

# Alzheimer's Disease- A Review

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## Abstract

**Aim:** To review about Alzheimer's disease and its prevention

**Objective:** This systemic review on Alzheimer's disease may throw light on the prevalence, causes, symptoms and prevention. Vast knowledge regarding disease and disorders will help people take precautions for not getting effected by it. This in turn will help reduce the number of Alzheimer's disease is a disorder that causes problems to a persons memory, thinking and behavior. It's the most common form of dementia. Mostly old adults are effected by it. This disease is related to brain damage. It's a progressive disease and as time progresses, more and more parts of the brain will get damaged. Memory related exercises will help people keep a check on the disease and its progress, this is one of the best ways to check for symptoms.

**Reason:** This review is being done so that people will be more aware about the consequences of Alzheimer's disease, and may be able to take precautions related to the disease.

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## INTRODUCTION

The word "Dementia" is associated with memory loss and difficulties with thinking, problem solving or language. It is the clinical condition which involves the deterioration of intellectual functions in an individual.[1] One of the most common forms of dementia is the Alzheimer's disease.[2] Dementia can either be reversible or irreversible. Alzheimer's disease is the cause for irreversible dementia. This disease was first diagnosed by a German psychiatrist and neuropathologist, Dr. Alois Alzheimer, on a patient who was a 51 year old woman.[3] This is mainly because the patients have a shortage of important chemicals in their brain which is necessary for the transmission of signals around the brain. When there is a shortage in these chemicals, the signals are not transmitted effectively.

Alzheimer's disease usually starts with mild conditions, and they get worse over time. They will, in the end, interfere with daily life. The earliest symptoms that are seen are memory loss. Patients will have trouble recalling recent events or learning new information. This occurs due to damage in the part of the brain called hippocampus which plays a role in day to day memories.[3] As the condition progresses, the memory loss will interfere with daily life activities and the patient will require help going through the day. Problems with memory loss, communication, reasoning and orientation will become more severe. In later stages, the patient may find difficulties eating or walking without help.

The general age group of the people who get affected by this disease is at about 65. For younger people under this age, who are affected by this disease, are said to have young onset dementia.[3] There are no particular treatments that cure this disease. Its diagnosis can be done through brain scans, CT scans etc. These scans will show if certain changes have taken place in the brain. Though there is no certain cure for this disease, there are a lot that can be done to enable someone to live well with the condition. It involves drug and non- drug care, support and activities. The treatments that involve the intake of drugs can temporarily alleviate some symptoms or slow down the progression of the disease in some cases. Drugs such as donepezil are prescribed.[4] They improve concentration

and help with daily aspects of living such as cooking, shopping or hobbies.

## CAUSES OF ALZHEIMER'S DISEASE

The main cause for this disease is still not known, with age as the greatest risk factor. Gene mutation is one of the triggers that lead to getting this disease. Early development of Alzheimer's disease (before the age of 65) is called "early onset" or "familial" Alzheimer's disease. Patients who suffer from Down's syndrome are more likely to get effected by this condition.[5] The prevalence of this disease is seen more in women which will explain their higher life expectancy rate compared to that of men.[3] The lack of education or knowledge about this condition is one of the major causes that are observed as well. Family history with cases of having this disease, injury to the head followed by losing consciousness will increase the risk factors for the development of Alzheimer's disease.

## NEUROPATHOLOGICAL ASPECT OF ALZHEIMER'S DISEASE

This disease is known as a progressive neurodegenerative brain disorder, which causes defect in the normal brain functioning. It is characterized by the loss of cortical neurons or pyramidal cells which disrupts the neural circuits which are necessary for memory and other functions. Degeneration of the brain cells usually start in the medial temporal lobe region and slowly spreads towards the parietal areas. [6] It then progresses to effect the limbic system which will result in behavioral changes. It has been theorized that the neural damages are due to the deposition of abnormal proteins within and outside neurons.

