Early detection & personalized management of dementia & Alzheimer's disease in elderly patients

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Abstract

Alzheimer's disease (AD) is sixth most common cause of death & the primary cause of dementia in the elderly. AD places a heavy financial strain on society and presents unique difficulties for parents and families that are affected. As the population ages, the issue will most likely become much worse soon. As of right now, there is no drug that can either cure or prevent the sickness. Alzheimer's disease (AD)-related dementia is one of primary causes of debilitation in elderly (over 65); early-stage AD cases, which make up around 2-5% of all cases, are also recognized. The improper classification of patients according to genetic variants and the lack of corroborating biomarker data for the pre-symptomatic registry seem to be additional factors causing this failure. Finally, the use of electronic health records (EHR) offers the chance to appropriately combine genetic, clinical, and biomarker data. In an effort to apply precision medicine to a greater variety of illnesses, governments everywhere are starting to put these initiatives into action. It is essential to diagnose Alzheimer's disease (AD) early in order to improve patient outcomes & enable timely treatment. Numerous strategies, such as artificial intelligence & enhanced imaging methods, are being investigated to improve medical accuracy & usability. Early identification has numerous benefits, but in order to improve outcomes for people who are at risk of Alzheimer's disease.

Keywords: Early Detection, Personalized Management, Dementia, Alzheimer's Disease, Elderly Patients

1. Introduction

Alzheimer's disease (AD) is a slowly developing neurological disease marked by buildup of toxic protein clumps in brain tissue, memory loss, & cell death (1,2). Currently, 5 million Americans have AD, which will cost the country 305 billion dollars in 2020 alone. It is projected that $1 trillion in fees and 14 million people would impact US society by 2050 (3).Unfortunately, no drug exists that may prevent, delay, or reduce the development of AD. Moreover, some hopeful studies in medicine have sadly failed in recent years. Indeed, some pharmaceutical firms have considered giving up on or significantly scaling down their hunt for AD-targeting medications (4,5). The various sign & symptoms of Alzheimer's disease are show in the Figure 1.

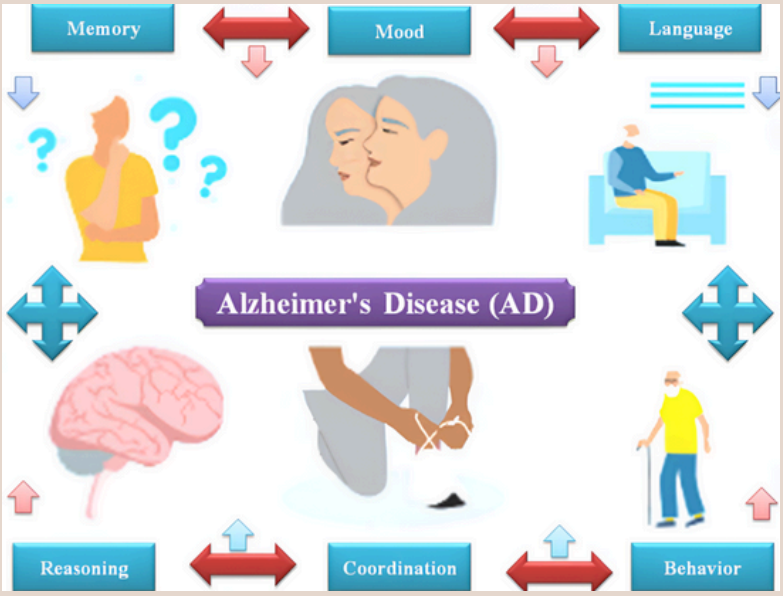

Figure 1. Sign & Symptoms of Alzheimer's Disease

In the field, the general consensus is that clinical studies have failed because sick individuals who already have severe and persistent dementia have been included in them (6). Pre-symptomatic treatment is required for the highest likelihood of success since damaged brain tissue in the central nervous system (CNS) cannot heal (7). The complex genetic variety linked with AD is a major limitation of the most recent clinical studies on the illness. Similar to cancer, the most prevalent types of AD seem to be caused by a confluence of many disease processes with similar clinical signs, each determined by an individual's own genetic composition and environmental circumstances (8).Great strides have been made in our understanding of AD sickness during the last several decades. Furthermore, we can now diagnose AD earlier and with greater accuracy because to developments in imaging and fluid biomarker technology (9,10).

2. Epidemiology

The illness affects around 57.4 million individuals worldwide, according to the most current estimates, which is a substantial health burden. The age distribution of population is thought to be rising as a result of lower fertility rates and higher life expectancies (11). To be more precise, the percentage of older people is increasing in comparison to earlier times. According to the Global Burden of Disease Study (GBDS) 2019, there will be a staggering 166% rise in dementia cases between 2019 and 2050, affecting over 152.8 million individuals (12). These approximations align with the World Health Organization's estimations. Furthermore, the highest rise in dementia cases up to 330% will most likely happen in countries with low Socio-demographic index scores, like India (SDI) (13).

