used in cardiovascular disease?
2. How is machine learning used in the prediction of CVD?

3. METHODOLOGY

3.1. Research Design:

Analysis and categorization both employ Random Forest methods. The data is organized into a tree, and predictions are based on that tree, even with a substantial number of recorded data lacking, the Random Forest algorithm can still produce the same outcomes when applied to huge datasets. The decision tree's produced samples can be preserved and used for different sets of data. In a random forest, there are two stages: first, generate a random forest, and then, using a classifier produced in the first stage, make a prediction. The goal of the suggested approach is to create a framework that can infer traits of the expected class from just a smattering of numerous other facts. This research determines to improve class prediction models based on chosen attributes. The current research uses the Random Forest online data sets categorization approach to accurately diagnose CVD and deliver the best therapy feasible. The data and patient

information are stored in databases using Advanced Encryption Standard (AES) encryption (Figure 1).

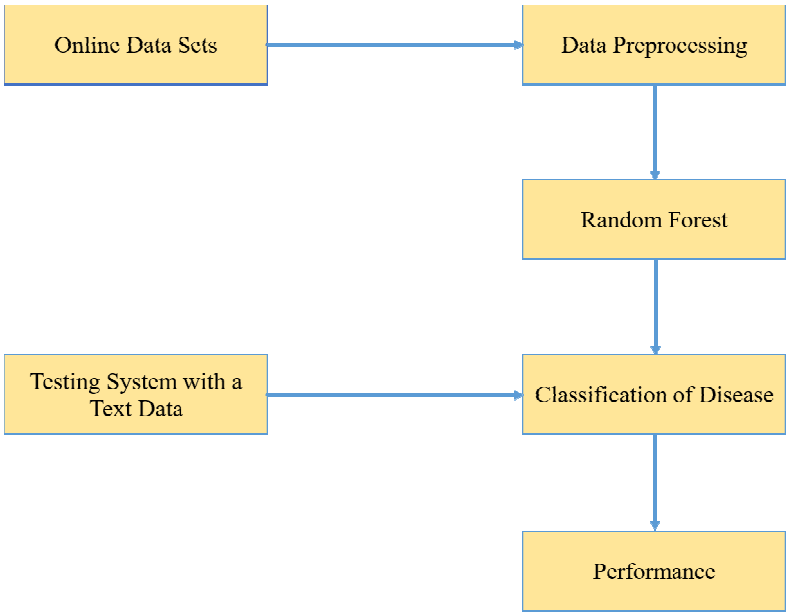

Figure 1: Illustrating the Block Diagram of the Proposed System Architecture for Cardiovascular Disease Prediction.

3.2. Sample and Instruments:

Firstly, picks some samples at random from the dataset provided by the online data sets. Predict each sample by building a Decision Tree for each Decision Tree's output, and cast a vote for each guessed outcome. Then choose as the outcome the prediction that receives the most vote's prediction.

3.2.1. Random Forest

The most effective and well-known machine learning algorithm is called Random Forest (RF). It is a part of managed computer learning. In machine learning, it is applied to classification and regression issues, the random forest method:

a. It assembles the data

b. It creates decision trees using various samples

c. It uses the decision tree average

Although it can handle datasets with categorical variables, it is slower than a single decision tree. Ignores values that are missing. [4], [11]. A supervised learning method called random forest is used for together sorting and regression. Random forest is primarily used for classifying-related concerns. As everyone is aware, a forest is comprised of trees, and a forest with more trees will be more stable. Similar to this, the arbitrary random forest method builds decision trees on samples of data, then gets predictions from each one before voting on the best choice. The outfit technique uses an average of the outcomes to prevent over-fitting, making it superior to a single decision tree.

3.3. Data Collection:

A database for diagnosing coronary artery disease utilizing machine learning random forest method. Health, Health and biomedical sciences, cardiovascular disease, coronary artery disease, and heart disease dataset. Here describe Random Forests and show how to use them to determine whether or not a person has heart disease as shown in Table 1.

Table 1: Illustrating the Dataset Description for Cardiovascular Disease Prediction System.

Chest pain	Good Blood Circulation	Blocked Arteries	Weight	Cardiovascular disease
No	No	No	125	No
Yes	Yes	Yes	180	Yes
Yes	Yes	No	140	No
Yes	No	Yes	170	Yes

After determining Table 1 finds that if the weight is low of the person, then the chances of cardiovascular are very less. People do not need to face all the diseases of the heart. Exercising, eating a diet high in green vegetables and low in fat. Heart disease can be lessened by leading a healthy lifestyle. Although men tend to have greater age-specific rates of CVD than women in most age groups, the real lifetime risk of CVD is comparable for both sexes. Evidence also points to the possibility of CVD rates varying within the same sex as well as between age and racial groups.

The prevalence increased with age, rising from 0.9% among individuals aged 18 to 44 to 5.9% among those in the 45 to 64 age range and 18.2% among those over 65. The average yearly rates of the first cardiovascular events increase from 3 per 1000 males between the ages of 35 and 44 to 74 per 1000 men between the ages of 85 and 94. Women experience comparable rates 10 years later in life. As people become older, the divide gets less. People 75 and older make up about 66% of CVD deaths.

3.4. Data Analysis:

To the fitness parameters that affect a patient's possibility for a disease of heart, data exploration, and predictive analysis are being conducted. To do this, the data will be explained and the health aspects of the dataset will be graphically analyzed. The introduction of the predictive modeling procedure will provide the context for assessing the logistic regression predictive model. Reviewing performance data from the confusion matrix will make up this evaluation. To show how the variables influenced the forecast, the model's calculation for a single case will then be explained [11].

While age and sex do not correlate with the cardio factor as strongly as age and sex, this does not mean that no inferences may be made from these variables. By examining patterns within and across groups of both age and sex, it is possible to further understand how these variables interact with the cardio factor and how a patient's age and sex can statistically affect their total risk for cardiovascular disease [12].

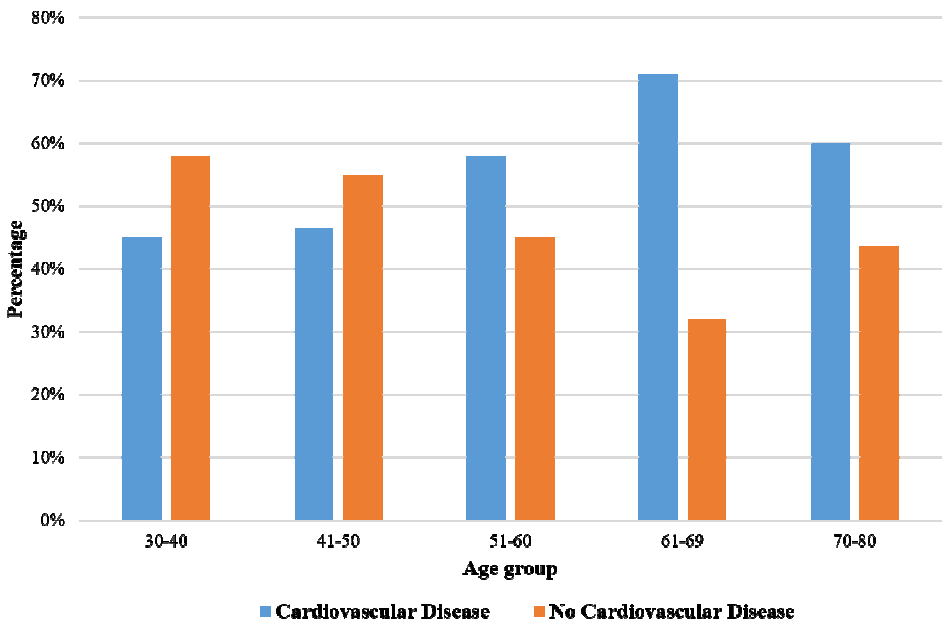

Figure 2: Illustrating the Graph of Cardiovascular Disease by Age Group.

The data, which is grouped by age in Figure 2 above, demonstrates that the prevalence of cardiovascular illness often rises with patient age. The only exception is in the group of those aged 69 to 77, where the prevalence of cardiovascular disease falls from 68.5% in the 62s to 57.7% in the 71s. A higher systolic blood pressure reading is related to a greater possibility of cardiovascular disease in together males and females. Males in the systolic blood pressure grouping are the only exception, decrease in disease prevalence from the grouping 62.5% to 60%. For females, the change in the risk of cardiovascular disease varies between each grouping rather steadily, whereas, for males, the change rises as blood pressure levels rise. For girls and males, respectively, the average change in illness risk between the groups is 11.89% and 11%. The difference in cardiovascular disease rates between males and girls in the dataset. Only 3.2% fewer men than women in the maximum blood pressure range, which is regarded as a measurement for a patient in hypertensive crisis, develop cardiovascular disease. This range is believed to be between, which is a normal measurement.

4. RESULTS AND DISCUSSION

The outcome of this research shows that the Random Forest procedure is the best effective procedure for predicting heart disease, with an accuracy score of 93%. In many cases, the random forest provides far more accurate predictions than straightforward CART/CHAID or regression models. These instances typically have a large sampling size and a large number of predicted factors. The results demonstrate that the CVD risk level is preceded by a diagnostic system that was built correctly. The suggested system to command a huge number of patient data can also leverage cloud computing technology. One of the recent global health challenges is heart disease. Many studies are being done right now to anticipate and identify cardiac problems. The identification and evaluation of machine learning, data mining, and deep learning methodologies used in HD research goals of this work. EHR in health Large-scale data production brought on by technological advancements has also sparked in-depth research into the

accurate diagnosis, prognosis, and treatment of diseases. Applying machine learning methods with the right algorithm has the potential to lower disease rates and mortality rates among the world's population. Achieved an accuracy of 86.5% for the calculation of heart illness using the random forest procedure, with sensitivity values of 91.5% and specificity values of 81.9%. According to the receiver operating characteristics, the accuracy of random forest's heart disease prediction is 94%. As shown in Figure 3 and Figure 4.

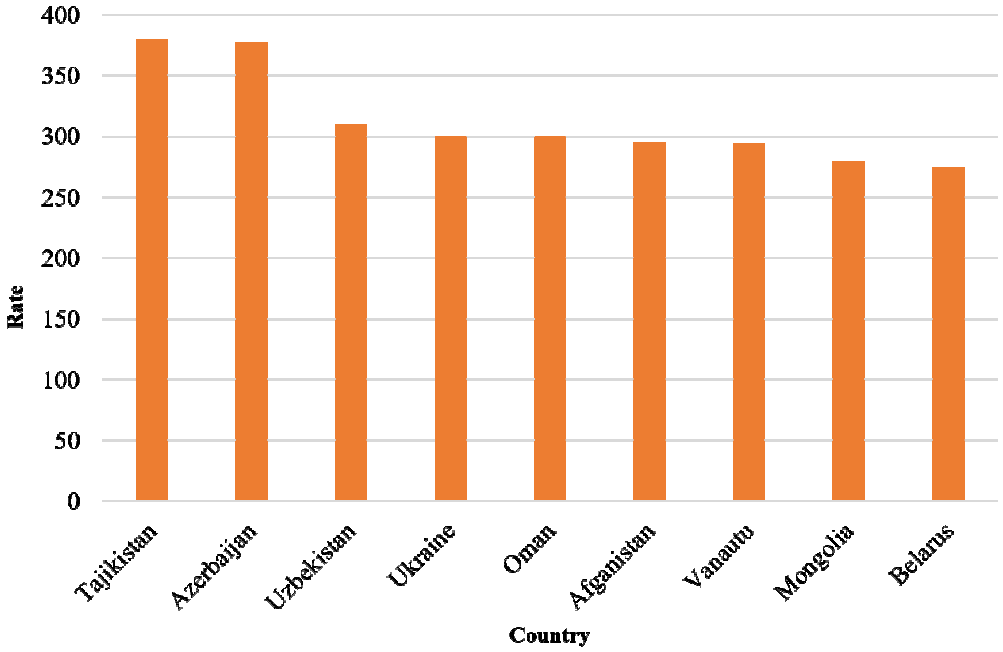

Figure 3: Illustrating the Graph of the Highest Ratings of Cardiovascular Diagnosis.

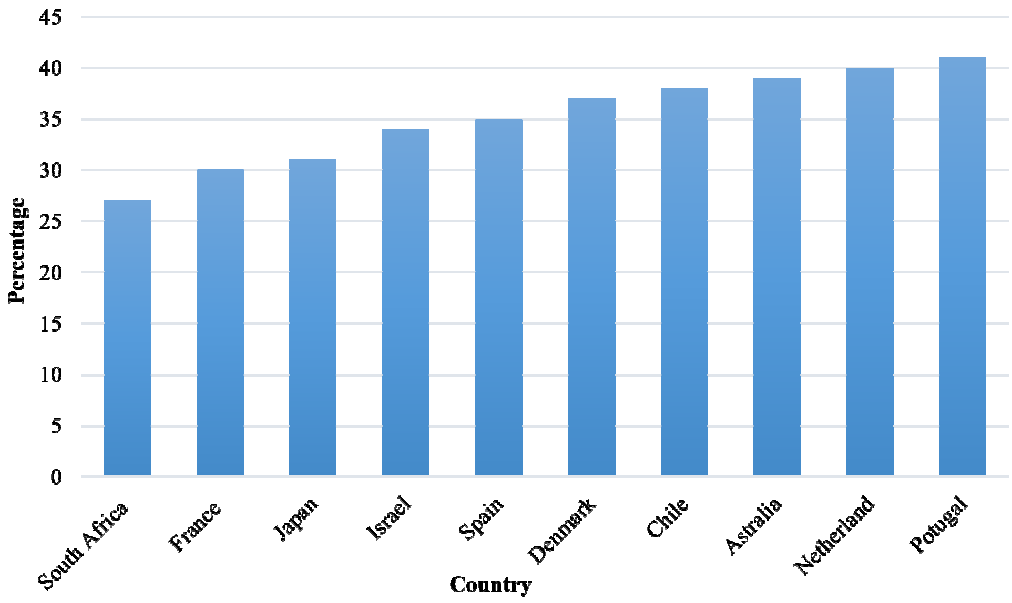

Figure 4: Illustrating the Graph of the Lowest Ratings of Cardiovascular Diagnosis.

4.1. Advantages of Using Random Forest:

One of the best efficient ensemble classification methods is the random forest algorithm. The RF method has been applied to probability estimation and prediction. The benefits of the random forest algorithm are described below:

1. The ensemble learning algorithm known as the random forest is precise.
2. For huge data sets, random forest performs well.
3. It can manage a large number of input variables.
4. Random forest calculates the key classification variables.
5. It can deal with missing data.
6. For class unbalanced data sets, Random Forest includes ways for balancing errors.
7. This method allows for the saving of generated forests for later use.
8. Overfitting is overcome by random forests.
9. RF is less susceptible to outliers in training data.
10. RF allows settings to be simply defined and does away with the requirement for tree pruning.
11. Automatically produced variable importance and accuracy in RF.

5. CONCLUSION

It is essential to create a system that can forecast heart diseases precisely and effectively given the rise in fatalities caused by heart diseases. The implementation of the random forest machine learning technique for heart disease prediction was done in this research paper. By combining the suggested system with additional machine learning algorithms for improved accuracies, such as Naive Bayes, K-NN, decision trees, linear regression, and fuzzy logic, it can also be used to predict the occurrence of other diseases.

In this reference, reducing ML applications' future performances will focus on more than just disease prediction. The outcome of this research shows that the Random Forest algorithm is the most effective algorithm for predicting heart disease, with an average accuracy of 89%. The research can be improved in the future by creating a web application based on the Random Forest method and using a data set than the one utilized in this research, which would help to deliver better results and aid healthcare professionals in accurately and efficiently forecasting cardiac disease.

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CHAPTER 8

A CRITICAL ASSESSMENT OF SCIENTIFIC LITERATURE ON RABIES AND ITS POSSIBLE PREVENTION STRATEGIES

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ABSTRACT:

Rabies can be viewed as a virus as well as a disease, where the disease can be prevented from spreading from rabid animals to warm-blooded organisms including humans. There is rabies in more than 150 countries and territories. Dog bites, which account for 99% of all human deaths, are the main cause. Rabies claims lives in emerging and developing countries. Rabies, a zoonotic viral disease, must be effectively controlled in many developing countries. Most of the current rabies management strategies are focused on giving effective "post-exposure prophylaxis" (PEP) to animal bite victims.

The prohibitive expense of rabies prophylaxis is a significant barrier to its widespread use for all animal bite patients, especially in areas with limited resources. The intradermal method of administration has been demonstrated to be cost-effective except for external sites. The main objective of this study is to learn more about rabies and its possible prevention strategies. In the future, this paper will aware of the people about harmful effects of rabies and its preventive strategies.

KEYWORDS:

Central Nervous System, Lyssavirus, Virus, Vaccine, Zoonotic.

1. INTRODUCTION

Rabies is a zoonotic disease that can be transmitted from animals to humans. Individuals can become contaminated by infected creatures and contract the disease. Canines, raccoons, skunks, bats, and foxes are among the animals most commonly associated with cases of rabies. Hydrophobia and rabies are two such diseases that harm dogs. Although dogs have been immunized against it in many Eastern and Western countries, the problem is still widespread. The rabies virus attacks the neurological system before releasing itself into the saliva. A human or animal can get rabies in several ways, like as:

1. Bites
2. Non-bites exposure
3. Humans to Humans

The transmission while the other two conditions are uncommon, rabid animal bites on humans are fairly prevalent. Rabies affects the spinal cord and the brain (central nervous system), although it first causes flu-like symptoms, fever, or headaches, it can also cause hallucinations, paralysis, and ultimately death [1], [2]. An acute viral encephalitis virus from the genus Lyssavirus in the family Rhabdoviridae is what causes rabies, which nearly usually results in death. The virus spreads to both animals and people when a rabid animal bites, scratches, licks at damaged skin, or contacts mucous membranes. Wild animals and all carnivorous species act as the virus's natural reservoirs [3].

Due to frequent, pervasive contact between humans and animals, the "South East Asia Region "of the "World Health Organization" (WHO) has seen the most exposure internationally. More than 1.4 billion people in this region are at risk of contracting rabies. Therefore, it continues to represent a significant danger to the Region's economic and public health [4]. In India, where rabies is an endemic disease, there are an estimated 17.4 million animal bites each year, or an incidence of 1.7%, posing a serious threat to public health. In India, 20,000 people are thought to die from rabies each year. Therefore, in a nation like India where rabies is common, any animal bite has the potential to be a rabid animal bite.

Since rabies is completely preventable by vaccination, prompt and appropriate post-exposure prophylaxis (PEP), which includes washing affected areas with soap and water, administering the full course of rabies vaccines, as well as locally administering rabies immunoglobulin in all Category III exposures, is almost always successful in preventing rabies, even following high-risk exposure. The disease, which is best described as a neglected zoonotic disease, mostly affects residents in rural regions. Rabies prophylaxis is, therefore, a crucial public health precaution in rural settings [5]–[7].

1.1. Etiology:

The Rhabdoviridae family member Lyssavirus genus is the cause of rabies. It has a single-stranded RNA genome but is shaped like a bullet. UV rays might cause the lyssavirus to spread. When exposed to air, sunshine, and dried blood with secretion, it quickly deactivates.

1.2. Transmission Mode:

The lyssavirus may develop in the cells of cold-blooded organisms, even though it can infect any warm-blooded species. The disease can be spread by bites, cuts, or small wounds to the skin, mucous membranes, or through the saliva of an infected animal. Given that the infected animal dies from a terrible illness, rabies is not a real zoonotic disease [8], [9].

A survey of sick dogs conducted in the USA revealed that all rabid dogs died about 8 days after being ill. Bites are the most common form of communication. Even though the sickness frequency is 50 times lower, the disease can occasionally occur from a scrape contaminated by saliva since the virus is produced in saliva. Although the virus seldom transmits from one person to another, transplant surgery has been associated with a very small percentage of cases [10], [11].

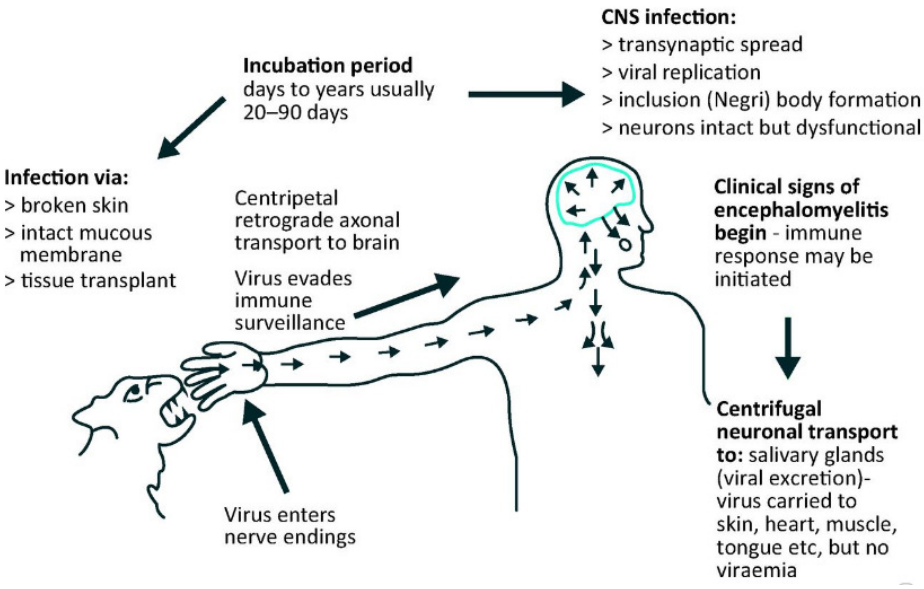

Figure 1: Illustrate the Rabies pathogenesis [12]**.**

Humans with the rabies virus develop deadly encephalomyelitis. It belongs to the Lyssavirus genus species. The other species, which primarily affect bats, are lyssavirus's connected to rabies this might be just as dangerous. Infection with rabies should be completely avoidable. However, a virus injected into a puncture wound could ascend intraneuronal to the brain, resulting in deadly encephalomyelitis, if adequate therapy is not accessible, economical, delayed, or complete, as shown in Figure 1.

1.2.1. Pathogenesis:

The lyssavirus can enter the body through cuts or direct contact with mucous membranes. It won't penetrate healthy skin. Before infecting the central nervous system, the rabies virus replicates inside the muscle tissue that has been bitten. The virions enter carrying vesicles without being absorbed by sensory or sympathetic terminals and move fast retrogradely via motor axons to the "central nervous system" (CNS). In most cases, subsequent metabolic or circulatory abnormalities, along with respiratory concerns, are brought on by a virus that reaches brain regions and culminates in death [13].

1.2.2. Clinical Symptoms:

It has been shown that an animal's behavior changes as the sickness progresses. Any confirmed rabies suspicion should be supported by a confirming lab test report. The main clinical symptoms might include anxiety, restlessness, anorexia or increased hunger, nausea, dilated pupils, diarrhea, a mild temperature, hyperactivity to any stimuli, along with excessive salivation. Usually, the first sign of post-vaccinal rabies is lameness in the leg that got the vaccine. The animals often display behavioral and emotional changes, and they might turn out to be weirdly hostile or extremely loyal [14], [15].

This study by humans takes into account the difficulties of eliminating canine-mediated rabies in nations where the illness is endemic sickness. The relationship between people and dogs, rabies

epidemiology, and the necessity of ongoing surveillance are all thoroughly covered before a brief overview of the difficulties these nations have in putting effective safeguards into place follows. Figure 2 illustrates how the One Health concept and potential methods for eradicating dog-mediated rabies were taken into account.

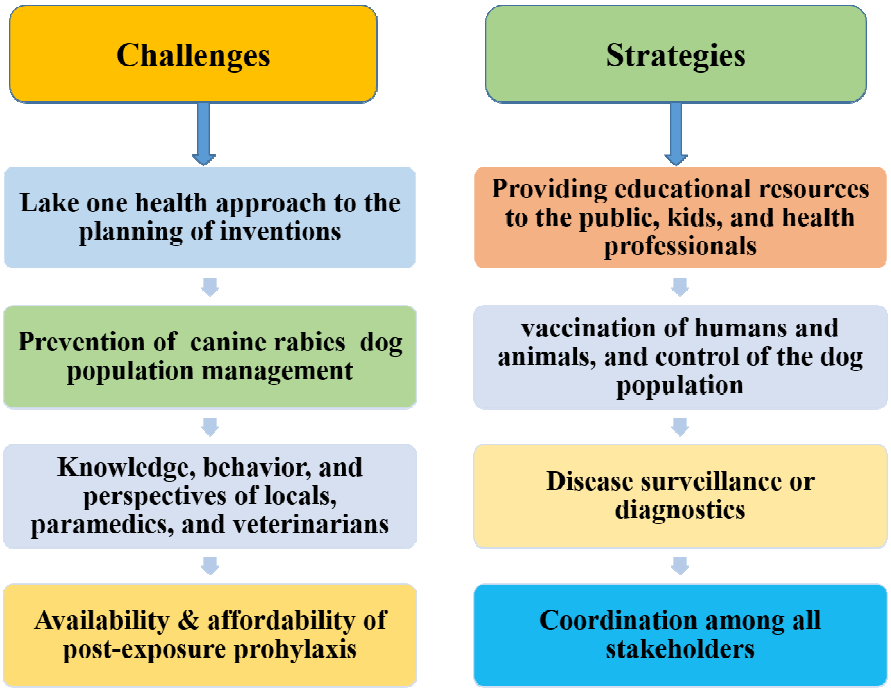

Figure 2:Illustration of the Issues and Plans for Eradicating Canine-Mediated Rabies in Endemic Countries.

This study is divided into different parts such as an introduction, literature review, discussion, and conclusion. In this study, the author talks about rabies disease, the transmission mode of rabies, and also talk the clinical mode of rabies. In the literature review section, the author discussed the previous study. In the discussion, the author talks about the detection of the rabies virus, the Clinical Diagnostics in Humans, and also talks about diagnosis and treatment of rabies and also concludes the study in the conclusion part.

2. LITERATURE REVIEW

Iqra Bano et al. studied Rabies Disease, its transmission, and treatment. Rabid animals reportedly die rapidly after becoming ill, making it a quasi-zoonotic acute disease. Since the virus is produced in the saliva of an infected animal, it can be transmitted to all homeothermic species. However, dogs are considered to be at higher risk, and in the US even bites from bats cause rabies. The incubation period of the disease can last for an average of six months, yet in some cases, it can be less than four days. After the incubation period is over, symptoms appear. Clinical signs or symptoms of this disease may be mistaken for tetanus, polio, or botulism [16].

Harish Kumar Tiwari et al. studied getting rid of dog-mediated rabies. The disease, which kills an estimated 59,000 people worldwide, is mostly transmitted through dog bites. Post-exposure prophylaxis (PEP) can be used to prevent the disease, which has been shown to eliminate it in many countries using several treatments at once. A health strategy to control dog-mediated rabies was considered in this paper. In some urban and rural parts of nations where rabies is prevalent, they promote the use of multiple strategies to combat the disease involving all stakeholders. Empirical evidence of disease freedom in targeted areas using one health strategy is needed to persuade decision-makers to allocate funds for rabies management and treatment at a national level [17].

Arnaud Tarantola et al. studied rabies in both humans and animals. The evolution of concepts over time has contributed to our current understanding of canine and human rabies, as well as its prevention, as passed down through extant and still accessible written texts. Developed, and included the first post-exposure prophylaxis (PEP) regimen and the first live, attenuated vaccine for humans. Sadly, etiological therapy has not advanced, rendering medical experts treating helpless animals or people showing symptoms of rabieslike their ancestors in Mesopotamia 40 centuries ago. The infectious disease that still claims the most lives is rabies. In rural parts of poor countries, there is a dire need for widespread access to PEP that is fast, efficient, and affordable [18].

3. DISCUSSION

The current review study was carried out using a database search on Google Scholar, Science Direct, PubMed, Research Gate, and other websites. In the review approach, terms like Central Nervous System, Lyssavirus, Virus, Vaccine, and Zoonotic were combined. The preliminary assessment of the records utilized title and abstract screening. Insufficient information, redundant research, or non-extractable data were some reasons to exclude the Records. More details about the review study's methodology are provided in Figure 3 below.

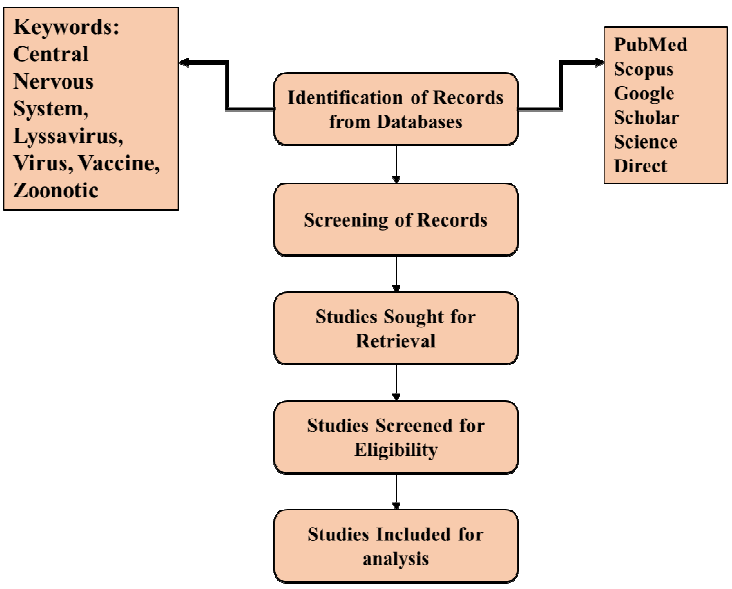

Figure 3: Illustrate the Design of the Methodology which Carry out for this Study.

A bite from an animal with rabies is the main method of transmission for this viral disease. If it is not treated right away, it frequently ends in death. It is an RNA rhabdovirus that can affect the body in two separate ways. It can enter the brain without first entering the peripheral nervous system. It may also grow in muscle tissue, which is immune-suppressed by the host. It then enters the neurological system after passing through the neuromuscular connections. The virus severely inflames the brain after entering the neural system. Rabies comes in two different forms. Eighty percent of human cases of rabies are enraged or encephalitic, and the likelihood is higher in those who exhibit hyperactivity or hydrophobia. Loss of mobility is the most common side effect of the second kind of rabies, often known as immobile or stupid rabies. The likelihood of transmission of rabies is highest in nations with a high stray dog population, with Africa and Asia accounting for 95% of cases.

3.1. The Virus is spread by Saliva:

A trustworthy source claims that if an infected animal assaults a human, rabies may spread. Infected animal saliva may also spread the disease if it penetrates an open wound or travels via a mucous membrane, such as the mouth or eyes. Meanwhile, the virus cannot enter healthy skin. The animal species most prone to spread the illness in the US are raccoons, coyotes, skunks, bats, and foxes. Except for Hawaii, every state in the US has bats that are rabies carriers. Any animal can carry and spread the virus, although smaller mammals, such as rodents, seldom contract the disease or spread it. Additionally, rabbits are unlikely to transfer rabies.

3.2. Detection of the Rabies Virus:

3.2.1. Examination of Animals:

Any portion of the afflicted brain can be used to diagnose rabies in an animal. To fully rule out rabies, the test must, however, utilize tissue from at least two distinct brain areas, preferably the brain stem, and cerebellum. As shown in Table 1, several diagnostic techniques, including direct fluorescent antibody, tissue culture infection method, mouse inoculation technique, and polymerase chain reaction, are available for the detection of rabies in animals. The WHO has given its clearance to each of these methods.

Table 1: Illustrate the Various Diagnosis Methods for Rabies.

Techniques	Specimen	Benefits/ drawback
"Technique for Tissue Culture Infection"	Related to DFA	Use only new tissues
"Direct Fluorescent Antibody Technique"	The best samples to use are from target organs such as the brain, liver, nuchal skin, spleen, salivary glands, and pancreas.	Suitable for the majority of tissue sources. In degraded tissue, not applicable
"Mouse Inoculation Technique" (MIT)	Similar to DFA	Only use fresh tissues
"Polymerase Chain Reaction" (PCR)	Similar to DFA, bodily fluids such as saliva, urine, and CSF are included.	Any tissue condition will work Expensive Want qualified technicians

3.3. Clinical Diagnostics in Humans:

Clinical rabies diagnosis can be made using one of three signs: prodromal, ecstasy (wild), or crippled (stupid). However, none of these phases should appear in a single individual. Neuropathic pain, which is present only at the wound site along with contamination and is caused by viral replication, is the first clinical symptom. Depending on the species, either the disease's excitation or paralytic forms follow the prodromal phase. Sometimes both. The fact that severe rabies affects cats more commonly than dogs is another well-known fact [19], [20]. Despite the absence of any symptoms, the rabies virus has been linked to an unexpected death in a few cases. Only laboratory studies on central nervous system tissue taken from the skull, ideally post-mortem, can provide the diagnosis. Additionally, tests are performed on skin biopsies, serum, or saliva taken from hair follicles around the nape of the neck.

3.4. Prevention and Treatment:

3.4.1. Treatment

If a person is bitten or scratched by a potentially rabid animal, or if the animal licks a large wound, they should seek medical attention immediately. Any nicks and scrapes should be washed in iodized sudsy water or cleaner for 15 minutes. As a result, the number of infectious particles may decrease. This should then prompt clinical consideration at that point. Potential rabies contamination can be addressed with a series of vaccinations after exposure but before negative symptoms appear. Because vets are occasionally unclear, it is advisable to assume that an animal has the sickness and to begin immunizing it. Even while a few people have managed to survive rabies, the majority of cases are deadly once symptoms appear and there is currently no cure. Instead, medical staff typically makes an effort to reduce whatever discomfort a patient may be experiencing. These people may also require breathing help.

3.4.2. Vaccine:

Rabies must be handled seriously and proactively. An injection of rabies-resistant globulin as well as a second injection of rabies vaccine when it is practicable after exposure to a bite or spits from an infected mammal can prevent rabies before ineffective side symptoms appear. Human rabies immune globulin is administered or instilled at the site of the bite as soon as practicable as it fights or prevents infection, slowing, or stopping viral spread through the sensory system. Timing is critical to patient endurance, as is the patient's ability for a forceful, flexible response. Rabies is nearly always deadly if not treated or handled incorrectly, and supportive care just makes the patient's suffering worse. An effective new rabies treatment strategy developed by scientists protects from the illness. The two treatment approaches are preexposure prophylaxis and postexposure prophylaxis.

1. Doctors frequently advise against receiving the rabies vaccine. Instead, they save it for individuals who are most vulnerable to contracting rabies, including those who are more likely to be bitten by animals, veterinarians, or laboratory workers who come into contact with the virus that causes the disease. These folks might be vaccinated according to protocol.
2. Other people could receive the immunization after getting the virus from an animal bite. The medical name for this is post-exposure prophylaxis.

3. Because rabies vaccination contains an inactivated or harmless form of the rabies virus, it cannot transmit the illness. It stimulates the production of antibodies by the immune system that stays in the body and works as a preventative measure against future rabies infections.
4. Rabies vaccination is administered by doctors via injection into the upper arm. Three doses are necessary for preexposure protection. A 28-day supply of rabies vaccination from a trusted provider.

Four doses of the rabies vaccine plus rabies immune globulin are required to provide post-exposure protection in patients who have already been exposed to rabies (RIG). To stop the virus from infecting the patient, medical professionals inject RIG as soon as they can, close to the bite wound. Depending on the timing and frequency of vaccinations, the WHO Trusted Source" lists several approaches to doing this.

3.4.3. After-exposure safety:

To reduce the risk of infection following an animal bite, the wound or any scrapes must be thoroughly cleaned with soap or water. As part of the post-exposure prophylaxis, five doses of the rabies vaccine as well as one dose of rabies immune globulin were given over 28 days. Blood donors with rabies vaccinations provide the antibodies for rabies immune globulin. The rabies vaccine functions by encouraging the body to produce antibodies that can block the rabies virus.

3.4.4. Pre-Exposure Drugs:

For those who fall within the high-risk category, pre-exposure prophylaxis is required. These people consist of veterinarians, animal handlers, and lab technicians. They also include international visitors who could encounter animals in rabies-endemic areas while traveling. All of these populations should have rabies vaccines to lower the chance of an unexpected disease.

3.4.5. Common Rabies Issues and Concerns:

There are a few issues that need to be fixed to stop the spread of this fatal sickness. The majority of countries, especially those in Asia, do not consider rabies to be a priority disease. Second, the surveillance techniques used in less developed countries are inadequate. In most developing countries, modern rabies vaccines and immunoglobulin are not available. The overall lack of awareness in high-risk countries is the biggest issue. If these problems can be properly handled, rabies can be prevented.

3.5. Recommendations:

The deadly viral zoonotic illness rabies is a serious public health issue. By implementing preventative measures, the vast majority of European nations completely avoided this epidemic. To educate the public about responsible pet ownership and routine veterinary care, workshops on public health education should be organized. Most cases of rabies exposure in animals or people can be avoided by increasing awareness of the disease's transmission routes, restricting contact with animals, or following a doctor's advice for treatment. The most crucial step in preventing human rabies is to stop people from coming into contact with rabid animals. They may also prevent human rabies by administering a human rabies immune globulin and vaccination to those who have been exposed to rabid animals. Local governments should launch and maintain

efficient programs to ensure that all cats, dogs, or ferrets are immunized and to get rid of stray and unwanted animals.

4. CONCLUSION

Both wild and domestic animals have the potential to transmit the viral illness rabies. Although the majority of nations on earth now have the designation of rabies-free zones, several still have the category of high-risk areas. This demonstrates that by implementing preventative methods, rabies may very well be successfully eradicated from high-risk locations. Modern medical advancements have made it possible to control rabies as well. Public awareness can make a big difference in this way. Several measures must be taken or lifestyle adjustments must be undertaken to prevent certain viral illnesses. The major goal of this study was to find out more about rabies and potential preventative measures. This paper will educate readers on the negative effects of rabies and its prevention measures in the future.

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CHAPTER 9

AN EXAMINATION OF THE MOLECULAR MECHANISM FOR HONEY'S ANTIOXIDANT PROPERTIES

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ABSTRACT:

Honey has been treasured as one of nature's finest gifts to mankind for thousands of years. Honey is used to treat a wide range of medical conditions, from cancer to wound care, in addition to being a nutritious food. Honey is a natural food that has been demonstrated to have positive benefits in lab and animal experiments due to the presence of some nutrients (such as vitamins, bioactive components like phenolic compounds, amino acids, proteins, enzymes, and minerals). Honey, a sweet and flavorful nectar, has several helpful compounds. Honey's medicinal potential in boosting health qualities and strengthening biological systems has been the subject of much investigation. The purpose of this study is to highlight honey's capability and the many therapeutic benefits it offers. Honey not only protects the neurological system, but also the digestive system, the lungs (especially against asthma and bacterial infections), and the lungs. Low-density lipoprotein oxidation in the blood is substantially stopped by honey. It has also been shown that honey has a positive influence on performance in athletes. In the study,the author also focuses on both completed studies and open research questions. The study suggests honey as a potential natural therapeutic antioxidant that merits additional experimental and clinical investigation, either on its own or as an adjuvant to other treatments.

KEYWORDS:

Apis Mellifera, Antioxidant, Antifungal, Honey, Nectar Flower.

1. INTRODUCTION

Honey is a chemical found in nature, made by bees from the nectar they collect from flowers (*ApisMellifera*; Family: *Apidae*) [1]. Humans have utilized honey for medicinal purposes dating back over 5500 years [2]. Most ancient peoples, including Honey, were utilized as a nutritional and therapeutic staple by ancient civilizations as diverse as the Greeks, Chinese, Egyptians, Romans, Babylonians, and Mayans. Plants generate nectar, a sugary liquid, in glands in the body nectaries or nectarines, either inside the flowers to entice pollinating insects or outside the flowers to offer a food supply for animal mutualists who defend the plant against herbivores. Animals including mosquitoes, dragonflies, wasps, honeybees, butterflies, moths, hummingbirds, honeyeaters, and bats are frequent pollinators that feed on nectar. It is believed that differences in nectar foraging behavior are largely responsible for the divergent evolution of the African honey bee, A. M. scutellate, and the western honey bee [3]. Figure 1 shows the Nectar Flower.