## DIAGNOSING ALZHEIMER'S DISEASE

Diagnosing this disease is best done with the help of observation. There are many common symptoms that will develop in a patient as Alzheimer's disease progresses in a patient. The most obvious symptom would be memory loss, when the patient starts to lose the ability to recall small and simple things in his/her daily life. Autopsy-based pathological evaluations can also be done.[7] They try to detect the presence of amyloid plaques in the brain. in

clinical settings, the doctors are able to diagnose this disease with the help of taking medical history and neurological examinations. The accuracy for these diagnosis would be about 70-90% right. Alzheimer's disease is usually diagnosed when there are cognitive or behavioral (neuropsychiatric) symptoms.

### **SYMPTOMS**

Main signs and symptoms of an Alzheimer's patient are usually related to cognitive and neuropsychiatric. Some of the symptoms of an Alzheimer's patient are the interference of the ability to carry out daily tasks, deterioration of progressive levels of functioning, has no signs of delirium or psychiatric disorders, and shows similar behavioral patterns as individuals with substance abuse. Cognitive impairment is detected and diagnosed through a combination of history-taking from the patient and a knowledgeable informant and an objective cognitive assessment.[8]

The Cognitive or behavioral impairment involves the inability of acquiring new knowledge and forgetfulness. Forgetting daily conversations and activities that the patient has been carrying out on a day to day basis before the onset of the disease. The individual will have trouble making judgments as well as poor decision making to make and carry our simple or complex activities. [9] The patient will also have a problem with facial recognition as well as common objects; it is possible for them to forget their close family members that they have spent most of their lives with. Alzheimer's also causes the patient to have an impairment of speaking, reading and writing. There will be a vast change in personality with mood swings, lack of interest in prior daily activities as well as a loss of empathy. Alzheimer's patients tend to develop obsessive compulsive behaviors (OCD).

Individuals with dementia are classified into probable, possible as well as probable or possible Alzheimer's disease. Probable Alzheimer's disease is diagnosed when the following characteristics such as an insidious onset, clear- cut history of worsening which can be seen in hereditary conditions as Alzheimer's disease dementia can be a hereditary condition. Probable Alzheimer's can be due to Amnestic and non-amnestic presentations.

Amnestic presentation is a syndromic condition includes an impairment of speaking, reading and writing as well as has trouble making judgments as well as poor decision making to make and carry our simple or complex activities. Non-amnestic conditions on the other hand cause a barrier in language and spatial cognition.[9] The most prominent deficits occurs when there is an impairment in judgment as well as solving problems either simple or complex that has been present in day to day activities of the patient.

Possible Alzheimer's disease dementia is usually characterized for patients with pathophysiological and Neuropathological conditions that can be observed in patients having Alzheimer's disease but they have no other signs or symptoms to support the diagnosis of the disease.[3] It can be misdiagnosed with HIV dementia, dementia of Huntington's disease as well as neuronal injuries biomarkers.

### **TREATMENT**

Although no cure has been found for the treatment of Alzheimer's disease, there are drugs that are able to curb the breakdown of acetylcholine in the brain. This drug slows down the onset of Alzheimer's symptoms.[4] Aricept is a drug used for mild to severe Alzheimer's while Razadyne and Exelon are used on patients with mild to moderate onset. [8] Namenda are used in moderate to severe cases, it is used by changing the amount of glutamate in the brain which controls the role of learning and memory. Namzaric is a combination of Namenda and Aricept and is used in patients consuming both the drugs together.

Other than the usage of drugs, the patient and their close ones can ensure the patient is safe and calm at all times. The patient can keep all the valuables at a specific place so they do not lose them, they should have mobile phones with trackers so their locations can be traced when they are confused about their whereabouts.[10] Use a calendar or whiteboard whenever possible to note down important details. Photographs can help jog the memory of a patient. Excess of furniture as well as mirrors should be removed to avoid clutter and cause confusion for the patient as they might be confused and run into the furniture. Handrails and support bars are placed in the bathrooms and kitchen. Ensure the appointments are done on the same day and time to avoid the patient from forgetting besides giving them medication on a once daily basis. All daily activities should be simplified for the patient to ensure the patients do not get confused or have an onset of mood fluctuations due to stress and frustrations.[3] Alzheimer's disease patients should be constantly watched and cared for by family members or closed ones as it is the best and most reliable form of treatment.