2.1. AD general background

Alzheimer's disease (AD) is most common kind of dementia & sixth leading cause of death in those over 65. Minor memory loss, severe cognitive deficits, loss of basic body functions, & even death are among range of symptoms (14). The deleterious protein aggregates stimulate the release of inflammatory cytokines, glial cell activation, disruption of synapses, and neuronal death (15).

2.2. Alzheimer's disease biomarkers

Early detection of AD neuropathological change (ADNC) has been made achievable by the combination of PET imaging, CSF, and blood biomarkers. The cost, invasiveness, and reagent consistency of AD biomarkers remain a number of constraints, and new PET methods and blood tests are now being investigated. In addition, the area of biomarkers is developing so quickly that it is now possible to identify AD often and accurately (16). The four main types of biomarkers for AD that have been found are Cerebrospinal Fluid (CSF), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET) imaging, and blood testing. Furthermore, composite cognitive tests have created to detect pre-clinical cognitive deterioration. Early diagnosis of AD using cognitive testing is a great technique to track the

effectiveness of therapy. To sum up, many biomarkers have been found to assess different aspects of AD pathology & establish illness's stage. AD biomarkers offer a potential means of lowering the risk and improving the chance of technical success. Understanding of AD is improving quickly, and key biological events are being found (17). In some cases these events are followed by biomarkers measured by brain imaging or in the cerebrospinal fluid (CSF) or blood. The use of these factors to improve the drug development process can de-risk AD drug development. The amyloid (A), Biomarkers have a key role in Alzheimer's disease (AD) drug research. Biomarkers can help in detection, show target interaction, support disease change, and watch for safety. The FDA's staging of AD contributes biomarkers to the staging strategy and aids in treatment development for AD patients in the predementia phases. Drug research initiatives may combine the development of companion and additional biomarkers with novel medications. The smart use of biomarkers has the potential to accelerate drug discovery for AD and assist in developing novel therapies for AD patients and those at risk (18).

Biomarkers for Alzheimer's disease (AD) are crucial for early diagnosis and tracking the progression of the illness. The current research reveals a number of putative biomarkers in different biofluids, particularly blood and cerebrospinal fluid (CSF), which may enhance the precision of diagnosis and efficacy of therapy.

2.2.1. Important Alzheimer's disease biomarkers:

- Cerebrospinal fluid (CSF) biomarkers: Neurofilament light (NfL), tau proteins (T-tau, P-tau), and amyloid-β (Aβ) are important indicators. Increased levels of these proteins have been linked to cognitive impairment and symptoms of AD.
- Biomarkers based on blood: New blood biomarkers with potential for non-invasive detection include plasma NfL and Aβ levels. They may foretell alterations in the brain and are connected to neurodegeneration.
- Imaging biomarkers: Methods such as tau- and amyloid-PET are often used in clinical investigations and serve as the primary gauges of therapy effectiveness.

Even with these advancements, standardizing these biomarkers for routine clinical usage still present challenges, particularly for blood-based indicators that still need further validation.

3. Personalized medicine for Alzheimer's disease

Precision medicine, according to the FDA, aims to offer security and medical treatment that considers each person's unique genetic makeup and lifestyle. By taking into account a patient's genetic background, lifestyle, and environment, precision medicine specifically aims to move clinical practice away from "one therapy fits all" approach. This is achieved by taking into account a patient's susceptibilities to a given disease or how a patient may respond to a therapy. The aging-related, chronic, complicated illnesses, such as dementia, heart disease, & cancer, have become biggest danger to human health in recent decades (19). The research of AD is quickly catching up in terms of describing disease mechanisms and underlying risk factors. An increasing amount of evidence indicates that AD is mostly genetically based. Numerous basic risk genes have been shown to be connected to a number of disease processes. Moreover, a variety of lifestyle decisions are connected to the risk to AD. In the end, strong data from AD clinical trials has shown that knowing etiopathology & accurately staging the illness are essential to deciding whether to start therapy. It seems that pre-symptomatic treatment is essential to ensuring possible outcomes that affect the illness (20).

Personalized medicine is an innovative method to treating Alzheimer's disease (AD). It centers on tailored therapeutics that consider the individual genetic, biochemical, and environmental factors of each patient. Enhancing treatment effectiveness and safety is the aim of eschewing a one-size-fits-all approach. AD is a complicated disorder involving amyloid-beta and tau proteins.

