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ALZHEIMER DISEASE

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ABSTRACT

Alzheimer's disease is the most common cause of dementia worldwide, and its prevalence increases with aging populations. The two main pathologies of this neurodegenerative disease process are typically defined as deposition of β-amyloid plaque and neurofibrillary tangles of hyperphosphorylated tau.[1] Alzheimer's disease is a chronic condition that takes 20 years to fully develop throughout the preclinical and prodromal stages, with an average clinical course of 8 to 10 years. In the population over 65, the disease is predicted to have a prevalence of 10-15% and an incidence of 1-3 percent.[2] We highlight the most significant advancements in the study of Alzheimer's disease in this seminar. This projection is three times greater when considering Alzheimer's disease according to a biological definition rather than a clinical one. The cellular phase of Alzheimer's disease occurs concurrently with amyloid β accumulation, causing tau pathology to proliferate. There are currently about 40 genetic risk loci linked to Alzheimer's disease, the most prominent of which is the APOE allele.[3] Up to 24 million people worldwide are thought to have dementia, and this number is expected to double every 20 years until 2040, creating a high and expensive disease burden. The primary cause of dementia is Alzheimer disease (AD), which is typified by a progressive reduction in cognitive function that usually starts with memory loss. Individuals with this disorder typically become dependent on caregivers before to death. The neuropathological hallmarks of the AD brain include widespread and neuritic extracellular amyloid plaques—which are typically flanked by dystrophic neurites—and intracellular neurofibrillary tangles.[4]

1. INTRODUCTION

The WHO has designated Alzheimer's disease (AD) as a "global public health priority" since there is currently no cure for the condition. Up until now, the cause and potential therapeutic targets of AD have only been well-stated notions and theories. Medication slows the progression of disease pathology based on this idea . Dementia in those over 60 is primarily caused by AD. Alzheimer's affects 50–75% of persons with dementia. Based on global statistical data, women are more likely than men to get AD, and the risk rises with age . Individuals suffering from diabetes, hypertension, and cardiovascular disorders.[5]

2. PATHOPHYSIOLOGY OF AD

older individuals, Alzheimer's disease (AD) is the most prevalent neurological illness, accounting for almost 80% of dementia cases globally. It causes a gradual loss of mental, behavioral, functional, and learning abilitie. AD's pathophysiology The discussion of the pathophysiology of AD dates back to Alzheimer's observation of the neuropathological characteristics of the disease in 1907, specifically amyloid plaques and hyperphosphorylated NFTs. To explain this complex condition, a number of hypotheses, including the cholinergic, Aβ, tau, and inflammatory hypotheses, have been proposed based on the different causal variables. It has been demonstrated recently that the most widely accepted Aβ hypothesis.[6] Given that various factors contribute to the disease's progression, combination medication is necessary for the effective treatment of AD. Anticipate multi-targeted medications to address various symptoms and underlying causes of the illness.

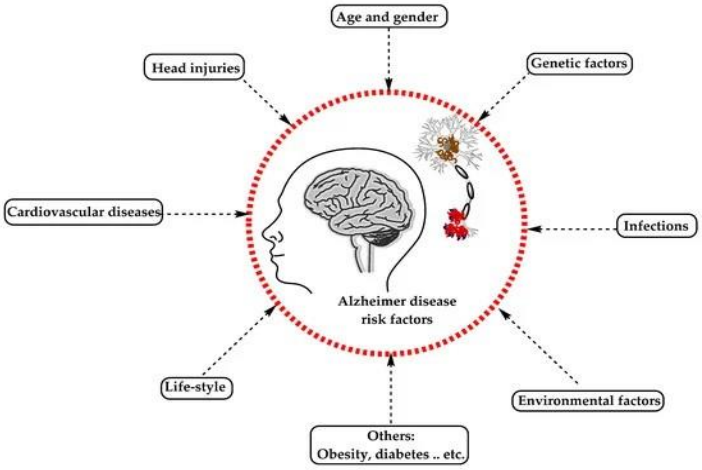

Fig 1 :-The Cause of Alzheimer's diseases and risk factor's

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Causes and Risk Factors of Alzheimer's Disease:-

AD has been considered a multifactorial disease associated with several risk factors .such as increasing age, genetic factors, head injuries, vascular diseases, infections, and environmental factors (heavy metals, trace metals, and others). It is currently unknown what causes the pathogenic alterations (Aβ, NFTs, and synaptic loss) associated with Alzheimer's disease. A number of theories have been put forth to explain AD, but only two are thought to be primary: one holds that changes in the synthesis and processing of amyloid β-protein serve as the primary initiating factor, while others contend that cholinergic dysfunction is a major risk factor for AD.