Figure 1: Displays the Nectar Flower.

Since honey can't be made without nectar, it has significant economic value. Because numerous predatory insects' adult stages consume nectar, it is also valuable in horticulture and agriculture. Nectar is the major food supply for several species of "parasitoid wasps", such as the "social wasp *Apoica flavissima"*. These wasps then feed their offspring on agricultural problem insects [4].

Honey is the only natural substance that comes from insects, and it has many uses in food, cosmetics, medicine, and industry. Reviewers agree that honey is a healthy addition to anyone's diet, regardless of gender or age. Honey doesn't need to be refrigerated since it doesn't go bad and may be kept unused at ambient temperature as long as it's dry. Honey's WA ranges from 0.56 to 0.62, and its pH is about 3.9 [5]. Many natural product brochures, general interest periodicals, and scholarly journals now include information about honey's use in treating human illness. Many studies have shown that honey has positive impacts on health, including those related to the immune system, inflammation, digestion, the lungs, the heart, and the brain [6].

Honey is an all-natural remedy that has been used for centuries. Approximately 200 different chemicals have been linked to it. Fructose, glucose, fructooligosaccharides, and a plethora of enzymes, amino acids, vitamins, and minerals are the primary building blocks of honey [7]. Honey's flavor and texture change depending on the flowers the bees visit. Some of the antioxidants that may be found in natural honey are vitamins C and E, tocopherols, catalase, superoxide dismutase, reduced glutathione, Millard reaction products, and peptides. Apigenin, pinocembrin, kaempferol, quercetin, galangin, chrysin, and hesperetin are all flavonoids, a subclass of polyphenols. The antioxidant impact of most of these substances is enhanced when administered in combination.

Raw honey varies somewhat in its chemical makeup depending on where you live. Because bees collect nectar from various flowers, the honey's overall variety depends heavily on its floral origin. Honey's positive effects come from the synergistic action of many of its beneficial

components, including ascorbic acid, antibiotic-rich inhibine, tocopherols, phytochemicals, flavonoids, catalase, phenolic acids, and peptides [8]. Much research has been conducted to obtain some scientific insights and provides evidence-based data on honey's usage as a "complementary and alternative medicine (CAM)" and apitherapeutic agent due to its widespread acceptance and effective use. Consolidating some of these separate data sets is necessary for further study of honey's nutraceutical properties and its use in modern health care [9].

Honey's method of action is complex and a still-developing field of study. Honey's potential function in illness regulation is discussed, as are the underlying processes. It also includes a summary of research that demonstrates how the various signaling pathways lead to their respective molecular targets. The study also highlights the theoretical underpinnings of honey's curative properties and research gaps and the also author looked at the historical and contemporary treatment of human sickness with natural honey.

2. LITERATURE REVIEW

Jing Sun et al. examined all three rapeseed bloom metabolites (stomach honey, mature honey, and mature honey) in the same season. MH has a more diverse physiological pattern than IMH, andDecenedioic acid is one of three metabolites produced by MH. Decenedioic acid was identified in GC-MS analyses of rapes, acacia, and jujube honey, all of which were produced by bees; this finding raises hope that it could serve as a biomarker for separating IMH from MH ($P < 0.01$). In addition, MH exhibited higher FAs than IMH ($P < 0.05$). From IMH to MH, this study demonstrates the FA process [10].

One research by Ahmad Ahmad et al. purpose of their research is to assess how often CAM is used by people with acne vulgaris and to identify any characteristics that may lead people to choose CAM over conventional treatments. "King Abdulaziz University Hospital (KAUH) in Jeddah", Saudi Arabia, participated in an acne education push and gathered data for cross-sectional research. In 2016, the study was conducted from the 21st to the 28th. In all, 658 people were surveyed; of them, 68% were female and 32% were male; 72.2% had a prior occurrence of acne. The face showed the highest signs of damage (90.7%).Women of middle age with higher educational levels did not use CAM at a lower rate. Community ideas and limits may have influenced their decisions [11].

In their analysis, Elijah Brown et al. five samples of honey were gathered from the Apis mellifera, the stingless Frieseomelitta nigra, and the Melipona likes bees. The physical properties and antimicrobial potency of several honey varieties were examined (fresh and aged honey). The apiaries from throughout Trinidad and Tobago provided the honey samples. Honey was also replaced with a sugar-based substitute for testing purposes. In terms of physical properties, we looked at things like color, acidity, moisture, sugar, and density. Agar diffusion assays were conducted to measure antimicrobial activity, and also the results were compared to a phenol equivalency. Honey samples had pH values between 2.88 "(from M. favosa of Tobago)" to 3.91 (from everywhere else),"(fresh A. mellifera)". A had the highest concentration of sugar. mellifera honey varieties (81.6 and 80.5°Bx), with a spread of 66.0% to 81.6%. Leaving old A at 16.9%, we have a wide range. The 32.4% concentration of Fructus mellifera honey in F. Species: nigra (from Tobago. The author determined that Tobago Stingless bee kinds of honey had the most antibacterial activity. Tobago's M. favosa honey has therapeutic effects [12].

Vicki J. Conrad et al. evaluated in their study to investigate honey bee (Apis mellifera) venom biotherapy for OA knee pain and functionality. In this double-blind research, The study randomized 538 individuals with radiographic Kellgren/Lawrence grades 1-3 knee OA and WOMAC pain level 2 to receive either a placebo ("histamine") or HBV. The pain and physical function subscales, as well as the "Visual Analog Scale (VAS)", "Patient Global Assessment (PGA)", and "Physician Global Assessment (PhGA)" were used for assessment. Regular safety parameters and the usage of rescue medicine (acetaminophen) were tracked. Seventy-seven to seventy-eight percent of patients in both groups required rescue acetaminophen. Injection site responses were more common in the HBV group (5%), but otherwise, there were no notable differences in the safety profiles of the two regimens. This large-scale, randomized study of HBV biotherapy for knee OA showed substantial reductions in pain and increases in function [13].

3. DISCUSSION

Raw honey has been a popular food item for human consumption for a long time. Pure, genuine honey has been used since antiquity, according to several sources, making it the oldest sweetener known to humankind [8]. Honey is a CAM for most illnesses because of the many bioactive chemicals it contains interacting in novel and synergistic methods to contribute to synergistic multiple ingredients factors (SMIF) [14]. Historically, NH has been used medicinally and therapeutically to treat infections, alleviate symptoms of illness, assist patients, and even aid healthy people. Honey is a naturally sweet substance that bees produce by fermenting the nectar of flowers. Honey is made when nectar or honeydew is brought back to the hive, where it is concentrated and the sugars are converted into honey by enzymes. The honey's composition is strongly influenced by the plants from which it came, in addition to its processing and ambient circumstances [15].

Honey has been utilized medicinally for a variety of conditions throughout ancient times, including but not limited to wound healing, tissue formation, and also the relief of gastrointestinal problems, gingivitis, or other similar conditions. Honey's healing properties come from the phenolic chemicals (like flavonoids and phenolic acid) that are present in honey [16]. Figure 2 shows that Consuming honey has several positive health effects.

Figure 2: Displays that Consuming honey has several positive health effects.

Multiple in vitro and in vivo studies have shown that honey possesses antibacterial, antiviral, antifungal, anticancer, and anti-diabetic effects. Furthermore, it has been shown that it safeguards the cardiac, neurological, respiratory, and gastrointestinal systems [17]. Figure 2 shows that honey has a protective impact on the bodies of athletes who engage in a variety of high-intensity physical activities. Honey's phytochemical components have a greater or lesser impact on human health depending on how well they are absorbed by the body, as well as the methodologies by which these substances are absorbed and metabolized.

3.2.Honey's Medicinal Properties and Mechanisms of Action:

3.2.1. Effect of Antioxidants:

Honey's natural antioxidants help keep food fresh and protect human health by neutralizing the free radicals that may otherwise cause problems like cardiovascular disease, leukemia, immune response deterioration, cataracts, inflammation, etc. Antioxidants are substances was using to combat damage brought on by oxidants like oxygen, hydrogen peroxide, superoxide, and lipid peroxyl radicals. Oxidative stress may cause various chronic and degenerative diseases including cancer, aging, atherosclerosis, and also the production of mutagens.

Honey is a naturally occurring food group that, thanks to the existence of bioactive substances, not only has nutritional value but also has medicinal effects. Honey's biologically active components fall into two broad categories: antibacterial and antioxidant. Furthermore, these two factors interact with one another, leading to honey's potent health benefits. Honey is antibacterial and bactericidal against a variety of human infections, particularly those such as Escherichia coli, Pseudomonas spp., and Staphylococcus aureus gram-positive bacteria [18].

Honey derived from a diverse range of floral sources and geographical locations has been shown to have exceptionally high levels of antioxidant activity. Honey has been demonstrated to have antioxidant properties due to the presence of phenolic acids and flavonoids. Sugars, proteins, amino acids, carotenoids, organic acids, Maillard reaction products, and reactive oxygen species (ROS) are examples of chemicals, and others, all play a part in the antioxidant effect. Additionally, honey's high concentration of free radical scavengers may help restore a healthy balance between free radical generation and antioxidant defenses.

Oxygen free radicals are produced as a result of normal biological metabolism, but they are harmful because they destroy cells and disrupt DNA. These are the mechanisms that lead to aging before their time. Antioxidants attach to free radicals, neutralizing them before they can do damage. Honey is a natural substance that does not have the potential for undesirable side effects like those of synthetic chemicals. Honey contains several substances with antioxidant characteristics, including glucose oxygenase enzymes, vitamin C, phenol compounds, catalase, and peroxides. Honey contains carotenoids and flavonoids as well. Antioxidants in honey may be reliably measured by their concentrations of these markers. In times of intense mental, physical, or emotional stress, the antidepressant qualities of honey's antioxidants may help [19].

3.2.2. Beneficial Effects of Honey on Wounds and Bacteria:

It's no exaggeration to say that antimicrobial drugs are crucial to lessening the worldwide impact of infectious illnesses. However, antibiotics lose some of their efficacy when resistant organisms proliferate. Since bacterial resistance to all types of antibiotics, including the most important treatments of last resort, is widespread, and is increasing globally, it poses a serious threat to

public health. As a result, there is a pressing want for new antimicrobial approaches, which has prompted a look back at some old cures, like honey, with fresh eyes [20]. The honey's antibacterial properties come from the presence of inactive antibiotic components. In particular, its low pH, the osmotic action of carbohydrates, and the formation of hydrogen peroxide by peroxidase all play a role. Nonperoxidase chemicals such as flavonoids, phenolic acids, and lysozyme are also helpful in promoting antibacterial activity.

Bee-produced hydrogen peroxide and floral pollen-derived catalase, are the primary antibacterial agents in honey. When honey is diluted, it produces H2O2, which is said to have an antimicrobial property.

This process is associated with the release of hydrogen peroxide and gluconic acid from glucose oxidation by the enzyme oxidase. The peroxide activity of honey may be quickly neutralized by heat or catalase under certain conditions. containing bactericidal components, which strongly destroy bacterial cells, and limiting the bacterial quorum sensing (QS) system, which further reduces the interpretation of the las, MVFR, and rhl regulons and their related virulence genes, are the two ways that honey can combat bacterial infections, according to a recent study.

Clotting cascade, inflammation, proliferation and differentiation, tissue formation, and restoration of injured tissue are all part of the normal wound healing process. Numerous kinds of wounds, including chronic ones, burns, necrotic ones, diabetic foot wounds, and postoperative divided skin wounds, have responded well to honey therapy.

3.2.3. Effects of Antifungal Activity:

The rise in antifungal medication tolerance has caught the attention of scientists. Candida albicans (C. Albicans) is a dimorphic organism that exists as a companion in the oral and vaginal mucosa and also the gastrointestinal tract of humans. Central venous catheter infections and fungemia have been linked to Rhodotorula sp. in addition to Candida albicans. In most cases, infections and lesions result from viral activity provoked by either native or universal stimuli. According to recent studies, honey may have antiviral effects.

Honey's antiviral properties may be traced back to the presence of several active components that are effective in the management of lesions. In the same way, as vitamin C inhibits viral translation and transcription, honey's H2O2, ascorbic acid, and flavonoids, also help to limit viral growth.

Honey impedes fungal development by preventing biofilm formation, disrupting existing biofilms, and inducing structural changes in exopolysaccharides. This compromises the biofilm's cells by causing their membranes to deform and shrink, which may cause apoptosis or growth inhibition. Scientists have discovered that the flavonoid component of honey slows the development of fungi, alters their outer shape and disrupts membrane function, and inhibits cell activities necessary for germ tube development.

Poor membrane growth is linked to the suppression of germ-tube development. The ratio of cells in the G2/M phase to those in the G0/G1 phase has been shown to decrease in honey flavonoid extraction, which has been reported to influence hyphal transition. Possible methods for honey's antifungal actions are shown in Figure 3.

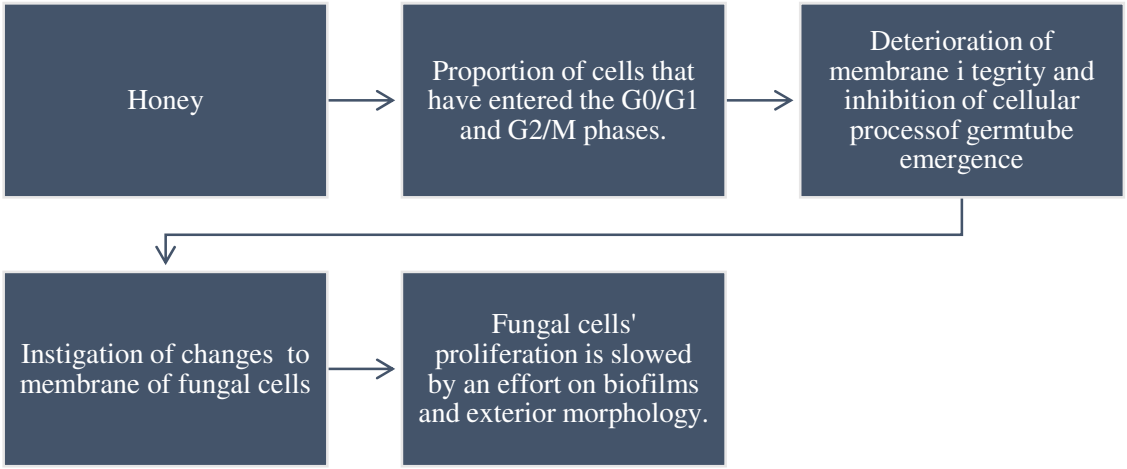

Figure 3: Displays Honey's antifungal properties and their underlying mechanisms.

The agar disc diffusion technique was used to determine whether or not honey has antifungal activity against the test bacteria. The test microorganisms were cultured by spreading about 100 L of their suspension onto plates of Sabouraud dextrose agar. The culture dilution was 1 x 107 CFU/mL. The screening was performed by placing sterile filter paper discs (5 mm in diameter) on top of infected medium agar plates and then impregnating them with 10 L of honey, which is equal to 0.1 mg of honey. The plates were chilled to 4 degrees Celsius for two hours, then 24 hours were spent incubating at 37 degrees Celsius. The discs showed evidence of antibacterial action in the form of clear inhibitory zones. Disk diameters and inhibitory zone diameters were both measured in millimeters. Controls had the same amount of water poured into them. Honey has powerful antibacterial qualities that have been related to an improved gut microbial balance, and this is assumed to be due to the high concentration of oligosaccharides in honey, which act as a substrate for the development of prebiotic germs. Research has shown that some varieties of honey may stimulate the growth and survival of beneficial bacteria like lactobacilli and bifidobacteria, two important microorganisms for maintaining the balance of the gut microbiota.

3.2.4. Other health advantages:

Diagnosis of a wide range of other health issues, including aches and pains all over the body, difficulty breathing, menstrual cramping, tiredness, vertigo, postnatal illnesses, male impotence, and breathing difficulties like coughs, bronchitis, pharyngitis, sore throats, and urinary tract infections (URTI), have also been linked to apitherapy. The antibacterial and anti-inflammatory qualities of honey, together with its high amount of energy, may explain these benefits. The benefits of Malaysian tualang honey on menopausal rats were documented by Zaid et al. [21] in reproductive research. Based on their findings that honey inhibited uterine shrinkage, the authors propose using honey in replacement of hormone replacement therapy (HRT). Natural honey has long been known for its therapeutic effects on gastrointestinal disorders. Recent studies show that honey is effective in treating a variety of GI issues, including ulcers, diarrhea, gastritis, and

gastroenteritis, lending credence to this age-old remedy. Osato et al. [22] revealed that the natural product's efficacy as a gastro-protective drug includes its ability to suppress Helicobacter pylori, the bacterium responsible for gastritis and peptic ulcers.

3.3.Honey's potentially harmful side effects:

Since honey has few negative side effects, it is a popular food choice. Honey may provide a temporary stinging sensation if applied topically. In other contexts, it is said to be calming, pain-relieving, non-irritating, and painless during a dressing change. Even though honey allergies are uncommon, anybody who is sensitive to pollen or bee proteins may also be allergic to honey. Honey's ability to heal may be diminished if applied in large enough quantities, although saline packs may replenish the fluids lost if honey is used excessively. When treating a major open wound in a diabetic, there is always the possibility that their blood glucose levels would increase. To reduce the possibility of botulism in wounds caused by Clostridium spores, gamma irradiation may be used without compromising the wound's natural antibacterial properties.

4. CONCLUSION

In comparison to manufactured pharmaceuticals, natural compounds may be more effective treatments, hence scientists are now focusing on them. Honey, one of the most valuable natural resources, has been used for therapeutic purposes for a long time. Honey has played a significant part in traditional medicine, and now it is widely recognized by both scientists and doctors as a potentially useful treatment for a wide range of illnesses. Honey's antibacterial properties are perhaps the best recognized of its many uses. An antimicrobial impact against yeast, fungus, leishmania, and maybe even viruses has been attributed to honey. Honey's exceptional effectiveness and its widespread use in apitherapy make it an alternative treatment for a variety of diseases and conditions, including cancer. Honey's therapeutic benefits come from the unique and honey ingredients work together to produce beneficial effects on the body on multiple levels (biological, physical, and chemical). For this reason, honey's distinctive "synergistic many components factor" may be explained by molecular insights into its overall protective properties.

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CHAPTER 10

EXPLORING THE POTENTIAL OF NANOTECHNOLOGY-DRIVEN WOUND HEALING AND INFECTION CONTROL

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ABSTRACT:

Wounds are extremely difficult to treat because of their great vulnerability to microbial infection. Furthermore, rapid and acceptable wound healing with minimal undesirable scars should be addressed. Nanotechnology is an emerging and major field with a wide variety of biological applications that give enhanced treatment for many types of wounds. While antibiotic-resistant pathogens are one of the most significant public health issues today, nanotechnology can provide novel treatment techniques in the post-antibiotic era. Nanoparticles can both eliminate bacteria and induce skin regeneration. In contrast to conventional topical treatments, the special attributes of Ag-NPs indicate that they can both successfully inhibit wound infections and promote the process of healing of injured tissues. The present paper aims at investigating the nanotechnology-driven wound healing solutions which can revolutionize the science of wound healing in the future. However, as nanotechnology is a relatively new science, the exploration to a greater degree of extent is not done yet. In addition to that, to take complete advantage of nanotechnology, there is also a need to have a deeper understanding of wound biology.

KEYWORDS:

Nanoparticles, Nanotechnology, Silver nanoparticles, Wounds, Wound Healing.

1. INTRODUCTION

By definition, a wound is a breakdown in the ability of the skin to protect its occupant; it involves the loss of epithelial tissue integrity, whether or whether underneath animal tissue also dies. The vital role of skin in maintaining fluid balance, preventing contamination, and regulating thermogenesis extends from childhood to old life. It can be devastating for the patient and society if this regenerating protective layer is disturbed. Many millions of unusual injury healing effects consume cases and 7 million chronic skin ulcers annually in the US that are brought on by pressure, blood vessel or venous insufficiency, and diabetes mellitus. This translates to annual costs of $9 billion to reduce the substantial failure and subsequent death of such serious skin injuries [1], [2].

There are many numerous explanations for why wounds develop; some are brought on by surgical treatment, others through trauma, yet others by external forces like stress or shearing, or by preexisting chronic diseases such as diabetes or vascular diseases [3], [4]. They are frequently

divided into acute wounds, including burns, surgical wounds, and chronic wounds, such as pressure ulcers, diabetic foot ulcers (DFUs), and leg ulcers, as a result of their underlying reasons. Whatever the origin, wounds have a significant but sometimes underestimated influence on the population who experience them, their caregivers, and the healthcare system. The prevalence of cases (in Millions) by wound types is illustrated in Figure 1 below whereas Figure 2 illustrates how the health resources are allocated to wound management.

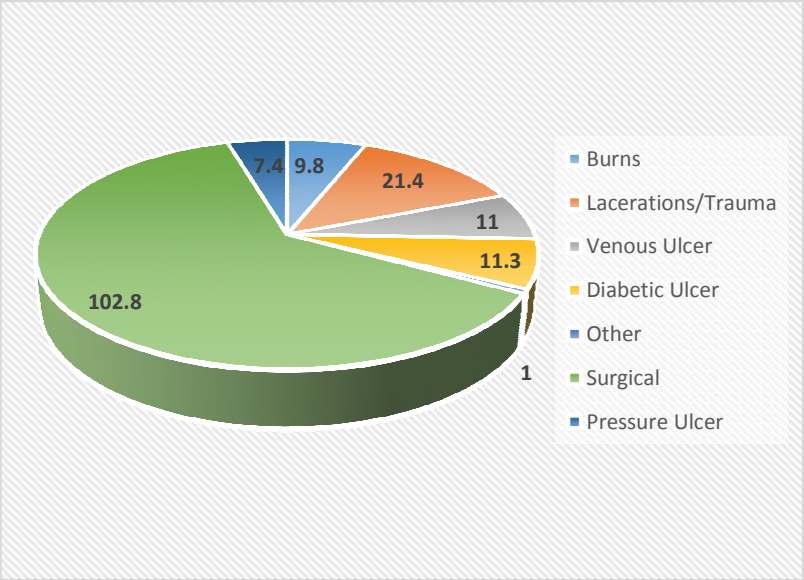

Figure 1: A Graphical Representation of Wound Incidence in Millions.

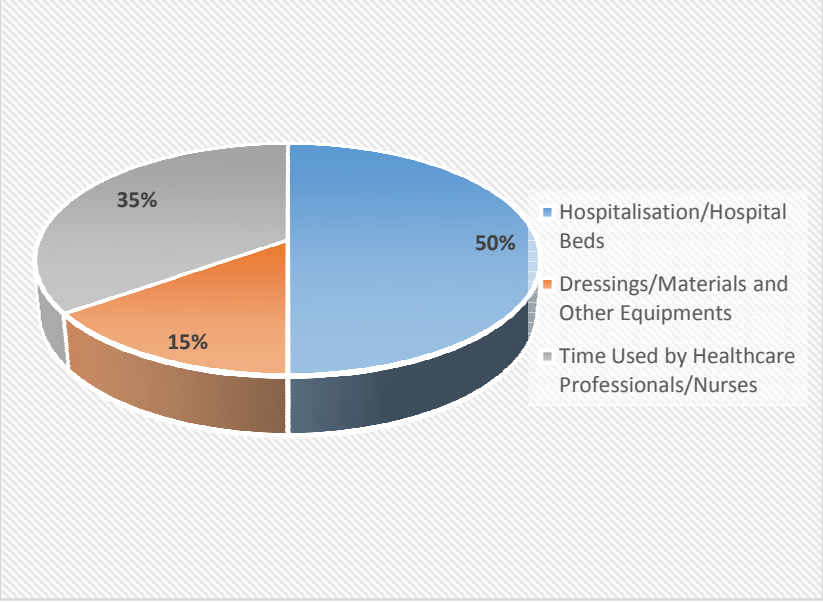

Figure 2: A Graphical Representation of Resources Used for Treating Wounds.

Silver compounds and ions have been employed for both hygienic and therapeutic purposes for ages due to their potent antimicrobial and bactericidal properties [5]. Several treatments containing silver are also used to heal chronic wounds by utilizing their antibacterial characteristics. Silver nitrate was used as a pigment in the 17th and 18th centuries. It was first introduced for the healing of wounds in 1960 and was already being used for ulcer treatment. Owing to an increase in drug-resistant bacteria and advancements in polymer technology, there has also been a resurgence in interest in silver in recent years, following a decline in the usage of silver salts as a result of the introduction of antibiotics in 1940.

Many Ag-containing dressings from multiple manufacturers became available in the marketplace around the end of the 1990s. Silver-based dressings are currently available in a wide range of fibers or polymeric scaffoldings that have been saturated or covered with an Ag salt or metallic Ag. They are all rapid-acting and have a broad spectrum of anti-bacterial action against Gram-positive and Gram-negative bacteria. The mode of action of silver has recently been studied: it appears that silver has a multilayer antibacterial impact on the extent to the blocking of respiratory enzymes pathways, as well as changes in microbial DNA and cell walls. Silver is efficient in fighting multidrug-resistant pathogens while being non-toxic [6]–[8].

The term "nanoparticle" (NP) refers to a particle with one or more dimensions of 100 nm or less. Silver nanoparticles (Ag NPs) have been demonstrated to exhibit peculiar physical, chemical, and even biological characteristics. Numerous reports have been conducted recently proving the usefulness of Ag NP-containing dressings, and these studies have shown that these dressings have a quick significant antibacterial activity against both Gram-positive and -negative bacteria. Since antiquity, the antibacterial properties of Ag salts have been recognized, and Ag is today utilized to inhibit bacterial development in a variety of applications, including dental procedures, catheters, and consume wounds [9]–[11]. Indeed, it is widely known that Ag particles and Ag-based combinations are extremely toxic to bacteria, with strong biocidal effects on up to 12 different species of pathogens, including E. coli. The number of in vivo investigations has, however, been rather small up to this point.

Therefore, the present study aims at studying the effectiveness of Silver-nanoparticles for wound healing. This publication is categorized into five sections, including one which offers a basic value and the relevance of conducting the review study, the second which explains the methodology, and the third which gives a focused review of related literature on the beneficial effects of silver nanoparticles in wound healing and care. The fourth part discusses the challenges and potential associated with the use of silver nanoparticles. In addition, the final section, the fifth section includes a concluding remark.

2. METHODOLOGY

To find the pertinent records, an electronic database search is performed on PubMed, Scopus, Science Direct, Research Gate, and Google Scholar. The following keywords are used in an approach called keyword combination to analyze the records: “wounds”, wound healing”, “silver-nanoparticles”, “nano-particles”, “wound dressings”, etc. In case any new research studies are missed, a search strategy is also conducted on the top 10 pages of Google Scholar. Records that include "No full information," "Non-Extractable Data," and "language other than English" are excluded. Figure 3 below provides an overview of the entire review approach.

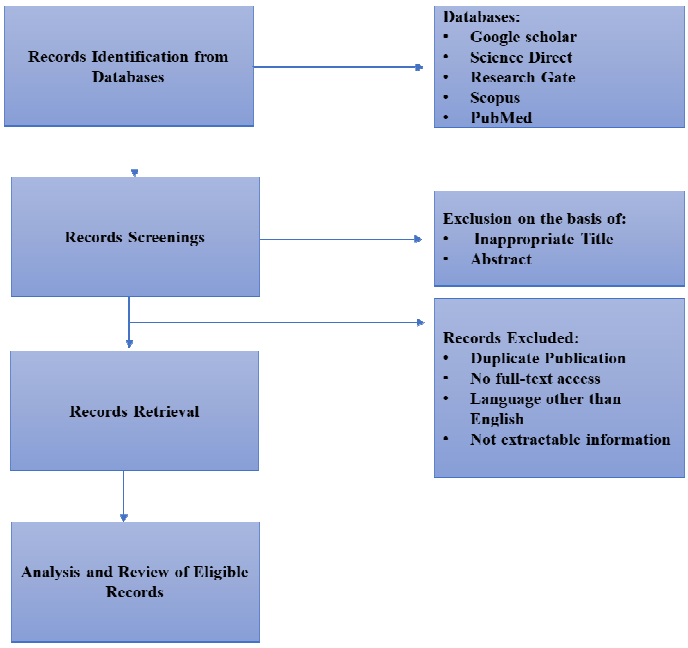

Figure 3: Illustrating the Design Use to Retrieve Relevant Records to Carry out the Review.

3. LITERATURE REVIEW

El-Aassar et al. carried out the development of a novel wound dressing of Hyaluronic acid, polygalacturonic embedded silver nanoparticles. In their study, the nanofiber-mates embedded AgNPs were administered to the injured location of albino rats in vivo. The wound was completely assessed histopathologically. In addition to that, the antibacterial activity of the synthesized wound dressing was further tested against gram+ve and gram-ve bacteria. The results of their study in albino rats revealed that 14 days of nanofiber treatment resulted in maximal wound epithelization and collagen deposition [12].

Another study was carried out by Satish et al. on the effectiveness of greenly synthesized silver nanoparticles (AgNPs) from *Gelidiella acerosa* against multi-drug resistant Vibrio spp. in terms of non-bactericidal and anti-virulence. The findings of their investigation showed that quorum sensing also controls the development of biofilms and the generation of EPS in vibrios. Its maintenance and architecture are also crucial factors in the creation of biofilms. In their tests, the scientists showed that AgNPs were useful for negatively altering the vibrios biofilms' structure and for lowering the colonies [13].

Diniz et al. carried out the synthesis of Gelatine/Alginate Hydrogel silver nanoparticles and checked the effectiveness in wound healing. They carried out the characterization of silver nanoparticles and then evaluated the efficacy against bacterial pathogens. The results of their study revealed the minimal inhibitory concentration of 53.0 µg/mL against *Staphylococcus aureus* and 0.50 µg/mL against Pseudomonas aeruginosa further demonstrating that the novel hyddr5ogel developed for wound healing has healing potential to be used for future [14]. Rath et al. demonstrated the utilization of a collagen nano matrix containing an AgNP reservoir to speed up the healing of wounds. Because of its natural anti-inflammatory, antibacterial, and hemostatic capabilities, in vivo, investigations demonstrated excellent wound-healing characteristics [15].

Tang et al. carried out the construction of skin adhesive using methacrylated hyaluronan–polyacrylamide (MHA–PAAm) hydrogels, integrated with silver nanoparticles (AgNPs) for hemostatic and antibacterial activity. In addition to the fabrication and characterization, they evaluated the developed skin adhesive on animal models. Animal investigations showed that the AHAs, which have tissue adhesion and antimicrobial characteristics, were simple to stretch and could halt bleeding in models of liver damage and amputation of the rat tail. AHAs reduce inflammation while also promoting the development of vascular tissue, collagen, and granulation tissue in wounds. These characteristics encouraged wound healing in rat models of wound infections, indicating the tremendous potential for using AHAs in clinical settings. The above studies have developed novel types of silver nanoparticles for wound healing and wound improvement. However, there is still a lack of expertise in nanotechnology, the escalation of which can enable the research community to harness the complete potential in wound healing.

4. DISCUSSION

The goals of current treatment for wounds include covering the wound, preventing bacterial infection, providing moisturization, removing dead tissue, and absorbing extra fluid. Platforms for nanotechnology have shown new potential and advantages in the sector because of their properties. The delivery of biomolecules like DNA/RNA or GFs that may be used in the treatment of chronic wounds has been made possible by recent advances in nanotechnology. These agents may be delivered intracellularly, are protected against deterioration, and have improved drug penetration due to their tiny size and physical and chemical characteristics. Together, they enable topical administration and half-life of these agents, reducing the number of applications and expenses. Additionally, diverse drug release patterns that can accommodate the needs of wound healing are made possible by the encapsulating of pharmaceuticals and biomolecules inside nano-carriers. The nano-carriers used for wound healing comprise nanogels, nanofiber, nano-material, and so on as illustrated in Figure 4.

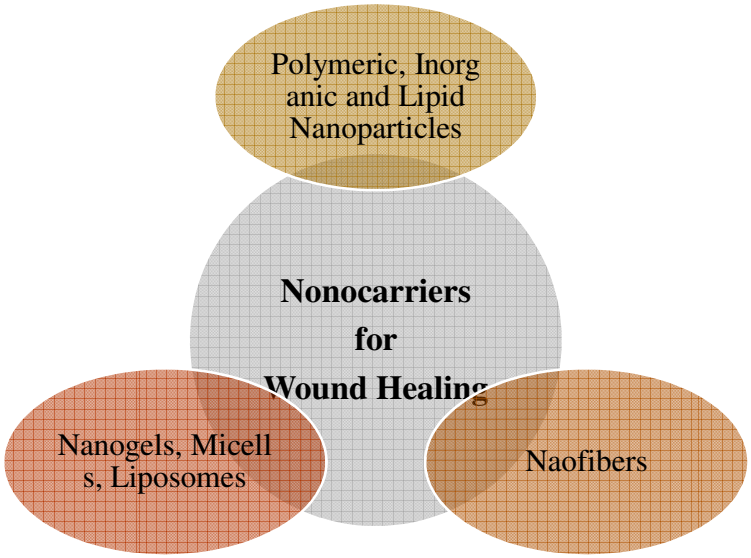

Figure 4: Illustrating the Different Nanocarriers; Nanoparticles, Self Assembled Nanocarriers, and Nanofibers for Wound Healing.

Although the exact process in many biological systems is still unknown, it has been determined that AgNPs can disrupt intra-cellular structures because of their increased nanometric size and surface area, which can cause them to cross the body of the microorganism. The binding of membrane protuberances to NPs, which are drawn into the cell by electrostatic attraction, causes total cell disintegration and the elimination of lipopolysaccharide (LPS) as illustrated in Figure 5. Additionally acknowledged explanations for the antibacterial action of silver nanoparticles include non-oxidative, metal ion release, and oxidative stress induction processes.

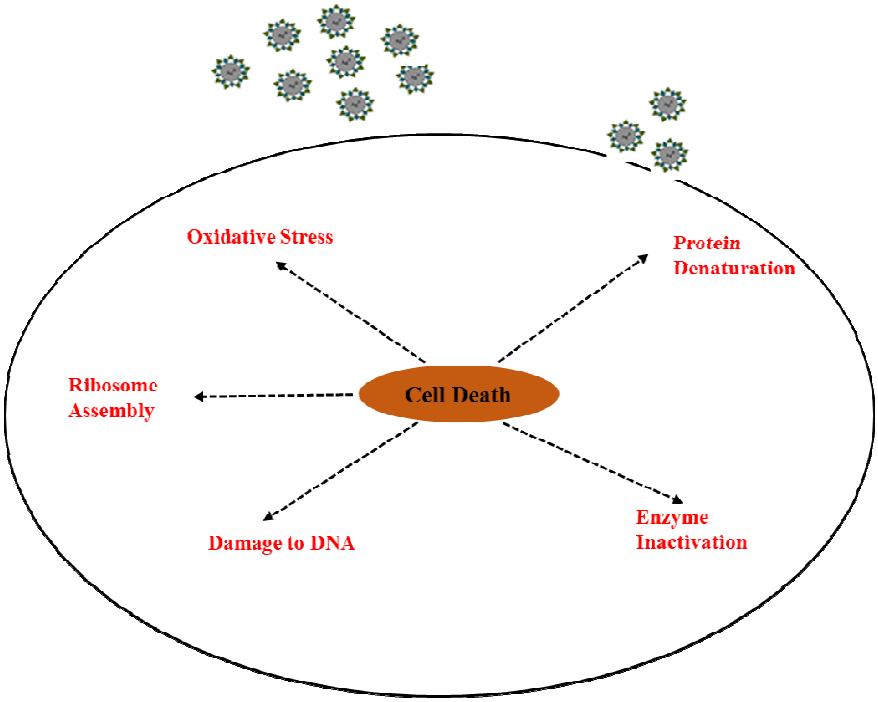

Figure 5: Illustrating the Schematic Representation of Different Mechanisms of Action of AgNPs for the Removal of Bacterial Pathogens.

The advancement of nanotechnology, particularly the production and characterization of nanoparticulate systems, has expanded the range of interventions that may be used to treat chronic wounds. The novel chronic wound nano-therapeutics are multidimensional platforms that facilitate the healing of wounds with minimum scar formation, prevent/treat bacterial contamination, and even deliver the active biomolecules contained at precise rates that correspond to wound healing requirements. They must also contain significant levels of the biomolecule and be highly biocompatible. To meet this need, they must also be simple to apply to the wounds, which calls for NPs and self-assembling carriers to be incorporated into another formulation.

Various obstacles need to be overcome for these technologies to be commercialized and for new therapeutic therapies to be developed. The main issue, from a biological standpoint, is the incomplete understanding of the pathophysiology of patients. Understanding the in vivo outcome of the interactions of NPs with tissue, cells, blood, and intracellular compartment is important in both normal and pathological situations. On the other hand, from a technical standpoint, the biggest challenge is to better understand the physicochemical characteristics of such nanoscale systems, as well as their toxicities and in vivo behavior.

The complexity of the development of nanotechnology systems needs to be reduced for them to have realistic clinical scalability and commercial transfer potential. Fabricating controllable, repeatable, and supervised nanotechnology systems is the purpose. As a result, to lessen the negative effects that these nanosystems have on the human body, it is necessary to enhance the synthesis and characterization of nanotechnology-based wound healing systems. Additionally, other factors like systemic absorption or the materials/polymers utilized in their manufacturing, which are often not FDA-approved materials, must be taken into consideration.

Resistance to antimicrobials by microorganisms has been a source of concern for the medical profession, that includes wound care and other concerns connected to the formation of wounds. Non-healing wounds following lengthy procedures continue to be a serious challenge for the surgical team, and a clinical investigation demonstrates that the healing process is directly related to wound comorbidities. Thus, the expense of the complex management of wound therapy, connected to biofilm, unique characteristics as vital treatment methods for a successful anti-biofilm course is required for future techniques such as nanotechnology and the production of nanoparticles with unquotable properties. Recent technological advancements enable the development of wound dressings for the application of active molecules or treatments to the wound environment.

Inflammation, proliferation, and remodeling all take place throughout the complex three-stage process of wound healing. The most significant internal component that might affect the physiology of the healing process is infection with germs. Researchers have worked hard to provide a variety of topical solutions that can offer a moist environment as well as antibacterial activity to produce a successful recovery with less scarring. But because of bacterium biofilms and multidrug-resistant germs, treating chronic wounds is still difficult. Due to their high surface-to-volume ratio, nanoparticles may be effectively used in a wide range of medicinal applications, including wound treatment. Gold, silver, and zinc metal nanoparticles have exceptional qualities including low toxicity and antibacterial activity, which make them ideal candidates for inclusion in wound dressings. Research by Pang et al. assesses the effects of silver nanoparticles on wound healing in Zebrafish. The results of their study discovered that when exposed during the epithelialization and blastema formation stages, AgNP treatment at a dose of 2 g/ml inhibited fin regeneration. Following AgNP exposure, cell growth in regenerating blastema was drastically reduced.

Additionally, recently established techniques with advantageous characteristics and properties have evolved, such as nanoscale architecture surfaces, substrates imprinted with cells, and three-dimensional and four-dimensional printing. In general, the next generations of wound-healing nanotechnology have been developed using various newly discovered nanosystems, present abilities in high tech, understanding of chronic wounds, molecular pathology, and genotype/phenotype features. The FDA-approved manufacture of high-purity scaffolds and nanoparticles is still a difficulty since the purifying and mass synthesis of the nanomaterials and polymers are frequently difficult processes.

5. CONCLUSION

The significant number of papers published in recent times demonstrates the rise of different nanotechnologies, particularly multifunctional systems, in wound healing, indicating the high expectations towards nano-therapeutic interventions in the wound-healing sector. The challenge, however, is accumulating adequate knowledge of the physical and chemical features of

nanoscale systems, as well as their expected behavior and toxicities in the human body. Furthermore, the high purity of the scaffolds and nanoparticles required by the FDA for commercial use is a challenge, as mass manufacture and refinement of the polymers and nanoparticles prepared are sometimes difficult. As a result, there is an ongoing need for improved synthetic techniques and analytical procedures to enable the translation of nanotechnology-based treatments to the clinic.