### **BIOMARKERS**

Several biomarkers are used in the approach to study Alzheimer's disease. Biomarkers are required to select patients during studies and also to identify high risk patients for early treatment as well as monitoring the patients disease progression or response to treatment. Some of the biomarkers that are used would include Magnetic Resonance Imaging (MCI), Position emission tomography and fluid biomarkers.

Magnetic Resonance Imaging uses a strong magnetic field and radio frequency waves, and measure the energy released by protons in various tissues and parts of the brain. it can be used to study the regional patterns of brain atrophy in patients. Positron emission tomography is a nuclear imaging technique and it helps measure the regional brain metabolism. The earliest signs of Alzheimer's disease can be detected on this. Fluid biomarkers are based on CSF and blood plasma; they are used for diagnosis purposes as well. [3]

Three biomarkers have been well-established and validated internationally to diagnose AD in CSF with ELISAs:  $\beta$ -amyloid(1-42) [ $A\beta(1-42)$ ], total tau and phospho-tau-181. CSF  $A\beta(1-42)$  was the most sensitive biomarker for AD in the autopsy cohort of CSF samples. The CSF biomarker signature of AD defined by  $A\beta(1-42)$  and t-tau in the

autopsy-confirmed AD cohort and confirmed in the cohort followed in ADNI for 12 months detects mild AD in a large, multisite, prospective clinical investigation, and this signature appears to predict conversion from mild cognitive impairment to AD. Despite strong efforts to characterize other potential biomarkers in CSF, several biomarkers have been tested in CSF that have displayed changes between AD and controls. Florbetaben is another radiotracer designed to detect beta-amyloid during a PET scan. Florbetaben is currently being reviewed by the FDA for approval as an amyloid imaging agent. However, no other single biomarker has been validated to date for routine diagnosis, because the changes are very heterogeneous and low, and data have differed between laboratories. Cognitive decline is highly correlated with loss of the neurotransmitter acetylcholine in the cortex or the hippocampus. Brain atrophy on structural magnetic resonance imaging (MRI) in a characteristic pattern involving the medial temporal lobes, paralimbic and temporoparietal cortices is a biomarker of AD-related neurodegeneration.

### CONCLUSION

There have been many advances made in the study of this disease since the first time it had been diagnosed. There have been many studies conducted in order to find a cure and to find better methods for its diagnosis. People have been able to learn more about the symptoms, diagnosis and the development of this disease from all the studies that were conducted. Large financial supports have been dedicated for the studies to identify new approaches and drugs. Relationships have been found that describes the development of the disease, such as, diet, cardiovascular risk, pharmaceutical products etc. With knowledge regarding the disease conditions, even though there is no known cure as of yet, people can diagnose the disease at early stages and take proper care.