AD is a complex disease that is influenced by a number of risk factors, including aging, genetics, head trauma, vascular disorders, infections, and environmental variables (such as heavy and trace metals). It is currently unknown what causes the pathogenic alterations (Aβ, NFTs, and synaptic loss) associated with Alzheimer's disease. Identification A person must be experiencing memory loss, cognitive decline, or behavioral changes that are interfering with their day-to-day functioning in order to be diagnosed with Alzheimer's disease. Prior to the individual experiencing dementia, friends and relatives may become aware of the signs. Alzheimer's disease cannot be diagnosed with a single test. A doctor will inquire about the patient's symptoms, experiences, and medical history if they have any reason to suspect the illness is present. They may also want to speak with the patient's relatives or caregivers. The following tests could also be performed by the physician: tests of cognition and memory to evaluate an individual's capacity for thought and memory tests of neurological function to A person may be evaluated using tests for blood or urine, a brain MRI or CT scan, genetic testing, balance, reflexes, and senses. It is customary to distinguish between the more common late-onset, sporadic Alzheimer's disease, which has an age of onset above 65 years and no obvious pattern of heredity, and the early-onset, familial type of the disease, which accounts for only approximately 5% of all cases and has a documented genetic etiology. The amyloid-cascade theory has become a key concept for the overall etiopathogenesis of Alzheimer's disease, despite the fact that there appears to be significant variation in the illness's genesis. .The regulation of amyloid plaques is essential for many cellular and molecular processes. Apolipoprotein E 4 is a well-established risk factor in addition to ageing. Another theory about the etiology of Alzheimer's disease is disruption of cerebral glucose metabolism, particularly in the hippocampus regions.[7]

Highlight:

Half of all clinical trials, and 68% of Phase 3 trials, are sponsored by the biopharmaceutical sector. Currently, there are 143 drugs in the pipeline for developing drugs to treat Alzheimer's disease (AD). Disease-modifying therapies account for 83.2% of the candidate treatments.50,575 volunteers must contribute 3,878,843 participant-weeks to current trials in order to be eligible to participate .[8]

Clinical trials for AD target a wide range of biological processes, most of which are identified in the CADRO classification. Despite the difficulties caused by the current epidemic, there has been a slight increase in the number of clinical trials. Biomarkers are increasingly being used to inform clinical trials, including their use in diagnosis and as outcomes. Since the monoclonal antibody aducanumab was approved, amyloid therapeutics have advanced. The pipeline of AD medication development includes therapies for inflammation, synaptic dysfunction, tau abnormalities, and other amyloid approaches. Alzheimer's disease (AD) is becoming more common as the number of elderly individuals increases. By 2050, there will be 12.7 million people in the US living with AD dementia, up from the present 6.2 million. Apart from persons with Alzheimer's disease (AD) in the advanced stages of dementia, around 10 million Americans suffer from moderate cognitive impairment . Physical Inspection Early in the disease process, the general physical examination is usually normal; localized neurologic symptoms suggest that there may be other or coexisting causes for the cognitive impairment. As the illness worsens, extrapyramidal symptoms may become evident. These symptoms may be associated with comorbid conditions like dementia with Lewy bodies (DLB), cerebrovascular disease, progressive supranuclear palsy (PSP).[9]

AD genes with an early start Both late onset AD (LOAD) and early onset AD (EOAD) are regarded as "polygenic" illnesses, notwithstanding the possibility that (rare) autosomal dominant gene mutations cause EOAD (Lambert et al., 2013; Escott-Price et al., 2015). The amyloid hypothesis has advanced largely because of the finding that mutations on three different genes that cause autosomal dominant AD (ADAD) all resulted in a change in the Producing or using Aβ (Tanzi and Bertram, 2005). For the past 20 years, the reduced complexity of the EEG in AD NDA has been extensively used to a variety of physiological data in order to understand the intricate dynamics of the underlying processes. Specifically, new mathematical techniques are needed for one of the most complex biological signals—the EEG. NDA's application to the EEG has provided insightful knowledge about brain .[10]

Understanding the pathogenic processes of Alzheimer's disease (AD) and improving early diagnosis have come a long way in the more than a century since Alois Alzheimer and Gaetano Perusini's initial study.

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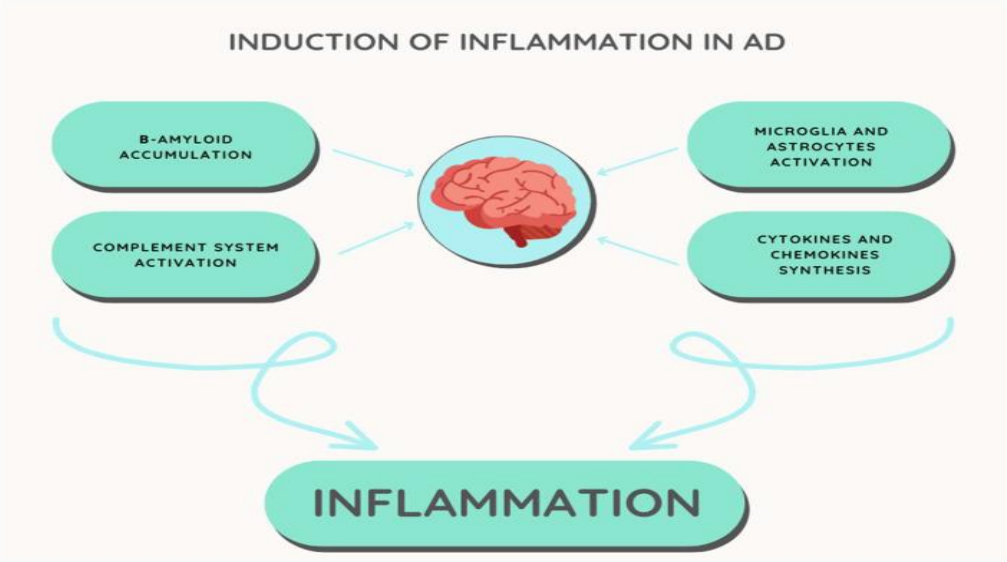