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CHAPTER 11

CURRENT STATUS, CHALLENGES, AND FUTURE PERSPECTIVES OF DOWN SYNDROME

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ABSTRACT:

One of the most prevalent but financially devastating conditions is Down syndrome (DS). Congenital heart problems, leukemia, Alzheimer's disease, Hirschprung disease (HD), and other conditions have all been linked to Down syndrome. Individuals with DS experience various traits to varying degrees, making it crucial to identify the factors that underlie this diversity. Down syndrome (DS) is a severe birth condition caused by chromosome 21 trisomy and has far-reaching medical and societal repercussions. The author discusses potential avenues for further study in light of technological developments. Particularly, large-scale investigations of genotype-phenotype interactions in patients and the application of chromosomal engineering to create novel trisomic mice models are expected to considerably increase the future understanding of DS. Down syndrome, sufferers experience Alzheimer's disease (AD) occurring more often and at a younger age. Examined are the pathogenic effects of the amyloid cascade and TAU pathology on the development of Alzheimer's disease.

KEYWORDS:

Alzheimer's disease (AD), Amyloid Precursor Protein, (APP), Chromosome, Down syndrome (DS).

1. INTRODUCTION

It is believed that between 1 and 3% of the general population has some kind of intellectual impairment. The prevalence percentage might range anywhere in that range. Aneuploidies make up a significant portion of the group of chromosomal abnormalities that are linked to up to 28 percent of all cases of intellectual disability. This includes both numerical and structural chromosome abnormalities. The most frequent kind of diagnosis is for Down syndrome (DS) of autosomal trisomy (chromosome 21C21), which occurs spontaneously in roughly one in seven hundred live births [1].

Millions of people with Down syndrome struggle with a wide range of health problems, such as difficulties with memory and learning leukemia, cancer, Hirschprung disease (HD), congenital heart disease, and Alzheimer's disease. Births with trisomy vary in frequency from somewhere between 1 in 319 and 1 in 1000, depending on the mother's age and geographical location as shown in Figure 1 [2]. Genetic complexity and phenotypic variation are both high in DS. Both

the genetic and phenotypic variations of DS are rather large. People with Down syndrome are more likely to have a wide range of health issues in general, and newborns with trisomy 21 are more likely to experience miscarriages during pregnancy. Due to recent developments, patients with DS now have a longer average lifespan in medical treatment and social assistance. In affluent nations, the average lifetime of those with Down syndrome is 55 years[3].

Figure 1: Demonstrates the presence of Down syndrome, which is brought on by an extra copy of the 21st chromosome in the baby [4]**.**

The condition is caused by an increase in the increased gene dosage causes the trisomic genes to express themselves, and it may impact all or select body cells. Down syndrome is characterized by intellectual disability, hematopoietic disorders, heart defects, digestive issues, low neuromuscular tone, dysmorphic features of the head, neck, and airways, impaired hearing and vision, distinctive facial and physical features, and a higher risk of developing other health issues. Pregnancies with a child with Down syndrome are more common among older mothers. Due to younger women's higher reproductive rates, more than 80% of children with DS are born to moms under the age of 35 [5].

Delayed physical and mental development, a tiny chin, slanted eyes, weak muscles, a large tongue, a single-hand wrinkle, and a flat nasal bridge are the most noticeable physical characteristics of this disease. Prenatal and postnatal chromosomal analysis (karyotype assessment) is one proposed method for diagnosing DS. To assess the likelihood of DS recurrence Investigation of cytogenetics is warranted because of its usefulness in genetic counseling [6]. Since there is currently no treatment for Down syndrome's cognitive impairment,

researchers have focused on determining which genes contribute to certain symptoms. Using preventative measures, including prophylaxis against the respiratory syncytial virus (RSV) and extra vaccines, is crucial since respiratory tract infections are the second highest cause of mortality in children with Down syndrome [7]. To that end, this study will provide a narrative summary of DS. The data presented here will provide optometrists with the fundamentals they need to establish a rapport and communicate effectively with their patients who have Down syndrome. The review covers the following topics: an explanation and summary of DS; a historical perspective and terminology; the etiology and genetic mechanism behind DS; the many forms of DS; the prevalence of DS; the medical and physical characteristics of DS; screening and diagnosis; and so on.

2. LITERATURE REVIEW

In their research, Kalpana V. Lakshmi et al. evaluated mild retardation incidence at 1% to 3%. Environmental and genetic variables are equally important. Chromosomal abnormalities (statistical and structural) cause up to 28% of mental impairment, including Down Syndrome (DS). Over 95percent of Down syndrome patients are trisomy 21-free. 2–4 percent have chromosomal 21 translocations (D or G group), while 1–2% have mosaics. This research examined chromosomal anomalies in 100 mentally retarded patients. There was an 18% incidence of trisomy. Three percent and one percent of Robertsonian translocations included the chromosomes “46, “XY”, and “t (21; 21) +21. 2 (2%)”. Mosaic “46, XY/47”, XY, Plus 21. Because the research is reported previously without case studies [1].

According to studies by Juan Fortea et al., people with Because of cognitive deficits brought on by dementias like Alzheimer's and other dementias, people with Down syndrome have a higher death rate than the general population. The “Cambridge Cognitive Examination for Older Adults with Down Syndrome (CAMCOG-DS)” was used to categorize patients with Down syndrome age, they develop cognitive impairment. The lowest ages at separation and 95% confidence intervals are also included where appropriate, and a first-order locally computed scatterplot smoothness curve was used to establish the order and age at which the biomarker abnormalities first appeared. Alzheimer's disease has a protracted preclinical period with persistent biomarker abnormalities over 20 years in Down syndrome. Due to the similarities between sporadic and autosomal dominant Alzheimer's disease and Down syndrome, this population is a great target for medications that prevent Alzheimer's disease [8].

In their study, Amy Y. Tsou et al. addressed the need to create a clinical practice guideline based on solid data for individuals living with Down syndrome. Thirteen contributors worked together to formulate 10 PICO (population, intervention, comparison, and outcome) questions regarding people with Down syndrome for inclusion in the World Down Syndrome Foundation's official publication, Health Recommendations for Adults with Down Syndrome. These questions include a wide range of clinical topics, such as mental health (2 questions), dementia, screening, and therapy. 20 relevant papers were found among 11,295 citations for 10 PICO queries. A new search revealed 2 more documents, bringing the total to 22 (3 systematic reviews, 19 primary research) examined and synthesized. 14 suggestions and 4 good practice statements were derived from this investigation. These evidence-based clinical guidelines promote primary care for people with Down syndrome, the author stated. Insufficient evidence weakens the conclusions and calls for further investigation [9].

Deborah Kinnear et al. studied multimorbidity in intellectually disabled persons with and without Down syndrome. All individuals (16+) with intellectual impairments recognized by general practitioners (GPs) and adults receiving intellectual disability healthcare or social worker services. 1023 out of 1562 potential individuals took part (65.5%), including 461 women and 562 men, both "aged 43.9. (16–83 years)". 837 people did not have Down syndrome. The average participant had 11.04 health problems, and 98.7% had multimorbidity. Most common ailments are unpleasant, debilitating, and life-threatening. Obesity, epilepsy, constipation, visual impairment, and ataxia/gait issues were widespread. Multimorbidity is disseminated throughout adulthood, unlike in the general population. The frequency of various diseases varies between people with and without Down syndrome. This is on top of communication and knowledge constraints. As their multimorbidity differs from the older general population, care routes, and recommendations are needed to enhance their healthcare [10].

3. DISCUSSION

The birth prevalence of this condition might be cut by more than half with a plan of concluding the family before the mother's age of 30. Pre-implantation genetic diagnosis should be available to women at high a priori risk, since this may increase the likelihood of a successful pregnancy with a very small chance of a child being born with Down syndrome. Due to the lack of conclusive data, large-scale clinical research is not required before considering an active prophylactic approach to folic acid supplementation. If a high enough quantity of folic acid is taken, the current supplementation strategies aimed at preventing neural tube abnormalities may also prevent Down's syndrome. Etiological understanding gaps are impeding primary prevention efforts, hence there is an immediate need to shift research priorities [11].

3.1.Several health disorders are linked to Down syndrome:

Clinical conditions such as Alzheimer's disease, irregularities of the heart, leukemia, hypertension, and digestive problems are indicated in Figure 2 as being connected with DS. Together, the causes of DS and its associated phenotypes need to be investigated at the molecular level to provide a fuller picture of the condition. A detailed discussion of a variety of phenotypes associated with Down syndrome follows:

1. *Neurological problems:*

Patients with DS are substantially more likely to experience the onset of AD earlier in life. The likelihood of developing dementia in people with DS rises beyond the age of 50 by as much as 70%. Young people's onset of Alzheimer's disease has been connected to some genes. Phosphatidylinositol-binding clathrin assembly protein Apolipoprotein E (APOE) (PICALM), beta-secretase 2 (BACE2), amyloid precursor protein (APP), and others have all been discovered as potential risk factors in the ongoing study. Amyloid precursor protein (APP), an important membrane protein present in brain synapses, is more often trisomic in people with Down syndrome, leading to speculation that It significantly contributes to dementia development in this group [12].

The degeneration of basal forebrain cholinergic neurons may be studied using several different mice models (BFCNs). Expression of APP trisomy is required for retrograde axonal transport in Ts65Dn mice. BACE2, which codes for the enzyme beta-secretase 2, has also been associated with the onset of Alzheimer's. Beta secretase is an enzyme that cleaves the amyloid precursor

protein (APP) in the body (BACE 2) genes both map to chromosome 21. Currently, available data on DS provide credence to the link between BACE2 haplotypes and AD. There are more genes than APP and BACE2 that are connected to how Down syndrome individuals acquire Alzheimer's illness [13].

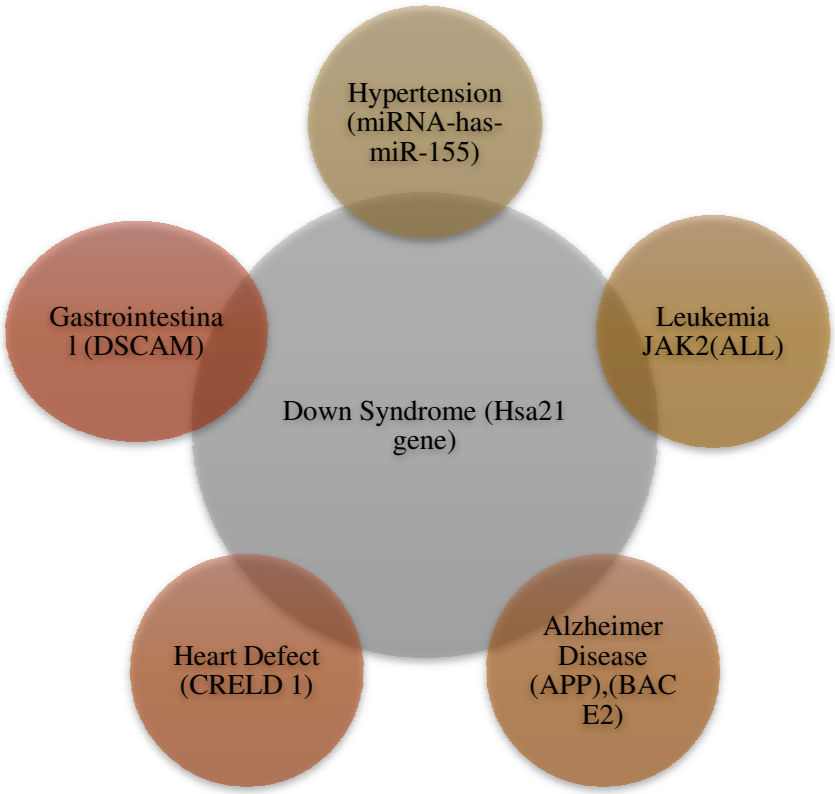

Figure 2: Displays the Numerous ailments linked to the genes that cause Down's syndrome.

2. *Hematological problems:*

There is a distinct range of malignancies seen in patients with DS, including both leukemia and solid tumors. In 1930, the disease was first reported in a person with Down syndrome; the first comprehensive investigation wasn't conducted until 1957. Down syndrome patients have a 2% prevalence rate for leukemia, making them more likely to get cancer by age 5 and 2.7% by age 30 according to studies [14]. GATA 1 is a transcription factor that is found on chromosome X and is essential for the maturation of megakaryocytic and erythroid cells. These mutations in GATA 1 cause a shorter GATA 1 protein to be produced, which in turn causes the unchecked growth of immature megakaryocytes. In contrast, around 30% of cases of ALL in DS have a mutation in the Janus kinase 2 gene that causes an increase in function [15].

3. *Hypertension:*

There seems to be a lower rate of hypertension in people with DS, according to reports. This is related to the Hsa-miR-155 trisomy, a mutation in the Hsa21 microRNA. The hypothesized mechanism through which Hsa-miR-155 lowers the risk of hypertension is that it targets a single AGTR1 allele, which is situated inside the type-1 angiotensin II receptor gene hence reducing

the expression of that allele. More research is needed to confirm this theory and identify any other genes that could prevent persons with Down syndrome from developing hypertension [16].

3.2.Etiology:

The primary factor that contributes to the development of Down syndrome is an extra copy of chromosome 21. The genetics of Down syndrome and the relationship between genotype and phenotype has been the subject of several hypotheses. An overabundance of Hsa21 genes is one example of a problem that might arise from an uneven distribution of copies of genes. Also discussed is the theory that different genes contribute to different characteristics of Down syndrome. The second widely recognized theory called the amplified developmental instability hypothesis, proposes that the genetic imbalance brought on by several trisomic genes has a bigger influence on the expression and function of numerous genes [17]. Therefore, the critical area theory is a household name. There are a small number of chromosomal regions (DSCRs) that are linked to Has21 partial trisomy. Many of Down syndrome's clinical characteristics may be traced back to the DSCR on 21q21. Multiple crucial areas or genes seem to have a role in the phenotypic aspects of trisomy 21, as was discovered after a comprehensive examination of various investigations, rather than a single critical region gene [18].

3.3.Evaluation:

Prenatal testing for Down syndrome may be performed in a variety of ways. Soft indicators, such as an enlarged small or missing nasal bone, a thick nuchal fold, and large ventricles, may be seen by ultrasound between 14 and 24 weeks gestation. Miscarriage rates range from 0.5% to 1%, making amniocentesis and chorionic villus sample a common choice for determining the diagnosis[19]. Several different techniques, both prenatally and postnatally, have been created and are employed for the speedy diagnosis of trisomy 21. The most popular method is fluorescence in situ hybridization (FISH), which uses whole Hsa21 or Hsa21-specific probes to examine interphase nuclei. Nowadays, techniques like the quantitative polymerase chain reaction (QF-PCR) are used. This method uses DNA polymorphic markers to determine which of three possible alleles is present. The existence of DNA and also the presence of informative markers are necessary for the success of this approach. Researchers have discovered that the Short tandem repeat (STR) marker approach may be used to diagnose Down syndrome in as many as 86.67 percent of patients [20].

Paralogue sequence quantification, a relatively new method, makes use of the Hsa21 copy number's paralogue sequence (PSQ). Using paralogue genes, a PCR-based approach may be developed for the identification of certain chromosomal number abnormalities. The identification of Down syndrome is being studied using some cutting-edge techniques, such as digital PCR and next-generation sequencing (NGS) [21].

3.4.Treatment and Management:

Multiple approaches are utilized to treat individuals with Down syndrome. The answer is condition-specific. Surgery, medication, and other psychotherapies are all used to treat this condition. To avert problems later in life, the following treatment procedure may be used. Patients with Down syndrome need a team approach to their care. If a newborn is suspected of having Down syndrome, karyotyping may be used to diagnose the problem. The parents should undergo genetic screening and counseling with a clinical geneticist, who should be suggested to

the family. Treatment of Down syndrome includes some factors, one of the most important of which is educating parents about the disorder and the numerous complications that may arise from it. Symptomatic treatment is the norm, and a full recovery is unrealistic.

Depending on the severity of an illness, a person may have varying degrees of both talents and impairments. There are medical issues that a person is born with and others that worsen with time. 43 Many of the health problems that often accompany DS are now more manageable, so individuals with DS may live longer and healthier lives than ever before. Table 1 provides a brief overview of the most common medical issues that occur in people with DS.

Table 1: Illustrates the Concerns raised by Down syndrome concerning health.

Disease	Conditions
Cardiac Disease	Between 44 and 50 percent of children born with DS have cardiac defects. Septal (wall of the heart) defects in the atrium and ventricles are the most common types.
Gastrointestinal (GI)	Reflux of the stomach's contents into the esophagus and trouble eating are two of the most frequent symptoms.
Neurology	Impairments in development, most significant intellectual disability
Central Nervous System (CNS)	Alzheimer's disease and other forms of dementia that strike older people
Ear, Nose, and Throat	Sleep-related respiratory issues (including sleep apnea), conductive and sensory-neural hearing loss, and persistent catarrh have all been linked to stress.
Immunological	Immune system malfunction; autoimmune diseases such as arthritic pain, baldness, and vitiligo. Children with this condition are more likely to get infections than their healthy peers.
Dental	Take into account dental cavities and crooked teeth
Reproduction	Male infertility is common, while female infertility manifests in a variety of forms, including miscarriages, early deliveries, and labor complications.

Quantifying the Hsa 21 copy number by paralogous sequences is a relatively new technique known as paralogous sequence quantification (PSQ). To detect specific chromosomal number aberrations PSQ is employed because it is a PCR-based approach that can accurately quantify paralogous sequences. Paralogous sequences share a lot of nucleotide base pairs, but they tend to acquire mutations in a certain way depending on where they were first discovered. With the use

of pyrosequencing technology, we can quantify these sequence variances, known as paralogous sequence mismatches (PSMs), and so assess the relative dosage across various chromosomes. Given that PSQ may be completed in under 48 hours, it is an option that has the potential to replace standard practice in diagnostic settings; it is also accurate, straightforward, and simple to implement for the detection of common aneuploidies.

4. CONCLUSION

The ocular and medical effects of DS, a hereditary disorder with serious implications, are substantial. The field of optometry plays an essential part in reducing the negative effects of visual impairments for people with Down syndrome. To perform this function effectively, optometrists need to learn the fundamentals of the condition. There is currently no medical treatment for Down syndrome, although it is a devastatingly expensive birth condition for both the healthcare system and society as a whole. This makes it essential to check all expectant mothers for DS. Since November 2011, NIPS has been used in clinical practice to diagnose fetal aneuploidy; nevertheless, owing to the likelihood of false positive and false negative test findings, it is not currently recognized as a diagnostic test. It is advised to undergo invasive diagnostic procedures like CVS or amniocentesis if the cfDNA fetal aneuploidy screening test is positive.

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CHAPTER 12

EXECUTING THE IMPACT OF OPTICAL MICROSCOPY IN MODERN BIOMEDICAL APPLICATIONS

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ABSTRACT:

Optical microscopy, frequently recognized as the "light optical microscope," is a microscope kind that enlarges images of tiny materials utilizing noticeable light and a set of lenses. The objective of optical microscopy is that they are in charge of making the principal images and have a significant impact on the standard of images the microscope can produce, microscope objectives are among the most crucial parts of an optical microscope. Optical microscopes employ visible light, which allows for direct visual observation of samples, they were unassuming to generate and they are mostly used nowadays. Usual light-sensitive cameras can record an optical microscope's image to create a micrograph. Upcoming microscope arrangements are undoubtedly going to be integrated and automated, with crafty operating choices that will deliver an extraordinary opinion of anything that occurs during a biomolecule.

KEYWORDS:

Non-linear Microscopy, Optical Microscopy, Optical Microscope, Re-construction microscopy, Sophisticated Optical Reconstruction.

1. INTRODUCTION

Optical microscope is also known as light microscopy, Optical microscope is an arrangement of optical microscopy which find out or magnifies pictures of tiny components consuming visible light and a bunch of lenses. The first type of microscope is an optical one, which may have been created in the 17th and 18th centuries in its present compound form. While many complex proposals struggle to recover perceptiveness and section distinction, basic spectrophotometers can be quite straightforward. Since they employ visible light and allow for direct visual inspection of samples, optical microscopes have historically been simple to create and are still widely used today. Modern optical microscopes frequently have a computer built into them because they have joined the digital era. Nowadays, major microscope producers have choices for automating their optical microscopes, allowing users to control a variety of operations via a tiny bit screen. The objective, sample chamber condenser, and image projection system are all moved automatically by motors, and they are all automatically tuned for lighting quality, resolution, and sometimes even focus.

An optical microscope uses an impartial lens to produce an exaggerated picture of a thing specimen and an eyepiece to identify its appearance more so the user container sees it with their unassisted eye. The major appearance (magnified image) A'B' of the exerted real picture is shaped with an objective lens, using material as AB. The eyepiece should then be set up so that

the principal image (A'B') is closer to the ocular than that of the anterior focus point, creating a larger, more erect virtual picture (A"B"). To view the larger image, position your bare eye in the eye (pupil) location on the eyepiece tub. Now that digital image capture equipment and image analysis techniques are working together, automated sample assessment is a genuine possibility. A skilled petrographic will always be needed to oversee the procedure and evaluate the findings, though. Automation offers considerable increases in productivity as well as the ability to significantly lower the cost per examination. Many common tests that have historically been carried out by less expensive and perhaps not as accurate chemical analysis techniques are expected to find a major alternative in automated modal analysis.

One method possibly the oldest method of truly overcoming the optical limit in fluorescence microscopy is optical microscopy. It operates in the optical near field region where the predominance of evanescent waves is associated with sub-wavelength objects. It is possible to get great optical resolution by having access to evanescent waves. Like other components of the SPM family of methodologies, NSOM got its start in various incarnations in the 90s. Even with the help of intricate staining, it is considerable difficulty to teach computers to recognize individual cells by their visual properties due to excessive calculation and a memory-intensive process. However, optical microscopy may still be the sole method available today for distinguishing tissue right down to the level of the individual cell. A non-metallic component's surface, such as one made of ceramic, plastic, or elastomer, can be examined using an optical microscope. These are comparable to metal samples, although problems can arise due to polymers' softness. Optical microscopy examination of polymeric surfaces requires experience to produce good results.

2. LITERATURE REVIEW

In a study [1], The author Mingyou Liu et al. Discussed Optical Microscopy and Electron Microscopy for the Morphological Assessment of Ligaments: A Mini Review. Confocal microscopy is a new ability to perform microbiological inspection towards pointing out what is good in this field and biological microscope Through the use of microscopy, the morphological traits of tendons have already been fully assessed. The most popular methods for observing tendon tissue are optical and electron microscopy. Both types of microscopy have different principles that govern how preparation and evaluation are done. Cells and extracellular are frequently observed with straightforward optical microscopy.

In a study [2], The author, Sparsha Shetty et al. Discussed Improvements in nonlinear optical microscopy techniques for in vivo and in vitro neuroimaging. One of the difficulties in neuroimaging is unraveling the mechanics of the brain using optical microscopy because of the intricate structures. Advanced neuroimaging methods offer a more thorough understanding of the pathomechanisms behind brain disorders, which is helpful in the early diagnosis of the pathological and physiological alterations brought on by different neurodegenerative diseases.

In a study [3], The author, Zhong Min Wagner et al. Discussed SEM/EDS and optical microscopy analyses of microplastics in ocean trawl and fish guts. Using optical microscopy and SEM/EDS, the size, shape, and chemistry of microplastic particles from Atlantic and Pacific

Ocean trawls, lab-fed rotting food, and ocean fish guts have been studied. We investigated the potential of these measurements as a quick screening method for the life orientation of the likely microplastic candidates using micro-spectroscopy.

In a study [4], The author Grubb, D. T. et al. Discussed Polymer Science: A Comprehensive Reference, 10 Volume Set. Through the use of microscopy, the morphological traits of tendons have now been fully assessed. The most popular methods for observing tendon tissue are optical and electron microscopy. Both types of microscopy have different principles that govern how preparation and evaluation are done. Many stains, including h&e, Van Gieson, Prussian blue, Yellow blue, and Fuchsin blue, are used to evaluate cells, collagen fiber arrangement, and noncollagenous components. Simple optical microscopy is frequently employed to observe cells and extracellular matrices.

In a study [5], The author, Jianquan Ma et al. Discussed Stochastic optical reconstruction microscopy (STORM). The way we study life has been transformed by extremely (SR) fluorescence microscopy, a family of optical imaging methods with temporal resolution below the diffraction limit, as recognized by the 2014 Nobel Prize in Chemistry. The commonly used SR technique known as stochastic optical reconstruction microscopy (STORM) is founded on the idea of single-molecule localization. When compared to traditional optical microscopy, STORM frequently delivers a resolving power of 20 to 30 nm, an eight gain.

In a study [6], The author Taewoo Senyuk et al. Discussed Optical microscopy of soft matter systems. fundamental ideas and variables are crucial to all microscopy modalities. The chapter examines cutting-edge three-dimensional (3D) imaging technologies like fluorescence microscopy and fluorescence optical coherence tomography in addition to traditional optical microscopy methods like bright field and polarising microscopy (PM). It offers a detailed explanation of nonlinear optical (NLO) microscopy methods and examines a particle-tracking method using a pre-designed probability density function (PSF) and its use in imaging.

In a study [7], The author L. Gu et al. Discussed Fibre-optic nonlinear visual microscopy and endoscopyThe essential laboratory tool for high-resolution imaging in dense tissue and living animals is nonlinear optical microscopy. There are a lot of prospects for advancements in nonlinear optical microscopy due to the quick growth of fiber-optic components in terms of increasing functionality and decreasing size. The only device that enables cellular photography within empty tissue passages or substantial structures that are unavailable to a normal optical microscope is fiber-based nonlinear optical endoscopy.

3. DISCUSSION

The earliest method, Near Field Scan Optical Microscopy (NSOM), is to truly surpass the optical microscope diffraction limit. It operates in optical close-up. field zone where its evanescent waves are connected to objects at sub-wavelengths predominant. It is possible to get great optical resolution by having access to evanescent waves. NSOM began in the same year as other scanning probe microscope (SPM) techniques did. the 1980s in a variety of forms. An elongated optically conducting substance, such as a drawn optical fiber, makes up the most basic type of NSOM probe. A metal, such as an alumina, can be placed on the probe to control and steer light that is a few tens of nanometers in wavelength. The electromagnetic wave equation's solution using the finite element approach was used to compute the TM field transmission into the probe.

A vital in situ assessment and observing method through numerous requests in several fields of resources research is high-temperature optical microscopy. The equipment utilized consists of heating microscopes, which are commercially accessible, and thermo-optical instruments, which are typically constructed to order and referred to as "high-temperature processing microscopes." Based on real-world examples taken from the literature, many high-temperature optical microscope applications are explored. This review discusses alternative applications of the technique, including the use of heating microscopes as "optical dilatometers" to examine the sintered metal kinetics of powder compacts, in addition to its traditional use to study the melting and weakening behavior of glass, slags, ashes, and other sulfate and ceramic materials. The benefits of the method over traditional dilatometry are emphasized in this regard.

The development of a variety of special devices to look into specific issues, like the excessive wear and twisting of cover mixtures throughout density, the cloistering of multiplayer online metal-ceramic and ceramic-ceramic systems, and the saturating behavior of water phase on rigid substrates, are described. A unique, multi-purpose high computation microscope is detailed as one example of such specially designed equipment, and its changes in strategies, which is far greater than that of commercial instruments, are outlined. This equipment is exceptional in that it combines the ability to observe materials both vertically and horizontally. It also offers the chance to examine relatively large samples (65 mm3), or around 10 times greater than those appropriate for commercial heated microscopes.

New techniques in optical microscopy are now possible thanks to the accessibility of high-resolution tiny spatial light modulators (SLMs). The SLMs covered in this article are tiny liquid crystal displays with micron-sized cells that may alter an optical wave front’s phase or amplitude. They can be employed as spatial Harmonic filters in the image route in microscopy or to regulate and sculpt the sample illumination. This article reviews a few of these applications. One of them, known as spiral phase contrast, produces interference fringes that have a spiral shape for thicker phase samples and isotropic edge enhancement for thin phase samples, allowing for the reconstruction of the phase topographic from either a single on-axis interferometer. For instance, this combination enables the Zernike inverted microscope concept to be generalized. The new SLM-based technology eliminates some drawbacks and artifacts of the conventional approach while enhancing effective resolution. The fundamental benefit of SLMs in the microscope is their adaptability. By electronically adjusting the phase pattern shown on the SLMs, one can achieve several operation modes within a single setup without the need to change any hardware components.

A novel optical microscopic method called confocal scanning optical microscopy (CSOM) has several benefits over traditional microscopy. In laser scanning fluorescence microscopy (SOM), a diffraction-limited laser beam scans the sample, and the light emitted by the in-focus lighted structure or component (voxel) of the sample, or the fluorescence emission that the input light stimulates within it, is focused onto a photoanode. The voltage efficiency after this sensor is shown at the proper three-dimensional position on even a TV monitor when the lighting spot is moved over the specimen, creating a two-dimensional image. In the confocal mode, an aperture is placed in the picture plane in front of the detector at a point confocal with the in-focus voxel. This aperture is often somewhat smaller in circumference than the Airy disc image. Thus, light coming from this in-focus voxel travels through the aperture and is detected by the detector, however light coming from any area either above or below the objective lens is lens blur at the reference plane and mainly prevented from doing so, adding virtually nothing to the confocal

image. Confocal skimming microscopy is ideally matched for the imaging and two-half tomography of discolored clinical materials because it can eliminate out-of-focus blur and so enable precise non-invasive optical sectioning. Multimodal NLO imaging makes use of NLO microscopy's potential for studying intricate biological tissues. Coherent generally pro-Raman scattering (CARS), second-harmonic generation, and multiphoton fluorescence have been coupled to enable the examination of a wide range of biological issues, including lipid metabolism, cardiovascular illness, cancer formation, and skin biology. A CARS microscope also has a great deal of promise for developing more sophisticated NLO techniques including electronic-resonance-enhanced multiple mixing, induced Raman scattering, and syphon photography. The development of methodological and investigative approaches is a key component of current advancements in both the biological and medical areas. The detection of the processes that cells engage in their natural and dynamic environments has become one of the most crucial issues in recent years related to cell biological applications.

The findings of the investigation of the macroscopic properties of the cells have improved thanks to the use of fluorescence microscopy. Particularly, the traditional light of microscopes has made it possible to observe fixed or living cells more quickly and directly, as well as to use several imaging modes, notably fluorescent. The study of the mechanical characteristics necessitated the invention and evaluation of new techniques, just as optical techniques were important for the biological decoding of cellular activities. Atomic force microscopes (AFM) were one of the most significant of them. AFM's greatest strength was its ability to do nondestructive measurements, together with good lateral resolution and the "liquid mode," which mimicked the environment found in biological material.

Numerous papers concentrated on the use of systems that permitted sample observation in both optical and AFM modes. More specifically, by employing an inverted microscopic configuration, it was possible to map the surface of the same sample from above using an AFM probe and to analyze the sample from below due to the transparency of biological samples. The "fluorescence-AFM" hybrid technology was unquestionably depicted as an AFM installed on an upright optical microscope. Following that, sample tests might be made in a variety of places and circumstances. Observations using light, alternative interface difference, phase contrast, fluorescence, confocal, or total internal reflection fluorescence have all been made possible by this method at the same time. Numerous parallel investigations have been undertaken in the past. It indicates that the same item was examined by two different instruments, one after the other. Due to the challenges this method entailed, it was required to connect the data collected using the second technique to the results of AFM manipulations. AFM acquisitions were collected concurrently with pictures taken using phase interference, epifluorescence, and transmitted light microscopy (Nagao and Dvorak, 1998). Among these, the combination of AFM and fluorescence microscopy brought about a significant advantage for the decoding of bioprocesses in terms of mechanical and morphology alterations of the molecules and labeling of cellular components.

High-resolution topographies were simultaneously supplied by the AFM. Additionally, a selective tracking of the particular membrane components that had previously been designated with the proper fluorochromes was established using fluorescence microscopy. To display the structure, differential interference contrast microscopy was typically used. The tip was also functionalized in their experiment to identify the membrane receptor SRBI, which was tagged with a fluorescent probe and viewed using fluorescence microscopy. A precise location of the protein targets was made possible by combining the photographs. There are two basic processes

in the construction of fiber-based optical probes: A transparent contour with a pointed apex is made, and then aluminum is added to the surface to create an opaque layer on the cone's walls and a transmissivity hole at the tip. The "boiling and tugging" technique and biological engraving are the two techniques for creating tapering visual fibers with a piercing point besides a suitable pinecone approach.

The heating and dragging technique works by first pulling the fiber apart and then locally heating it with Laser energy or a filament. The degree of hotness and time of warming and dragging, as healthy as the size of the animated part, have a significant impact on the tip shapes that are created. The pulling technique has the benefit of a very smooth glass superficial to the flame, which enhances the quality of the vanished metallization. Turner's etching technique made the mechanical etching of optical fibers in HF solutions mainstream. The fiber is submerged in an HF solution and then coated with an organic solvent. At the meniscus that develops at the thread's contact amongst High Fluorensce and flush, tips are formed. The meniscus height's relationship to the remaining fiber diameter serves as the foundation for the mechanism. Chemical etching makes it possible to produce larger numbers of probes in a single process with greater reproducibility, paving the way for "mass manufacturing" of optical probes on a laboratory scale. Selected applications, including phase and amplitude components,are defined, and fluorescence imaging, Raman spectroscopy, and near-field optical decomposition are provided to highlight the technique's potential. These examples show that scanning near-field confocal microscopy has developed into a useful technique and is no longer an uncommon technique.

The optical probing should incorporate two key characteristics to provide the best performance in aperture SNOM: The aperture diameter-based spot size should be as tiny as possible. The light intensity at the lens should be as great as possible at the same time. This can be done by either increasing that maximum input power or by either increasing the metal coating's damage threshold or total light throughput. Finally, it should be as convenient as practical to supply light to the area around the aperture. Aperture probes made from common optical fibers are a good fit for this purpose. The optical scanning should have the following two features to work optimally in aperture SNOM: The plot size based on the opening width will be as insignificant as conceivable. The lens should receive as much light as is simultaneously possible. This can be accomplished by raising the metal coating's damaging threshold, total light throughput, or maximum input power.

The light should be supplied to the area around the aperture as conveniently as is practicable. For this use, optical fiber-based aperture probes are an excellent fit. In the far field, the aperture's power output is frequently measured. The no propagating field constituents at the opening will not affect the time-averaged Poynting vector, hence this is correct in theory. However, the immediate electronic grounds dominated light substance communication in practically all experimental circumstances. As a result, the near-field impacts of field enhancement are not reflected in the far-field transmission coefficient. On the other hand, knowing the far-field transmission ratio can be helpful when comparing tips with the same aperture size. The properties of a conical tip are governed by the two primary structural elements: the component that directs light toward the area around the subwavelength aperture. The guiding portion of conventional fiber probes is a tapering, metal-coated dipole waveguide. The mix of propagation modes in the curved waveguide determines how well light is guided to the aperture. Figure 1 shows the overall process of optical microscopy.

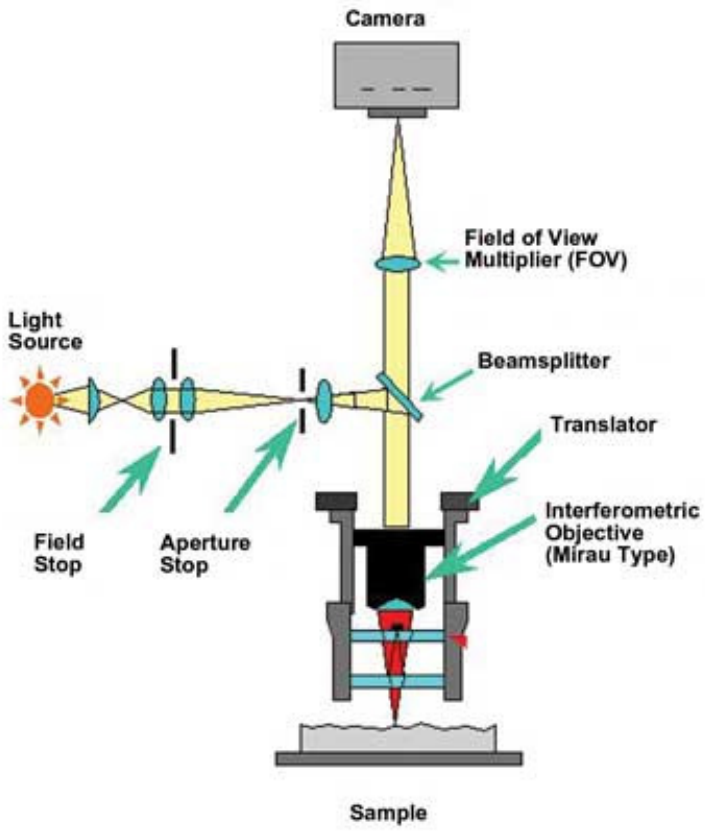

Figure 1: Depicts the overall process of optical microscopy.

3. CONCLUSION

Adaptive optics, a technique initially created for planetary observatories, has remained adapted to the electron microscope process to recuperate deflection limited imaging presentation profound within existing material. This technique may adjust for the deviations presented by organic samples. This automation has remained utilized, in particular, to enhance the picture excellence or to offer an additional precise definition of together the anatomy and occupation of neurons in a range of active creatures. Among its numerous accomplishments, adaptive optical microscopy has enabled the imaging of The resolution of synaptic connections over 500 meters deep in the brain area, the enormous regions with chromatic aberration resolutions in vertebrate embryonic brains, and the more accurate definition of the orientation adjustment properties of ventricular boutons in the primary retinal cortex of waking pests.

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CHAPTER 13

RISK FACTORS, DIAGNOSIS, TREATMENTS OF AUTOIMMUNE DISEASES WITH EMPHASIS ON MODERNTECHNOLOGIES

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ABSTRACT:

There are significant and growing unmet clinical requirements in autoimmune diseases, which are brought on by the immune system's mistaken host targeting. Generally speaking, modern medicines are non-disease specific and have a broad spectrum of effects, which leads to a variety of adverse effects. Autoantibodies then target normal cells, causing harm to bodily components and causing autoimmune illness. An autoimmune disease can affect one or more types of human tissue by causing the body's immune system to target healthy cells. There is a critical need for precise and prompt intervention techniques. There is no specific cause for autoimmune diseases; they have a relapse and recurring trends and thus are challenging to recognize since various diseases have varied potential signs and individuals' symptoms vary. Therefore, here the present paper provides a comprehensive approach to the fundamentals of autoimmune diseases. In addition to that, the author also provides a discussion on recent trends, opportunities, challenges, and future perspectives for the treatment and management of autoimmune complications.

KEYWORDS:

Autoimmune Disease, Autoantibodies, Immune System, Diabetes.

1. INTRODUCTION

An autoimmune disease develops when the body's immune system, which defends the body from disease, misidentifies healthy cells as alien and undesirable cells. A mistake can cause the body to fail to distinguish between foreign and self-cells, resulting in autoantibodies. Autoimmune diseases can affect almost any part of the body, including the nerves, heart, brain, lungs, joints, skin, lungs, and eyes [1]. As opposed to SLE (Systemic Lupus Erythematosus), which can damage the skin, blood vessels, heart, kidneys, joints, and other organs, type 1 diabetes can have an impact on the kidneys, eyes, glands, muscles, and more. The exact etiology of autoimmune disorders is not known. Infections (bacteria, viruses, medications, chemical irritants, etc.) or other environmental variables can trigger some immunological conditions. On the contrary hand, several autoimmune conditions tend to advance genetically that can be triggered by an outside intrusion. Autoimmune diseases come in approximately 80 different varieties. It is difficult to determine whether this illness may be present because so many of them exhibit identical symptoms [2]–[4]. Inflammation, which can result in fever, exhaustion, swelling, discomfort, and redness, is a typical sign of an autoimmune illness.

