



## A CLINICAL UPDATE ON ALZHEIMER'S DISEASE

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### ARTICLE INFO

### ABSTRACT

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Alzheimer's disease (AD) is a progressive and eventually fatal dementia of unknown cause characterized by loss of cognitive and physical functioning, commonly with behavioural symptoms. AD is not a normal part of ageing; it is a disease condition of the brain that causes problems with behaviour, thinking & memory. Signature findings include intracellular neurofibrillary tangles (NFTs), extracellular amyloid plaques in the cortex and medial temporal lobe, and degeneration of neurons and synapses and cortical atrophy. Density of NFTs correlates with severity of dementia. The disease may cause a person to become misplace things, or have trouble with language, confused & get lost in familiar places. The most common symptom is the short term memory loss. This may cause due to the genetical problems, depression, hypertension and also because of head injury. Following is a review about some recent updates of AD from all over the world.

### INTRODUCTION:

Alzheimer's disease that is that the commonest form of dementia, that sometimes starts in adulthood or in late time of life, leads to impaired thinking, progressive cognitive state, disorientation and changes in temperament and mood.<sup>1</sup> There is a degeneration of brain neurons particularly within the cortex. In 1906 Dr. Alois Alzheimer, a German medical practitioner was 1st delineate this disease. Regarding 3% of men and girls ages 65 to 74 have AD. Each year, about 3, 60, 000 new cases of Alzheimer's are diagnosed. The early stages of Alzheimer's disease are tough to diagnose. He was progress from gentle cognitive problems, like memory loss through increasing stages of non cognitive and cognitive disturbances, eliminating any chance of independent living. The transitional period between normal cognitive functioning and dementia is the mild cognitive Impairment.<sup>2</sup> Life expectancy of

the population with the disease is reduced. The mean life expectancy of AD is around seven years. Fewer than 3% of patients live quite fourteen years. Associate magnified severity of psychological feature impairment, history of falls, reduced functional level and disturbances within the neurologic examination are the disease features considerably associated with reduced survival.<sup>3, 4</sup> The risk of AD and its progression related to the increased accumulation of cerebral iron, that has been coupled to many pathological processes.<sup>5-10</sup> Presence of the apolipoprotein E (ApoE) ε4 gene and genetic predisposition, that is that the strongest notable genetic risk issue for late-onset AD and it's significantly affected the progression of AD.<sup>11-15</sup> It is expected that the amount of individuals plagued by AD worldwide can exceed 100 million in 2050, by the lack of disease modifying therapies and within the absence of clear

prevention ways.<sup>16</sup> Thus for research in each domain and pharmaceutical companies, it's urgent to develop the disease modifying medical aid for AD. AD have two principle hallmark events: 1) the aggregation, brain deposition and the misfolding of amyloid- $\beta$  ( $A\beta$ ) peptide in amyloid plaques, and 2) Misfolded tau protein deposition in neurofibrillary tangles (NFT).<sup>17</sup> In the AD field, the pre-eminence of the amyloid hypothesis<sup>18</sup> for drug development, various forms of  $A\beta$  aggregates; these include alteration and reduction of APP processing, prevention of  $A\beta$  misfolding and minimization, aggregation or elimination of its neurotoxicity, degradation and acceleration of its clearance<sup>19-24</sup> as well as passive and active vaccination strategies to remove amyloid deposits.<sup>25</sup> In neurodegenerative diseases, an ever-increasing body of evidence implicating tau,<sup>26, 27</sup> supports it as a potential target for the development of disease modifying therapeutics.<sup>28, 29</sup> By the inhibition of phosphorylation, potential therapeutics may manipulate tau<sup>30, 31</sup> activation of proteasomal or proteolytic degradation pathways,<sup>32, 33</sup> microtubule-binding drugs (eg, paclitaxel) for stabilization of microtubule networks microtubule binding drugs were used,<sup>34, 35</sup> inhibition of aggregation by small molecules,<sup>36, 37</sup> or clearance by immunotherapy.<sup>38-41</sup>

### **Role of meditation and music**

A recent study from West Virginia University found that, the practice of simple meditation and music listening programme have a beneficial effect on older adults who is suffering from preclinical memory loss. Both the meditation and music programme marked a significant improvement on 60 adults randomly taken by the University research team in their subjective memory function and objective intellectual performance at 12 weeks (3 months). The regained memory and intellectual performance can be improved and maintained at 6 months. This two simple practices not only regain the memory and objective cognition but also the sleep, mood, stress and quality of life.<sup>42</sup>

