Journal of The Gujarat Research Society

ISSN: 0374-8588
Volume 22 Issue 1, January 2020

A Study on Several Aspects of Alzheimer ’s disease

Dr Kamala Kant Parashar

SOMAS, Sanskriti University, Mathura, Uttar Pradesh, India

Email Id- principal.son@sanskriti.edu.in

ABSTRACT: ***Alzheimer's disease is one of the most frequent types of dementia that affects nerve cells throughout the brain. Pathologically, it is caused by intracellular neurofibrillary tangles and extracellular amyloidal protein, which leads to plaque formation and obstructs nerve cell transmission, resulting in this neurodegenerative illness. Alzheimer's disease need early detection in order to get successful treatment. Because the number of Alzheimer's disease patients is increasing at an alarming rate, new technology must be used to battle the condition. This paper discusses several concepts related to Alzheimer’s disease. It discusses several risk factors in Alzheimer’s such as diabetes, hypertension, obesity, etc. It also discusses several reasons which might be the cause behind this disease. It also discusses several prevention methods for this disease. Several other important concepts have been discussed. Many studies on biomarkers, proteomics, and genomes have been done in recent years and continue to be conducted. Despite these studies, there are still a number of obstacles that must be addressed. Technology alone will not be enough to combat the disease; standardisation of procedures and approaches is critical for preserving consistency and achieving a high level of reliability.***

KEYWORDS: ***Alzheimer's, Dementia, Diabetes, Hypertension, Obesity.***

1. INTRODUCTION

Alzheimer's disease (AD) is the leading cause of dementia, affecting over 44 million people worldwide. It has been noted that only symptomatic therapies are available for Alzheimer's disease, and there is no cure. It is a neurodegenerative illness first described by Alois Alzheimer in 1906, and neurodegenerative disorders are one of the biggest health-care issues today. It's a multifaceted, complicated disease with a pathophysiology that's yet unknown, but it's characterised by neuronal destruction, memory loss, and other symptoms. Deposition of amyloid- (A) plaques surrounding neurons, neurofibrillary tangles, a reduction in acetylcholine content, and other neurotransmitter dysregulation are the major pathological hallmarks of Alzheimer's disease. Oxidative stress, obesity, diabetes, hypertension, air pollution, smoking, hypercholesterolemia, and other risk factors all have a part in the development of Alzheimer's disease and the development of preventative strategies. Physical activity and dietary variables have been found to be protective and aid in the prevention of it. We utilise biomarkers in the cerebrospinal fluid and positron emission tomography to diagnose it. Currently, the Food and Drug Administration (FDA) has authorised two traditional pharmacotherapies for Alzheimer's disease: acetylcholinesterase inhibitors tacrine, donepezil, rivastigmine, galantamine, and N-methyl-D-aspartate glutamate antagonist (NMDA)-memantine [1].

Alzheimer disease (AD) was first recognised as a progressive and neurodegenerative illness by Alois Alzheimer in the 1906s. Alzheimer disease is one of the most serious neurodegenerative illnesses that the contemporary health-care system has to deal with. Since the dawn of the twenty-first century, it has been recognised as the most common form of dementia among the elderly. Alzheimer's disease is the most prevalent form of dementia, accounting for 60-80

ISSN: 0374-8588
Volume 22 Issue 1, January 2020

percent of all dementia cases globally. It is defined by the gradual loss of neurons, brain processes, and cognition function [2].

1.1 Risk Factors:

Diabetes, oxidative stress, hypertension, air pollution, hypercholesterolemia, atrial fibrillation, alcohol, smoking, and other genetic, environmental, and nutritional risk factors for Alzheimer's disease exist. These risk factors have influenced the development of Alzheimer's disease prevention strategies[3].

1.1.1 Diabetes:

Insulin-degrading enzyme acts as an insulin and amyloid cleavage enzyme. Because insulin signalling is disrupted in type 2 diabetes, the synthesis of insulin-degrading enzyme is reduced, resulting in A buildup and hyperinsulinemia. It was also shown that insulin and amyloid were fighting for the same insulin-degrading enzyme, resulting in a reduction in A clearance. Insulin is also thought to control tau protein phosphorylation, and they all have a role in the development of Alzheimer's disease[4].

1.1.2 Hypertension:

It may increase the risk of Alzheimer's disease by decreasing the vascular integrity of the blood-brain barrier (BBB), which can lead to protein extravasation in brain tissues and the buildup of A 32, 33, 34. Hypertension is a risk factor for a variety of pathological disorders, including myocardial infarctions, strokes, ischemic white matter lesions, atherosclerosis, and cardiovascular diseases, among others. All of them are linked to the year AD 35. According to a study, increased midlife systolic blood pressure (160 mmHg) is linked to a higher number of senile plaques and lower brain weight in the hippocampus and neocortex, while increased late-life diastolic blood pressure (95 mmHg) is linked to an increase in the number of neurofibrillary tangles in the hippocampus 36.