The symptoms of autoimmune disease vary depending on which bodily organ has been attacked. In Graves' disease, for example, the targeted body component is the thyroid, which leads to weight gain, muscular pains, and fatigue. Skin is compromised in systemic sclerosis, systemic

lupus erythematosus (SLE), and vitiligo, causing blisters, color changes, blisters, and rashes. Because there is no effective medication for autoimmune illnesses, the current therapeutic practice focuses on alleviating symptoms and preventing complications. Examples of the most frequent autoimmune diseases include: A person might have many autoimmune disorders at the same time. However, based on published studies and original data gathered from smaller nations with superior epidemiological resources, researchers have estimated the incidence of autoimmune diseases in the US. According to these projections, there are 10 million persons in the US who are affected by all autoimmune diseases together as shown in Figure 1 [5].

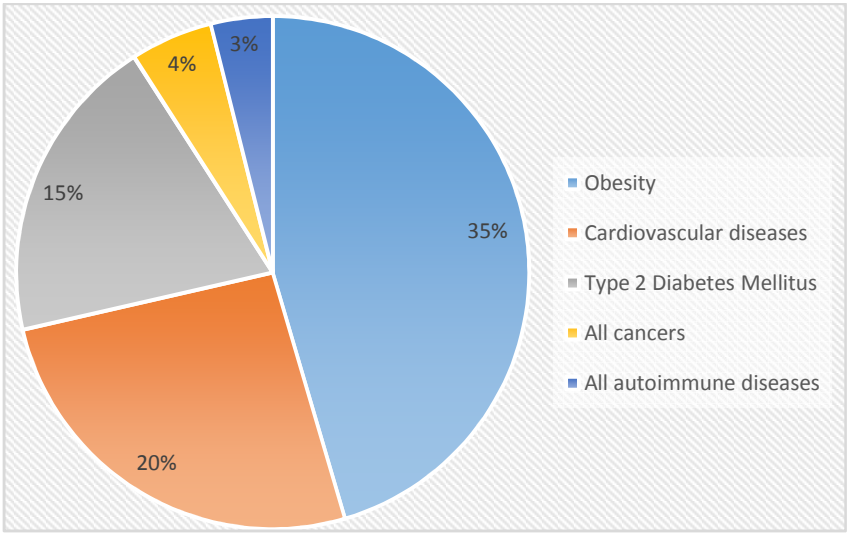

Figure 1: A Graphical Representation of the Prevalence of Different Diseases in the U.S. Population by Percentage.

At least one autoimmune disease affects 4% of individuals worldwide, according to estimates. The number is almost double that in the US. Men and women experience these diseases at differing rates (see "Balance of the sexes"). Additionally, there are disparities between the sexes in the severity and timing of symptoms [6], [7]. Some of the initial hypotheses to account for these differences centered on sex hormones, which control the innate and adaptive immune systems via a variety of routes and receptors on immune cells. Hormones may aid in understanding why some patients with autoimmune diseases experience an improvement or worse in their symptoms in response to changes in hormone levels, such as those that occur during puberty, pregnancy, and menopause. Women with multiple sclerosis, for instance, report a 70% decrease in relapses during the second part of pregnancy, when estrogen levels soar. However, symptoms often return after giving birth when estrogen levels fall, and women with lupus never have this respite.

The hormone idea, however, is disputed. Some scientists hypothesize that sex chromosomes may be at blame. Even though all the mice are genetically altered to have the same sex organs and hormones, two X chromosome mice acquire diseases like lupus more commonly than XY mice do in research on animals. In addition, men with Klinefelter syndrome, who have an additional X chromosome, also experience similar levels of lupus and Sjögren's syndrome development as women. The current review paper is divided into a total of five sections where the first section provides the significance of carrying out the study with a little introduction about the topic. The

second section provides a literature review. In addition, another section provides the methodology used to retrieve the relevant records for carrying out the review study. The fourth section provides the future recommendation for use followed by the conclusion in the final fifth section

2. LITERATURE REVIEW

Yasuda et al. discussed the modulation of Th17 development and chronic tissue inflammation by pathogenic Th17 cells in animal and human models of autoimmune disorders was reviewed, as well as the involvement of proinflammatory cytokines and environmental factors. The control of pathogenic Th17 cells by intestinal microbiota and immunometabolism in rheumatoid arthritis is another new development they emphasize [8].

Conrad et al. sought to establish if and to what degree this was true for a wide spectrum of autoimmune diseases. They put together a cohort of up to five people who were similar in terms of age, sex, socioeconomic position, area, and year of birth and who were free of cardiovascular and autoimmune disorders up to 12 months following study admission. These findings call for more investigation into the pathophysiological processes behind these consequences as well as specific cardiovascular preventive interventions, especially in younger patients with autoimmune disorders [9].

Salvi et al. looked examined how changed miRNA levels affected the production of many cytokines, including IL-10, the IL-17/IL-23 axis, type I interferons, and main pro-inflammatory cytokines, which all have important pathogenic roles in autoimmune disease.

Regulation might be "direct" on the targeted cytokines or "indirect," where a specific miRNA post-transcriptionally controls the production of a protein, which in turn affects the amount of the cytokine.

Additionally, miRNAs linked to extracellular vesicles can control cytokine secretion in adjacent cells whether post-transcriptionally or by activating innate immune RNA sensors [10].

Zhou et al. suggested that circRNAs play a crucial part in intricate human diseases. Notably, the prevalence and progression of autoimmune disorders are significantly correlated with circRNAs, crucial immune system gene modulators. Intending to shed new light on the diagnosis and treatment of autoimmune diseases like multiple sclerosis (MS), systemic lupus erythematosus (SLE), primary biliary cholangitis (PBC), rheumatoid arthritis (RA), psoriasis, authors concentrate on the positions of circRNAs in the immune system and immune regulation [11].

Hedman et al. assessed the strength of the connections for the reciprocal links between autoimmune diseases and EDs. Swedish registries were connected to create a cohort of more than 2.5 million people for their population-based study that was conducted nationally. It was shown that there was a significant, bidirectional association between the two sickness groups, meaning that having a diagnosis in one illness class raised the likelihood of having one in the other. The results of the study demonstrated the links between EDs and autoimmune disorders are supported by their interactions. The two-way risk pattern seen in females points to either a common mechanism or a third mediating factor that contributes to the relationship between these disorders [12].

3. METHODOLOGY

The data for this review was found and gathered using electronic resources such as Scopus, PubMed, Science Direct, Research Gate, and Google Scholar. A variety of crucial keywords were used to discover and arrange relevant literature. More information on the strategy used to discover relevant data can be seen in Figure 2.

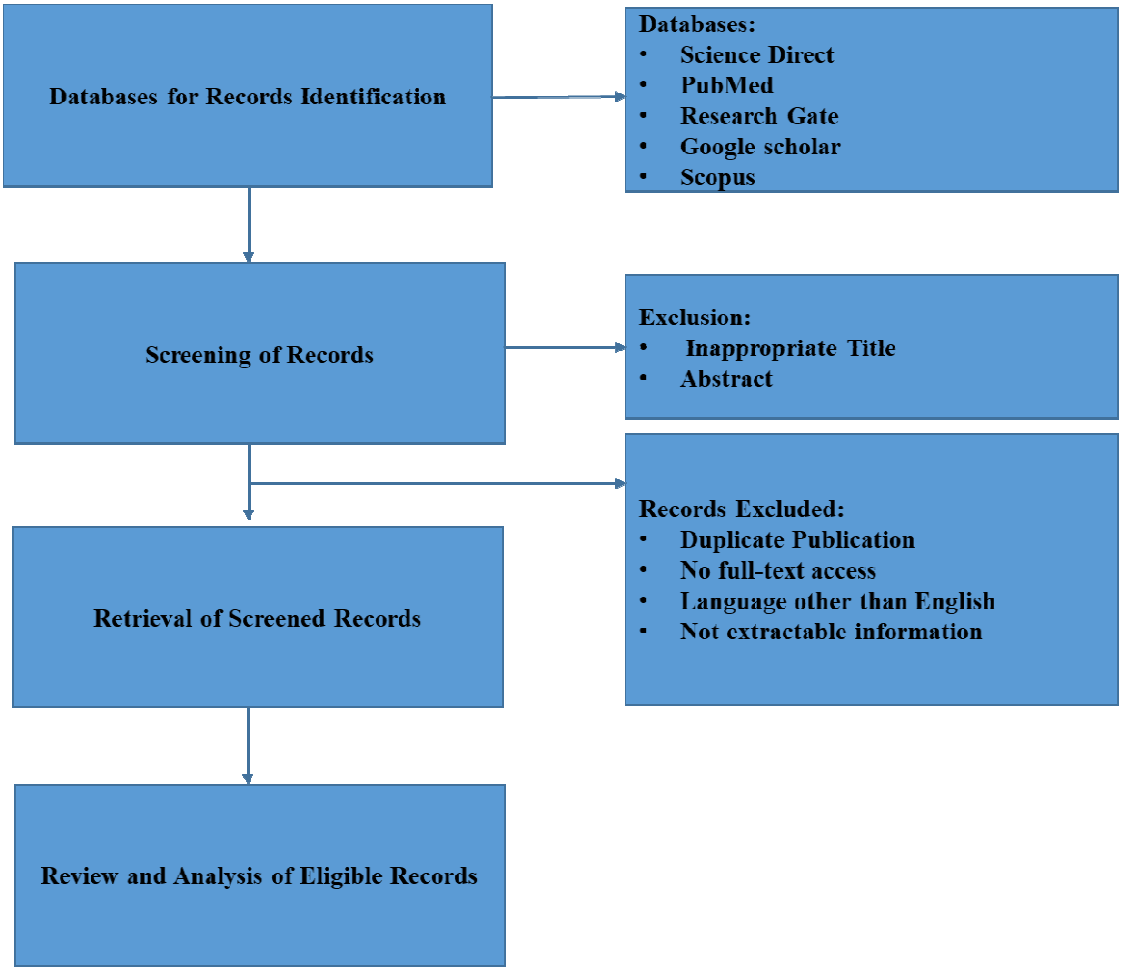

Figure 2: Illustrating The Methodological Design Used To Retrieve Relevant Publications.

4. DISCUSSION

In promoting, developing, or moderating autoimmune diseases, environmental influences may play a variety of functions. If and when particular environmental variables cause autoimmune disorders, they may well influence how quickly symptoms appear, how they appear initially, or even if an autoimmune disease that is present internally in a person will ever show. Among the most significant initiators influencing the onset and kind of an autoimmune condition is the environment. A particular mix of different chemicals, infectious agents, medications, and immunizations can define the type of condition in one person, in an autoimmune-prone family. The Factors affecting the development of autoimmune disease are illustrated in Figure 3.

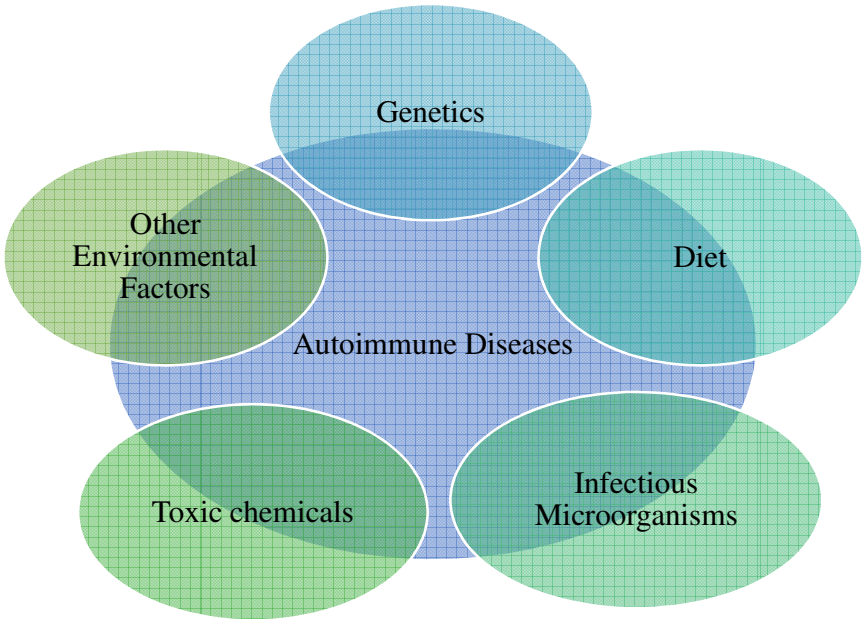

Figure 3: Illustrating the Factors Influencing the Development and Progression of Autoimmune Diseases.

4.1.Risk Factors

*Smoking:*Tobacco use constitutes one of the most potent risk factors for autoimmune diseases. Tobacco has already been linked to systemic lupus erythematosus; the highest prevalence and proportions for present and previous smoke for disease development were determined to be 1.6. The link between smoking and rheumatoid arthritis is becoming increasingly recognized. Smoke combines with genetic risk factors such as HLA-DR alleles, resulting in a 21-fold increase in disease risk. Cigarette smoke can lead to autoimmunity through a variety of processes, including the formation of free radicals, the release of metalloproteinase, and the stimulation of Fas expression on lymphocytes. Smoking causes an inflammatory response by increasing fibrinogen levels, inducing leucocytosis, and elevating intercellular adhesion molecule, C-reactive protein.

*Infections:*Possible mechanisms, involving viral replication damage, molecular mimicry, bystander activation, antigenic dissemination, production of cryptic self-peptides, and the adjuvant effect, have been hypothesized for just how infectious diseases might cause autoimmune disease. The idea of molecular mimicry holds that whenever an infection takes place, autoimmunity is produced, and the antigens of pathogenic microorganisms closely resemble self-antigens. Whenever the immune response is unintentionally activated by an infection, a condition known as bystander activation can take place. This condition causes autoimmunity to become active in those who are genetically predisposed to it. The adjuvant effect is a term used to explain the particular stimulation of the innate immune response by microbial antigens, such as when adjuvants are administered in vaccinations. Self-antigens can

be administered with adjuvants to experimentally create a variety of autoimmune illnesses, such as rheumatoid arthritis with collagen and myocarditis with cardiac myosin.

*Stress:*The body can suffer greatly from chronic stress, and it may even contribute to autoimmune disease. Constant stress can deplete the body of essential nutrients and put a strain on the intestines and neurological system. Over time, it may also weaken the immune system and cause problems with control. In recent research, more than 100,000 persons with stress-related diseases were examined. It was shown that those who had been given a diagnosis of a stress-related ailment were more likely to also have an autoimmune disease, and they were also more likely to have numerous autoimmune diseases.In addition to these autoimmune variables, such as gut bacterial disturbances and virus exposures, stress may also play a role.

Toxic Chemicals: The immune system assists in protecting us from external intruders, but when it is overburdened by pollutants and chemicals from the environment, complications may develop. Finding a single environmental toxin to blame for an autoimmune disease is quite difficult because there are hundreds of them. However, some studies indicate that some pollutants, like mercury, BPA plastic, and asbestos, could perhaps cause autoimmune disease.

Diet: A condition known as celiac disease can be brought on by gluten, a kind of protein present in various bowls of cereal including wheat, rye, and barley. Whenever the immune system produces autoantibodies towards gluten, these antibodies also target adjacent tissues, like the lining of the small intestine. Although the exact cause is unknown, molecular mimicry may be to respond. In addition to type 1 diabetes and other autoimmune diseases involving the thyroid gland, joints, skin, and neurological system, wheat and celiac disease are connected. There are, however, a large number of additional possible dietary triggers, particularly those that affect the immune system or gut flora.

*Genetic triggers:*There is a hereditary predisposition that runs in families with many autoimmune illnesses. The genes can increase the likelihood to acquire any autoimmune disease in principle or acquiring one or more particular disorders. A greater chance of getting coeliac disease eventually exists in those who screened positive for particular versions of the Coeliac HLA gene, for instance. People who tested negative for these variations, however, have a chance of acquiring it of less than 1%. For instance, one individual may have rheumatoid arthritis, while another person may have type 1 diabetes.

4.2. Diagnosis

Biomarkers are clinical indicators or the outcomes of laboratory tests that are associated with the beginning or development of an autoimmune disease. Thus, biomarkers show significant potential for earlier and more precise diagnosis of autoimmune diseases, greater forecasting of illness flare-ups, and enhanced tracking of disease progression and therapeutic response. Currently, some biomarker efforts are active.

Finding at-risk individuals before permanent organ damage takes place is one of the main objectives of autoimmune disease research. Recently developed assays have been used by researchers to identify lupus-related autoantibodies in serum, which are frequently present years before a patient has symptoms. Additionally, Epstein-Barr virus-reactive antibodies were discovered in blood samples from lupus patients, which further supports the theory that a virus may be the cause of lupus. High levels of T cells and autoantibodies in the blood were

discovered to be indicators of a fast course of the disease in another investigation of rheumatoid arthritis [13], [14].

4.3. Treatments and Emerging New Technologies

Since most autoimmune disorders presently lack treatment, patients commonly have to deal with lifelong, incapacitating symptoms, loss of organ and tissue function, and expensive medical care. Therapies for many autoimmune diseases aim to lessen long-lasting symptoms and immune system activity while keeping the immune capacity to combat external invaders intact. Depending on the exact ailment and the symptoms, many treatments are available. People with Type I diabetes, for instance, need to restore their insulin levels, typically by injections. Patients with autoimmune disorders like Type I Diabetes could require supplements to provide their bodies with the hormones or vitamins they're missing [15], [16].

The majority of autoimmune disorders have treatments that lessen symptoms, but permanent cures have not yet been discovered. There are now two main types of therapy methods accessible. The first entails replacing or correcting the damaged function. Patients with type 1 diabetes mellitus, for instance, might take insulin to make up for the hormone that their impaired pancreatic islet cells are unable to generate. Thyroid-stimulating hormones are also effective in treating people with autoimmune thyroiditis. Even though the individual may experience remission when undergoing symptom-based therapy, such treatments do not stop the auto-immune process. Nevertheless, the patient will often need replacement therapy for the rest of his or her life. A diseased organ may occasionally be replaced by transplantation. For instance, researchers are now examining the efficacy of islet cell transplantation as a diabetic therapy. Patients who have dilated cardiomyopathy or end-stage renal disease may be eligible for a kidney or heart transplant. Stem cell therapy may one day make it possible to replace or repair damaged organs. The likelihood of a satisfactory outcome from replacement treatment is highest when the reduced function is restricted to a single organ system.

Autoimmune disease study is now utilizing several innovative technologies. For instance, the application of microarray techniques that show patterns of gene expression in clinical specimens allows us to define pathological conditions at the molecular scale. Scientists can evaluate the state of proteins in tissues and antibodies in blood by studying the form, function, and expression patterns of proteins, or through a process known as proteomics. Researchers may collect a lot of genomic and proteomic data using high-throughput technologies, and they can also keep track of the biological reactions and activities of the systems they are studying. T cells may now be sorted and analyzed depending on their identification of particular antigens thanks to devices called MHC-tetramers.

These potent tools are being used more frequently in clinical research as well as at the lab bench. Finally, several sophisticated computational tools are required for the mining and analysis of the data obtained from such investigations. Results from these strategies are starting to emerge in the detection and treatment of cancer. Although only getting started, a focused effort to use these technologies to treat the family of autoimmune illnesses has enormous potential. The discovery of disease susceptibility and resistance genes will proceed much more quickly now that the reference human genome sequence is available. It will also be crucial for understanding the genetics of autoimmune illnesses to continue attempts to comprehensively sequence the genomes of animal models, such as the mouse and rats.

5. CONCLUSION

Regarding the particular genesis of the majority of autoimmune illnesses, there are still many unanswered concerns. Scientists in the field are still unable to determine the precise nature of the inciting antigen, the regulatory processes that control the onset and scope of the autoimmune response, the processes through which spontaneous periods of remission and flare-ups occur, the role of environmental exposures and also how they trigger and propagate autoimmune reactions and the individuality and mode of action of genetic makeup that makes a person more susceptible or accelerate autoimmunity. Future research initiatives will be focused on these important concerns.

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CHAPTER 14

EMPIRICAL STUDY OF THE MOST WIDELY USED TECHNIQUES FOR FOOD PRESERVATION

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ABSTRACT:

The many methods used to keep food from going bad after harvest or slaughter. They have been practiced since the Stone Age. Techniques for food preservation keep food safe and satisfying to eat in the future by avoiding bacterial development and other sorts of food degradation. Food may be preserved in a variety of ways, from the simple act of freezing to more complex procedures like canning the process of processing and treating food to stop or postpone food deterioration, loss of nutritional value, or edibility while allowing for extended food storage. To preserve anything, you must postpone the oxidation of potentially rancid lipids and stop the development of bacteria, fungi, and other organisms. The many methods of food prevention are the topic of this research. Several creative options let you experiment with ingredients at home or sell food in various packaging. Food preservation keeps harmful microorganisms to a minimum, maintains food quality, and lowers expenses for both domestic customers and commercial sectors. Chemical Additives and Radiation: Irradiation and chemical additives are two potential food preservation techniques in the future.

KEYWORDS:

Bacteria, Chemical, Food, Food Preservation, Microbes.

1. INTRODUCTION

Food preservation is one method for avoiding the growth of undesirable germs on food. We cover the rice and curries with lids after the dinner is prepared to preserve them as well as safeguard them and keep flies and other insects out. By doing this, we are protecting it from any sickness that it could cause. This condition is temporary. Contrarily, food preservation is done to keep food fresher for a longer period of time the process of processing and treating food to stop or postpone food deterioration, loss of nutritional value, or edibility while allowing for extended food storage.

Preserving requires postponing the oxidation of potentially rancid lipids as well as preventing the development of bacteria, fungi, and other microorganisms. It may be summed up as the method by which we manage and treat food to reduce or eliminate food loss in terms of quantity, nutritional content, and edibility. We can preserve food for a longer period of time thanks to food preservation. To preserve anything, it is often necessary to stop the development of bacteria, fungus, and other microbes. By using techniques like salting, drying, etc., this form of food preservation is employed for a variety of food items including fruits, vegetables, meat, and fish [1]–[5].

1.1.Methods to Preserve Food and Causes of Food Spoilage:

1. The expansion of insects or germs like bacteria, fungi, etc.
2. Enzymes, which are proteins, are present in all plants and animals.
3. Rancidity or color changes are brought on by oxidation by air.
4. Physical (freezing, burning, drying), chemical, biological, and environmental elements all contributed to the modifications.
5. Spoilage affects food safety, nutritional value, and organoleptic quality (smell, touch, taste, and appearance).

1.2.Preservation of Food Is Important:

Although some methods work by contaminating the food with benign bacteria or fungi, food preservation prevents the growth of microorganisms (like yeasts) or other germs and postpones the oxidation of lipids that lead to rancidity [1], [6]–[9]. Food variety is increased via food preservation. For instance, during the sweltering summer, canned or dried peas could be substituted for fresh peas. Food preservation extends its shelf life. For a very long period, cherries, pineapples, and other fruits and vegetables may all be preserved using several techniques. Food preservation increases the availability of food. Food preservation helps to prevent food waste. When excess foods that might have otherwise gone to waste are processed and preserved, food waste is reduced. Food preservation makes it simpler to reduce nutritional inadequacies. The preservation of food helps to vary the diet. For instance, due to the dryness of the country, no vegetables are grown in several Middle Eastern nations. This deficit is filled by importing fresh and preserved fruits and vegetables. Preserving food primarily aims to prevent microorganisms from causing it to spoil.

Its guiding concepts are as follows:

1. Preventing microbes from getting into the food being preserved, or upholding asepsis
2. Getting rid of microbes
3. Restricting the development of microorganisms using a variety of techniques, such as low temperatures, drying, chemical usage, etc.
4. Using techniques like heating and radiation to kill the germs.

The oldest method of food preservation, salting, has been used for countless years. The most important intrinsic and extrinsic factors for food preservation are water activity (aw), temperature (low or high), and preservatives. These intrinsic and extrinsic components have limits when employed independently. However, each activity is significantly enhanced when combined with the others or utilized concurrently or consecutively. This effect is akin to a series of hurdles that get harder to overcome as more obstacles are added. A hurdle effect, a synergistic form of food preservation, is the final result. To fully comprehend the effects of these obstacles on microbial populations, extensive study has focused on establishing the critical constraints for the growth, survival, and death of the most significant microbes connected to the food supply. Thanks to the information provided, designing effective food preservation systems now has a strong foundation.

Due to the enzymes they contain, several dietary components may self-decompose. In these situations, the enzymes are turned off during food preservation. Some foods are also vulnerable to insects or other animals, therefore it is necessary to use the right chemicals to kill them and stop them from contaminating the meal. Food preservation lowers food waste, landfill waste, and environmental impact. It also benefits your cash and the neighborhood economy. It's surprisingly simple to can, dry, and freeze food with the right knowledge and practice.

2. DISCUSSION

Food preservation is the process of preventing edibles like fruits and vegetables from spoiling. The foods that have been preserved retain their original flavor, color, and nutritional value. This prolongs the shelf life of the food product and makes storage and supply possible. According to Wikipedia, food preservation is "the science that deals with the process of preventing food from decaying or spoiling so that it can be stored in a fit condition for future use." Food quality, edibility, and nutritional value are all guaranteed by preservation. The process of preservation involves delaying the oxidation of fats to lessen rancidity and inhibit the growth of bacteria, fungi, and other microorganisms (Table 1).

Table 1: illustrating the Various Methods and their Impact on Microbial Growth.

Methods	Impacts on Microbial Growth
Refrigeration	Reduced temperature to slow growth
Freezing	Freezing Low temperatures, decreased water activity, and slowed oxidation reactions inhibit microbial development.
Drying, curing, and conserving	Reduced water activity that is sufficient to postpone or stop microbial development
Vacuum as well as oxygen-free modified atmosphere packaging	Low oxygen tension prevents the development of facultative anaerobes and inhibits stringent aerobes.
CO_2-enriched and or modified atmosphere packaging	certain microbial species are inhibited
Addition of weak acids; e.g. sodium lactate	Microorganisms' internal pH is decreased
Lactic fermentation	pH value reduction caused by in-situ microbial activity, with additional inhibition sometimes provided by the lactic and acetic acids produced as well as other microbial byproducts. (Bacterocins, ethanol, etc.)
Sugar preservation	Cooking with a lot of sugar creates an osmotic pressure that is too high for most microbes to survive.
Ethanol preservation	Alcohol-based cooking or steeping results in harmful microorganism inhibition. it is possible to combine sugar preservation
Emulsification	Foods made from water-in-oil emulsions exhibit compartmentalization and nutrient restriction within the aqueous droplets.

Several food preservation techniques may be used to halt, delay, or otherwise significantly reduce food degradation. With the aid of preservers, food may be produced, maintained in storage, sold, and kept in the house of the consumer for a respectable period of time, prolonging its shelf life. A key component of food preservation strategies is keeping or generating nutritional value, texture, and flavor, even when certain procedures have dramatically altered the composition of the preserved foods. Many of these alterations, including cheese, yogurt, and pickled onions, are now seen as desirable traits. Any modification that renders food unfit for human consumption is referred to as food degradation. These alterations might be brought on by microbial contamination, insect invasion, or endogenous enzyme breakdown (those present naturally in the food). Food degradation may also be accelerated by physical and chemical changes, such as the rupturing of plant or animal tissues or the oxidation of certain food ingredients. Foods derived from plants or animals quickly lose their nutritional value after being harvested or slaughtered. Any mechanical damage produced during postharvest processing may cause the enzymes that are stored in the cells of plant and animal tissues to be released. These enzymes disassemble the components of cells. Food quality declines as a result of the chemical processes that enzymes catalyze because of the emergence of bad tastes, degradation of texture, and nutritional loss.

When it comes to keeping food from going bad after being harvested or slaughtered, the term "food preservation" refers to a broad variety of techniques. These customs have existed since the dawn of mankind. the process of processing and treating food to stop or postpone food deterioration, loss of nutritional value, or edibility while allowing for extended food storage. In order to preserve anything, you must postpone the oxidation of potentially rancid lipids and stop the development of bacteria, fungi, and other organisms. Drying, chilling, and fermentation are some of the oldest methods of preservation. Canning, pasteurization, freezing, irradiation, and chemical addition are only a few examples of contemporary techniques. Modern packaging advancements have significantly improved food preservation.

2.1. Categories Food Preservation Techniques:

One of the aforementioned categories best describes the frequently used food preservation techniques [10]–[13]. The main goal of all these techniques is to either stop or delay food from spoiling as shown in Figure 1.

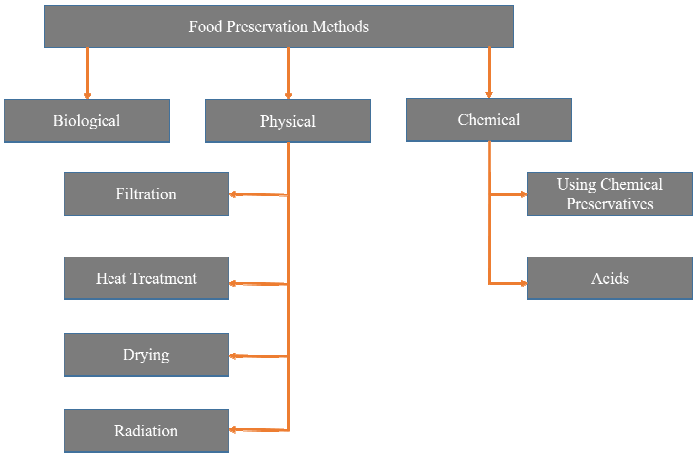

Figure 1: Illustrating the Three Main Categories of the Food Preservation Methods.

2.1.1. Filtration:

Juices and other liquids get this treatment. The liquid is forced through an extremely tiny sieve as part of the procedure. As a consequence, the resultant liquid is sterile since the liquid may pass through but the microorganisms cannot.

2.1.2. Heat therapies

Several heat treatments may be used, such as pasteurization, boiling at or above 100 degrees Celsius, and sterilization (as done in the case of milk)

2.1.3. Use of low-temperature therapies

The approach that is most often employed, even in homes, involves a refrigerator. The low temperature that the refrigerator maintains inhibits the development of microorganisms and prolongs the freshness of food. Another low-temperature technique for food preservation is freezing, which keeps the temperature at -18 degrees Celsius.

2.1.4. Using preservatives or chemicals

These are additives that are put into food to stop or delay deterioration. Before being approved for use as food preservatives, additives must meet several requirements. Preservatives should be able to block a broad variety of bacteria, be safe for ingestion by humans, and not modify the taste, flavor, color, or other characteristics of the food being preserved. They also shouldn't cause any other changes to occur in the food being preserved. Sulfites, sorbic acids, sodium nitrate, and benzoic acid are all frequently used preservatives.

2.1.5. Acids

Common organic acids used to preserve foods including pickles, sauces, chutneys, and vegetables include citric acid and acetic acid. They are good food preservatives because of their acidic nature, which prevents the development of microorganisms.

2.1.6. Dripping

Many items, including chips, papad, and vegetables like methi or ginger, are preserved by drying or dehydrating them. By removing the moisture from these materials during dehydration, microorganisms are unable to grow on them, protecting them from deterioration.

2.1.7. Radiation

Meat, fish, and poultry are routinely preserved using this technique to extend shelf life. These dietary ingredients are exposed to radiation, which helps eradicate any diseases and bacteria that may be present there and stop the spread of more. People have sought to preserve their food and other perishable goods for centuries. Although the techniques have changed or developed, the goal has not altered.

2.1.8. Crystallization

Sugar is used to preserve fruits, either as fruit syrup (for apples, peaches, and apricots) or in crystallized form, which involves boiling the fruit in sugar until it crystallizes and storing it in a dry environment.

This method may be used to process citrus (candied peel), ginger, as well as angelica peels. When producing glacé fruit, such as glacé cherries, this process is adjusted such that the fruit is first preserved in sugar before being taken from the syrup and sold, preserving both the fruit's sugar content as well as the thin syrup coating. Brandy and other alcoholic drinks sometimes include alcohol and sugar to preserve expensive products like fruit. These shouldn't be confused with alcoholic beverages that contain additional fruit scents, such as cherry brandy.

2.1.9. Smoking

Food that spoils quickly is smoked to increase shelf life. This result comes from exposing food made from burning plant materials, like wood, to smoke. The majority of the time, cured fish and meat are preserved using this method. Although mostly for cooking or flavoring, smoking is also done on cheeses, spices, and drink ingredients like malt and tea leaves. Fruits and vegetables like paprika are also occasionally done. It is believed to have emerged after the invention of cooking over fire and was one of the first methods of food preservation.

2.1.10. Additives

Food preservative additives may be antimicrobial. These prevent the development of bacteria or fungi, including mould, whereas antioxidants, such as oxygen absorbers, prevent the oxidation of food ingredients.

2.1.11. Pickling

A food preservation technique called pickling uses a palatable antibacterial liquid. Chemical pickling and pickling by fermentation are the two basic categories into which pickling may be split.

2.1.12. Canning

Cooking the food, putting it in sterile canisters or pots, and then sterilizing the containers by boiling them to kill or weaken any microorganisms is called canning. Foods may need the last step in a pressure cooker since they have varied degrees of natural spoiling prevention. High-acid fruits like strawberries need just a brief duration of boiling and no preservatives, while marginal foods like tomatoes need longer boiling times and the inclusion of additional acidic ingredients. Low acidity feed ingredients like vegetables and meats call for canning pressure. After opening the can or bottle, food preserved by canning or bottling is immediately in danger of spoiling.

2.1.13. Pasteurization

It is described as the fast cooling to 7°C after heat treatment of food material at 72°C for 15 seconds, 63°C for 30 minutes, or 90°C for 0.5 seconds. Because they cause less harm to the nutritious content and sensory qualities of meals, high-temperature-short-time (HTST) treatments are preferred over low-temperature-long-time (LTLT) therapies.

2.1.14. Sterilization

Sterilization fully eradicates microbes. Unlike non-acidic vegetables, which must be sterilized at 116°C for 30 minutes, fruits and acidic vegetables, such as tomatoes, may be sterilized at 100°C for 30 minutes.

2.1.15. Freezing

When kept at 4°C or below, many food items may have their shelf life increased. Meats, eggs, dairy products, fresh fruits and vegetables, and dairy products are all often refrigerated goods. Low temperatures, however, may be destructive to certain things, such as tropical fruits (bananas, for instance). Foods' nutritional content may be preserved quite well by freezing. It takes place between -18°C and -4°C in temperature. Most juices are preserved by freezing.

2.1.16. Dehydration

To preserve food items, dehydration is the act of taking the moisture out of them. Dehydration occurs at a temperature that begins at 43°C and subsequently increases to 60–66°C for vegetables and 66–71°C for meat (for fruits).

2.2. Microbes that cause disease

Consuming tainted foods or drinks results in foodborne disease. Foods may be contaminated by a wide range of pathogens or disease-causing bacteria, leading to a wide range of foodborne diseases [14]–[18]. Foodborne illnesses are typically caused by bacterial, viral, and parasitic infections. Food poisoning caused by harmful toxins or substances is another illness. It should be noted that a significant number of foodborne pathogens can also be contracted through contact with animals or their surroundings, drinking or recreational water, or through person-to-person transmission. Food preservation has been crucial to human survival since the dawn of time because it increases the stability and safety of different meals. The modern food industry still preserves food using age-old techniques like heating, drying, fermenting, and salting. Since then, there has been a significant advance in the knowledge of the main factors contributing to deterioration, which has reduced losses from food contamination and spoilage.

When a meal is unspoiled and non-sterile compared to the same rotten food, the food's microbial profile differs significantly. The first case often includes a wide variety of microorganisms, including viruses, yeasts, moulds, and bacteria from several genus, maybe from more than one species, and even from the same species in many strains. When the same food spoils, it is discovered to have mostly one or two varieties, and they could not even have been present at all in the unspoiled or fresh product. Only those species with the shortest growth times under storage circumstances among the several species originally present and capable of growing in a certain food reach the numbers quickly and cause spoiling. Food degradation refers to any change that renders food unfit for consumption. These alterations may be caused by a variety of factors, including endogenous enzyme breakdown, insect invasion, and microbial contamination (those present naturally in the food). Physical and chemical changes, such as the tearing of plant or animal tissues or the oxidation of certain food components, may also promote the degradation of food. Foods manufactured from plants or animals begin to degrade shortly after harvest or slaughter. The enzymes that are housed in the cells of plant and animal tissues may be released if there is any mechanical damage caused during postharvest processing. The biological elements begin to dissolve as a result of these enzymes. The chemical reactions that the enzymes catalyze cause food quality to decline, which includes the appearance of unpleasant flavors, degradation of texture, and loss of nutrients (Figure 2).

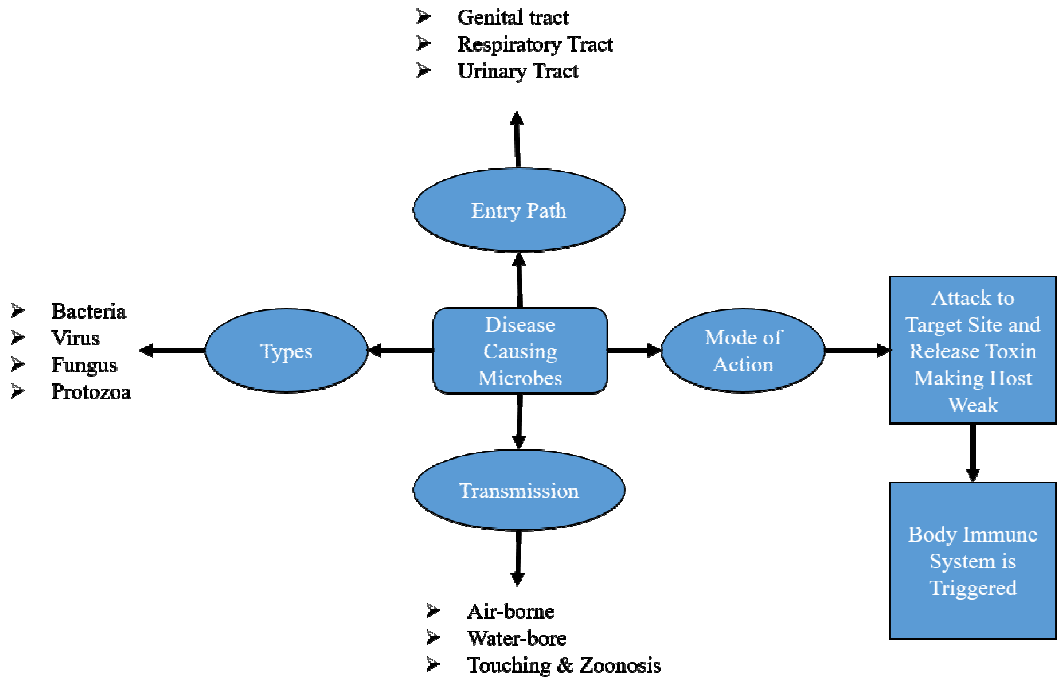

Figure 2: Representing the Disease Caused by the Microbes.

2.3.Benefits of food preservation:

Food preservation is advantageous since it enables us to safeguard the food's nutritional content and avoid deterioration [19]–[21]. It prevents food-borne microbe growth, survival, or reproduction. The quantity of enzymes and poisons produced by bacteria decreases as their activity diminishes. As a consequence, regardless of the season, food may be preserved longer. Various microorganisms' life circumstances are altered during preservation using physical, chemical, biological, or a combination of these techniques to hinder or entirely stop their growth and reproduction.

1. Food preservation stops enzymes and bacteria from causing the food to deteriorate.
2. Food preservation lengthens the time that food may be stored safely.
3. It makes goods that are out of season more readily available.
4. It promotes the accessibility of different meals, even in remote and difficult-to-reach locations. In other terms, it facilitates the delivery of food ingredients.
5. Food preservation compensates for dietary deficits.