### **Alzheimer's Memory test: women perform better than men**

Another update by Dr. Pauline Maki, Professor of psychiatry and psychology at the University of Illinois is that women do better on verbal memory test than men with the same amount of neurotoxic protein in their brains. "Women have better verbal memory than men, in general. One key factor is their higher levels of estrogen," she said. "We see this in women whose ovaries are removed – their verbal memory worsens and when they take estrogen, their memory bounces back. So the advantage women have over men on this test is real, and the issue is that these tests might not detect the early stages of AD in women. This is a big problem for women, because the earlier that mild cognitive impairment is diagnosed, the earlier treatment can begin to slow its progression." <sup>43</sup>They found it through several steps of observation. They wanted to know that, who(male or female) will perform well in the tests of AD and come to a conclusion that, women had significantly better in delayed recall scores among men and women with low to moderate levels of amyloid beta. Scientists and Clinicians had reported that AD in women is different from that of in men and majority of the victims of this disease are women where men are suffering from the precursor to AD which is mild cognitive impairment. If the amyloid beta level is increased, the effect will be worse on women than men.<sup>43</sup>

### **Importance of brain SPECT imaging**

It is really difficult for a clinician to prescribe a diagnosis for depression and cognitive disorders because both of these disorders have some overlapping symptoms. A new report according to the Journal of AD is that we can distinguish between depression and cognitive disorders on the basis of the neuro imaging of decreased blood flow in specific regions of the brain. Researchers who have examined about 4541 subjects of this kind had made an inference that there was reduced blood flow particularly in hippocampus, temporal and parietal lobes for the people who have

diagnosed with cognitive disorders compared to those with depression. Another mode of distinguishing both these disorders is by SPECT (Single-photon emission computed tomography).<sup>44</sup>

### **Risk in off-label uses of drugs**

Transitional state between dementia and normal age related changes in cognition is known as cognitive impairment. Many AD patients display symptoms similar to this condition. The most prescribed medicine used for AD is donepezil. It was tested as a possible treatment for mild cognitive impairment but it was not approved by the FDA. But still this drug is prescribed as off-label for this condition. A study was led by the sophie sokolow, an associate professor at the USLA school of nursing researchers discovered that for people who carry a specific genetic variation the K variant of butyrylcholinesterase or BchE-K donepezil could accelerate cognitive decline. Hence donepezil should not be prescribed for people with mild cognitive impairment without a genetic test.<sup>45</sup>

### **Early recognition of Alzheimer's disease by diagnostic biomarker in saliva**

A recent update of investigators at the Beaumont research institute revealing that they are hopeful in their study involving small molecules in saliva will help to identify those at risk of developing Alzheimer's disease. They found salivary molecules as reliable diagnostic markers. They used a newer technique called metabolomics, to study molecules involved in metabolism. Their goal was to find unique patterns of molecules in the saliva of their study participants that could be used to diagnose Alzheimer's disease in their earlier stages, when treatment is considered most effective. So it's a necessary first step to design prevention and early intervention research studies.

### **Perseverance time instrument for the people with dementia**

The people with dementia who needs informal care which is non professional care

provided by patient's caregivers, is a large and crucial part of all necessary care.<sup>46</sup> Day by day patients with dementia is rising and the demands of health care resources increases. Hence, it is important that those willing and able to provide informal care to their loved ones can maintain the care situation for as long as possible.<sup>47</sup> A recent study from Netherland intended to extend insight into psychometric properties of the perseverance time instrument, specifically the construct validity, responsiveness and predictive validity within the population of informal caregivers for people with dementia.<sup>48</sup> This study supports previous finding regarding the construct validity of the perseverance time instrument and adds new evidence of good construct validity, responsiveness and predictive validity. The predictive power of perseverance time scores for living situation exceeds the predictive power of other burden measures and indicates informal care as an important factor for maintaining the patient at home.

### **CONCLUSION**

Currently available therapies of AD are symptomatic, but do not alter underlying disease progression. The first case of AD was described by Alois Alzheimer more than a century ago. Many progressions have been made in understanding the clinical aspects and biology of the disease. Several substantial advances have been made in characterizing pre-dementia stages and improving the diagnostic and therapeutic options available for managing AD. According to recent updates several factors plays an important role in controlling and preventing AD. Our ability to find the 'cure' for AD ultimately depends not only on having an accurate view of the molecular and cellular processes that go awry but also on having optimal biomarkers to enable early diagnosis and timely therapeutic intervention in at-risk individuals. Recognizing the urgent need to develop clinically useful neuro imaging and other biomarkers for the early detection of AD.

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