### REFERENCE

- Gilman, S., *Oxford American Handbook of Neurology*. 2010: Oxford University Press.
- Plassman, B.L., et al., *Prevalence of dementia in the United States: the aging, demographics, and memory study*. *Neuroepidemiology*, 2007. **29**(1-2): p. 125-132.
- Korolev, I.O., *Alzheimer's Disease: A Clinical and Basic Science Review*. *Medical Student Research Journal*, 2014. **4**: p. 24-33.
- Winblad, B., et al., *Donepezil in patients with severe Alzheimer's disease: double-blind, parallel-group, placebo-controlled study*. *The Lancet*, 2006. **367**(9516): p. 1057-1065.
- Busse, A., et al., *Mild cognitive impairment long-term course of four clinical subtypes*. *Neurology*, 2006. **67**(12): p. 2176-2185.
- Bozoki, A., et al., *Mild cognitive impairments predict dementia in nondemented elderly patients with memory loss*. *Archives of neurology*, 2001. **58**(3): p. 411-416.
- McKhann, G.M., 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 & dementia*, 2011. **7**(3): p. 263-269.
- Khachaturian, Z.S., *Diagnosis of Alzheimer's disease*. *Archives of Neurology*, 1985. **42**(11): p. 1097.
- McKhann, G., et al., *Clinical diagnosis of Alzheimer's disease Report of the NINCDS-ADRDA Work Group\* under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease*. *Neurology*, 1984. **34**(7): p. 939-939.
- Etminan, M., S. Gill, and A. Samii, *Effect of non-steroidal anti-inflammatory drugs on risk of Alzheimer's disease: systematic review and meta-analysis of observational studies*. *Bmj*, 2003. **327**(7407): p. 128.
- Etminan, Mahyar, Sudeep Gill, and Ali Samii. "Effect of non-steroidal anti-inflammatory drugs on risk of Alzheimer's disease: systematic review and meta-analysis of observational studies." *Bmj* 327.7407 (2003): 128.
- Costa-Bouzas J, Takkouche B, Cadarso-Suarez C, Spiegelman D. HEPiMA: software for the identification of heterogeneity in meta-analysis. *Comput Methods Programs Biomed* 2001; **64**: 101-7.
- Busse A, Hensel A, Guhne U, Angermeyer MC, Riedel-Heller SG. Mild cognitive impairment: long-term course of four clinical subtypes. *Neurology* 2006; **67**: 217685. doi: 10.1212/01.wnl.0000249117.23318.e1
- Manly JJ, Tang M-X, Schupf N, Stern Y, Vonsattel J-PG, Mayeux R. Frequency and course of mild cognitive impairment in a multiethnic community. *Ann Neurol* 2008; **63**: 494506. doi: 10.1002/ana.21326
- Farias ST, Mungas D, Reed BR, Harvey D, DeCarli C. Progression of mild cognitive impairment to dementia in clinic- vs community-based cohorts. *Arch Neurol* 2009; **66**: 11517. doi: 10.1001/archneurol.2009.106
- Mitchell AJ, Shiri-Feshki M. Temporal trends in the long term risk of progression of mild cognitive impairment: a pooled analysis. *J Neurol Neurosurg Psychiatr* 2008; **79**: 138691. doi: 10.1136/jnnp.2007.142679
- Bozoki A, Giordani B, Heidebrink JL, Foster NL. Mild cognitive impairments predict dementia in nondemented elderly patients with memory loss. *Arch Neurol* 2001; **58**: 41116.
- Gauthier S, Reisberg B, Zaudig M, Petersen RC, Ritchie K, et al. Mild cognitive impairment. *Lancet* 2006; **367**: 12621270. doi: 10.1016/S0140-6736(06)68542-5
- He J, Farias S, Martinez O, Reed B, Mungas D, Broich K, et al. Differences in brain volume, hippocampal volume, cerebrovascular risk factors, and apolipoprotein E4 among mild cognitive impairment subtypes. *Arch Neurol* 2009; **66**: 13939. doi: 10.1001/archneurol.2009.252
- Rabinovici GD, Seeley WW, Kim EJ, Gorno-Tempini ML, Rascovsky K, Pagliaro TA, et al. Distinct MRI atrophy patterns in autopsy-proven Alzheimer's disease and frontotemporal lobar degeneration. *Am J Alzheimers Dis Other Dement* 2007; **22**: 47488. doi: 10.1177/1533317507308779 48. Wh
- Korolev, Igor O. "Alzheimer's Disease: A Clinical and Basic Science Review." *Medical Student Research Journal* 4 (2014): 24-33.
- Mosconi L, Pupi A, De Leon MJ. Brain glucose hypometabolism and oxidative stress in preclinical Alzheimer's disease. *Ann NY Acad Sci* 2008; **1147**:180-195
- Mosconi L, Mistur R, Switalski R, Tsui WH, Glodzik L, Li Y, Pirraglia E, De Santi S, Reisberg B, Wisniewski T, de Leon MJ. FDG-PET changes in brain glucose metabolism from normal cognition to pathologically verified Alzheimer's disease. *Eur J Nucl Med Mol Imaging* 2009; **36**(5): 811-822
- Mosconi L. Brain glucose metabolism in the early and specific diagnosis of Alzheimer's disease. FDG-PET studies in MCI and AD. *Eur J Nucl Med Mol Imaging* 2005; **32**(4): 486-510.