3. CONCLUSION

Food preservation keeps harmful microorganisms to a minimum, maintains food quality, and lowers expenses for both domestic customers and commercial sectors. To mention a few, techniques for preserving food include smoking, canning, chemical processing, and sugaring. Food may be preserved in a variety of ways, from the simple act of freezing to more complex procedures like canning. A lot of them are creative options that let you experiment with

ingredients at home or sell food in a variety of packaging. Others help you preserve your inventory in a commercial kitchen for a lot longer, reducing waste and increasing revenue. We should always consume fresh foods without additional preservatives if we want to maintain excellent health. Only a few items need to be preserved, such as potato chips and rice chips, which are done utilizing antiquated methods like sun drying and food preservation using castor oils, among others. Low-temperature preservation is preferable to other long-term preservation procedures because it is more successful at preserving the flavor, color, and nutritional content of food while being only somewhat good at preserving texture. It takes less time to preserve something, in comparison. There are additional methods of food preservation that make use of cutting-edge scientific techniques and can keep food for a long time. Food may be preserved in a variety of ways, from the simple act of freezing to more complex procedures like canning. A lot of them are creative options that let you experiment with ingredients at home or offer meals in a variety of packages. Others help you maintain your inventory in a commercial kitchen for a lot longer, reducing waste and increasing revenue. Irradiation and chemical additives are two potential food preservation techniques in the future. Even though these techniques are already in use, further growth and development are anticipated.

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CHAPTER 15

IN SILICO STUDY OF "PROTEIN KINASE C ALPHA" (PRKCA) USING VICINE FOR HEART DISEASE

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ABSTRACT:

Cardiovascular diseases (CVDs) are the major cause of death, accounting for 17.8 deaths globally per year. To create novel organically based pharmaceuticals, extensive study has been done on these botanicals as a consequence of the recent development of new knowledge of traditional medicines. Recent concerns about the side effects of synthetic medicines have led to a decrease in patient visits, drug abuse, and a disruption in the precise management of sickness. As a result, the current research intends to investigate the Vicine capacity to target the protein PRKCA, which is a key player in the onset and progression of cardiovascular disease. The calculating method utilized in this work, Autodock4, resulted in a negative binding energy of -6.87 Kcal/mol, highlighting the potential of PRKCA for the effective treatment of cardiovascular diseases.

KEYWORDS:

Cardiovascular Disease, Molecular Docking, Pharmacological, PRKCA, Vicine.

1. INTRODUCTION

The heart is the most important organ of the circulatory system since it pumps blood to the body's numerous organs. Heart disease refers to a variety of illnesses or syndromes that impair heart function. Critical health problems and even early death may result from any cardiac condition. In terms of causes of death, heart disorders come at the top. According to the "World Health Organization" (WHO), around 17.8 million people die each year from cardiac disorders, accounting for 31% of all fatalities. Of these, 85% are heart attacks. Therefore, it is crucial to identify cardiac disorders as soon as feasible [1], [2]. There are plenty of documents about patient healing signs after recurrent heart attacks. However, the latent that we require to help us predict similar potential consequences in seemingly stable adults are not being seen. For instance, according to the Indian Heart Association's figures, 50% of heart attacks occur in those under the age of [3], [4].

Both the heart and the blood arteries are affected by cardiovascular disorders (CVDs). In addition, 50% of Americans have some kind of cardiac disease. A person's lifestyle may need to be changed, or a doctor may prescribe medication, to treat heart disease. Treatment is much simpler when cardiovascular disease is caught early. Depending on the specific kind, various reasons may result in a distinct form of cardiovascular disease. For instance, atherosclerosis contributes to peripheral arterial disease and coronary artery disease. Scarring of the heart muscle, coronary artery disease, genetic diseases, or unfavorable pharmacological side effects may all cause arrhythmias. Age, infections, or atherosclerosis may all cause valve problems [5], [6].

The lock-and-key idea put out by Fischer, in which the ligand fits into the receptor like a lock or key, is an early explanation for the ligand-receptor binding process. This notion served as the foundation for the first known docking techniques, which considered the ligand and receptor as rigid things. The "induced-fit" idea put out by Koshland then advances the “lock-and-key” theory by asserting that interactions with the ligands cause the protein's active site to be continuously altered. According to this hypothesis, while docking, the ligand or receptor should be viewed as flexible. As a result, it might better capture the binding events than the rigid treaty [7], [8].

The protein kinase C (PKC) family of enzymes, which are selective for the amino acids serine and threonine, may be activated by calcium as well as the second messenger diacylglycerol. It is well known that members of the PKC family take part in a variety of cellular signaling pathways and phosphorylate a wide variety of protein targets. PKC family members serve as crucial phorbol esters receptors, a type of tumor promoter. Each member of the PKC family has a distinct pattern of expression and is assumed to have a different role in cells. This gene encodes a protein that belongs to the PKC family. This kinase has been associated with a wide range of biological processes, including cell adhesion, cell transformation, cell cycle checkpoints, and cell volume control. According to mice knockout investigations, this kinase may be a fundamental regulator of cardiac contractility and Ca (2+) processing in myocytes [9], [10].

For the ligand-receptor binding process, they provide a heterogeneous parallel molecular docking strategy in this work. The rigorous and accurate binding free energy landscape is the goal of the ligand-receptor binding procedure. The binding pocket of the receptor is split into subcubes (lattices), the ligand is docked into each lattice, as well as the binding configurations are produced within the lattice to model the ligand-receptor binding process.

With fewer myocytes, the heart cannot continue to contract efficiently. Apoptosis is one of the primary mechanisms causing cardiomyocyte loss in failing hearts in both human patients and animal models. Anti-apoptosis has been introduced as a provocative new paradigm for both preventive and therapeutic approaches for CVD, even though the underlying cause and pathophysiological relevance of apoptosis remain unclear.

An attractive method for preventing or treating heart failure may be the selective inhibition of Protein kinase C alpha” (PRKCA) proteolytic activity [11]. Diuretics, ACE inhibitors, and beta-adrenergic receptor blockers are just a few of the drugs used to treat and control the effects of heart failure. Some adverse effects, nevertheless, make them difficult to use and difficult to control. Consequently, chemicals from natural sources, particularly those of plant origin, are currently being investigated to contribute to the creation of medications that are successful in preventing CVD [12], [13].

The rest of this research is divided into the following sections: The parallel scheme for the ligand-receptor binding process is proposed in Section 2, along with implementation details for the parallel scheme. Section 2 also provides a short description of the molecular docking for the ligand-receptor binding process. The experimental findings made possible by the parallel programs that are presented are described in Section 3. Section 4 provides findings and recommendations for further study.

2. LITERATURE REVIEW

Swagatam Sahoo et al. studied examining the capacity of Santalol to target the protein CD36, which is important for the onset or development of atherosclerosis. To create novel organically based pharmaceuticals, much study has been done on such botanicals as a consequence of the recent development of new knowledge of traditional medicines. The potential of -Santalol for the efficient treatment of cardiovascular disorders like atherosclerosis is highlighted in this study by a calculation technique utilizing Autodock4 that indicated negative binding energy of 9.10Kcal/mol. The results of this study still need to be confirmed by both in vivo and in vitro experiments, however.

Diwakar Chauhan et al. studied a docking process between the Cox-2 target structure as well as the selected phytochemical terminic acid. When the oxygen supply to the heart muscle is inadequate in one or more locations, a myocardial infarction occurs. Due to expensive medication, its management becomes prohibitively expensive in impoverished countries. Additionally, the unforeseen side effects of the medication used to treat myocardial infarction highlight the necessity for alternative medicine research. Future use of the protein in the therapy of myocardial infarction may be made possible by the initial posture of both the protein as well as the ligand combination, which demonstrated binding energy of -7.79 kcal/mol. However, further research is needed, including larger trials and in-vitro studies, to establish its drug-likeliness.

Chung F Wong studied Virtual screening has grown more common because of molecular docking. Although it is quick, docking tiny molecules to a stiff biological receptor may lead to many false negatives and the discovery of fewer, more varied chemicals. This issue has been resolved thanks to flexible receptor docking. The number of real actives discovered by ensemble docking may increase if the structural ensemble is reduced in size and the structures that bind few ligands poorly are removed. Further study is required in this area, although ensemble docking's capacity to locate more true positives at the top of a rank-ordered list is also influenced by the techniques used to score and rank compounds [14].

Julio Cesar Batista Ferreira et al. Studied About To identify alterations in electrophysiological parameters as well as the molecular processes underlying the illness, cardiovascular disease animal models or pharmacological or genetic modification of cardiac cells are utilized. A key function in cardiac electrophysiological remodeling is played by Protein Kinase C (PKC) and several other kinases. As a result, the primary objective of current research is to develop particular medicines that control these kinases. Clinical benefits from targeted and efficient pharmaceutical therapies to restore cardiac electrical activity and treat cardiac arrhythmias would be substantial [15].

Kamaruddin et al. provided a quick look at the biologically active phytochemicals that have vascular protection properties. They conducted a thorough literature study, which turned up a ton of information supporting the role of phytochemicals including epigallocatechin-3-gallate, curcumin, cyanidin-3-glucoside, resveratrol, berberine, and quercetin in heart protection. They recommended more research into these phytochemicals to speed up the process of developing medications for several heart disorders.

Phytocompounds of aqueous extract of "Acacia Senegal (L.)" were used in research by Charan et al. To treat dyslipidemia and atherosclerotic plaque. They conducted several analyzes in their research, including in silico, in vitro, and in vivo tests. Additionally, in vivo, investigations showed that HMG-CoA reductase was inhibited. In addition, they performed an in silico experiment using HMG-CoA reductase and three extract-derived chemicals, linoleic acid, flavan-3-ol, or eicosanoic acid, which showed a significant or strong interaction with the docked complex as well.

Muhammad Ali Shah et al. studied the potential for cardioprotection of compounds originating from plants. The author of this research employs phytochemicals, which are naturally occurring bioactive compounds that are derived from medicinal herbs, vegetables, or fruits and are effective in treating a wide range of ailments. It is crucial to fully examine the plant variety's medicinal and pharmacological potential. Among the resources searched for research describing the cardioprotective qualities of medicinal plants were the Directory of Open Access Journals, PubMed, Medline, and Google Scholar. The present research examines the potential cardioprotective effects of phytoconstituents/molecules as plant secondary metabolites and provides information on the use of medicinal plants, particularly against cardiac diseases [16].

3. METHODOLOGY

In structural molecular biology or computer-assisted drug creation, molecular docking is a crucial technique. Predicting the dominant binding mode(s) of a ligand with a protein having a known 3D structure is the aim of ligand-protein docking. Essentially, the goal of molecular docking is to use computational techniques to anticipate the structure of the ligand-receptor complex.

To perform docking, two related processes must be taken: first, the ligand's conformations in the protein's active site must be sampled; then, these conformations must be ranked using a scoring function. The experimental binding mode should ideally be reproducible by sampling methods, and it should also be given the best score among all created conformations. Here, we provide a succinct introduction to fundamental docking theory from these two angles.

3.1. Design:

Data mining and a comprehensive examination of the available literature were conducted to discover the potential and effective ligand structure for the management of cardiovascular disease (CVD) using alternative medicine.

The current work explores the targeting potential of certain ligands and target proteins using a computational method and docking technique. After completing data mining and a thorough examination of the literature, it was discovered that Vicine is an inhibitor of PRKCA, a potential target protein for cardiovascular disease. To conduct the research, the protein and chemical were obtained from their respective databases, ready for docking, as shown in Figure 1. Autodock4 was then used to accomplish the docking, and the complex was then visualized using a different program called BIOVIA Drug Discovery Studio.

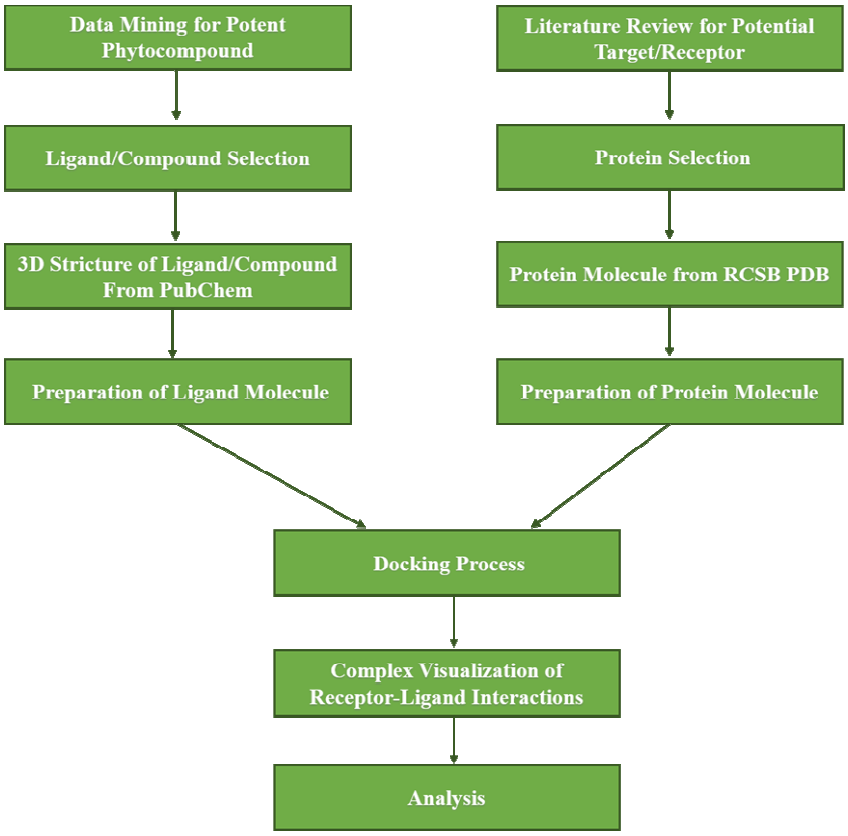

Figure 1: Illustrate the Docking Process Methodology.

3.2. Instrument:

Using the RCSB: PDB and PubChem databases, the structures of the protein and ligand are retrieved. All users, from computational biologists to structural biologists and beyond, may access PDB data for free via the Research Collaboratory for Structural Bioinformatics Protein Data Bank (RCSB PDB), the US data center for the global PDB repository. It acts as a database for the three-dimensional structural data of important biological substances, including proteins and nucleic acids. Biochemists and biologists from all around the globe give the data, which is often gathered using NMR spectroscopy or, increasingly, cryo-electron microscopy and X-ray crystallography.

PubChem is a database of chemical substances and related biological test procedures. The National Center for Biotechnology Information (NCBI), a section of the National Library of Medicine, which is a component of the National Institutes of Health in the United States, is in charge of managing the system (NIH). Through a web interface, PubChem is accessible without charge. Through FTP, millions of chemical structures and descriptive data are readily downloadable. Small compounds with less than 100 atoms and 1,000 bonds may be found in PubChem along with descriptions of many other substances. The PubChem database is constantly growing and is provided by more than 80 database suppliers.

One of the most often mentioned pieces of software in the scientific world, Autodock4, was utilized for the molecular docking procedure. The program uses a docked log file that is then evaluated by the use of a graphical tool called BIOVIA drug discovery studio to assess receptor-

ligand interactions and forecast how a substance or a ligand would bind to a protein or a receptor in a real biological system.

3.3. Sample:

3.3.1. Compound Collection and Preparation:

The compound molecule is obtained for PubChem in XML format, which was then transformed into.pdb format using a simple, openly accessible application called open babel GUI. For further processing, the compound was exported to the Autodock tool. After performing the ligand preparation, the ligand was then stored in the.pdbqt format, which is required to complete a subsequent docking operation. Figure 2 below shows the ligand molecule's structure.

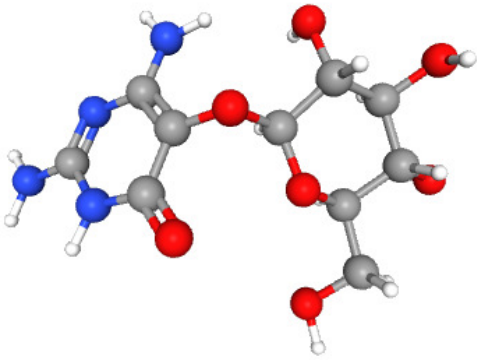

Figure 2: Illustrate the ball and Stick Structure of Vicine; the Red ball represents oxygen, the blue ball represents Nitrogen, and the Gray ball represents Hydrogen.

3.3.2. Protein Preparation:

The RCSB PDB was used to acquire the structure of the protein PRKCA, which was then trimmed to remove the water molecule and the associated ligand molecule. The protein molecule was then transferred to Autodock for further preparation, including the insertion of polar hydrogens to speed up the docking process. The protein molecule was then stored in. pdbqt format for additional docking. Figure 3 below shows how the protein's 3-D structure looks.

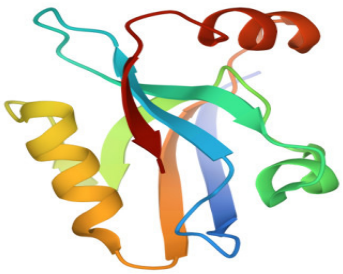

Figure 3: Illustrate the Three-Dimensional Structure of Protein (PRKCA).

3.4. Data Collection:

The protein and selected ligand are docked to acquire multiple confirmations and locations for the effective binding of the two molecules to create the complex. The. gpf file was used to run the auto grid and the. gpf file was used to run the autodock4 program to finish the docking process. The docking technique was carried out by making a protein or other macromolecule rigid and the ligand flexible. Using the auto dock tool, the binding energies of different docked confirmations were calculated and recorded in the DLG file (Docked log file). Figure 4 uses the confirmation with the largest negative binding energy to depict the interaction. The visualization and analysis process was subsequently completed, and the complex.pdbqt file was created.

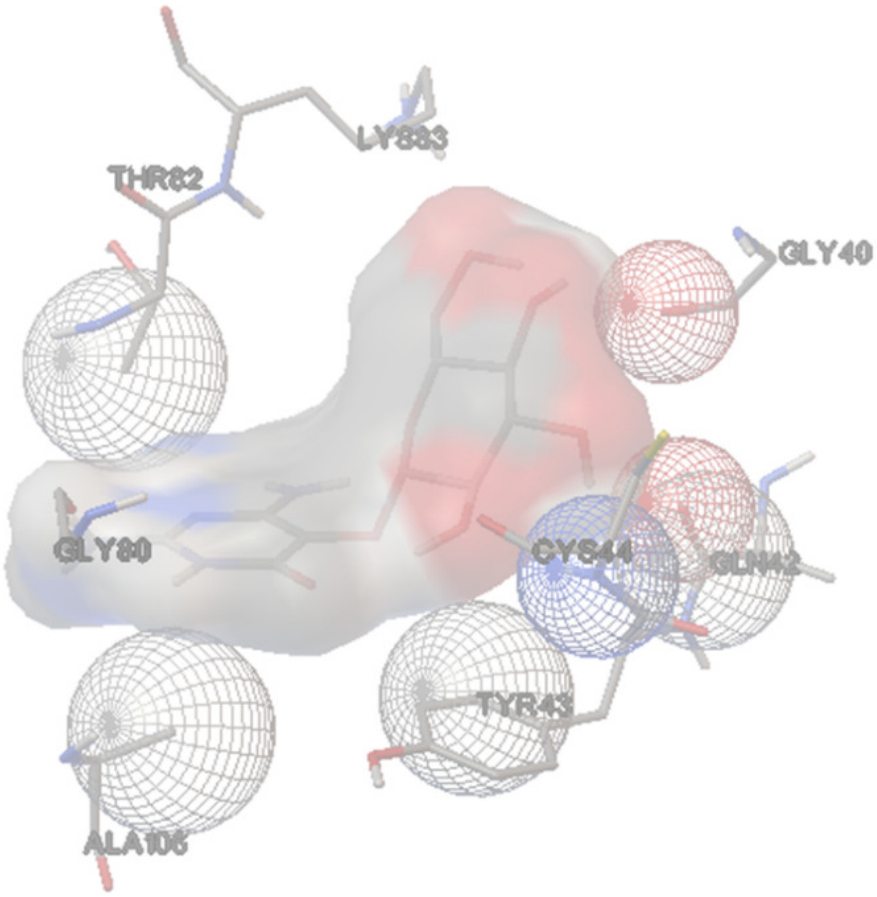

Figure 4:Illustrating the Interaction of Docked Protein and Ligand Complex

3.5. Data Analysis:

Using BIOVIA Drug Discovery Studio, the analytical complex that had the greatest negative binding energy was examined. The exact interaction between the ligand molecule and the protein's amino acids is shown in Table 1. The two-dimensional structure shown in Figure 5 was created to clearly understand the sorts of linkages required in the creation of a stable complex. The amino acids involved in the formation of the complex involved CYS44, ALA106, GLY80, GLN42, GLY40, LYS83, and ALA106.

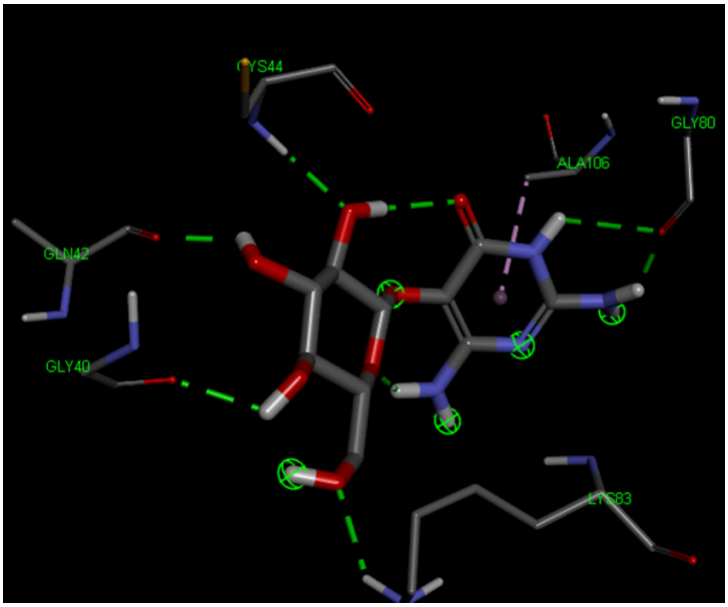

Figure 5: Illustrate the Ligand Molecule and the Amino Acids of Protein Involved in the Interaction.

Table 1: Illustrate the Distance, Bond Type between the Ligand and the Amino Acids of the Protein.

Compound: Protein	Bond Category	Distance	Bond Type
UNL1 : CYS44	Hydrogen bond	2,03381	Conventional Hydrogen Bond
UNL1 : LYS83	Hydrogen bond	2,23941	Conventional Hydrogen Bond
UNL1 : GLY80	Hydrogen bond	2,59025	Conventional Hydrogen Bond
UNL1 : GLY80	Hydrogen bond	1,90126	Conventional Hydrogen Bond
UNL1 : GLN42	Hydrogen bond	1,97775	Conventional Hydrogen Bond
UNL1 : GLY40	Hydrogen bond	2,1005	Conventional Hydrogen Bond
UNL1 : ALA106	Hydrophobic Bond	4,07727	Pi-Alkyl

4. RESULT AND DISCUSSION

The interaction energies for polar, non-polar, and non-bonded contacts are added together to determine the binding free energy. To calculate binding energy, the final total internal energy, total intermolecular energy, and torsion-free energy must all be added together. The energy of an unbound system is then reduced by this energy. The DLG file format was used to get the docking results and a list of the binding energies. The general rule is that the protein and ligand combination is more stable the more negative the binding energy there is. According to the calculation of the binding energy, the chosen ligand "Vicine" and receptor/protein "PRKCA" produced a stable complex with a variety of bond topologies. This complex's binding energy was -6.87 kcal/mol.

5. CONCLUSION

Heart-related diseases are increasing day by day, and it is a very biggest problem nowadays. Heart disease is now one of the most significant socioeconomic issues. Changing one's lifestyle is crucial for avoiding cardiovascular disease, particularly nutritional changes. As a result, research is now being done to find alternatives that could include a phytocompound. In the current work, the targeting potential of a phytocompound against PRKCA, a newly discovered target protein for cardiovascular disease, was investigated. The findings showed encouraging inhibition, as shown by negative binding energy. The current study's weakness is that significant in vivo and in vitro research is required to corroborate the results**.**

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CHAPTER 16

PREDICTION OF MYOCARDIAL INFARCTION USING MACHINE LEARNING ALGORITHMS

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ABSTRACT:

Acute myocardial infarction (MI) and coronary artery disease have seen amazing advancements in therapy over the last 20 years, yet MI is still the most prevalent cause of heart failure (HF). Three clinical presentations were seen, each with a different etiology, clinical features, and prognosis, depending on the timing of the onset of the MI and the development of HF. Nowadays, the prediction of any disease condition is becoming more important in order to treat and manage the condition. Machine learning algorithms are now being used for predicting the likelihood which can further help in managing patients using simple health parameters. To predict and categorize the patient with a likelihood of developing myocardial infarction, we employed several machine learning techniques, such as KNN and logistic regression, and random forest. The model was trained and tested with 70% and 30% of the dataset. The results of the study demonstrated the highest accuracy when classification was performed using the KNN classification algorithm which was found to be 91%. However, a good accuracy percentage was also observed with rest two classifiers.

KEYWORDS:

Cardiovascular Disease, Machine Learning, Myocardial Infarction, KNN, Random Forest.

1. INTRODUCTION

Monitoring demographic patterns in incidence as well as subsequent clinical outcomes after the acute presentation is important for planning the healthcare supply for acute cardiovascular disease. Public health policy must take into account how these patterns have been influenced by changes in risk factor profiles throughout time. Although myocardial infarction & stroke share many pathophysiological processes, lifestyle factors, and treatment options, they have only occasionally been examined together [1]. Myocardial infarction (MI), sometimes referred to as a heart attack, is a disorder of the blood arteries feeding the heart muscle (myocardium), also known as coronary heart disease. Myocardial infarction is the medical term for when a portion of the heart muscle has either no blood flow or blood flow that is so little as to be unable to support cardiac muscle function. The haemoglobin is completely deoxygenated as a result of the muscle fibres simultaneously utilizing the blood's final remaining oxygen [2]. As a result, the infracted region develops a bluish-brown hue. Later phases include extremely permeable artery walls that leak fluid, edematous local muscle tissue, and swelling of the cardiac muscle cells due to decreased cellular metabolism. The heart muscle cells expire after a few hours with essentially little blood flow. Cardiac muscle needs roughly 1.3 milliliters of oxygen per 100 grams of muscle tissue every minute merely to stay alive [3], [4].

MI may be divided into two basic groups: Transmural: involving important arteries and related to coronary atherosclerosis. It may also be described as superior, inferior, or anterior. It often happens when the blood supply to the afflicted area is entirely cut off that transmural infarcts, which permeate the whole thickness of the heart muscle, develop. Subendocardial: A small area of the ventricular septum, the papillary muscles, or the left ventricle's subendocardial wall may be involved. Subendocardial infarcts are thought to result from a localized decrease in blood flow, perhaps as a result of coronary artery constriction. This kind of illness is more common in the Subendocardial area, which is the furthest from the heart's blood supply. The clinical subdivisions of MI include ST elevation MI and non-ST elevation MI based on changes to the ECG [5], [6].

Epidemiology Ischemic heart disease often manifests as MI. According to WHO estimates, ischemic heart disease caused 12.6% of all fatalities globally in 2002. Heart illnesses are the number one killer in the US, outpacing cancer in terms of mortality (malignant neoplasm). One in five fatalities in the United States is caused by coronary heart disease. This indicates that an American dies from a coronary episode about every 65 seconds [7], [8]. The biggest cause of mortality in India is cardiovascular disease (CVD). Fatalities in India from CVD accounted for 32% of all deaths in 2007 and are projected to increase to 2.03 million by 2010 from 1.17 million in 1990 and 1.59 million in 2000. Despite being a relatively recent pandemic in India, cardiovascular disease (CVD)-related mortality is predicted to more than treble between 1985 and 2015.

Major expenditures related to MI that increase the financial burden it exerts on public health include the cost of hospitalization and treatment during the acute period, as well as cardiovascular care and secondary and tertiary prevention. There is also a social cost associated with MI; people who have one have a worse quality of life and are more likely to have functional limitations and reliance. In this situation, projecting the burden of MI in the future might assist stakeholders in planning for future treatment and preventative requirements as well as in adjusting to public health policies [9], [10]. To predict the prevalence of chronic diseases in the future, a strategy that takes into account the mortality tendency for both sick and healthy individuals is required, especially for illnesses that are more prevalent in the elderly [11], [12]. 10 Multi-state models, in specific "illness-death" models, shine as an alternative to conventional survival models and are especially well suited for prevalence projection. Through using the "illness-death" approach, we aimed to provide a French national estimate of the incidence of MI in 2035 as well as other epidemiological factors.

The prediction of cardiovascular issues via data mining is one of the most fascinating and challenging tasks. The creation of a rapid and effective detection system is crucial due to the shortage of specialists and the high percentage of patients with inaccurate diagnoses. Automated techniques for myocardial infarction prediction are useful for predicting CVD in the healthcare sector. This essay tries to provide a detailed analysis of the many data mining techniques that may be used in these automated systems. Additionally, this automation will reduce the number of tests a patient must undergo.

2. LITERATURE REVIEW

A hitherto unexplored topic in the ml algorithms for the healthcare domain, Ibrahim et al. showed an approach to foresee the onset of AMI utilizing 713,447 recovered ECG samples and associated auxiliary data from the longitudinal and comprehensive ECG-ViEW II database. The

study's findings highlighted the potential use of comprehensible machine learning in the field of cardiovascular event prediction, showing that the top CNN, RNN, and XGBoost models had high accuracy in prediction of 89.9%, 84.6%, and 97.5% and ROC curve areas of 90.7%, 82.9%, and 96.5% [13].

To anticipate the incidence of myocardial infarction (MI) utilizing harmonized EHR data, Mandair et al. contrasted baseline logistic regression using just "known" risk markers with deep learning and machine learning models. In contrast to the 2.25 million patients who did not have a MI diagnosis, 25,000,911 people received one. Compared to previous techniques, a deep neural network with random undersampling produced higher categorization [14].

A study by Khera et al. revealed that although machine learning algorithms may not significantly improve the ability to forecast the probability of mortality after an AMI, they may provide a higher level of risk resolution, which may help to more clearly define each person's risk for negative consequences [15].

Han et al. suggested a method for predicting the site and severity of myocardial infarctions (MI) utilizing 12-lead electrocardiograms and deep learning as well as a knowledge graph. The average accuracies for predicting the acute period of MI patients were 93.65%, 94.86%, 97.76%, and 94.27%, respectively. For localizing MI, the F1 was 86.88% .

3. METHODOLOGY

3.1. Design:

The goal of the prediction approach is to create a framework as shown in Figure 1 that can infer properties of the projected class from merely a collection of many other facts. The purpose of data mining in this research is to develop models for class prediction based on chosen characteristics. The current research employs the Random Forest - classification technique to precisely forecast the chance of having a myocardial infarction and provide the best therapy available. The results demonstrate that the appropriately developed diagnostic system predates the myocardial infarction level.

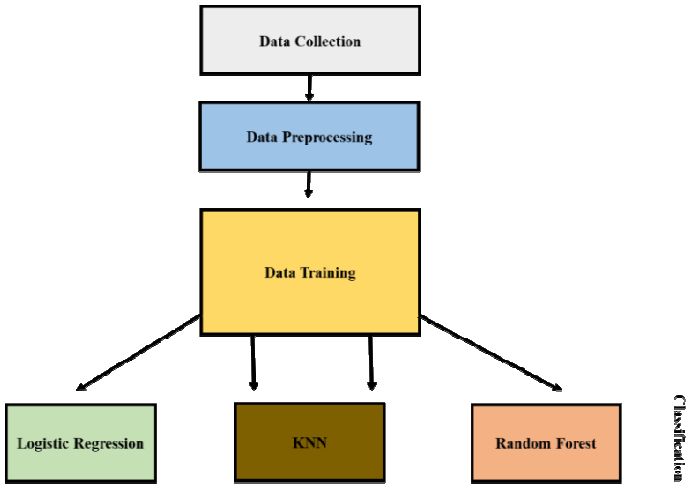

Figure 1: Illustrating the Methodology used to carry out the research.

3.2. Sample and Data Collection

The data sets from the free database "Kaggle (https://www.kaggle.com/ronitf/ heart-disease-uci/)" was employed. The collection includes information on 14 parameters gathered from 303 individuals who investigated European research facilities. "Age", "chest pain type (cpfasting blood sugar (FBS)", "serum cholesterol (chol)", "sex", "resting blood pressure (trestbps)", "resting electrocardiographic results (restecg)", "maximum heart rate (thalach)", "ST depression (oldpeak)", "slope of the ST peak", "presence of exercise-induced angina (exang)", "the number of major colored vessels (ca)", and "thalium(thal)" stress results were the factors researchers used to forecast MI (or lack thereof).

Table 1: Dataset Description for cardiovascular disease prediction system.

Sr. no.	Attributes	Description	Labeling
1.	Age	Age in Year	
2.	Sex	A classification of the sex of the person	value 1: Male; value 0: Female
3.	Cp	Chest pain type	value 1: typical type 1 angina, value 2: typical type angina, value 3: nonangina pain; value 4: asymptomatic
4.	Testbps	Resting blood pressure	-
5.	Chol	Serum cholesterol	-
6.	Fbs	Fasting blood sugar	(fasting blood sugar>120? yes=1, no =0)
7.	Restecg	Resting electrocardiographic results	(value 0:normal; value 1: having ST-T wave abnormality; value 2: showing probable or definite left ventricular hypertrophy)
8.	Thalach	Maximum heart rate achieved	-
9.	Exang	Exercise-induced angina	(value 1: yes; value 0: no)
10.	Oldpeak	ST depression induced by exercise relative to rest	-

The dataset is split into 2 portions: "training dataset" and "testing dataset". Training Data consists of 70% and testing data was consist of 30% of the whole dataset.

3.3. Instrumentation

In the research, we looked at the results of the "random forest classifier", "K-nearest neighbors (KNN)", and "logistic regression" techniques.

Logistic regression: The early twentieth century saw the usage of logistic regression in the biological sciences. This led to several social science applications using it. Whenever the goal (dependent variable) is a categorical variable, logistic regression is utilized. In order to calculate the likelihood that an event will occur, a mathematical model called logistic regression is utilized. A value of 1 is assigned to event y in the case that it happens, while a value of 0 is assigned in the absence of the event.

Binomial: The target variable may only have one of two potential kinds, such as "0" or "1," which might also indicate "win" vs. "loss," "pass" vs. "fail," "dead" vs. "alive," etc.

Multinomial: The target variable might include three or more alternative kinds that are not ordered (i.e., types have no quantitative importance) like "illness A" vs. "disease B" vs. "disease C"

Ordinal: It works with target variables that have categorized options. Example categories for test results include "extremely poor," "poor," "excellent," and "very good." A score of 0, 1, 2, or 3 may be assigned to each category in this case.

k-nearest neighbors algorithm (also referred to as KNN or k-NN): The k-nearest neighbor method, sometimes referred to as KNN or k-NN, is a supervised, non-parametric learning methodology that makes predictions or forecasts about the clustering of a single data point using proximity. Although it may be used for classification or regression issues, it is often employed as a classification strategy since it is predicated on the idea that comparable points can be discovered close together. The k-nearest neighbor method, sometimes referred to as KNN or k-NN, is a supervised learning classifier that relies on closeness to make classifications or predictions about the grouping of a single data point. Although it may be used for classification or regression issues, it is most often employed as a classification tool since it is predicated on the idea that adjacent comparable points can be located.

When it comes to classifying problems, a majority vote is applied, which means that the label that is most often associated with a certain data point is selected. Although this process is officially known as "plurality voting," the term "majority vote" is more often used in literature. The distinction between the two concepts is that "majority voting" requires a majority of more than 50% to be considered legitimate, although "majority voting" usually works when there are only two options. If there are many classes—say let's four—you don't necessarily need 50% of the vote to decide which class wins; you might assign a class label with a vote of more than 25%.

The k points in the training data that seem to be nearest to the test value are used by the KNN to determine the distance between each of these categories. The category within which this distance is the least is one that the test result falls within.

Random forest: Random forests, as the name indicates, are collections of several decision trees that collaborate to get choices. The class with the greatest votes is selected as the forecast by our model from among the individual class predictions produced by each tree in the random forest. By doing this, the training data's unwanted over-fitting is corrected. During the training phase, a

replacement sample is routinely picked at random from the training set, and the trees are subsequently matched to these samples. Each tree is grown without being trimmed, and the size of the ensemble affects the choice. Numerous movable hyperparameters are included in the Scikit-Learn documentation for random forest classifiers.

3.4. Data Analysis

To help make up for the absence of real-world data, the dataset is split into a "test set" (30% observations) and a "training set" (70% observations) before the analysis is conducted. Care is taken to balance the "class distributions" within the divide. The model has been trained using the "training" dataset, which the model uses to see and pick up new information. The resulting model fits the training dataset and is then evaluated objectively using the "test" dataset. In several instances, we ran manifold experimentations to authenticate model results using different splitting ratios.

4. RESULTS AND DISCUSSION

There has been research done on the use of logistic regression, random forest, and KNN classification algorithms for the prediction of myocardial infarction. The datasets utilized in this analysis, with a total of 303 records and 14 attributes in the training dataset and others in the testing dataset. According to preponderant statistics, males are 58.32% more likely than women to face myocardial infarction. The accuracy of three classifiers was used and compared to assess the developed model. Accuracy is the percentage of the proportion of all instances of the dataset that were accurately predicted out of total instances. The accuracy of all four tested algorithms is given in Table 2.

KNN classification outperformed the random forest and logistic regression with the highest accuracy percentage of 91%. On the other hand, random forest and logistic regression demonstrated good and similar accuracy of 86 and 84%. Our research used 30% of the testing data from the cardiovascular disease dataset and 70% of the training data during the testing phase. Table 2 provides the accuracy %.

Table 2: Enlisting the Accuracy of Different Classifiers.

Classifier	Accuracy
Logistic regression	**86%**
k-nearest neighbors algorithm	**91%**
Random forest	**84%**

One industry where data mining techniques have been used is healthcare. The goal of this study is to determine if heart attack predictions may be made using fewer criteria than those suggested by earlier research. We use 14 parameters (out of the 13 recommended), including: "Age," "Chest Pain Type," "Fasting Blood Sugar," "Serum Chol," "Sex," "Resting Electrocardiographic Results," "Maximum Heart Rate," "ST Depression," "Old Peak," "Slope of the ST Peak," "Presence of Exercise-Induced Angina," "Number of Major Colored Vessels," and "Thalium Stress." These parameters were chosen for this investigation because they are straightforward

measures and are routinely reported. If we evaluate studies using 14 parameters with KNN to those using different numbers of parameters, as well as other data mining techniques like logistic regression and random forest, we find that the accuracy is excellent. As a consequence of this study, we can demonstrate that 14 straightforward characteristics are reliable enough to be employed in heart attack predictions. It may be employed as a variable in machine-to-machine (M2M) technology-based remote monitoring of patients, particularly for patients receiving care at home or in outlying clinics, according to our future study. A prediction system will be included as a unique element in the end-to-end M2M architecture.

Traditional CVD risk scores have several drawbacks, such as discrepancies across validation cohorts, especially in some groups, including rheumatoid arthritis patients. The Framingham score may overstate the risk of CVD in some situations, which might result in overtreatment20. The majority of the time, these risk ratings only take into account a small number of predictors and leave out a lot of crucial elements. To better precisely estimate the burden of CVD, new reliable prediction techniques are required given the shortcomings of the most extensively used risk models. The use of machine learning (ML) for risk prediction has gained popularity due to improvements in computing capacity for handling massive volumes of data, although doctors often have little knowledge of this approach. As a result, we have used a meta-analytic method to define the insights that ML modeling may provide for CVD research.

Unfortunately, we do not know how or why the authors of the examined research picked the particular algorithms they did from the wide range of alternatives. Researchers and writers could have chosen plausible models for their datasets and run many models (for example, running in parallel, changing hyperparameters) while only reporting the best model, which overfitted their data. Most notably, pooled investigations show that ML algorithms often provide good predictions of cardiovascular disease. ML algorithms are accurate in predicting CAD and stroke in a subgroup analysis of each ML algorithm. There has only been one other published meta-analysis of the ML literature so far, and it used a similar basic idea to ours. The researchers examined the diagnostic abilities of several deep-learning models and doctors using medical imaging. The researchers concluded that deep learning algorithms were intriguing but they also noted several methodological obstacles to reaching clinician-level accuracy. Though our research points to the potential of boosting models for predicting likelihood, further research contrasting human experts and ML models are required. Because there were so few studies for each model of myocardial infarction, we were unable to use meta-analytic techniques. According to observations, the KNN classification algorithm seems to be more effective at identifying than other predictive algorithms.