1.1.3 Obesity:

Studies show that a diet heavy in cholesterol and saturated fats increases the risk of Alzheimer's disease (AD 37). Obesity is characterised by a persistent mild systemic inflammation that leads to a brain inflammatory process marked by increased cytokine production at first. It is a pro-inflammatory factor, and tumour necrosis factor alpha (TNF), interleukin-1beta (IL-1), chemokine, and interleukin-6 (IL-6) 40 are the main cytokines involved.

1.1.4 Oxidative Stress:

According to numerous research, oxidative stress appears to have a negative impact on the development of Alzheimer's disease. Reactive oxygen species such as superoxide, hydrogen peroxide, hydroxyl radicals, nitric oxide radicals, and others are produced in an infinite amount as a result of oxidative stress. It is linked to the oxidation of nucleic acids, proteins, lipids, and carbohydrates, which causes oxidative damage to these components. Endogenous sources such as mitochondria, cytochrome P450, peroxisomes, etc., antioxidant defences such as vitamins (A, C, and E), glutathione peroxidase, catalase, and glutathione, and exogenous sources such as UV, ionising radiations, inflammatory cytokines, etc. are all involved in the production of reactive oxygen species (ROS).

1.2 Protective Factors[5]*:*

Journal of The Gujarat Research Society

ISSN: 0374-8588
Volume 22 Issue 1, January 2020

1.2.1 Physical Exercise:

Several pieces of data suggest that regular aerobic exercise improves cognitive performance 48, and that it may be used as a preventative approach for the treatment of various stages of Alzheimer's disease. Physical exercise has been shown to increase the quantity of neurotrophic factors such as brain-derived neurotrophic factor (BNDF), which has a neuroprotective impact on Alzheimer's disease by enhancing cognition. Routine exercise also acts as an antidote to oxidative stress and reactive oxygen species (ROS), protecting against neurodegeneration and Alzheimer's disease by decreasing ROS-induced protein degradation. Physical activity also lowers levels of tumour necrosis factor alpha (TNF-) and interleukin-1 alpha (IL-1), which reduces amyloid-induced neuroinflammation in the brain and has a protective impact on cognition or dementia. It also raises the amount of nitric oxide in the brain by increasing endothelial nitric oxide synthase activity, which improves neuronal blood flow and reduces brain damage. The cleavage enzymes neprilysin (NEP) and insulin degrading enzymes (IDE) control and determine the quantity of amyloid accumulation and protect neurons from amyloid toxicity. Physical activity activates IDE and NEP, preventing A buildup, which is thought to be the most significant element in Alzheimer's disease pathogenesis[6].

1.2.2 Nutritional Factor:

Nutritional factors appear to be a significant protective factor against Alzheimer's disease. It has been observed that consuming a high-cholesterol, high-carbohydrate, and high-fat diet has a negative impact on AD 59. It has been shown that consuming dietary vitamin E but not taking additional vitamin E supplements is linked to a lower risk of Alzheimer's disease at the age of 60. Inadequate folate, vitamin B6, and vitamin B12 results in a rise in homocysteine level and homocysteine concentration, which is linked to AD as a neurotoxic.

1.3 Causes of the Disease:

Alzheimer's disease is responsible for 60 percent to 70 percent of dementia cases. It's a long-term neurodegenerative illness that generally begins slowly and worsens over time. Plaques, according to one idea, prevent nerve cells in the brain from communicating properly. Tangles may make it more difficult for cells to obtain the nutrients they need. It's understood that as Alzheimer's progresses, specific nerve cells die and a growing number of nerve cells, also known as neurons, are destroyed[7].

1.3.1 Age:

The most important determinant in the development of Alzheimer's disease is one's age. After 65 years of age, your chances of having the disease double every five years.

1.3.2 Down's syndrome:

Down's syndrome patients are more likely to acquire Alzheimer's disease. This is because the genetic flaw that causes Down's syndrome may also cause amyloid plaques to build up in the brain over time, which in some people can lead to Alzheimer's disease.

1.3.3 Genetics:

Based on analyses of twin and family studies, the genetic heritability of Alzheimer's disease (including memory components thereof) ranges from 49 percent to 79 percent. Around 0.1 percent of instances are familial variants of autosomal (non-sex-linked) dominant inheritance

ISSN: 0374-8588
Volume 22 Issue 1, January 2020

that manifest before the age of 65. Early onset familial Alzheimer's disease is the name given to this kind of Alzheimer's disease. Though it is uncommon, a tiny number of people get Alzheimer's disease before they reach the age of 65. Amyloid precursor protein (APP), Presenilin 1 (PSEN1), and Presenilin 2 (PSEN2) are three genes associated to the development of Alzheimer's disease (PSEN2).