3.1. Personalized therapy options based on genetic and biomarker data are essential:

- Genetic and biomarker profiles are used in precision medicine.
- Combination treatments utilize multimodal approaches, such as BACE inhibitors & monoclonal antibodies, to address many disease processes concurrently (21).

3.2. The role that epigenetics plays:

Epigenomics of drugs improved knowledge of epigenetic mechanisms has led to the discovery of predictive biomarkers, facilitating quicker diagnosis and more individualized treatment.

3.3. Collaborative research initiatives

A Dutch project called the ABOARD Cohort guarantees that patient viewpoints are taken into account while examining AD pathways and individualized treatment strategies. It also promotes public engagement in research (22).

Despite these developments, integrating personalized medicine into standard care remains difficult, necessitating modifications to clinical trial designs and healthcare laws (5). To fully grasp the possibilities of specialized therapy, further study and cooperation are needed due to the complexity of AD. The different imaging techniques for AD diagnosis are show in the Figure 2.

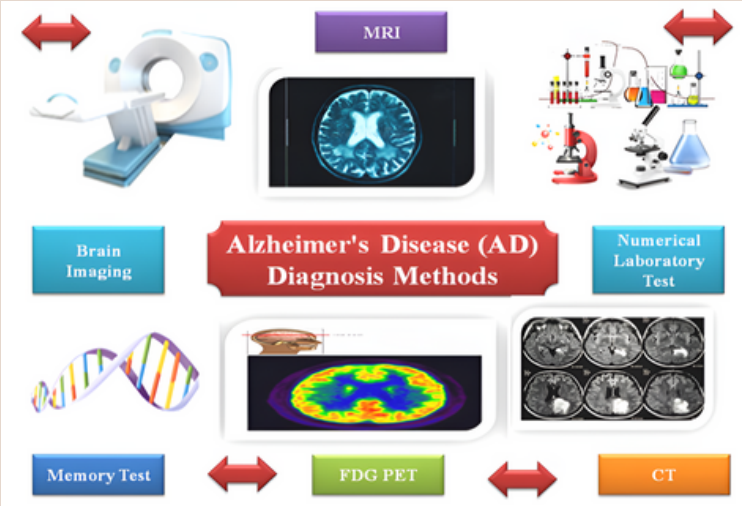

Figure 2. Different imaging techniques for AD diagnosis

4. Current drug pipeline for AD

Five drugs now approved by FDA to treat AD. Three cholinesterase inhibitors galantamine, rivastigmine, & donepezil one NMDA receptor blocker (memantine), & combination of memantine & donepezil. Sadly, the existing drugs can only briefly ease symptoms; they cannot change how the condition progresses (23). A cooperative multinational phase III study involves Europe, the United States, and China. Aducanumab is the most likely drug in the US. It is a monoclonal antibody made by Biogen that inhibits Aβ fibrils. When additional trial participants were included in the study, it was shown that there was less tau brain buildup, amyloidosis, and cognitive deterioration at higher dosages (24,25). However, solanezumab and crenezumab have not proven effective in protecting against monomeric and oligomeric Aβ when used as passive vaccines. γ-secretase modulators & β-secretase inhibitors, two more strategies for Aβ production, were withdrawn due to their toxicity, adverse effects, and decline in cognitive performance (26).

5. Future trends

The overall management of AD involves not only giving every dementia patient the standard care they need, but also implementing presymptomatic diagnostic protocols, accurately identifying and treating concurrent pathologies, improving diagnostic accuracy, customizing pharmaceutical treatments, & initiating prevention programs in population at risk. Important problems in management of AD include inadequate medicine, poly-pharmacy connected to related disorders, and excessive and wasteful use of psychoactive substances, especially in nursing homes (27).Ninety-five percent of patients older than eighty take ten or more different medications every day for conditions like arthropathies, metabolic disorders, cerebrovascular insufficiency, cerebral microinfarctions, and cardiovascular diseases and related pathologies that aggravate the clinical picture of dementia. Integrating pharmacogenetic techniques into ordinary clinical practice is the greatest way to improve the available medical tools and minimize adverse drug responses and dose-related injuries once pharmacogenetics achieves a mature level of development (28,29).

6. Conclusion

Even if several efforts to create AD disease-modifying medications have failed, there is now a unique chance to move AD treatment approaches toward precision medicine thanks to recent technology developments in the domains of genetics and biomarker testing. Early diagnosis of the condition will be straightforward and accurate using blood biomarker tests, such as P-Tau. Further diagnostic procedures, including as CSF, MRI, and PET scans, will identify the stages of the illness and maybe identify its cause. Thanks to genetic testing, future medical experts will be better equipped to determine the etiology of illnesses based on SNPs, odd mutations, & polygenic risk genes.

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