Even if ML-based algorithms seem to perform well, they are still far from ideal. Several methodological obstacles might skew findings and amplify variability. First, since technical details like hyperparameter tweaking in algorithms are often kept a secret from the public, there is a significant level of statistical variability. In actuality, heterogeneity assesses the variation in impact magnitude across research. Furthermore, since there are no set use standards, the data partitioning is similarly arbitrary. Furthermore, the pooled data can be unreliable since there is a limited sample size for each kind of CVD. The methods and strategies used for feature selection are random and diverse. Fourthly, we couldn't categorize the kind of custom-built algorithms owing to their ambiguity. Diverse assessment matrices are reported by research (some did not record positive or negative instances, sensitivity/specificity, F-score, etc.).

Due to the need to aggregate raw data from studies without accounting for differences across research, which might lead to bias, we did not provide the confusion matrix for this meta-analytic technique. Even though ML algorithms are reliable, some researchers did not provide comprehensive assessment metrics, such as "positive or negative" instances.

5. CONCLUSION

To quickly calculate the risk of developing myocardial infarction, the MI clinical decision support tool includes straightforward and objective data which are normal health parameters obtained using a high-sensitivity test. It could be used to differentiate between people with probable myocardial infarction who have a low or high likelihood of developing the condition.

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CHAPTER 17

IN SILICO STUDY OF BERBERINE WITH INTERLEUKIN-6 FOR MANAGEMENT OF PERIPHERAL ARTERY DISEASE (PAD)

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ABSTRACT:

Atherosclerosis, or the accumulation of fatty plaque in the arteries, is the main cause of peripheral artery disease (PAD). Although PAD may occur in any blood artery, it tends to affect the legs more often than the arms. Leg discomfort reduced quality of life in terms of health, immobility, tissue loss, and a higher chance of serious adverse events, such as myocardial infarction, stroke, revascularization, amputation, and death, are all symptoms of PAD. Antithrombotic medicines, such as aspirin and clopidogrel, as well as pharmaceuticals to address dyslipidemia, hypertension, and diabetes mellitus are known therapies for PAD. It has been found that the compound "berberine" can inhibit interleukin-6 with a considerable negative binding energy of 9.59 kcal/mol. Therefore, the current work may aid researchers in investigating the potential for enzymatic and chemical modification of the molecule. Patients having a history of coronary artery involvement are encouraged to have long-term follow-ups.

KEYWORDS:

Arteries, Berberine, Coronary Arteries Disease (CAD), Interleukin-6, Peripheral Artery Disease (PAD).

1. INTRODUCTION

Peripheral artery disease (PAD), is a disorder during which your arteries constrict and can't deliver as much blood to your extremities, such as your arms and legs. It is classified as a kind of peripheral vascular disease. One of the earliest warning indications of PAD is cramping which starts when you move and goes away when you relax. It is most often felt in the legs, although it may occur in other places of the body as well. PAD might affect your limbs, head, intestines, and kidneys. PAD is significantly associated with a poor prognosis, underrecognized, poorly understood, and a lot more frequent than previously assumed. The term will be used in this article to refer to vascular illnesses associated with atherosclerosis of the abdominal aorta, iliac, and shorter arteries, which results in stenosis. In primary care practices throughout the United States, 40% of patients over the age of 70 or the age of 50 with a history of cigarette smoking or diabetes have been diagnosed with PAD.

Congestion in the arteries, which transport blood away from the heart, is the most prevalent cause of PAD. This is known as atherosclerosis. It occurs when substances in your circulation, such as fat and cholesterol, create plaques that accumulate in your arteries, and some Plaques are largely formed of adipose and are first waxy. They accumulate slowly, so you just don't notice they're there. Plaque development makes your arteries stronger and weaker over time. It's similar to antiquated plumbing in a home. Water drains slowly when there is muck in the pipes, and the

pipes begin to clog. When plaque builds up in your arteries, blood flow slows and your body does not receive enough oxygen.

Not only was the diagnosis of PAD commonly ignored, but the cardiovascular risk factors were not addressed as thoroughly as they were in coronary arteries disease (CAD) patients. For two crucial reasons, the assessment of PAD should not be neglected. To begin, individuals with PAD may encounter a variety of issues, including claudication, ischemic rest discomfort, ischemic ulcerations, frequent hospitalizations, revascularizations, and limb loss. These factors contribute to a low quality of life and a high incidence of depression. Even individuals without leg symptoms had worse functional performance, lower quality of life, a smaller calf muscle area, and more calf muscle fat than an age-matched group of patients without PAD.

The chronic cardiovascular illnesses PAD and CAD have an etiology and a nearly perfect association with atherosclerosis. Using the general quality of life assessment instrument, the SF-36, patients with PAD and patients with CAD who were anticipated for surgery were compared as similar groups for this research. The findings suggest that both patient groups' overall quality of life has significantly declined. Compared to individuals with CAD, people with PAD had considerably lower levels. Although they defy the widespread belief that CAD has a bigger effect on the quality of life (QOL), which is based on the fact that it is more life-threatening, these findings are consistent with the literature.

In this research, the author performed the docking with the ligand, and protein such as berberine and the interleukin-6 is used for the PAD. The current study is broken into 5 sections, with the first portion providing an introduction to the research's context and the second section reviewing the literature. The third portion outlines the study methodology, followed by the results, discussion, and conclusion in the fourth and fifth sections.

2. LITERATURE REVIEW

Aday et al. in their study embellish that lower extremity atherosclerotic PAD is being increasingly recognized as a major cause of myocardial morbidities, affecting about 230 million individuals globally. In this paper, the author applied a methodology in which they stated that Common health conditions such as older age, smoking, and diabetes have all been related to an increased risk of PAD. The results show that PAD has previously been undervalued in comparison to coronary artery disease and stroke, increased focus on PAD in recent years has resulted in significant new epidemiological findings in the areas of coagulation, inflammatory processes, dyslipidemia, and microvascular illness. The author concludes that furthermore, poly-vascular disease, or subjectively visible atherosclerosis in numerous artery beds, is being increasingly recognized as a uniquely malignant cardiovascular disease deserving of special clinical attention and additional investigation. It is worth noting that PAD may raise the risk of bad outcomes in the same way as vascular atherosclerosis or stroke might [1].

Sánchez et al. in their study disclose that a relatively prevalent condition is (PAD). Its treatment and prognosis are impacted by the fact that it often coexists with other cardiovascular disorders. PAD of the lower extremities is brought on by the arteries' increasing stenosis-obstruction. In this paper, the author applied a methodology in which they stated that the most common cause is atherosclerosis, which is connected to cardiovascular risk factors smoking, diabetes mellitus, etc. The results show the clinical signs and symptoms change depending on how severe the blood deficiency is. The course of the illness is classified by the Fontaine categories as asymptomatic,

intermittent claudication, discomfort at rest, and trophic lesions. Ankle/arm index with/without stress test, physical examination palpation of pulses, and medical history all help with diagnosis, categorization, and therapy recommendation. The author concludes that To design surgical therapy, angiography or computed tomography (CT) is used [2].

Klarin et al. in their study disclose that Peripheral artery disease, also known as atherosclerosis of the abdominal aorta and the arterial bed of the lower extremities, is a complicated condition involving both environmental and genetic causes. In this paper, the author applied a methodology in which they stated that Amputation, persistent limb-threatening ischemia, severe functional impairment, and increased death are all consequences of untreated illness. Significant progress has been made in figuring out the genetic cause of this prevalent, complicated illness during the last ten years. The results show the main genetic analyses for peripheral artery disease, such as heritability and linkage studies, as well as more recently genome-wide association studies based on biobanks. The author concludes that Future research should focus on finding the genes that cause peripheral artery disease, doing rare variant and structural variant analysis utilizing data from whole-exome and whole-genome sequencing, and including people with various genetic ancestries, among other things [3].

Flores et al. in their study embellish that when peripheral artery disease, an atherosclerotic ailment, is present, patient outcomes are likely to be poor. In this paper, the author applied a methodology in which they stated that Low diagnostic rates encourage bad treatment, which results in limb loss and higher than average rates of cardiovascular morbidity and mortality. The results show that in several areas of health care, including reliably diagnosing illness, forecasting patient outcomes, and automating image interpretation, machine learning algorithms, and artificial intelligence have shown considerable promise. The author concludes that Although these technologies have just recently been applied to peripheral artery disease, they hold enormous potential [4].

Bonaca et al. in their study suggested that Systemic atherosclerosis manifests itself as a peripheral arterial disease (PAD). Lower extremity atherosclerosis is caused by modifiable risk factors such as cigarette smoking, dyslipidemia, diabetes, poor food quality, obesity, and physical inactivity as well as underlying hereditary factors. In this paper, the author applied a methodology in which they stated that the chance of significant adverse cardiovascular events, such as myocardial infarction, stroke, and cardiovascular mortality is raised in patients with PAD who often also have the coexisting coronary or cerebrovascular illness. The results show that Patients with PAD often have decreased mobility and run the risk of critical limb ischemia, which may cause substantial adverse limb outcomes including peripheral revascularization or amputation. Patients with past critical limb ischemia, prior soft tissue surgery, or amputation have an elevated risk of major adverse limb events. The author concludes that Patients with poly-vascular disease are identified as the greatest risk patient category for major adverse cardiovascular events [5].

Piotrkowska et al. in their study embellish that the variables affecting sufferers with peripheral artery disease's acceptance of their condition and level of life satisfaction Peripheral artery dysfunction are more prevalent in elderly people, who also have a higher risk of cardiovascular illnesses, death, and amputation. In this paper, the author applied a methodology in which they stated that one of the most crucial aspects of adapting to every day with a chronic condition is accepting the sickness. Cross-sectional survey research design questionnaires for patients. The

results show that the Patients with vascular disease made up the participants. The author concludes that the Acknowledgement of Illness Scale and the Pleasure with Life Scale were used as conventional research methods in the study [6].

Farhan et al. in their study disclose that one of the COVID-19 pandemic's epicenters was New York City. In this paper, the author applied a methodology in which they stated that for health care systems and medical staff, managing peripheral artery disease (PAD) throughout this period has been a significant problem. The results show the experiences of professionals from several medical specialties who treated patients with PAD during the epidemic in hospitals around New York City. The author concludes that the recommendations are based on several factors, such as the patient's clinical PAD presentation and the COVID-19 infection status. Our case-based algorithm intends to direct the safe and effective treatment of PAD patients during the epidemic [7].

Malik et al. in their study embellish that to evaluate the relationship between chronic self-perceived stress and the results of patients health condition who have peripheral artery disease. In this paper, the author applied a methodology in which they stated that From June 2019 to December 2021, 1565 patients with symptoms of peripheral artery disease were included in the prospective registry known as the PORTRAIT trial at 54 locations in the US, the Netherlands, and Australia. From a chart review, demographic, comorbidity, and diagnostic data were extracted. The results show that at the baseline, 3- and 6-month follow-ups, self-reported stress was measured using the 4-item perceived stress scale. The author concludes that higher ratings indicate more stress. Scores range from 0 to 16. Sum scores were computed and averaged at each time point to determine the average amount of stress experienced from enrollment through six months [8].

Eid et al. in their study disclose that PAD, which mostly affects the peripheral arteries in the lower limbs, is the clinical manifestation of atherosclerosis. In this succinct overview, we discuss the epidemiology and disease burden of PAD in the United States, with a focus on high-risk groups. In this paper, the author applied a methodology in which they stated that even though males and older adults tend to have greater rates of PAD, women in lower socioeconomic strata are impacted at rates that are twice as high as men. Black and African-American patients have a greater incidence of illness and less access to preventive treatment than other racial/ethnic groups. The results show that the Furthermore, high-risk groups continue to be disproportionately impacted despite an overall decline in amputation rates among all patients with PAD. The author concludes that Patients in rural locations, those who identify as African-American or Native American, and those with a poor socioeconomic position are more at risk for amputation [9].

Skeik et al. in their study embellish that over the age of 45, (PAD) is thought to afflict 8.5 million people in the US and is linked to severe morbidity, death, and disability. In this paper, the author applied a methodology in which they stated that In contrast to other atherosclerotic illnesses like coronary artery disease (CAD) or stroke, risk factor reduction often receives less attention despite the severe negative limb and cardiovascular (CV) outcomes found in individuals with PAD. The results show that the In the most recent research, statins have been proven to benefit patients with PAD by lowering mortality, major adverse CV events, major adverse limb events, and improving symptomatic outcomes. Additionally, PCSK9 inhibitors are emerging as an alternative lipid-lowering treatment for individuals with PAD. The author

concludes that PCSK9 is a proprotein convertase subtilisin type 9 enzyme. However, individuals with PAD are routinely undertreated with lipid-lowering medications, despite current guideline guidelines based on expanding data [10].

In this paper, the author elaborates that Age, smoking, and diabetes are all common health issues that have been linked to an increased risk of PAD. According to the findings, PAD has historically received less attention than coronary artery disease and stroke, and current attention to PAD has led to important new epidemiological discoveries in the fields of coagulation, inflammatory processes, dyslipidemia, and microvascular sickness. In addition, poly-vascular disease, or subjectively evident atherosclerosis in several artery beds, is becoming recognized as a particularly malignant cardiovascular illness that merits special therapeutic attention and further research, according to the author's conclusion.

3. METHODOLOGY

3.1. Design:

In this research, docking is performed in which the selection of the phytocompounds based on text mining is performed after that the retrieval of phytocompounds structure from the PubChem and the Ligand preparation simultaneously the working of the selection of the target protein is formed, and the retrieval of target protein from the protein data bank, protein preparation is formed. After this docking is formed from the auto dock and the visualization of the complex is formed. Figure 1 discloses the framework of the docking process.

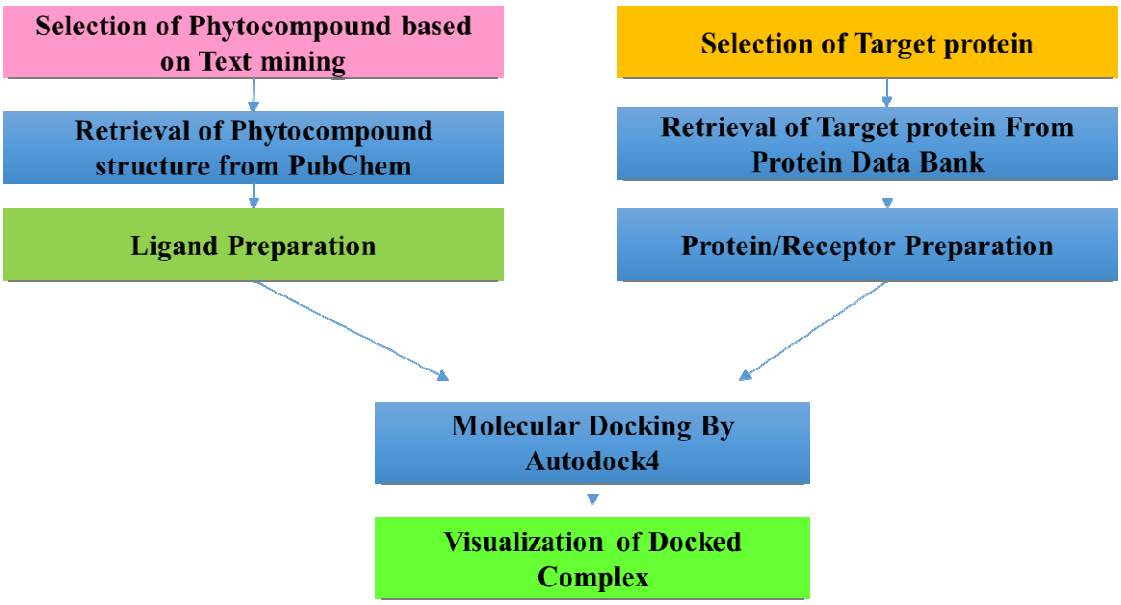

Figure 1: Discloses the framework of the docking process.

3.2.Sample And Instruments:

The protein and ligand structures are derived from the PubChem and RCSB: PDB databases. The "Research Collaboratory for Structural Bioinformatics" is the enlarged form of RCSB, while the

"Protein Data Bank" is an enhanced version of PDB. It serves as the focal point for the world's PDB repository and makes PDB information freely available to all scientists, including those working in the medical field and far beyond. It serves as a database for three-dimensional information on significant biological elements, such as proteins and nucleic acids. The information, which is often acquired via NMR spectroscopy or, increasingly, cryo-electron microscopy and X-ray crystallography, is provided by biologists and physicians from all over the world.

A database of different chemicals and associated biological test methods is called PubChem. The system is managed by the "NCBI," or "The National Center for Biotechnology Information," a division of the National Library of Medicine, a part of the National Institutes of Health in the United States (NIH). PubChem is freely available using a web browser. Numerous chemical components and descriptive data are easily available through FTP. In addition to information on many other chemicals, PubChem has information on small compounds with less than 100 atoms and 1,000 bonds. Over 80 database providers contribute to the ever-expanding PubChem database.

The molecular docking process was carried out using Autodock4, one of the scientific community's most often discussed software applications. A docked log file is used by the program to examine receptor-ligand connections and predict how a substance or ligand will attach to a protein or a receptor in a true biological system. This tool is called BIOVIA drug discovery studio. Berberine is used as a ligand in this research. Figure 2 discloses the Berberine structure in this with carbon, hydrogen, and oxygen.

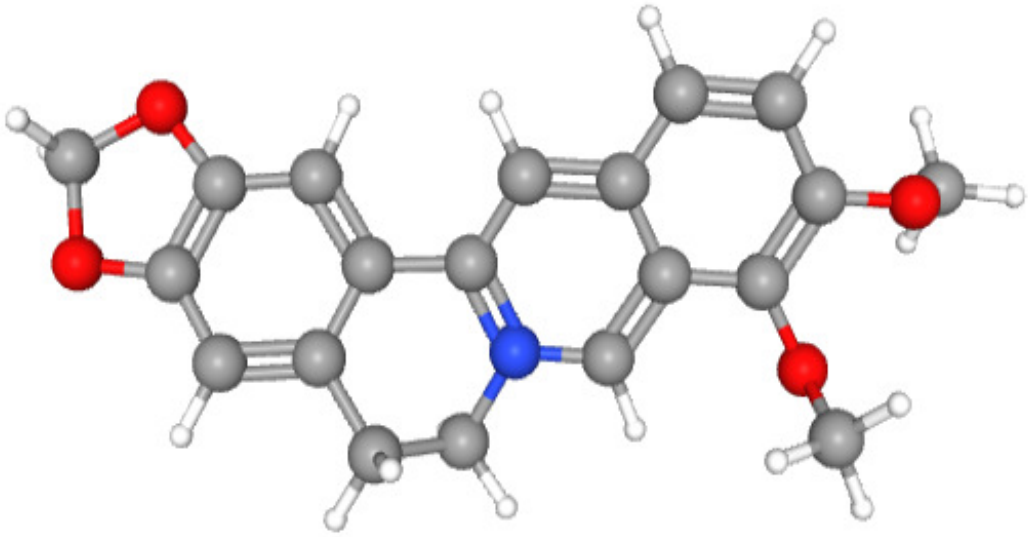

Figure 2: Discloses the Berberine structure in this with carbon, hydrogen, and oxygen.

Interleukin 6 is used as a protein in this research for effective working in the docking Figure 3 embellishes the Interleukin 6 structure.

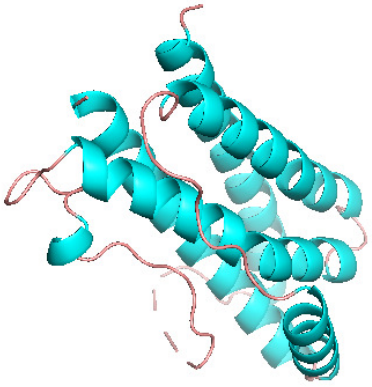

Figure 3: Embellishes the Interleukin 6 structure.

3.3.Data Collection:

After "docking" a protein with a certain ligand, there are several confirmations and places where the successful binding of the ligand and proteins may be discovered. To complete the docking operation, the autodock4 software was launched after the auto grid application was launched using the. pdf file. Hardening macromolecules or proteins and making the ligand flexible allowed for successful docking. It was feasible to get the binding energies of various docked confirmations in the DLG file by using the auto dock tool. The complex. pdbqt file used to do the visualization and analysis procedure was written using the confirmations with the largest negative binding energy. Figure 4 discloses the docked structure of the receptor and the ligand.

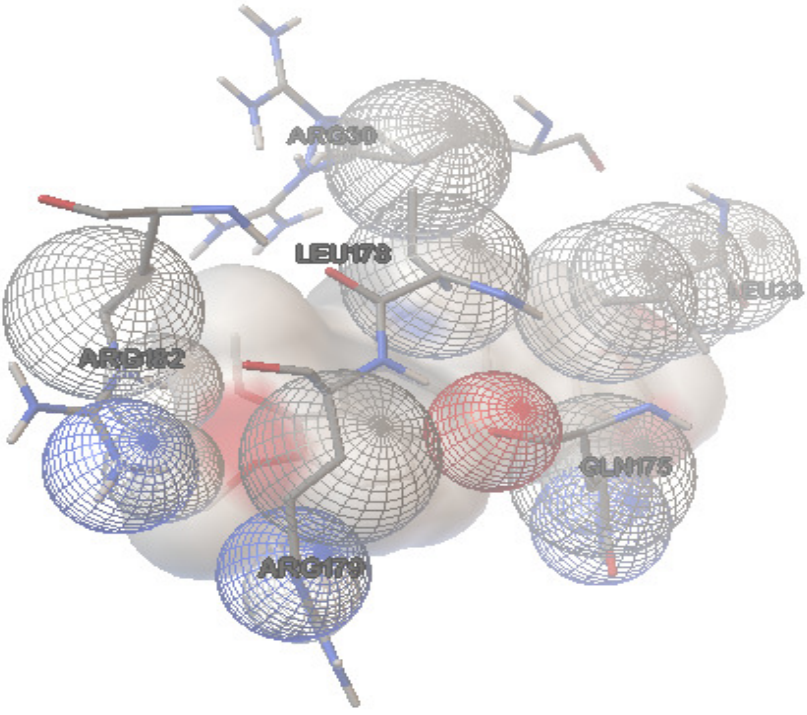

Figure 4: Discloses the docked structure of the receptor and the ligand.

3.4.Data Analysis:

In this research, all the data is collected and analyzed from the ligand and the protein structure Berberine and Interleukin 6 are used in this research, and docking is performed. The distance and the bond between the binding forces are shown below. Figure 5 shows the interaction between the amino acid of protein and the ligand. Figure 6 discloses the distance between the bonds and their energy in Armstrong (A*).

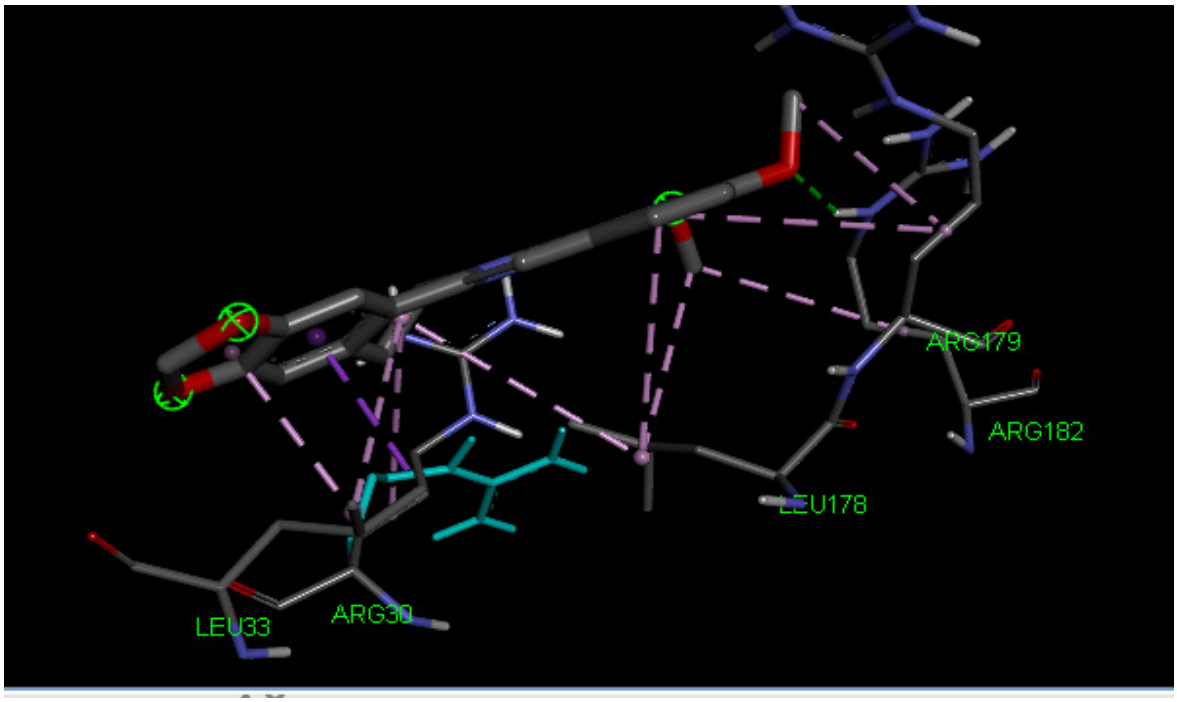

Figure 5: Discloses the interaction between the amino acid of protein and the ligand.

	Name	Visible	Color	Parent	Distance	Category	Types
1	A:ARG182:HE - :UNL1:O	☑ Yes		Ligand Non-bond Monitor	2.69268	Hydrogen Bond	Conventi..
2	A:LEU33:CD1 - :UNL1	☑ Yes		Ligand Non-bond Monitor	3.45131	Hydrophobic	Pi-Sigma
3	A:ARG30 - :UNL1	☑ Yes		Ligand Non-bond Monitor	4.99415	Hydrophobic	Alkyl
4	A:LEU33 - :UNL1	☑ Yes		Ligand Non-bond Monitor	4.87729	Hydrophobic	Alkyl
5	A:LEU178 - :UNL1	☑ Yes		Ligand Non-bond Monitor	5.22605	Hydrophobic	Alkyl
6	:UNL1 - A:LEU33	☑ Yes		Ligand Non-bond Monitor	3.57241	Hydrophobic	Alkyl
7	:UNL1:C - A:LEU178	☑ Yes		Ligand Non-bond Monitor	4.45973	Hydrophobic	Alkyl
8	:UNL1:C - A:ARG182	☑ Yes		Ligand Non-bond Monitor	4.59747	Hydrophobic	Alkyl
9	:UNL1:C - A:ARG179	☑ Yes		Ligand Non-bond Monitor	4.17886	Hydrophobic	Alkyl
10	:UNL1 - A:LEU178	☑ Yes		Ligand Non-bond Monitor	4.90729	Hydrophobic	Pi-Alkyl
11	:UNL1 - A:ARG179	☑ Yes		Ligand Non-bond Monitor	5.03405	Hydrophobic	Pi-Alkyl

Figure 6: Discloses the distance between the bonds and their energy in Armstrong (A*).

4. RESULTS AND DISCUSSION

The binding free energy is calculated by adding the interaction energies for polar, non-polar, and unbonded contacts. The ultimate total internal energy, total intermolecular energy, and torsion-free energy must all be summed together to determine binding energy. The energy of an unbound system is then decreased by this energy. The docking findings and a list of the binding energies were obtained in the DLG file format. Generally speaking, the more negative the binding energy there is, the more stable the protein and ligand combination is. The selected ligand “Berberine” and receptor/protein " Interleukin 6" created a stable complex with a range of bond topologies, according to the computation of the binding energy. Figure 7 shows the 2d structure of the protein-ligand complex.

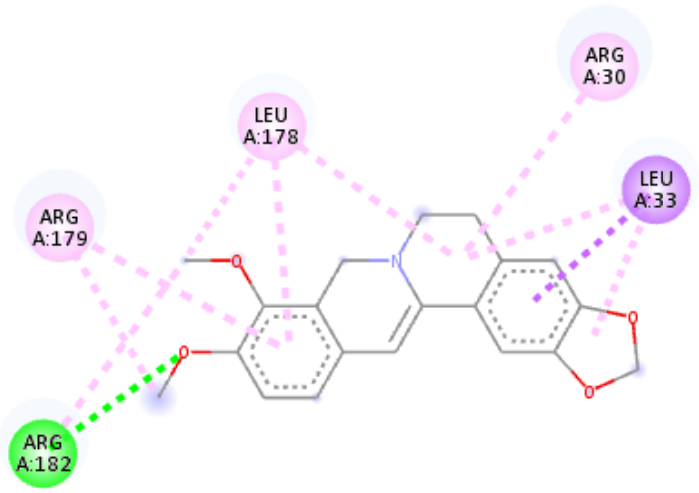

Figure 7: Discloses the 2d structure of the protein-ligand complex.

5. CONCLUSION

Peripheral artery disease (PAD) has a detrimental effect and significantly lowers patients' quality of life in all areas of their physical and mental health. The clinical signs of the illness and the test results only partly represent the patients' quality of life. Patients with PAD have a comparable or even larger detrimental effect on CAD patients who are scheduled for surgery. The results of this research are consistent with those of other studies, showing that quality of life is a crucial component of therapy in people with peripheral artery disease and may represent a new therapeutic target, in addition to the traditionally recognized criteria. Health-related quality of life will continue to be utilized and progressively established as a treatment endpoint result in patients with peripheral arterial disease. Doctors will be better able to grasp the impact of the illness and make better clinical judgments and use more efficient treatment methods as a result of the continuous and systematic evaluation of the quality of life.

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CHAPTER 18

IN SILICO STUDY OF ARJUNGENIN AGAINST NON-STRUCTURAL PROTEIN-3 OF CHIKUNGUNYA VIRUS (CHIKV)

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ABSTRACT:

Chikungunya Virus is an alphavirus from the Togoviridae family which poses a significant health burden with manifestations including fever, severe joint pain in knees, ankles, toes, and muscular soreness. Different kinds of efforts have been already been made to find and develop an effective treatment against the Chikungunya virus to stop its transmission and proliferation in humans. However, no effective treatment has been developed. Phytocompounds are now receiving great attention to be used as potential compounds for antiviral therapy against a range of viruses. In this research, the aim is to find out the future potential of Arjungenin, a natural product found in several medicinal plants against non-structural protein-3 of CHIKV. To carry out the assessment, docking between the target protein "NSP3 Macrodomain" and the selected ligand "Arjungenin" was performed and the affinity scores were then analyzed to check the interaction as well as inhibition activity of the ligand against the selected target. The affinity of -8.4 kcal/mol was observed between the protein and ligand complex which further implies that it can be used for future research studies to make it a potential inhibitor against CHIKV.

KEYWORDS:

Arjungenin, Chikungunya Virus (CHIKV), Docking, Medicinal plants, Non-structural protein.

1. INTRODUCTION

Chikungunya virus (CHIKV) belongs to the Togoviridae family that induces an acute febrile disease with severe, painful polyarthralgia. It is mostly spread to humans through the bite of a mosquito that is infected. From 2005 to 2007, a global outbreak of the Chikungunya virus reached 40 nations and constituted a serious public health concern [1]. CHIKV frequently causes large outbreaks that infect one-third to three-quarters of the populace in the afflicted areas. Severe joint pain in wrists, elbows, knees, toes, and ankles and fever are the most typical manifestations of CHIKV infection [2]. Chikungunya virus infection has also been reported in joint swelling, muscular soreness, and headache as some of the other symptoms. CHIKV has also caused outbreaks in Africa, Europe, Asia, the Americas, the Caribbean, the Indian Ocean, and the Pacific Ocean. Infected tourists have the potential to transfer the illness to unaffected places [3]. Despite increasing health burden and risk, there is no treatment or vaccine available to prevent or treat chikungunya virus infection. Mosquito bite prevention is an effective way for

travelers to protect themselves. Use insect repellent, long-sleeved shirts, and pants, and remain in areas with air conditioning or window and door screens while visiting nations where the chikungunya virus is present [4].

Many synthetic antiviral agents have been developed during the last few decades as a result of expanded scientific research, and they are effective against a wide range of viral infectious illnesses [5]. Unfortunately, a slew of side effects has been recorded from these synthetic pharmaceuticals. They may become ineffective against evolving virus resistance strains in some circumstances. Furthermore, the population of developing countries cannot afford these costly synthetic drugs for viral disease treatment. Given the global burden of viral infections and the high cost of antivirals, new tactics for finding effective and affordable antiviral treatments are urgently needed. Medicinal plants and their bioactive metabolites have recently become one of the most frequently researched areas in the hunt for effective and inexpensive drugs to address growing demands [6], [7]. Traditional indigenous herbal medicine has a long history of treating a broad range of chronic and infectious diseases. Therefore, the hunt for new antiviral agents is centered on plant-derived metabolites as well as synthetic mixtures. A range of plant metabolites can prevent viral replication with few side effects and without compromising the physiology of the host. These natural compounds could have the capacity to regulate the immunological responses of the host opposing viral infections in addition to direct impairment of viral replication.

From a pre-existing understanding of herbal medicines, there is so much to learn and understand about plant restorative characteristics that can be investigated for diverse uses as prospective antiviral drugs. It is simple to locate plants that can be studied; however, past knowledge must be transformed into medical formulations in the development of innovative drugs, ultimately taking it from the laboratory bench to the patient.

Even though various medicinal plants and plant-derived compounds have been shown to have antiviral properties, suitable integrated substantial studies of prior research with mechanistic insights are lacking. For the development of pharmaceuticals, investments in research & development are rapidly adopting plant-based methods. To develop novel drug agents and treatments, pure phytochemicals and extracts from plants have been explored. Terpenoids, tannins, lignans, flavonoids, and alkaloids are secondary metabolites found in plants that have a range of anti-infection and antioxidant properties [8].

Phytochemicals are exploited as antiviral drugs in several different ways. Carotenoids terpenoids, phenolics, and alkaloids are some of the compounds found in plants [9][10]. To combat viral infection, many techniques have been employed. The host receptors or the binding targets in viral agents can be blocked to prevent viral attachment. At different phases of infection, a virus can be prevented from being multiplied. Attacking DNA/RNA polymerase, post-translation alteration of viral proteins or viral packaging, and other NSPs are some of the ways that effectively impede viral replication. Phytochemicals limit viral replication through a variety of methods.

CHIKV nonstructural proteins (NSPs) are produced as one or two polyprotein precursors that are directly translated from virus genomic RNA. These polyproteins are precisely processed to provide matured NSPs. CHIKV proliferation requires both precursors and matured NSPs. CHIKV NSPs, like other alphaviruses, not just conduct viral RNA duplication but are also required for infectious agent and pathogenicity. Secondly, the NSPs play a variety of roles in

host-virus interaction, notable responses to antiviral evasion. These functions are more virus-(and/or cell-type) specific, which requires further care and attention to develop a potent compound that can make use of NSP proteins as a potential target [11].

Three different domains are present in Alphavirus NSP3. The N-terminal region of 160 aa is designated as the macro domain, and the structure of the CHIKV macrodomain has already been discovered. The macrodomains are called after macro histones, which are uncommon forms of histone proteins that, in addition to the normal histone domains, include the macrodomain. Macrodomains may also be found in other proteins. Rubella virus, hepatitis E virus, alphaviruses, and the other unrelated coronaviruses all exhibit macrodomains in Viruses having RNA as genome [12]. Most macrodomains have the biological function of binding mono-ADP-ribose or poly-ADP-ribose. Therefore, it presents to be a potential target for emerging inhibitors [13][14]. The present study is therefore aimed at testing some of the most potential phytocompounds from plants against non-structural protein 3 macrodomain of CHIKV using virtual screening and molecular docking using Autodock Vina.

2. LITERATURE REVIEW

Research by Puranik et al. assessed the antiviral activity of halogenated Dihydrorugosa flavonoids with NSP3 of CHIKV. They conducted an in silico study on derivatives of Dihydrorugosaflavonoids with NSP3 due to the importance of NSP3 in the replication of CHIKV. They found intrinsic binding of Dihydrorugosaflavonoids with the macrodomain of the NSP3 protein of CHIKV. Two derivatives of Dihydrorugosaflavonoids demonstrated docking scores of −6.86 and −7.54 kcal mol^{-1}. Several in vitro experiments were carried out to demonstrate their anti-CHIKV action.

The “3-(4, 5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide test” was used to establish a non-toxic dosage at 100 M. The inhibiting ability of compounds for CHIKV was assessed using a plaque reduction assay and cytopathic effect test that demonstrated inhibition of up to 95 and 92 percent for 70 M concentrations of the compounds, respectively. The ability of derivatives to decrease viral RNA levels in cells infected with CHIKV to about 95 and 93 percent concentrations at 70 M concentrations of compounds was validated in a “quantitative real-time polymerase chain reaction (qRT-PCR)” experiment. Furthermore, the inhibitory ability of these drugs against CHIKV was confirmed using an immunofluorescence test. Therefore, their study demonstrated the antiviral potential of chloro derivative of dihydro rugosa flavonoid and Bromo derivative of rugosaflavonoid which can be explored in future research [15].

Another study by Hussain et al. also undertook a density functional and molecular docking theory-based approach to determine and screen out the flavonoids from medicinal plants of Indian and Pakistan origin against the 4 NSPs of CHIKV. They carried out a docking study against four NSPs of CHIKV after screening out the pharmacological properties of the compounds. Screening and reducing the number of flavonoids for further investigation is done using an 8.5 kcal/mol threshold. By using DFT, the reactivity of flavonoids that were already screened was investigated.

They found that “5,7,3′,4′-tetrahydroxyflavone”, “Cirsimaritin, tamarixetin”, and “apigenin” from “*Andrographis paniculate*” demonstrated high affinity with NSP1 whereas the tamarixetin, medioresinol, and rhamnetin demonstrated high bind affinity with NSP2. The flavonoids tamarixetin, 5,7,4′-trihydroxy flavone, 5,7,3′,4′-tetrahydroxyflavone, and rhamnetin

all had a high binding affinity against NSP3, but apigenin had a significant binding for NSP4. Therefore, their research provided the above 8 screened compounds with the potential antiviral activity which can be explored more in future research using in vivo and in vitro studies [16].

Chaudhary and Sehgal also performed *in silico* identification of natural ligands having antiviral properties to inhibit the NSP3 macrodomain as a potential inhibitor. Apigetrin, Rutaecarpine, Luteoloside, Baicalin, Amentoflavone, and Baloxavir are six plant-based natural antiviral agents identified as potent inhibitors of the NSP3 macrodomain of CHIKV.

The chosen compounds indicated drug likeliness based on ADMET predictions and target analysis. Simulations revealed that the NSP3 macro domain and the chosen antiviral drugs form energetically favorable complexes. Additionally, using the concepts of each trajectory interaction investigations were performed. The findings indicate that these compounds have a significant likelihood of inhibiting NSP3MD and might be considered for pharmaceutical development for Chikungunya fever [17].

Another research by Keramagi and Skariyachan evaluated lead compounds, their potential, and pharmacokinetic features using data from 43 herbal sources. They also performed molecular docking experiments to examine the binding affinity of chosen plant-based ligands against the selected targets including non-structural proteins and envelope proteins. Their research revealed that Chymopain and Kaempferol are natural flavonols found in "*Carica papaya"*, and Gossypetin, a flavonoid found in "*Hibiscus sabdariffa"* demonstrated significant binding affinity to the presumed drug targets of DENV and CHIKV. The chosen lead compounds exhibited optimal drug likeliness, as well as the ADMET properties essential for drug development which provides a likeliness of the phytoligands for the potential of scale-up [18].

The present study assesses the interaction between the novel triterpene "Arjungenin" which is a natural compound found in *Combretum punctatum, Rudgea viburnoides, and other organisms* against the NSP3 macrodomain of CHIKV. Above studies have demonstrated different Phyto ligands affinity towards the NSPs of CHIKV by using different kinds of methodologies, followed by variety of tests, However, this study focuses on the NSP3 macrodomain to develop and check efficacy of selected phytoligand.