1.4 Prevention of the Disease:

1.4.1 Through diet:

Nutritional assistance might potentially delay the course of dementia and enhance the quality of life of Alzheimer's patients without affecting their survival rate. Fish, fruits, vegetables, nuts, and even Indian spices have been shown to reduce the incidence of Alzheimer's disease by up to 45 percent. Fructose should be consumed in amounts of fewer than 25 g per day, as stated in our review. According to several studies, having a high amount of magnesium in the brain reduces the symptoms of Alzheimer's disease. Vitamin D, with its immune-boosting and anti-inflammatory characteristics, is also advantageous to Alzheimer's disease. Vitamin B12-rich foods, as well as omega-3 fatty acids, should be eaten[8].

Folic acid raises levels of -3 PUFAs (polyunsaturated fatty acids) including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are known to help with dementia and Alzheimer's disease prevention and therapy. Both EPA and DHA increase NO production, inhibit the production of pro-inflammatory cytokines, and boost brain acetylcholine levels, which are low in Alzheimer's disease[9].

Beta amyloid is an aberrant protein that can also be detected in arterial plaques. Beta-amyloid is a poisonous intruder that appears when the body is in 'emergency mode,' causing inflammation when the immune system overreacts. So, if inflammation is the problem, the damage to the brain might be reversed by including natural anti-inflammatory elements in the diet, such as anti-oxidants and omega-3. Antioxidants like vitamin A, beta-carotene, vitamins C and E, and others are present in low amounts in Alzheimer's sufferers, thus restoring their concentration to normal might be the key to curing the illness[10].

1.4.2 Through astrocytes:

Astrocytes were implanted into the hippocampus of AD mice in a study using cultured adult and neonatal animals. These astrocytes were identified mostly around a deposits seven days later, and they internalise human an immuno-reactive material in vivo. The significance of astrocytes as active a clearance cells in the brain is supported by this work, which might have major implications for the future development of AD treatment methods.

1.4.3 Through stem-cells:

Without affecting A deposits, neural stem cell transplantation causes a significant increase in BDNF-mediated hippocampal synaptic density and improves spatial learning and memory impairments in AD animals. In the future, manipulation of neurotrophin levels might be a realistic method in the development of stem cell-based treatments to treat Alzheimer's disease, according to this study. Researchers discovered a decrease in neuronal death after transplanting human umbilical cord blood derived mesenchymal stem cells into the hippocampus of AD mice, which rescued the host mice's memory impairments.

Journal of The Gujarat Research Society

ISSN: 0374-8588
Volume 22 Issue 1, January 2020

The BFCNs are involved in many areas of cognitive function, including learning, memory, and attention, and cholinergic blockage impairs normal human cognitive performance. Numerous studies have demonstrated significant damage to basal forebrain cholinergic innervation and decreased cholinergic neurotransmission in the brains of Alzheimer's disease patients, even in the early stages of the disease. Of addition, the temporal lobes, particularly the hippocampus, are the most seriously damaged regions in the AD brain. These findings show that BFCN degradation contributes to the cognitive impairments and pathogenesis of Alzheimer's disease, implying that BFCNs might be an appropriate kind of donor cell to alleviate the cognitive symptoms associated with the disease.

1.5 Biomarkers:

From the standpoint of diagnostic accuracy, sensitivity, and specificity, biomarkers play a critical role in the screening of Alzheimer's disease. The aim is that if we can detect Alzheimer's before symptoms appear, future medicines may be able to target the illness in its early stages, before permanent brain damage or mental decline occurs. Only clinical evaluations and post-mortem brain pathology may presently be used to diagnose it. It is critical to discover verified biomarkers for Alzheimer's disease in order to enhance diagnosis and speed the development of novel treatments. The bulk of Alzheimer's disease cases are sporadic (risk age > 60 years), and only around 5% have a hereditary component. A perfect biomarker would be one that aids in early diagnosis and distinguishes Alzheimer's disease from other types of dementia. The most widely acknowledged technique for diagnosis is to use an ELISA kit to screen for beta-amyloid (1-42), total tau, and phosphor-tau-181 in CSF fluid.

2. DISCUSSION

Alzheimer's disease is a progressive neurological illness that is rapidly spreading around the globe. Because of the disease's complex pathology, variable symptoms, and lack of a specific diagnosis, current treatments such as acetylcholinesterase inhibitors (tacrine, donepezil, rivastigmine, galantamine) and glutamate antagonists (memantine) provide only symptomatic relief and have limited efficacy, there is currently no cure. Because there has been a significant increase in understanding regarding AD aetiology and its underlying pathophysiological process in recent years, research in this subject has a very broad scope, and a treatment for it is still a long way off. This article addresses a number of topics that are related to one another. This paper discusses several concepts related to Alzheimer’s disease. It discusses several risk factors in Alzheimer’s such as diabetes, hypertension, obesity, etc. It also discusses several reasons which might be the cause behind this disease. It also discusses several prevention methods for this disease. Several other important concepts have been discussed.