Fig.2

Fig 3:- induction of inflammation in Alzheimer Disease.

Widespread loss of neurons, neurofibrillary tangles, and senile plaques in the entorhinal cortex, neocortex, hippocampal, and other brain regions are hallmarks of AD neuropathology (DeCarli, 2001, Selkoe, 1994). Amyloid β-peptide extracellular aggregates cause senile plaques, while tau protein aggregations cause neurofibrillary tangles. The primary protein component of neurofibrillary tangles is hyperphosphorylated tau, which is created when there is an imbalance between protein phosphorylation and dephosphorylation as a result of a reduction in the activity of protein phosphatase-2A, which controls the activities of tau kinases (Iqbal et al., 2002, Smith et al., 2002). While broad diffuse and neuritic amyloid plaques grow preferentially throughout the neocortex, tangles are mostly located in the limbic structures, specifically in the hippocampus and parahippocampal areas (Price and Morris, 1999, Price et al., 2001)[11]

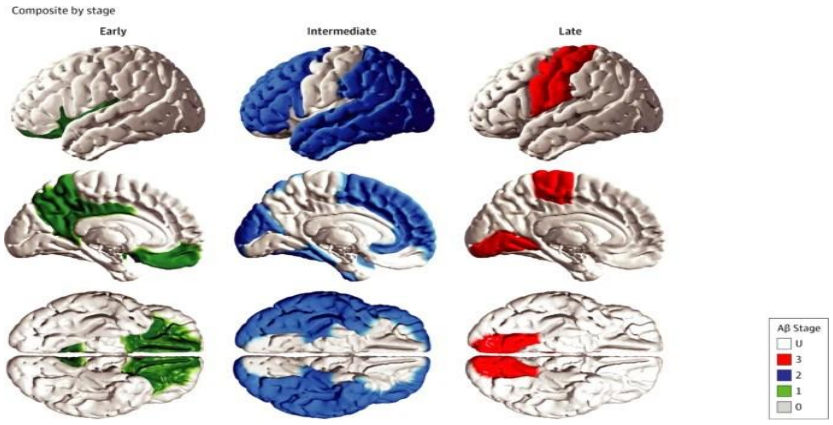

Fig 4 :- Techniques of in vivo Alzheimer's disease amyloid-β pathway staging, along the clinical continuum, based on molecular imaging and innovative algorithms.Neocortical distribution of -florbetapir is shown in a composite representation according to Aβ stages. Early composite (positive in stage 1 in green; left), intermediate composite (positive in stage 2 in blue; middle) and late composite (positive in stage 3 in red; right) can allow global and regional assessment of amyloid plaque deposition.

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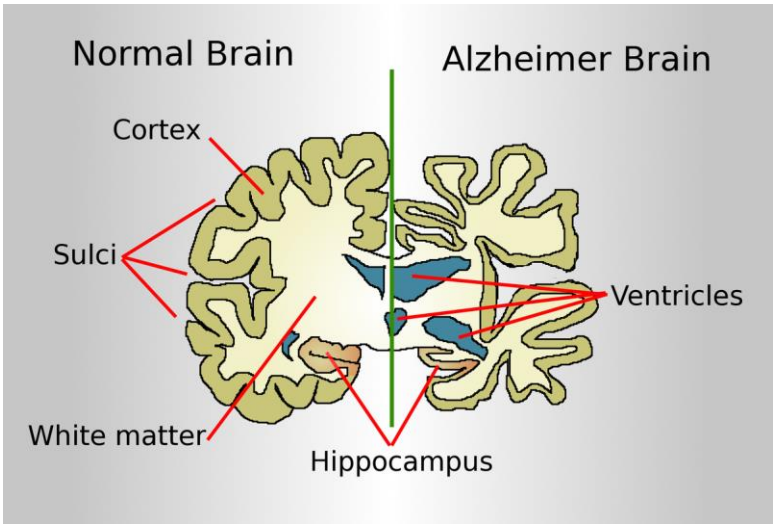

Fig 5 :- Alzheimer Disease.

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