3. METHODOLOGY

3.1. Design

Virtual screening and molecular docking were performed with Autodock Vina. In the present study, the crystal structure of the CHIKV NSP3 macrodomain was retrieved from Protein Data bank RCSB with PDB ID 6VUQ in .pdb format.

The three-dimensional structure of Arjungenin was retrieved from PubChem in the format of XML which was then converted into .pdb format using the Open Babel tool. Docking was then performed using both protein and ligand files in .pdb format. Vina is used to perform the docking and then visualized using Pymol and Biovia drug discovery studio for which each step in given in Figure 1 below.

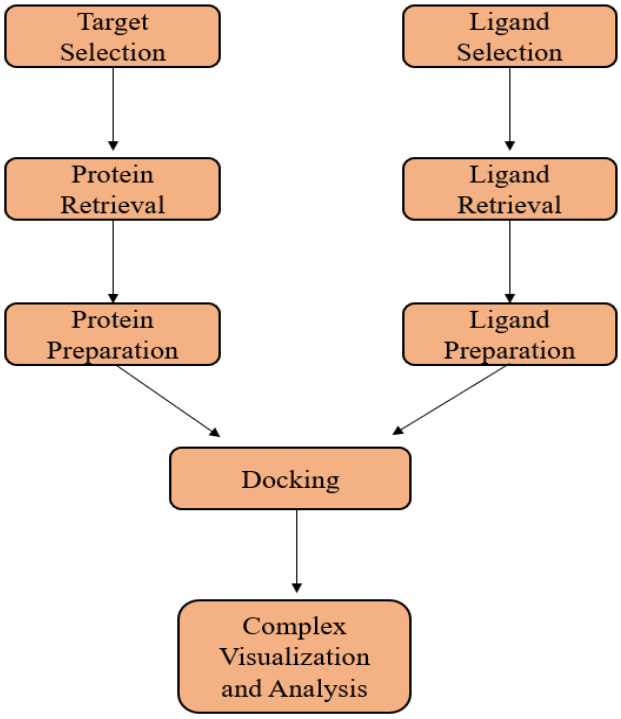

Figure 1: Illustrates the process and the steps to carry out the docking between Arjungenin and NSP3 Macrodomain of CHIKV.

3.2. Sample

The structure of the protein i.e, CHIKV NSP3 Macrodomain is given in Figure 2 below and the ball and stick structure of Arjungenin is represented in Figure 3. In protein structure, red color structures are presenting beta-pleated sheets whereas the cyan-colored spiral structures are representing alpha-helices. In the ball and stick structure of selected ligand arjungenin, green balls are representing carbon, and red oxygen and white balls are representing hydrogen molecules.

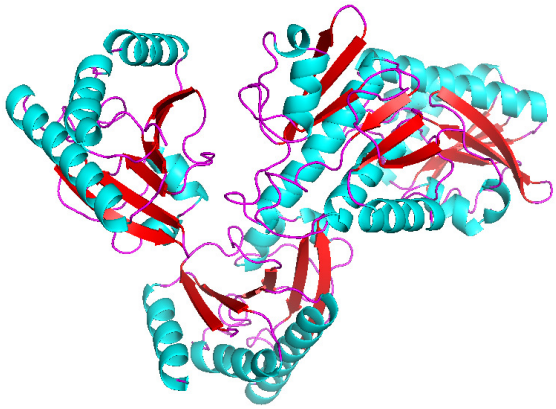

Figure 2: Illustrates the Quaternary structure of the NSP3 macrodomain of CHIKV, where the red ribbons represent the beta-pleated sheet and cyan-colored spirals represent the alpha-helices.

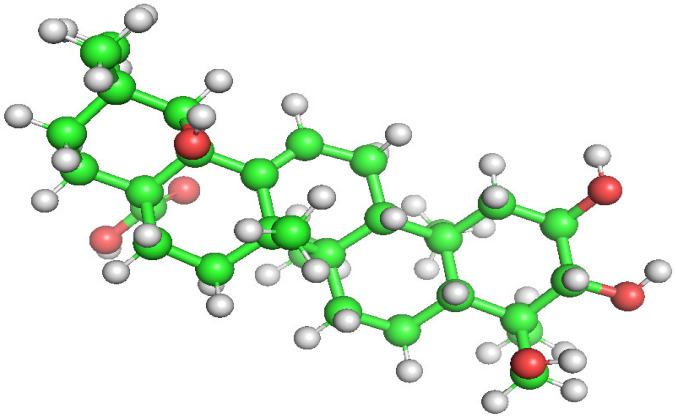

Figure 3: Illustrates the Ball and Stick Structure of Arjungenin.

3.3. Instrument

The 3D structure of Arjungenin was obtained from PubChem. PubChem is the largest collection and database of chemicals, and compounds as well as their activity against experimental assays. This repository is open and maintained by the "National Center for Biotechnology Information (NCBI)", a part of the "National Library of Medicine (NLM)". The three-dimensional structure of the NSP3 macrodomain of CHIKV was downloaded from "Research Collaboratory for Structural Bioinformatics Protein Data Bank", maintained by the "Worldwide Protein Data Bank (wwPDB)", most commonly known by its short-form RCSB PDB. The download of protein was performed in .pdb format under the ID of 6VUQ. This database contains 3-D structural data of nucleic acids and proteins collected and generated from different techniques such as spectroscopy, X-ray crystallography, and cryo-electron microscopy and is freely available.

Further, these structures were prepared with auto dock tools. The protein structure was first refined by using pymol, eliminating unwanted compounds and attached molecules that may hinder the docking process, and falsifying the results. The water molecules were deleted and the polar hydrogens, as well as the Kolman charges, were added. In addition to that ligand was also prepared and the Autodock run was carried out by Autodock Vina which is an open and easily accessible tool that is used to check the binding affinity of the protein-ligand molecule as well as the protein and protein interaction. The interaction between the protein and ligand with a bond as well as the bond lengths can also be identified. After that, the docked complex was recovered and then the Drug Discovery studio and pymol were used for visualization and further analysis was carried out. The bond formation and the distance between them were further visualized using accessory tools which further helped in the analysis of ligands to block and inhibit the selected protein.

3.4. Data collection

The docked files were obtained in the format of .pdbqt after the docking was performed using Autodock Vina. After opening the file in pymol, the interaction between the protein and the nine poses of ligand was analyzed giving the first pose the most attention for visualization. After visualization, the Biovia Drug Discovery studio tool was used to check different kinds of bond formation between the protein and ligand complex obtained from 1st pose, given in Figure 4 as well as the 2 D structure was also retrieved from Biovia drug discovery studio which is given in

Figure 5. The affinity scores of different poses with the NSP3 protein of CHIKV are given in Table 1 in order from most affinity score to least affinity score.

Table 1: Illustrates the docking score and the affinity of poses between Arjungenin and NSP3 Macrodomain.

Mode	Affinity(kcal/mol)	Dist from the Best mode	
		rmsd l.b.	rmsd u.b.
1	-8.4	0.000	0.000
2	-8.3	1.763	2.218
3	-8.1	11.670	15.987
4	-8.1	11.219	14.858
5	-8.0	25.787	29.995
6	-8.0	12.004	15.088
7	-7.9	11.620	14.784
8	-7.9	26.494	30.459
9	-7.8	28.508	30.719

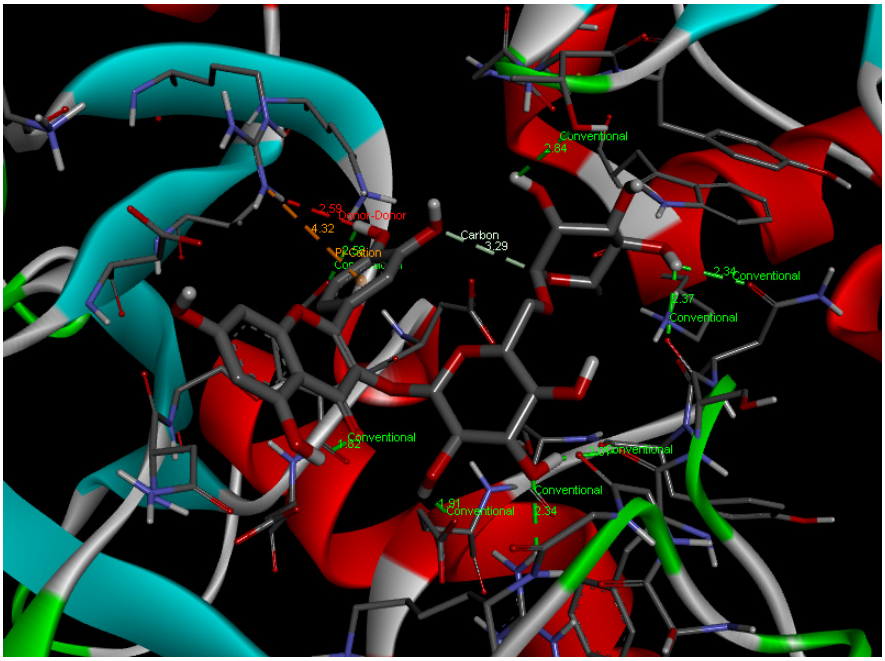

Figure 4: Illustrates the 3-D structure of Interaction between amino acids of protein and ligand (Grey sticks) representing the nature of bonds and the distance between them.

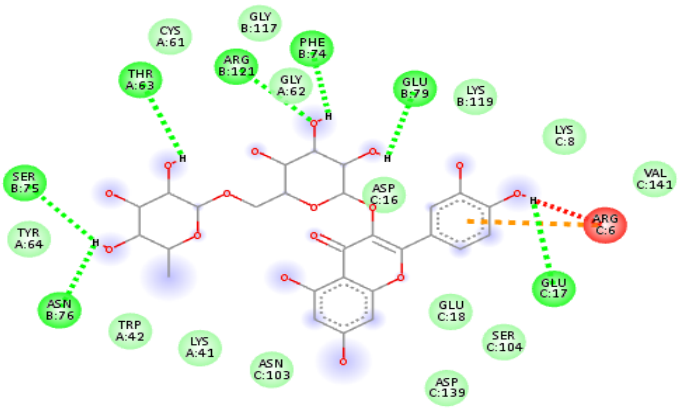

Figure 5: Illustrates 2 D Docked structure representing the amino acids involved in the interaction.

4. RESULTS AND DISCUSSION

A molecular dynamic study was performed and assessed the protein and ligand interaction in terms of binding energy which is simply defined as the total intermolecular energy exhibited by the target protein called receptor and the selected compound called ligand. After docking using Vina, the log file as well as the output file were recovered which were then used to check the most affinity pose of the ligand with amino acids of the protein. It should be noted that the more negative the energy between protein and ligand demonstrates that the stabilization of protein and ligand is stronger. It was noted that the affinity of the very first pose was -8.4kcal/mol which further implies the stability of the docked structures. Hydrogen bond formation was also noted between the ligand and the amino acids of the protein namely ARG121, GLU17, GLU79, SER75, ASN76, THR63, PHE74, and electrostatic bond formation was observed with ARG6:NH2. Apart from that, a close distance was also observed between the protein and ligand interaction with specific distances in terms of Angstrom which is given in Table 2.

Table 2: Illustrates the interaction of amino acids and ligands with their respective Distance, bond categories, and types.

Ligand: Protein	Distance (Å)	Bond Category	Types
UNL1 : ARG121	2.339	H – Bond	Conventional H – Bond
UNL1 : GLU17	2.582	H – Bond	Conventional H – Bond
UNL1 : GLU79	1.914	H – Bond	Conventional H – Bond
UNL1 : SER75	2.365	H – Bond	Conventional H – Bond
UNL1 : ASN76	2.341	H – Bond	Conventional H – Bond
UNL1 : THR63	2.839	H – Bond	Conventional H – Bond
UNL1 : PHE74	2.006	H – Bond	Conventional H – Bond
UNL1 : ARG6	4.315	Electrostatic	Pi – Cation

There is very little information about the NSP3 macrodomain of CHIKV and its inhibitor molecules. The current investigation is critical for discovering potential antiviral compounds against CHIKV. In future research, the precise binding mechanisms of the discovered inhibitors need to be explored more using more calculations of affinity binding between protein and ligands, and their inhibitory activity of the ligand needs to be validated using experimental research and large trials. Furthermore, the current study provides important information for developing drug candidates in ligand-based drug design and for producing chemical pools used in the development of anti-CHIKV agents.

5. CONCLUSION

Arjungenin is a new triterpene discovered to have significant anti-viral and anti-inflammatory activity against a range of viruses. Plant-based triterpenes have received a lot of attention in recent years due to their potential to be used in anti-viral therapy which can be supported by the current study about its effect on CHIKV NSP3 macrodomain is one the essential and imported target to stop the viral replication. Furthermore, it can explicate the Arjungenin with appropriate modifications and can be proven to be a deserving candidate for further study to find out the mechanistic insights for their effective Anti-CHIKV activity.

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CHAPTER 19

COMPREHENSIVE INVESTIGATION OF THE EFFECT OF POSTPARTUM PERIOD ON THE QUALITY OF A WOMAN'S LIFE

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ABSTRACT:

A woman has the power to create, nurture and transform. Giving birth to a child is an important part of a woman's life. It is a fact that 35-50% of females face baby blues or postpartum blues (Type of Postpartum Experience) after childbirth. Pain experienced during childbirth critically affects the maternal psychological state. It has been reported in many cases that after the child's birth maternal postpartum depression increases. The current study is conducted to understand the relationship between quality of life and postpartum experience. A total of 332 responses were collected from the females that have recently given birth to new ones with normal delivery in India. Our study found that the higher values of social support predicted higher quality of life while the lower values of trauma and loneliness predicted lower values of quality of life. Based on the obtained results, the current study also suggested a few strategies and approaches that can be implemented by the women or the mother of a newborn to cope-up with the postpartum experience.

KEYWORDS:

Childbirth, Loneliness, Postpartum, Social Support, Trauma, Quality of Life.

1. INTRODUCTION

The experience of childbirth is considered multidimensional. The delivery experience is influenced by a sense of control and security, participation in decision-making, the information offered, intrapartum analgesia, previous births, midwifery care, personal support, and the amount of labor pain experienced [1]–[5]. Maternal discontent is linked to unplanned medical interventions during labor, such as the requirement for neonatal intensive care, surgical vaginal births and emergency cesarean, intrapartum problems, and oxytocin augmentation. Postpartum depression is a kind of depression that occurs after a woman has given birth to a child. It impacts more than 25% of the population. Psychological mood swings, difficulty caring, guilt, worry, exhaustion, and frequent sobbing for their newborn are all symptoms of postpartum depression [6]–[8].

Having a child is a once-in-a-lifetime event. Parenting is exciting, but it can also be exhausting and stressful. It's natural to feel concerned or unsure, particularly if you're a first-time parent. If a person experiences great loneliness or sorrow, as well as strong mood fluctuations and frequent sobbing episodes, then the person may be suffering from postpartum depression. PPD

(postpartum depression) is a kind of depression that occurs after a woman has given birth. The individual who gives birth is not the only one who suffers from postpartum depression [6], [9]–[13]. It may also have an impact on surrogate mothers and adoptive families. After having a kid, people go through social, economic, emotional, hormonal, and physical changes. Symptoms of postpartum depression might arise as a result of the aforementioned alterations [14]–[16].

1.1.Postpartum Mood Disorders are divided into three categories:

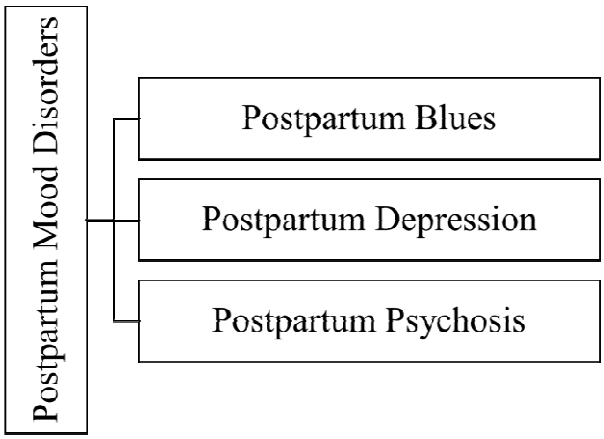

Figure 1: Representing the Three Categories of Postpartum Mood Disorders

1. Baby blues or postpartum blues:

Between 50-75 % of adults experience the baby blues just after giving birth to a child. A person will experience regular, extended episodes of crying without any reason, unhappiness, and worry if he/she is suffering from baby blues. The problem frequently happens during the initial weeks after birth (one to four days). Notwithstanding the unpleasantness of the situation, it usually passes in 2 weeks without any therapies (Figure 1) [17], [18].

2. Postpartum depression:

Postpartum depression, which affects around one in every seven new parents, is significantly more severe than baby blues. If some experienced postpartum depression previously, the chances of getting it again rise to 30% with each pregnancy. He/she might encounter consecutive up and downs, as well as feelings of incapacity, worry, and guilt to care for the infant, and also frequent weariness, irritability, and sobbing. Symptoms may vary from moderate to severe, and they might emerge suddenly or gradually (even up to a year after birth). Even though symptoms might continue for months, antidepressants or psychotherapy are highly effective treatments [10], [19], [20].

3. Postpartum psychosis:

It is an exceptionally severe type of PPD that requires instant medical intervention. This is a rather uncommon disease, affecting just 1 in 1,000 persons after birth. The symptoms usually appear soon after birth and are severe, lasting a few weeks to months (2-3 months). Severe agitation, mania, quick speech, hyperactivity, hallucinations or delusions, paranoia, sleeplessness, feelings of humiliation and despair, and disorientation are a few symptoms of

Postpartum psychosis. Postpartum psychosis necessitates immediate medical attention due to the increased possibility of suicides and damage to the newborn. Therapy plans usually include hospitalization, therapy, and medications [21]–[25].

1.2.Symptoms of Postpartum Depression:

Postpartum depression is a very frequent occurrence. After giving birth, up to 75% of individuals suffer from baby blues. Up to 15% of these women will have postpartum depression. Postpartum psychosis affects one out of every 1,000 women. After giving birth, many individuals experience baby blues. The symptoms of baby blues and postpartum depression are identical. The signs of baby blues, on the other hand, endure around ten days and are less severe. Signs of postpartum depression may last weeks or months, and they are more intense. Precise symptoms of postpartum depression are given in Figure 2 [26], [27].

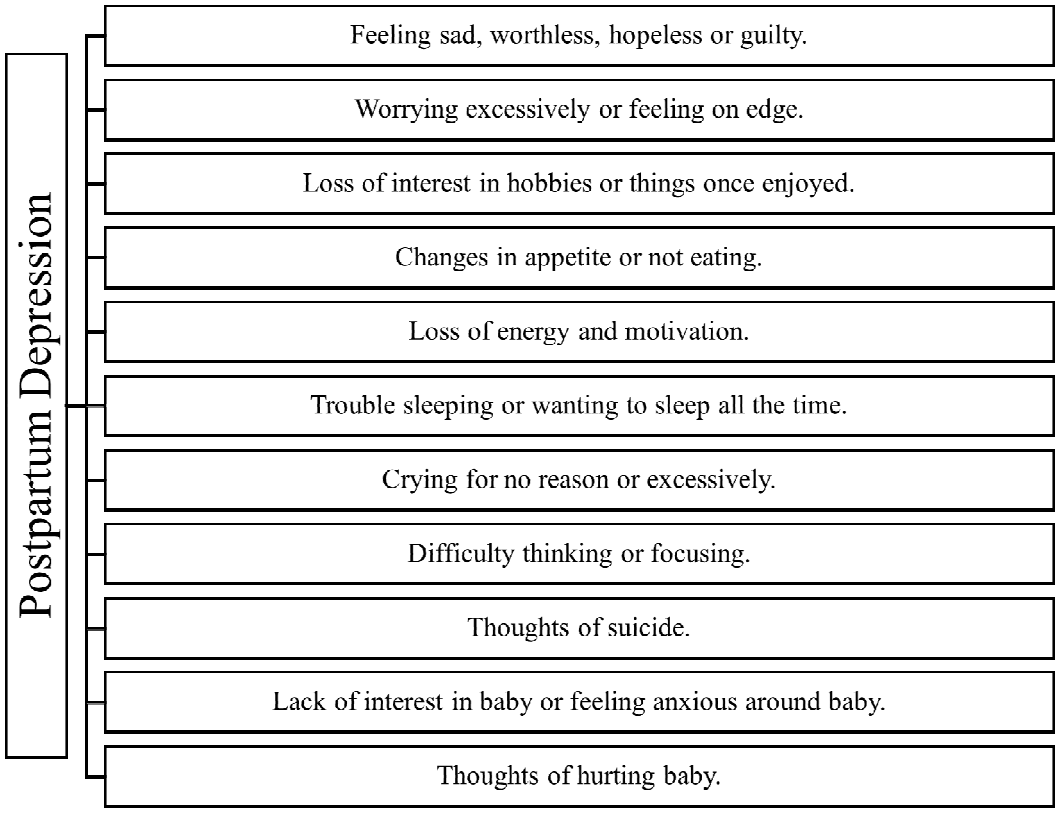

Figure 2: Representing the Various Symptoms of Postpartum Depression

There is very less literature available to determine the rapid decrease or instant drop in the hormones after giving birth to a baby. It has been suggested that the two main hormones in the female life cycle i.e., estrogen and progesterone, increase around ten-fold during pregnancy but a sudden drop is faced after childbirth which causes major mood swings. The current study is conducted to understand how the postpartum experience affects the life quality of a woman.

2. LITERATURE REVIEW

Dencker et al. conducted a study to develop a questionnaire to assess the experience of females that gave childbirth for the first time. In their study, a total of 920 responses were collected from

primiparous women. They used 22 item questionnaire, this questionnaire gave 4 factors which accounted for a total of 54% of the variance. The authors of this study concluded that the developed child experience questionnaire has potential and can be used as an instrument to recognize the negative experiences faced by women and develop strategies for their improvement[28]**.**

Fernandez et al. in their study found that the case women who work at night require fertility treatment as compared to women who work the day shift or that do not work at all. The authors collected the data from the South Australian Perinatal Registry. In this study, the authors found that women who are less than 35 years old and work the night shift had more chances to go for fertility treatment. They also found that the women who seek fertility treatment have more ratio of night shift workers [29]**.**

DeYoung & Mangum conducted a study in the United States to understand the influence of the COVID-19 Pandemic on pregnancy, childbirth, and postpartum experience. In this study, the authors included 34 states of Unites states from the regions of Central, Southeast, Midwest, Southwest, and Northeast. The authors found that there were several factors for stress during the period of pregnancy in a woman. The authors concluded in their study that COVID-19 is associated with the activation of psychological trauma within the time frame of postpartum and also affects the mental health of mothers[30]**.**

Powell et al. discussed the efficacy and safety of the brexanolone drug to treat PPD. They conducted a review study and tried to gain maximum knowledge on the efficacy and safety of the article published under Food and Drug Administration (FDA) approval. With this review, the authors found that many medications are available for the treatment of PPD but only brexanolone is approved by the FDA. They concluded that brexanolone can be used to treat severe as well as moderate PPD[31]. A similar study was also conducted by Barak & Glue, in their study, they stated that PPD is dangerous for both infants as well as mothers. Authors concluded that medications of brexanolone can help in managing PPD but it is costly. They suggested the oral administration of progesterone for the betterment of the postpartum experience[32].

The current study is conducted to collect information on how the postpartum experience affects the quality of life of a woman. This study can aid in the introduction and development of new strategies for the management of postpartum experience. The current study has also suggested a few strategies based on the responses provided by the respondents.

3. METHODOLOGY

3.1.Design:

In the year 2021, a survey was launched in India through social media sites like Facebook, Twitter, etc. The privacy of every person was maintained during the collection of data by removing the name of the respondent. In the current study, responses were collected from January 2021 to October 2021. Most of the respondents were in their postpartum phase when they received the questionnaire while some were in their pregnancy phase. The questionnaire had a total of 24 questions about loneliness, trauma, Quality of life, and Social Support. For trauma authors used the PCL Scale (PTSD (Post-traumatic stress disorder) Checklist) is used. For the quality of life, the Satisfaction with Life Scale (SWLS) is used. Likert Scale is used to calculate Loneliness and Social Support.

3.2.Sample:

A total of 332 responses were collected from January 2021 to October 2021. It was reported that the majority (72%) of the respondents either graduated or received secondary education (Table 1). As shown in Figure 3, the majority (54.8%) of infants were recently born. It was also reported that the majority (55.4%) were ready to lactate their child for 3 months only (Figure 4).

Table 1: Illustrating the Level of Education Attained by the Selected Respondents

		Frequency	Percent
Education Level	10th	27	8.1
	12th	114	34.3
	Graduation	125	37.7
	Masters	35	10.5
	Doctorate	31	9.3
	Total	332	100.0

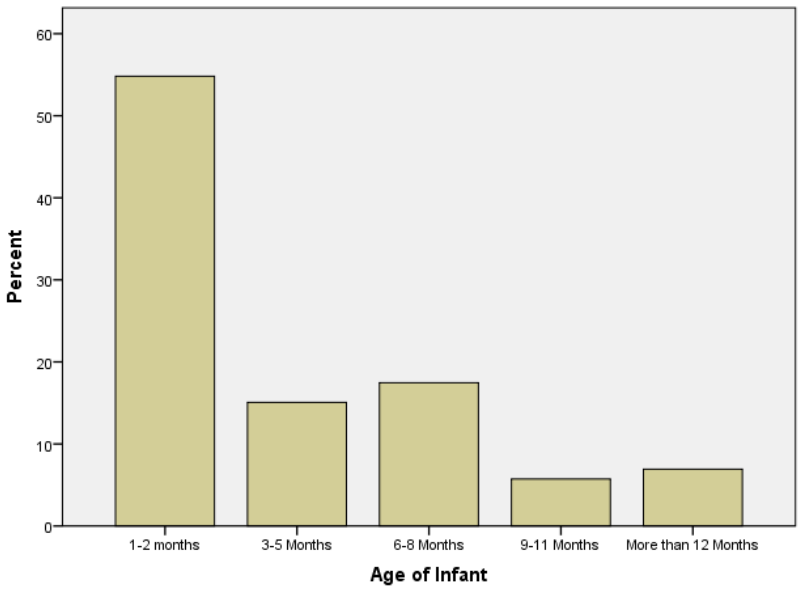

Figure 3: Represents the Age of New-born Infants versus the Total Percent Surveyed (During the Attempt of Questionnaire)

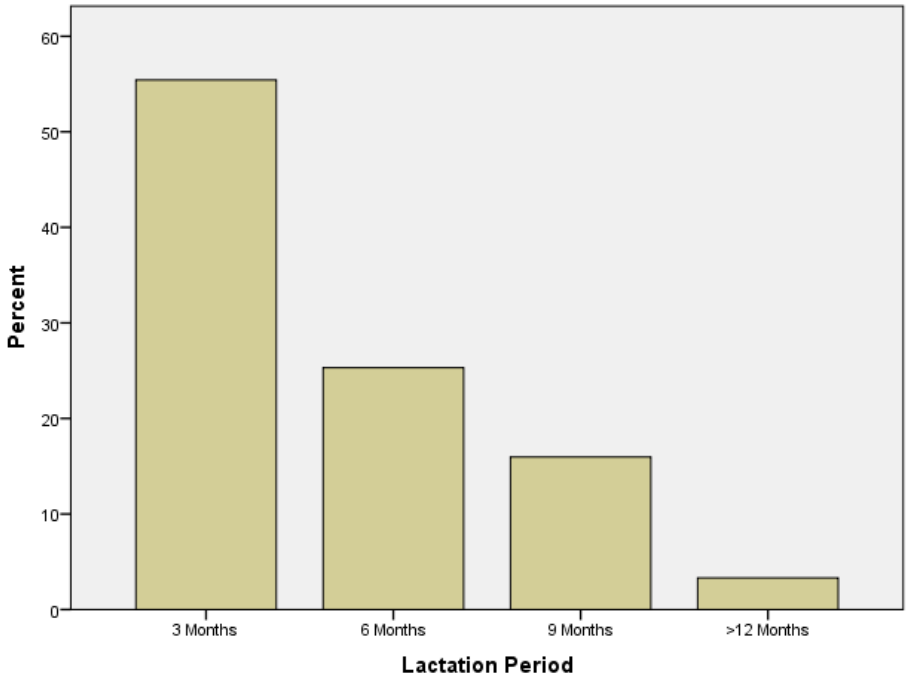

Figure 4: Representing the Duration of Lactation of a Child by Their Mothers versus Total Percent Surveyed

3.3.Instruments:

4. PTSD Checklist Scale: It is a 17-item standardized self-report rating scale for PTSD that corresponds to the main symptoms of the disorder [33]. The PCL is available in two versions: PCL-M is particular to PTSD produced by military events, while PCL-C is used to describe any traumatic incident. In our current study, 10 Items were selected to measure the trauma. These 10 items will measure the frequency of repeated unwanted memories, negative thoughts, stressful situations, disturbing dreams, physical reactions, loss of interest, feeling cut off, easily startled, trouble sleeping, and less concentration.

5. Satisfaction With Life Scale (STWS): This scale has 5 items for the measurement of the subjective well-being of a person [34]. In the current study, all 5 items are used for the measurement of quality of life.

3.4.Data Collection:

Bivariate correlation was conducted on 5 items i.e., Age of infant, Trauma, Quality of life, loneliness, and social support as shown in Table 2. It was found that none of the factors was significantly related to the age of the infant. Trauma, loneliness, and Social Support were statistically significant with Quality of life. Trauma and loneliness were negatively correlated while Social Support positively correlated with the quality of life. The age of the infant is excluded from the regression as it was not statistically significant. Further linear regression was conducted to measure the impact of postpartum experience on the quality of life.

Table 2: Illustrating the Bivariate Correlation between the Age of the Infant, Trauma, Quality of Life, Social Support, and Loneliness. Here 'r' represents Pearson's Correlation Coefficient.

		Age of Infant	Trauma	Quality of Life	Social Support	Loneliness
Age of Infant	r	1	0.023	0.075	0.052	-0.013
	Sig. (2-tailed)		0.678	0.171	0.347	0.807
	N	332	332	332	332	332
Trauma	r	0.023	1	-0.123*	0.044	-0.008
	Sig. (2-tailed)	0.678		0.025	0.427	0.886
	N	332	332	332	332	332
Quality of Life	r	0.075	-0.123*	1	0.105	-0.166**
	Sig. (2-tailed)	0.171	0.025		0.056	0.002
	N	332	332	332	332	332
Social Support	r	0.052	0.044	0.105	1	0.004
	Sig. (2-tailed)	0.347	0.427	0.056		0.947
	N	332	332	332	332	332
Loneliness	r	-0.013	-0.008	-0.166**	0.004	1
	Sig. (2-tailed)	0.807	0.886	0.002	0.947	
	N	332	332	332	332	332

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

3.5.Data Analysis:

Descriptive Statistics of the factors are represented in Table 3. The mean of trauma, quality of life, loneliness, and social support was found to be 35.048, 17.340, 3.367, and 4.048. Overall, the suggested model is significant at $p < 0.005$ with an adjusted R square value of 0.47 (Table 4).

Table 3: Representing the Descriptive Statistics of Trauma, Quality of Life, Social Support, and Loneliness.

	Mean	Std. Deviation
Trauma	35.048	6.9250
Quality of Life	17.340	3.8218

Social Support	3.367	0.9881
Loneliness	4.048	0.9283

Table 4: Represents the Summary of the Model Used in the Current Study

Model	R Square	Adjusted R Square	Std. An error in the Estimate
1	0.55	0.47	3.7314

a. Predictors: (Constant), Social Support, Loneliness, Trauma

4. RESULTS AND DISCUSSION

For the regression analysis, the Dependent variable is chosen to be the quality of life, as previously written, the age of the infant is not considered in the regression analysis since it was not statistically significant. As shown in Table 5, β values for Trauma, Loneliness, and Social support, while keeping the dependent variable as Quality of life, are -0.130, 0.111, and -0,167 respectively. Similarly, the p-values for Trauma, Loneliness, and Social support were 0.0.16, 0.039, and 0.002, and the t-values for Trauma, Loneliness, and Social support were -2.411, 2.075, and -3.112 respectively. Our model suggested that a higher value of quality of life is associated with the higher values of social support, similarly, the higher values of trauma and loneliness are associated with the lower values of quality of life.

Table 5: Representing the Multi-Regression Analysis. (Dependent variable = Quality of Life).

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig. (p)	95.0% Confidence Interval for B		Collinearity Statistics	
		B	Std. Error	Beta			Lower Bound	Upper Bound	Tolerance	VIF
1	(Constant)	21.178	1.535		13.793	0.000	18.157	24.198		
	Trauma	-0.071	0.030	-0.130	-2.411	0.016	-0.130	-0.013	0.998	1.002
	Loneliness	0.431	0.208	0.111	2.075	0.039	0.022	0.840	0.998	1.002
	Social Support	-0.688	0.221	-0.167	-3.112	0.002	-1.122	-0.253	1.000	1.000

a. Dependent Variable: Quality of Life

5. CONCLUSION

During and after pregnancy, a woman's body and psyche undergo several changes. For more than 2 weeks throughout or following childbirth, people experience lonely, emotionless, or unhappiness almost all the time. Women get a feeling that they do not love or care for the baby,

they may be suffering from postpartum depression. Management for depression, like counseling or medication, isn't completely prevented in postpartum depression. It is beneficial to be aware of the condition's warning symptoms as well as the elements that raise your risk.

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CHAPTER 20

A CROSS-SECTIONAL STUDY ON THE PREVALENCE OF PSYCHOLOGICAL HEALTH DISORDERS AMONG URBAN ELDERLY

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ABSTRACT:

There is strong evidence that psychological health disorders are prevalent among the Elderly people. Though little is known about the psychological health disorders of elderly people living in urban surroundings. A Cross-sectional study was used to assess the psychological health of the urban elderly. The current study was carried out on 1671 individuals (aged more than 60 years), from 12 sample areas of 12 cities in India. Psychological Health was measured using the "Cognitive Impairment Test (CIT)", "Geriatric Depression Scale (GDS)", and "Perceived Stress Scale (PSS)". Using the aforementioned scales and tests it was found that Urban elderly males are more prone to all three psychological disorders as compared to females. It was also reported that with increasing age, there are increases in the levels of Cognitive impairment and Geriatric Depression by 71.2% and 11.9 % but somehow there was a slight decrease in the level of stress by 22%. The prevalence of Depression was the highest in the Urban Elderly with 30.9% of the total respondents followed by mild cognitive impairment at 11.4% and Severe cognitive impairment at 17.7%. Similarly, moderate stress was 46.8% but severe stress only accounts for 3.8% of total respondents. Urban Elderly in the range of 70-80 Years has more chances of multiple psychological disorders. The involvement of urban elderly in physical activity and vegetarian diets can help in the reduction of these risks.

KEYWORDS:

Cognitive Impairment Test (CIT), Geriatric Depression Scale (GDS), Perceived Stress Scale (PSS), Psychological Health,Urban elderly.

1. INTRODUCTION

There is strong evidence that aging is one of the major concerns for public health, which is incurable. People who are in their 60s are expected nowadays to live more and most importantly with good health[1]. It has been reported in several literatures that there is rapid population growth which is directly proportional to the increase in elderly people [2]. It has been estimated by the World Health Organisation (WHO) that by the year 2030, there will be 1 person in every 6 people whose age will be more than 60 years. WHO also stated that the population share of older adults (age > 60) will be doubled, from 1 billion in 2020 to 2.1 billion in 2050 [3]. It has been estimated that the elderly age population of Asia only will increase to 24% in 2050 from 12 % in 2020 [4].

It has been reported that older adults living in urban areas are more likely to face several psychological health disorders apart from the other disorders. It is reported that the years of life that are lived with good health are still consistent, which suggests that the extra life years that people are living today are expended in bad health conditions [5], [6]. Individuals' capacity to carry out the activities they cherish would be comparable to that of a child or teenager whether they can enjoy such additional years of life in healthy conditions and a nurturing environment [7], [8]. The consequences for elderly adults and the community are more severe if these extra years are characterized by decreases in physical and psychological capabilities [9]–[12].

In several studies, it has been reported that depression is the most frequent condition that affects the psychological health of elderly people residing the urban areas. It is also reported that these psychological disorders also affect the quality of life of older adults.

Despite this, psychological disorders are not considered serious health concerns in urban elderly people. Since research is scarce on the psychological health of the urban elderly, we have attempted to raise this issue. The current study is conducted on elderly people residing in urban areas. This study will help in the assessment of the psychological health of elderly people residing in urban areas.

2. METHODOLOGY

2.1.Design:

The current study is a cross-sectional analysis conducted in the year 2018 to 2019 on 1671 older adults living in urban areas. Data of 7 self-reported diseases (Hypertension, Diabetes, Cardiovascular Disease, High Cholesterol, Sensory Impairment, Stroke, Psychiatric Illness, Joint Pain, or any other illnesses) and several demographic details (age, gender, marital status, residence, education, employment, present work status, and economic status)was collected from these individuals.

Further, the effect of Health determinants (Diet, Physical Activity, Duration of physical activity, substance habit, sleep, Bowel Clearance pattern, and Body Mass Index range), self-reported diseases, and Number of Multimorbidities on the psychological health of urban elderly was evaluated in this study.

2.2.Sample:

As shown in Table 1, the majority of the respondents were between the age of 60 to 70 years. A total of 516 (30.9%) elderly people living in urban areas were suffering from Cognitive Impairment, 487 (29.1%) elderly people living in urban areas were suffering from Geriatric Depression, and a total of 845 (50.6%) elderly people living in urban areas were suffering from Stress.

It was reported that non-vegetarian elderly people have more prevalence of all psychological disorders. Elderly people who indulge themselves in physical activities had less prevalence of all three psychological disorders. Elderly people who had no drug and no previous substance habit had less prevalence of all three psychological disorders. Elderly people who had normal sleep, and normal bowel clearance patterns but BMI was normal and obese had more prevalence of all the psychological disorders.

Table 1: Illustrating the Prevalence of Psychological Disorders based on Various Health Determinants

		Cognitive Impairment	Geriatric Depression	Stress
		N (%)	N (%)	N (%)
Diet	Vegetarian	237 (14%)	219 (13%)	371 (22%)
	Non-vegetarian	250 (15%)	297 (18%)	474 (28%)
Physical Activity	No	166 (10%)	119 (7%)	187 (11%)
	Yes	321 (19%)	397 (24%)	658 (39%)
Multiple Drug	No Drugs	344 (21%)	373 (22%)	648 (39%)
	Single Drug	102 (6%)	89 (5%)	142 (8%)
	Multiple Drugs	41 (2%)	54 (3%)	55 (3%)
Substance Habit	Nil	344 (21%)	374 (22%)	648 (39%)
	Current	55 (3%)	57 (3%)	96 (6%)
	Past	88 (5%)	85 (5%)	101 (6%)
Sleep	Normal	324 (19%)	319 (19%)	612 (37%)
	Distributed	163 (10%)	197 (12%)	233 (14%)
Bowel Clearance Pattern	Normal	333 (20%)	327 (20%)	641 (38%)
	Constipation	154 (9%)	189 (11%)	204 (12%)
BMI	Underweight	17 (1%)	20 (1%)	24 (1%)
	Normal Weight	248 (15%)	298 (18%)	414 (25%)
	Obese	222 (13%)	198 (12%)	407 (24%)
Total		516 (30.9%)	487 (29.1%)	845 (50.6%)

2.3.Instruments:

The "Perceived Stress Scale (PSS)' is a tool that is utilized to assess the perception of stress. This psychological tool is utilized to measure the stress level of an individual's life circumstances. In this tool, items are selected to replicate the measurement of the overburdened, unmanageable, and unexpected life of an individual. For this test, education of at least 0-5 years is required [13].