With a threshold of > 600 pg/ml, intra-neuronal inclusions of the microtubule-associated protein tau are considerably higher than in healthy people. In Alzheimer's disease, tau is hyperphosphorylated (at 39 different locations), resulting in axonal transport failure and a loss of function. With a cut-off of > 60 pg/ml, detection of tau phosphorylated at position 181 in AD is considerably increased compared to controls. Additionally, secretases cleave extracellular A plaque from amyloid precursor protein (APP), and processing of amyloidogenic pathways creates a 42-amino-acid peptide [A (1-42)] that can form in the brain under specific conditions. With a cut-off of 500 pg/ml, there is a significantly lower A in AD patients.

3. CONCLUSION

ISSN: 0374-8588
Volume 22 Issue 1, January 2020

We have presented some reasoning and potential therapy methods for Alzheimer's disease in this review. Extracellular amyloid plaques, intracellular neurofibrillary tangles, synaptic degradation, and neuronal death, according to several studies, are the causal metabolic processes that contribute to AD as a neurodegenerative illness. Genetics accounts for around 70% of the risk of Alzheimer's disease at any given age. The epsilon 4 allele of the apolipoprotein E gene is the most prevalent genetic risk factor for Alzheimer's disease (ApoE). Apart from the genetic and molecular aspects, a vitamin D deficient diet, in which the active form regulates nerve growth factor, appears to be another cause of Alzheimer's disease. Furthermore, in Alzheimer's disease, brain glucose metabolism decreases, resulting in diabetes for three reasons that are yet unknown. Finally, we'd like to point out that biomarkers and stem cell therapy may be developing approaches for early detection and treatment of Alzheimer's disease. Many research are now being conducted in order to find a cure for Alzheimer's disease. In recent years, several interesting studies have been conducted with some novel options, including as medicines that target amyloid- in various ways. Secretase promoters, -secretase inhibitors, secretase inhibitors, immunotherapy (anti-amyloid antibodies), and other current AD research efforts include As a result, with many major breakthroughs in innovative therapeutic agents in the next years, we will be able to give more complete and unique pharmacotherapy for Alzheimer's disease.

REFERENCES:

[1] C. A. Lane, J. Hardy, and J. M. Schott, “Alzheimer’s disease,” *European Journal of Neurology*. 2018, doi: 10.1111/ene.13439.

[2] J. Gaugler, B. James, T. Johnson, K. Scholz, and J. Weuve, “2016 Alzheimer’s disease facts and figures,” *Alzheimer’s Dement.*, 2016, doi: 10.1016/j.jalz.2016.03.001.

[3] C. R. Jack *et al.*, “NIA-AA Research Framework: Toward a biological definition of Alzheimer’s disease,” *Alzheimer’s and Dementia*. 2018, doi: 10.1016/j.jalz.2018.02.018.

[4] “2018 Alzheimer’s disease facts and figures,” *Alzheimer’s Dement.*, 2018, doi: 10.1016/j.jalz.2018.02.001.

[5] J. Weller and A. Budson, “Current understanding of Alzheimer’s disease diagnosis and treatment,” *F1000Research*. 2018, doi: 10.12688/f1000research.14506.1.

[6] G. M. McKhann *et al.*, “The diagnosis of dementia due to Alzheimer’s disease: Recommendations from the National Institute on Aging-Alzheimer’s Association workgroups on diagnostic guidelines for Alzheimer’s disease,” *Alzheimer’s Dement.*, 2011, doi: 10.1016/j.jalz.2011.03.005.

[7] P. Scheltens *et al.*, “Alzheimer’s disease,” *The Lancet*. 2016, doi: 10.1016/S0140-6736(15)01124-1.

[8] S. D. Stites, R. Milne, and J. Karlawish, “Advances in Alzheimer’s imaging are changing the experience of Alzheimer’s disease,” *Alzheimer’s and Dementia: Diagnosis, Assessment and Disease Monitoring*. 2018, doi: 10.1016/j.dadm.2018.02.006.

[9] X. Du, X. Wang, and M. Geng, “Alzheimer’s disease hypothesis and related therapies,” *Translational Neurodegeneration*. 2018, doi: 10.1186/s40035-018-0107-y.

[10] J. P. Chhatwal *et al.*, “Preferential degradation of cognitive networks differentiates Alzheimer’s disease from ageing,” *Brain*, 2018, doi: 10.1093/brain/awy053.