The "Six Item Cognitive Impairment Test (CIT)" is a 5-minute cognitive function test frequently utilized in primary care surroundings. This test contains 3 components: memorizing a single address, reversely reciting the months of a year, and counting backward from 20. 6CIT has a strong correlation with the "Mini-Mental State Examination (MMSE)", which is copyrighted and now costs money to use [14].

The “Geriatric Depression Scale (GDS)” is a screening tool for detecting depression symptoms in senior people. The GDS is a self-report instrument with a "yes/no" format that was created by J.A. Yesavage and colleagues in 1982. It comprises a series of questions that evaluate a person's degree of pleasure, interest, social contacts, and other factors. In acute, long-term, and community settings, the GDS is routinely utilized as a part of a full geriatric evaluation. It is suitable for both healthy and medically unwell persons, as well as those with mild to moderate cognitive impairments [15].

2.4.Data Collection:

A Pearson product-moment correlation was run to determine the relationship between Cognitive Impairment, Geriatric Depression, and Stress. As seen in Figure 1, Stress vs Geriatric Depression, the slope is maximum, which suggests that there is a positive and strong correlation between both psychological disorders as compared to other psychological disorders relationships. Urban elderly suffering from stress had more probability/likelihood of having Geriatric Depression. There was a strong, positive correlation between Cognitive Impairment and Geriatric Depression, which was statistically significant ($r = 0.264$, $n = 1671$, $p = 0.000$). It indicates that people who have cognitive Impairment have 26.4% more chances of having Geriatric Depression. There was a weak, positive correlation between Cognitive Impairment and Stress, which was statistically significant ($r = 0.121$, $n = 1671$, $p = 0.000$). It indicates that people who are suffering from cognitive impairment have 12.1% more chances of stress. There was a strong, positive correlation between Geriatric Depression and Stress, which was statistically significant ($r = 0.445$, $n = 1671$, $p = 0.000$). It indicates that people who have Geriatric Depression have 44.5% more chances of Stress.

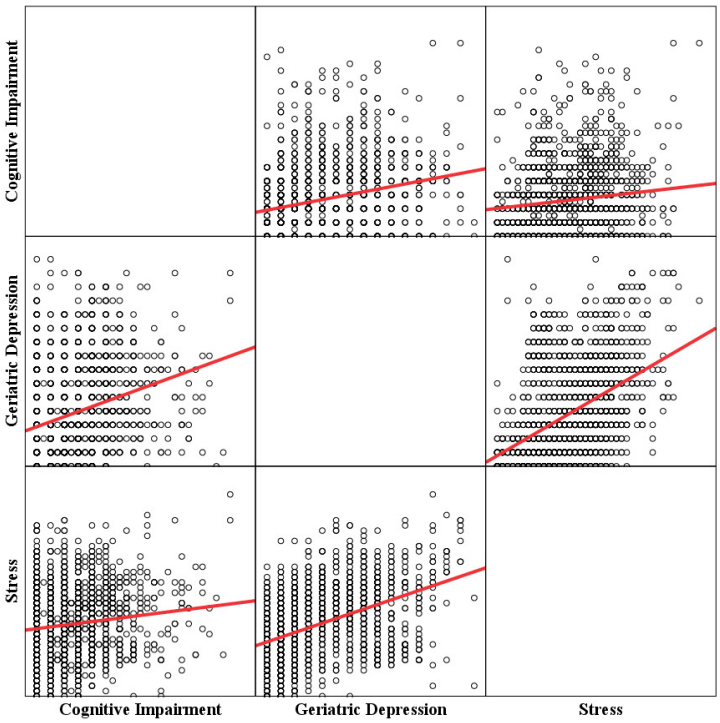

Figure 1: Pearson Correlation Slope between the Cognitive Impairment, Geriatric Depression, and Stress.

Table 2: Pearson Correlation between the Cognitive Impairment, Geriatric Depression and Stress

S. No.	Morbidity	1	2	3
1.	**Cognitive Impairment**	1	0.264	0.121
2.	**Geriatric Depression**	-	1	0.445
3.	**Stress**	-	-	1

3. RESULTS

As shown in Figure 2, Severe Cognitive Impairment and Depression rates in the urban elderly are high as compared to the levels of Severe Stress. It was reported that the prevalence of Mild Cognitive Impairment was 11.4% while Severe Cognitive Impairment was 17.7% in Urban elderly. Around 30.9% of the respondents were suffering from Depression. The prevalence rate of Moderate stress was 46.8%, though, severe stress was low about 3.8% in urban elderly.

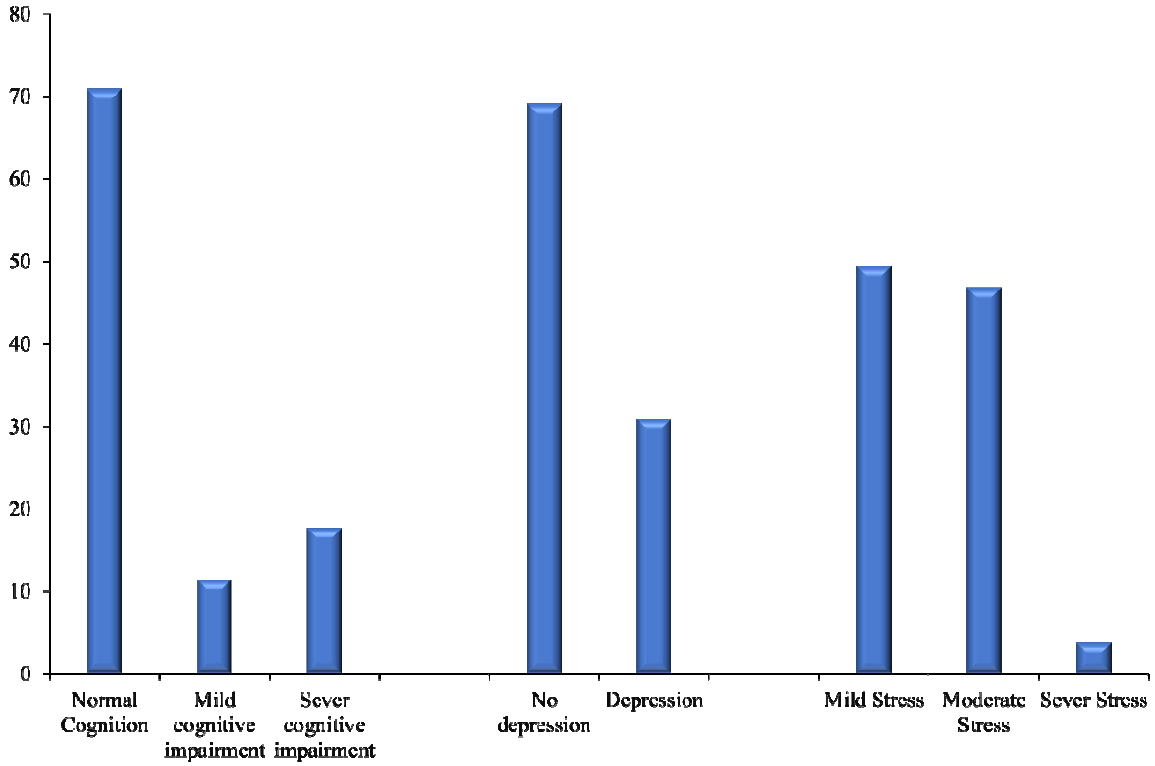

Figure 2: Prevalence of Cognitive Impairment, Depression, and Stress in Urban Elderly

Multiple regression was run to predict Cognitive Impairment, Depression, and Stress from Any other illness Duration, BMI, Psychiatric Illness Duration, Heart Disease Duration, Stroke

Duration, Sensory Impairment Duration, Physical Activity Duration, Total Years of substance use, Diabetes Duration, Joint Pain Duration, Age, High Cholesterol Duration, Years of employment, Hypertension Duration, and Years of education (Table 3). These variables statistically significantly predicted Cognitive Impairment, Depression, and Stress with F (15, 1656) = 28.854, $p < 0.0005$, $R^2 = 0.207$; F(15, 1656) = 15.179, $p < 0.0005$, $R^2 = 0.121$ and F (15, 1656) = 7.726, $p < 0.0005$, $R^2 = 0.065$ respectively. Out of 15 Variables, For the prediction of Cognitive Impairment; Age, Years of Education, and Duration of Physical Activity were added statistically significant. In the prediction of Geriatric Depression; Years of Education, Years of Employment, Duration of Physical Activity, BMI, and Joint Pain Duration were added statistically significant while for the prediction the Stress; Years of Education, Duration of Physical Activity, and Joint Pain Duration was added statistically significant, $p< 0.05$. The R^2 scores indicate that stress is more related to these factors as compared to cognitive impairment and depression.

Table 3: Prevalence of Cognitive Impairment, Depression, and Stress

Psychological Disorder	R	R Square	F	Sig.
Cognitive Impairment	0.455	0.207	28.854	0.000
Geriatric Depression	0.348	0.121	15.179	0.000
Stress	0.256	0.065	7.726	0.000

In Table 4 below, the unstandardized coefficient, B, for age is equal to 0.008. This means that for each one-year increase in age, there is an increase in Cognitive Impairment of 0.008. For one year's increase in education and physical activity, there is a decrease in Cognitive impairment of 0.035 and 0.101 respectively. Similarly, for one year increase in Education, Employment, Physical Activity, and BMI there was a decrease in geriatric Depression of 0.028, 0.002, 0.039, and 0.008 while for one year increase in Join Pain, there was an increase in Geriatric Depression of 0.013. For one year increase in Education and Physical Activity there was a decrease in Stress of 0.016 and 0.054 while for one year increase in Joint Pain, there was an increase in stress of 0.016.

Table 4: Significance of Cognitive Impairment, Depression, and Stress

	Cognitive Impairment		**Geriatric Depression**		**Stress**	
	B	**Sig.**	**B**	**Sig.**	**B**	**Sig.**
Age	0.008	0.000	-0.001	0.537	-0.004	0.067
Years of education	-0.035	0.000	-0.028	0.000	-0.016	0.000
Years of employment	-4.69E-06	0.99	-0.002	0.000	0.000	0.356
Duration For Physical	-0.101	0.000	-0.039	0.008	-0.054	0.001

Activity						
Total Years of substance use	0.002	0.06	0.002	0.034	0.001	0.424
BMI	-0.004	0.148	-0.008	0.005	8.86E-05	0.977
Hypertension Duration	0.001	0.356	-0.001	0.435	0.000	0.821
Diabetes Duration	-0.003	0.044	-0.002	0.128	0.003	0.132
Heart Disease Duration	-0.004	0.162	-0.005	0.082	-0.002	0.548
High Cholesterol Duration	0.002	0.575	0.005	0.21	0.005	0.294
Sensory Impairment Duration	-0.001	0.786	-0.002	0.686	-0.003	0.48
Stroke Duration	-0.011	0.151	0.012	0.133	0.01	0.269
Psychiatric Illness Duration	-0.002	0.803	0.007	0.425	-0.003	0.738
Joint Pain Duration	0.000	0.963	0.013	0.000	0.016	0.000
Any other illness Duration	0.001	0.676	0.000	0.957	0.003	0.186

Table 5 represents the prevalence of lifestyle on psychological disorders. These variables were predicted statistically significant for Cognitive Impairment, Depression, and Stress with F (7, 1664) = 29.904, $p < 0.0005$, $R^2 = 0.112$; F(7, 1664) = 43.165, $p < 0.0005$, $R^2 = 0.154$ and F (7, 1664) = 17.937, $p < 0.0005$, $R^2 = 0.07$ respectively. The R^2 scores indicate that stress is more related to these factors as compared to cognitive impairment and depression.

Table 5: Prevalence of Lifestyle on Cognitive Impairment, Depression and Stress

Psychological Disorder	R	R Square	F	Sig.
Cognitive Impairment	0.334	0.112	29.904	0.000
Geriatric Depression	0.392	0.154	43.165	0.000
Stress	0.265	0.07	17.937	0.000

In Table 6 below, it was reported that Diet, Multiple Drug, and BMI was not added significantly to be the predictor for Cognitive Impairment. Physical activity accounts for the reduction in cognitive impairment while Substance Habit, Sleep, and Bowel Clearance patterns were responsible for the increase. Physical Activity and Substance habit was not added significantly to be the predictor for Geriatric Depression. For one year increase in Diet, Multiple drugs, sleep, and BMI, there was an increase of 0.097, 0.094, 0.226, and 0.22 resp. to the levels of depression. only diet, and sleep was added significantly to the model of stress. For

one year increase in Diet and Sleep, there was an increase in stress of 0.191 and 0.16 respectively.

Table 6: Significance of Cognitive Impairment, Depression, and Stress on Lifestyle

	B	Sig.	B	Sig.	B	Sig.
Diet	0.03	0.166	0.097	0.000	0.191	0.000
Physical Activity	-0.23	0.000	-0.02	0.457	-0.052	0.085
Multiple Drug	-0.021	0.585	0.094	0.014	0.027	0.536
Substance Habit	0.081	0.011	-0.025	0.423	-0.017	0.628
Sleep	0.142	0.000	0.226	0.000	0.16	0.000
Bowel Clearance Pattern	0.13	0.000	0.22	0.000	0.056	0.079
BMI	-0.029	0.127	-0.094	0.000	0.013	0.544

4. DISCUSSION

A logistic regression was performed to ascertain the effects of age and gender on the likelihood that participants have Cognitive Impairment. The logistic regression model was statistically significant, $\chi^2(2) = 1.754$, $p < 0.005$ for Cognitive Impairment and $\chi^2(2) = 0.101$, $p < 0.005$ for Geriatric Depression. The model correctly classified 70.9%, 69.1%, and 52% of cases for Cognitive Impairment, Geriatric Depression, and Stress respectively (Table 7). Increasing age was associated with an increased likelihood of exhibiting Cognitive Impairment and Geriatric Depression by 71.2% and 11.9 % but increasing age was associated with decreasing likelihood of exhibiting Stress. These percentages relate to the results of a study conducted by Nayak et al. in which they found that 25% have Severe Cognitive Impairment[16]. Another study by Hua et al. also found similar results in which they reported that 15.8% of urban elderly had depression [17]. As the age increase, people start to experience several health-related conditions at the same time. In other words, older age can be characterized by the emergence of several health-related concerns or geriatric syndromes [18]–[20]. Ruchi Dhar et al. stated that the rate of depression in India's older population ranges from 14% to 26%. Depression with the help of GDS The result of this study found that there are 40% of old age people survived depression, 32% person had mild depression and another 7% to 8% had serious depression [21]. Males were 1.304, 1.083, and 1.171 times more likely to exhibit Cognitive Impairment, Geriatric Depression, and Stress than females (Table 8).

Table 7: Model Fit for Cognitive Impairment, Depression, and Stress

Morbidity	Chi-square	Percentage Corrected
Cognitive Impairment	1.754	70.9 %
Geriatric Depression	0.101	69.1 %
Stress	0.004	52 %

Table 8: Prevalence of Psychological Disorder on Age and Gender

Variables		B	S.E.	Wald	Sig.	Exp(B)	95% C.I. for EXP(B)	
							Lower	Upper
Cognitive Impairment	**Age**	0.538	0.111	23.296	0.000	1.712	1.030	1.067
	Gender	0.266	0.109	5.961	0.015	1.304	1.052	1.612
Geriatric Depression	**Age**	0.113	0.111	1.03	0.310	1.119	0.985	1.019
	Gender	0.08	0.106	0.562	0.453	1.083	0.876	1.328
Stress	**Age**	-0.118	0.103	1.301	0.254	0.889	0.976	1.007
	Gender	0.158	0.098	2.585	0.108	1.171	0.967	1.420

The logistic regression model was statistically significant, $\chi 2(2) = 13.964$, $p < 0.005$ for Geriatric Depression and $\chi^2(2) = 13.964$, $p < 0.005$ for Geriatric Depression. On the other hand, a model was not statistically significant, $\chi^2(2) = 5.313, p > 0.005$ for Cognitive Impairment. One morbidity had to decrease the likelihood ofGeriatric Depression while increasing the likelihood of exhibiting Cognitive Impairment and Stress (Table 9). Two or more two morbidities had to decrease the likelihood of Cognitive Impairment while increasing the likelihood of Geriatric Depression and stress. Cognitive Impairment was 1.138 times more likely to be one morbidity but had to decrease, 0.845 times, odds for two or more morbidities. On the other hand, Geriatric Depression had 1.477 times more odds for two or more morbidities and decreasing odds for one morbidity. Stress was 1.780 and 1.677 times more likely to be exhibited in one or more morbidities (Table 10).

Table 9: Model Fit of Psychological Disorder on Morbidity

Morbidity	Likelihood Ratio Tests		
	Chi-Square	df	Sig.
Cognitive Impairment	5.313	2	0.070
Geriatric Depression	13.964	2	0.001
Stress	22.198	2	0.000

Table 10: Prevalence of Psychological Disorder on One or Multiple Morbidity

Morbidity		B	Std. Error	Wald	df	Sig.	Exp(B)	95% Confidence Interval for Exp(B)	
								Lower	Upper
One Morbidity	**Cognitive Impairment**	0.129	0.147	0.770	1	0.380	1.138	0.853	1.519
	Geriatric	-0.062	0.154	0.163	1	0.686	0.940	0.695	1.271

	Depression								
	Stress	0.577	0.133	18.760	1	0.000	1.780	1.371	2.311
Two or More Morbidity	**Cognitive Impairment**	-0.169	0.145	1.348	1	0.246	0.845	0.635	1.123
	Geriatric Depression	0.390	0.147	7.041	1	0.008	1.477	1.107	1.969
	Stress	0.517	0.130	15.924	1	0.000	1.677	1.301	2.162

5. CONCLUSION

The current study measured the prevalence of psychological disorders (Cognitive Impairment, Geriatric Depression, and Stress) in elderly people living in urban areas of India. Results conclude that the in later life there are more probabilities or prevalence of Cognitive Impairment and Geriatric Depression but less prevalence of Stress. Also, the inclusion of several health policies or the involvement of elderly people living in urban areas in physical activities and following a healthy vegetarian diet lifestyle can help in the reduction of psychological disorders.

6. LIMITATIONS

In the current study, elderly people living in urban areas are considered. Elderly people living in rural areas are also the victim of several psychological disorders, deprived of major life-easing facilities.

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CHAPTER 21

EXPLORING THE EFFECT OF ORAL INFECTION ON THE HUMAN BODY

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ABSTRACT:

Oral Infections are the infections cause by airborne disease or by polluted infections which undergoes inside the mouth and make the mouth structure with lots of problems. The need to study about the oral infections because they are very dangerous for humans, Oral infections can be very dangerous because it damages the oral structure of the humans. The objective of the study is to analyze the effects of the oral infection on human body and related causing problem of the oral infection. The outcome of the study gives more information about the oral infections and precautions to take care from the oral infections. In future, oral infections wants to take more serious actions, to control the oral infection more methods have to be come.

KEYWORDS:

Human Body, Human Diseases, Infections, Oral Infection,Polluted Infections.

1. INTRODUCTION

The majority of human diseases are oral infections. Numerous studies have linked periodontitis and other mouth infections to an increased risk of atherosclerotic cardiovascular disease. From early childhood to late age, some mouth infections are frequent. Discover the eight most typical oral infections, their warning symptoms and signs and when to seek medical attention, teeth, gums, and tongue are all susceptible to infections and diseases, just like any other part of your body. The severity of various oral infections varies. However, you can avoid them if you are knowledgeable about these frequent oral infections, their origins, and the normal symptoms.

Over the past two decades, the connection between dental and overall health has gained more recognition. Numerous epidemiological studies have connected poor oral health to a range of illnesses, including cardiovascular disease, poor glycemic management in diabetics, low birth weight in preterm infants, and others, include osteoporosis and rheumatoid arthritis. Oral infections are acknowledged as an issue for people with a variety of chronic illnesses, such as cancer, a human immunodeficiency virus infection, and patients with ventilator-associated infections.

Improvements in the knowledge, prevention, and historically, oral illnesses have been treated 50 years have resulted in a dramatic rise in the proportion of people keeping more of they can keep their natural teeth longer. But several of these tooth have already been severely damaged. Repaired and vulnerable to future deterioration, and this growing population of dentate

individuals is at periodontal disease risk. Oral health is the end objective of contemporary dental treatment, although it is not always possible to acquire or maintain it. In many cases, just a halting of the disease's course can be achieved, and persistent chronic asymptomatic infections are possible. Additionally, mucosal chronic or malignant illnesses are becoming more prevalent. As a result, the mouth has emerged as oral infection holder.

Periodontal diseases (gingivitis, periodontal, see dictionary) and dental decay are the most prevalent oral infections (tooth decay). The attachment mechanism that surrounds and secures teeth to the alveolar process of jaws is made up of the cementum, which is the tooth root's outermost calcified layer, and highly structured collagen fibres known as periodontal ligaments. Due to the involvement of these structural components in infectious activities that directly cause bacteremia, systemic exposure to tooth infections frequently occurs. Since dental caries only affects the hard surfaces of teeth, it does not result in a systemic bacterial exposure. But if ignored, dental caries advances to the dentine (nervous system the blood vessels of the molar), causing a root canal disease that spreads to the bone and other supporting structures, greatly increasing the levels of systemic exposure. Any infection brought on by one of these species should make the clinician aware of the likelihood of an oral source, as the mouth is unquestionaba major reservoir of germs. Although there have been some cases of oral bacteria causing brain abscesses, the classic example is endocarditis brought on by viridians group bacterial spores. Anatomical obstacles or tissue divisions, such as muscle and bone, typically act as barriers to stop the recurrence of oral infections. However, it is possible for an infection to migrate back and down toward the esophagus and the abdomen. An important tenet is that successful treatment has always been based on correctly executed dental operations, and that treating oral infection cannot be accomplished solely through the use of antibiotics. In Figure 1 shown the overall oral system of the mouth which could be get infected by oral infections.

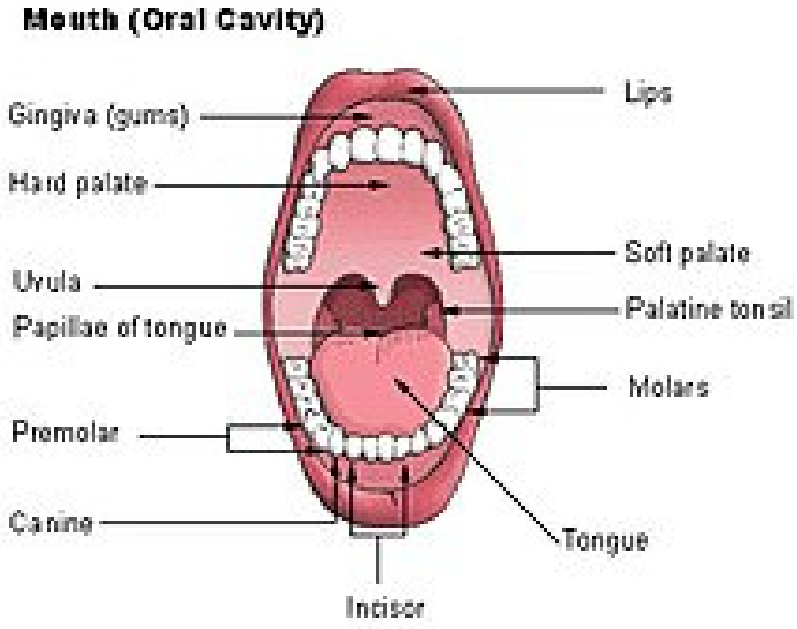

Figure 1: Depict the overall oral system of the mouth which could be get infected by oral infections.

More and more systemic disorders, including rheumatologically and gastroenterological conditions, are being treated by moderate-to-severe immunosuppressive drugs. A growing percentage of the population is also affected by cancer and the treatments that go along with it. The total management of patients with weakened immune systems and medical conditions depends critically on their oral health. Oral infections frequently have little symptoms and are persistent in nature.

2. LITERATURE REVIEW

Stina Syrjänen [1]discussed Oral appearances of human papillomavirus contagions that One of the earliest viruses ever discovered, papillomaviruses have been around for 330 million years. Human infections (HPV) have evolved into hijacker of human cells and immunological systems where they proliferate and remain dormant during the course of this lengthy evolution. The author concludes summarizes the state of knowledge regarding the virus, its methods of transmission, and the whole range of oral HPV infections, including asymptomatic infections, benign, potentially cancerous oral blemishes, and basal cell carcinoma.

Niculescu, and Adelina Gabriela Grumezescu [2] et al. discussed Natural compounds for preventing ear, nose, and throat□related oral infections that Preserving general wellbeing requires maintaining oral health. Commensal microorganisms can defend against external pathogenic threats by maintaining the intricate equilibrium inside the oral microbes. But when there is an imbalance, the organism is open to a wide spectrum of illnesses. In order to aid the body in combating the fungal, fungal, or viral burden, synthetic medications might be given. The author also concluded. In order to fully portray the state of the art in oral preventing infection in the ear, nose, and vocal (ENT) sector, the plant-based, algae-based, and beehive products were studied for their antibacterial characteristics.

Farah Al-Tawalbe and Deniz M Alnaqeeb, [3] et al. discussed Medicinal plants for the treatment and management of oral infections that Since ancient times, herbal medicines were used to treat a wide range of illnesses. Natural sources are one of the most crucial areas of research for minimising the effects of oral infections. The usage of traditional remedies has decreased as a result of the development of chemical treatments. The author conludes In order to create natural pharmaceuticals that are both efficient and without side effects in the management of chronic infections, future polyphenol and pharmaceutical studies should concentrate on frequently mentioned therapeutic plants.

Levi, Marilyn and E. Eusterman [4] et al. Oral contagions and antibiotic therapy Grown-ups' odontogenic origins and children's tonsil and lymphatic sources are where oral infections typically start. Periodontal disease or severe dental caries are the causes of oral infections. The authors also conlude the seriousness and potential risk of oral infections are discussed, as well as the antibiotics that can be used to treat them. Understanding the microbiota, the area architecture, the illness process, the therapy options, and interprofessional collaboration collaboration are necessary for successful treatment.

Lihua Zhang and Hualin Liu et al. [5] dicussed in examination of the oral contaminations and displays seen in patients with advanced cancer to examine the epidemiology of mouth infections in patients with advanced cancers and the influences of treatment plans and risk factors on oral infection incidence, a prospective, study was undertaken.The author concludes Patients with

advanced cancer frequently get oral infections, which are linked to medication regimens and risk factors. The people with advanced malignant tumours should receive more dental care.

, X. Kolltveit and K. M. Tronstad [6] explained Complete viruses caused by oral taint that A prospective study was conducted to investigate the demographics of oral infections in patients having terminal malignancies and the effects of treatment regimens and risk factors on the occurrence of oral infections. The author conludes three variables, including shared risk factors, subgingival biofilms functioning as gram-negative bacteria reservoirs, and the periodontal acting as both a reservoir of proinflammatory cytokines, may contribute to periodontitis' ability to influence the host's vulnerability to systemically disease.

3. DISCUSSION

Numerous risk factors, including advancing age, male sex, blood pressure, diabetes, dyslipidemias, and smoking, are very well contributors to vascular disorders. Recent research has also discovered links between previous infections and the onset of myocardial or brain infarction. Patients with coronary or cerebral infarction are said to experience preceding acute respiratory disease more frequently. A cerebral infarction may occur after bacterial meningitis, infectious endocarditis, or any other septicemia disease. Chronic bacterial infections like oral infections are very prevalent. While oral infections are localized, they can cause temporary bacteremia’s, which can cause systemic problems, as well as other systemic effects, such as toxic or immunologic ones. In two Finnish case-control studies involving myocardial and cerebral infarction, the relationship between oral infections and blood diseases was investigated. In these case-control investigations, it was discovered that patients with cardiac or cortical infarction experienced oral infections more frequently than their age- and gender-matched population controls.

Numerous variables, including diabetes, smoking, and alcohol misuse, may increase the risk of developing myocardial infarction as well as oral infections. Therefore, causality between them should be assumed, and it is possible that the observed link among bacterial diseases and vascular disorders is due to these shared predisposing variables. However, there are a number of ways that oral infections and ischemia might be related. Patients who've had poor oral health need education programs, listening closely to those common predictors of bacterial diseases and blood diseases, even though the causative relationship between oral infections with infarction cannot be established. Their oral illnesses should also be addressed because they may put them at risk for developing infectious complications that could cause an infarction.

3.1 Some causes of oral infections

This section is composed of some or oral infections causes and by this what the impact occurs in the mouth, some problems are summarize below:

3.1.1 Cavity:

Cavities, sometimes referred to as dental caries, are among the most prevalent oral infections and result in holes developing in your teeth as a result of tooth decay. Baby teeth, also known as primary teeth, can become lost due to dental caries, and the bacteria "Streptococci," which eats sugary, sticky foods and drinks, can develop holes in teeth. according to the Research Centre of

Oral and Craniofacial Research realize that your body also converts carbohydrates to sugar Rice and other common meals, such as chips, cause your body to produce glucose. Therefore, as you ingest more sugar during the day, the bacteria make more acid, which causes more decay.

3.1.2 Gingivitis:

A gum infection known as gingivitis, or "early gum disease," can progress to more serious periodontitis. When bacteria colonise the gumline and start producing toxins, gingivitis results. When you put it in your mouth, you may notice bleeding gums because your gumline is irritated from gingivitis, which causes pain and infection in the gums. By eliminating the bacteria there at gumline and well below with brush and brushing, gingivitis can be avoided. Additionally, your dentist's office can provide treatment for gingivitis.

3.1.3 Periodontal Diseases:

Gingivitis should be treated as a warning indication to focus on readjusting a healthy tongue because that might develop periodontal problems. When an oral infection extends below the gum line and damages the jawbone and supporting tissues, periodontal disease results. Pockets start to form as the gums pull away from the teeth, which causes more inflammation and bone thinning, which can cause teeth to become loose. Periodontal disease, the most prevalent causes of tooth loss in women, affects up to 47.2% percent adults aged 30 and older, according with Centers of Disease Control (CDC).

3.1.4Thrush:

An overabundance of "Candida albinos," a naturally occurring fungus, results in thrush. Outbreaks can be brought on by medical procedures like chemotherapy, radiation, and antibiotics. White, curd-like patches on the inner lips, lips, the roof of the mouth and back of throat are typical signs. Thrush is more likely to occur in people with HIV.

3.1.5 Hand, Foot, and Mouth Disease:

Per the University of Illinois, toddlers and classroom children are commonly affected by hand, foot, and mouth disease, a viral infection of the mouth and other regions of the body. It most likely results from the "Coxsackie A16" virus. Although it sounds terrifying, the infection frequently goes away within three days. After a few days of fever and sore throat, little, somewhat uncomfortable blisters appear on the mouth, palms, bottoms of the feet, buttocks, inside the cheeks, and elsewhere.

A week to ten days may pass between outbreaks of fluid-filled ulcers in the tongue or on the lips brought on by oral herpes.

The scabs are painless for another few days after the blisters break. The virus herpes simplex virus is the root of this infection. In the United States, up to four out of five persons are thought to carry the herpes simplex virus. Blisters, ulcers, and flu-like symptoms on the tongue and gums can all be signs of the first oral strep infection. However, there can be absolutely no observable symptoms. The virus will remain in the body continuously once it has been infected. In youngsters, oral herpes appears differently.

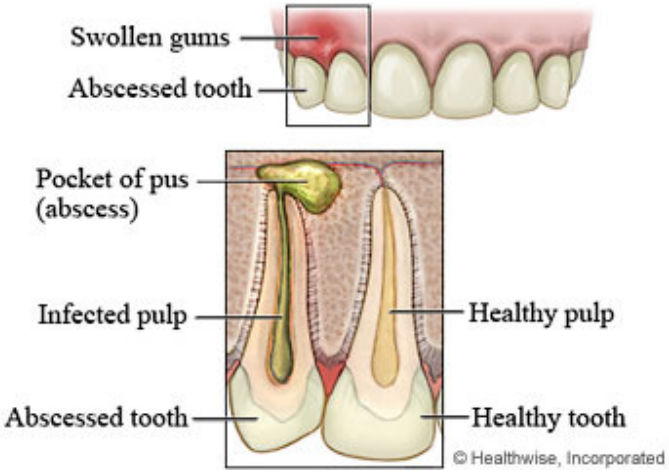

Figure 2: Depict the mouth infections causes of mislinearcy among mouth.

Herpes gingivostomatitis can occur in simplex virus carriers who are between the ages of one and four. Swollen gums and tiny blisters are symptoms. The kid can become agitated and exhausted, as well as get a temperature. Ulcers typically develop around the mouth a few days following the small blisters on the gums. Just like adult wounds, these sores and ulcers go away on their own. Most of the time, the virus remains dormant, but stress, trauma, sunshine, and the typical cold can make symptoms return. The genomic DNA of a number of periodontal bacteria has been found in human atheroma's, contributing to the atherosclerotic process. Others who discovered several bacterial species in atheroma's replicated and expanded these findings. Eventually, it was shown that human atherosclerotic plaques contained invasive Porphyromonas gingivitis and Actinobacillus enables the identification that were still alive and well. Numerous mechanism of action and animal model studies have been done in an effort to evaluate the seven "proofs" that have been suggested as being required to show that gum disease bacteria are a contributing cause of atheromatous disease. These studies showing the selectivity of oral organisms in atheromatous plaques have led to this.

Anatomical impediments or tissue divisions, such as muscle and bone, typically act as barriers to avoid the growth of oral infections. However, it is possible for an infection to migrate back and down toward the pharynx and the mediastinum. An important tenet is that therapeutic efficacy is always based on correctly executed dental operations, and that treating oral illnesses cannot be accomplished solely through the use of antibiotics. Nevertheless, antibiotic therapy is crucial, and as was said before, penicillin and metronidazole should really be taken into consideration. It is now commonly acknowledged how important inflammation and infection are in the beginning and development of endothelial damage in atherosclerosis. One of the most common chronic infections in people is chronic inflammatory periodontal disease, which is seen all around the world. Even after controlling for many of the conventional risk factors, those with severe chronic periodontitis have been shown to have a significantly higher risk of acquiring cardiovascular disease, such as atherosclerosis, myocardial infarction, and stroke.

Inflammation is a crucial factor in both Cardiovascular Diseases CVD and dental illnesses like periodontitis. Bacteria in the biofilms that make up the microbiome that develop on the teeth cause oral irritation. Hyperlipidemia, hypertension, smoking, as well as a number of other known and unknowing variables, cause vascular inflammation. The next sections discuss the most recent

research on the connection between oral infections and CVD as well as the implications of oral bacteria on systemic and local inflammation. It is important to distinguish between an active bacterial invasion and a viral infection that is the cause of inflammation. The eradication of the initial component might not be enough to halt the subsequent chain of events after the inflammation cascade has started. The primary infection in this situation turns into a secondary contributing component.

Over the past two decades, the connection between dental and overall health has gained more recognition. Numerous epidemiological studies have connected poor dental health to a number of diseases, including rheumatoid arthritis, osteoporosis, low birth weight preterm babies, and poor glycemic management in diabetics. Oral infections are acknowledged as an issue for people with a variety of chronic illnesses, such as cancer, a human immunodeficiency virus infection, and patients with ventilator-associated asthma. In Figure 2 shown the condition of dental healthcare when precautions are taken.

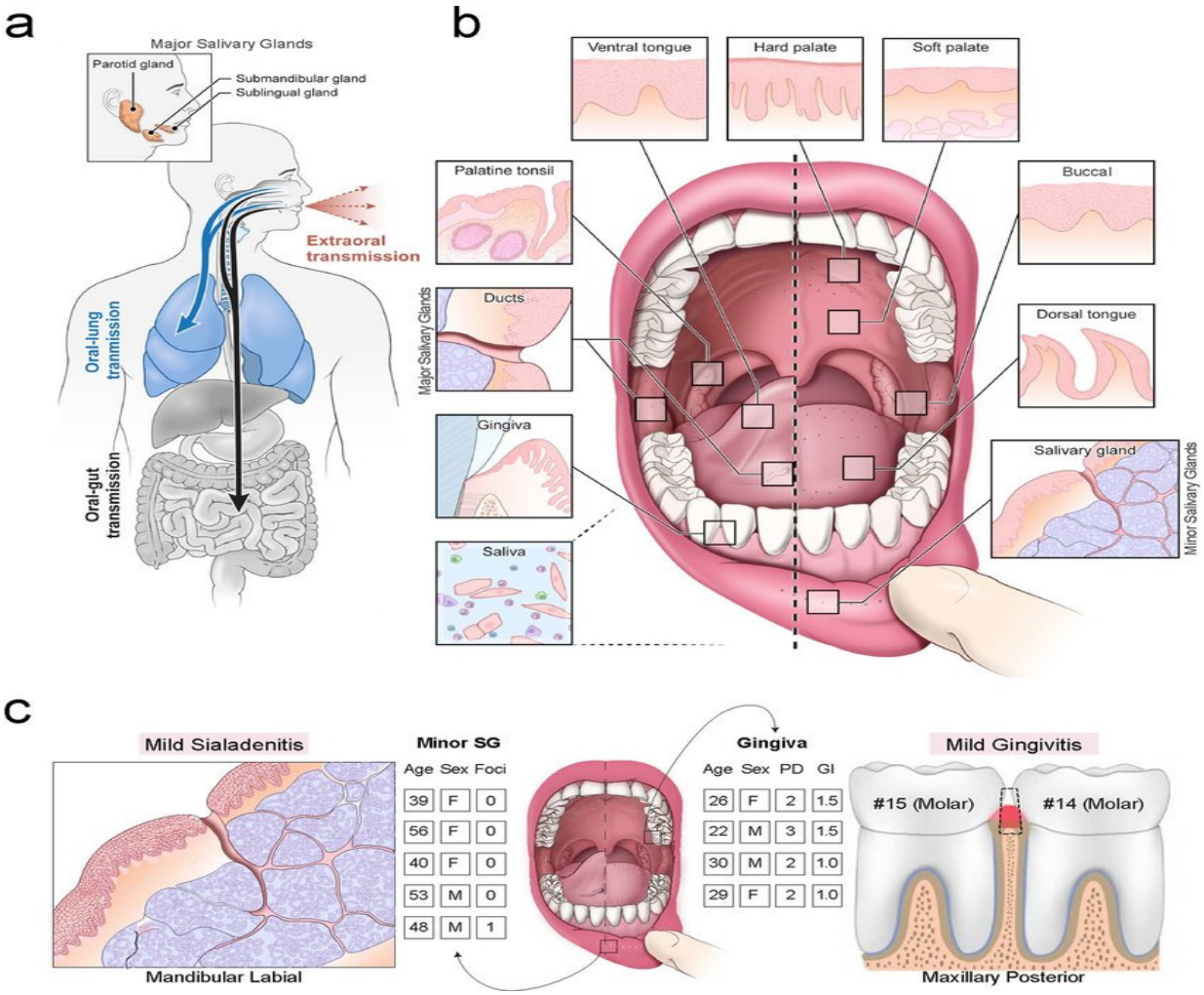

Figure 2: Depicts the condition of dental healthcare when precautions are taken.

Dental healthcare requires individualized monitoring and care, and some aspects of our growing understanding of the microbiome can be put to good use in this regard. Precision dentistry and

individualized oral healthcare will be made possible by continuously monitoring microbiological factors, either alone or in conjunction with immune parameters, in a quick and affordable manner before treatment such as during maintenance. The creation of point-of-care tools for microbial and antigenic detection that would help doctors with diagnosis, observation, and treatment decision-making is in progress.

4. CONCLUSION

Over the past few decades, more people have begun to keep more of their natural teeth for extended amounts of time. Adequate dental hygiene is challenging to attain, and oral mucosa, supporting tissues, and tooth infections that don't cause any symptoms are frequent. For individuals with acute illnesses or those who are medically challenged, maintaining dental health can be particularly difficult. All clinicians should carefully consider the mouth as a substantial potential cause of infection and inflammatory that adds to the improvement burden of disease and to overall health. Additional research will help clarify open questions and deepen our comprehension of the relationship between chronic periodontitis and CVD. The variety of the data gathered reduces the generalization ability of epidemiologic studies of a connection. Future research with defined methods of therapy, measurements, diagnostic standards, and descriptions of disease and wellness will produce a more reliable body of information.

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