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Medicine

RISK FACTORS STUDY OF CLINICALLY DIAGNOSED ALZHEIMER'S DISEASE

KEY WORDS: Alzheimer's disease, risk factors.

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ABSTRACT

INTRODUCTION - Alzheimer's disease is most common neurodegenerative disease of old age. Determining risk factors for Alzheimer's disease may assist in identifying candidates for future prevention.
METHOD AND MATERIAL - We had studied 50 patients of clinically diagnosed Alzheimer's disease. A structured questionnare was administered to identify possible risk factors. All such risk factors were analysed.
RESULTS - Most patients were of late onset Alzheimer's disease. Females outnumbered men. Those having lower educational level, lower grade of principal occupation and sedentary lifestyle were common. Family history, diabetes and head injury were associated with Alzheimer's disease.
DISCUSSION -Alzheimer's disease should be searched in old age people, specially those having positive family history, diabetes and Head injury. Providing HRT, improving educational level and employment grade would help in reducing risk of Alzheimer's disease. Engaging people in physical exercise and cognitive stimulating activity would decrease chances of future Alzheimer's disease.

INTRODUCTION

Alzheimer's disease is one of the most common neurodegenerative disorder. Incidence increases with age. Due to increased life expectancy of people is India it is going to be important health problem in future.

Pathogically, it is characterized by loss of specific neuron cells, senile plaque of Amyloid- and neurofibrillary tangles of protein tau. Pathological lesions first appear in the enthorhinal regions of the hippocampus and then become wide spread.[1] Neurotransmitters are decreased in Alzheimer's disease, most prominent among them is forebrain cholinergic system.

Clinically, it tends to follow characteristic pattern. In early stages, memory impairment is followed by language and visuospatial deficit. In late stages, delusions are common usually simple with common themes of -theft ,infidelity or misidentification. In end stages, Alzheimer's disease patient become rigid, mute, incontinent and bed ridden.

METHOD AND MATERIAL

We had studied 50 patients of clinically diagnosed Alzheimer's disease admitted in hospital from 2017-2019. Criteria for clinical diagnosis of Alzheimer's disease is shown in Table I.

We had modified original criteria of Guy Mckhann MD etal by adding biomakers. They are recommended by Alzheimer's association work group 2011.[4] Biomarkers are indicators of specific pathophysiological changes that characterizes Alzheimer's disease. They are used in our study to increase the patho-physiological specificity. Biomarkers are shown in table II.

MRI brain is the biomarker used in our study because it is easily available. Neuroimaging helps to rule out neoplasms, infarction, subdural hematoma, NPH or diffuse white matter disease. Serial MRI demonstrates increased rate of atrophy in Alzheimer's patient than normal.[9]

Table I : Guy Mckhann etal's modified criteria for clinical diagnosis of Alzheimer's disease.2

1. Dementia established by MMSE.
2. Deficits of 2 or more areas of cognition. Progressive worsening of memory and other areas of cognition. (language, perception and motor skills(praxis))
3. Age > 40 years and insidious onset.
4. No abnormality in consciousness.
5. Exclusion of systemic or brain disease that could cause progresive decline in memory and cognition.
6. Significant interference in daily activities at work.

For supportive evidence- Biomarkers are used.

87% of clinically diagnosed Alzheimer's disease patients full field histological criteria for Alzheimer's disease in autopsy.3

We had evaluated our patients by history, MMSE, Test for long term memory, Neurological examination and MRI brain. Relevant investigations were done to rule out systemic or brain disease that could cause progresive decline in memory and cognition. Eg:- TSH, Serum Vitamin B12, MRI brain, etc,.

Preferred clinical strategy is to investigate multiple risk factors and to establish diagnostic or therapeutic decisions based on risk factors pattern. A structured questionnare was administered to identify possible risk factors.

Following possible risk factors associated with the disease were noted and analysed :- Age, Sex, Family History in first degree relatives, Diabetes mellitus, Head injury, Education level, participation in cognitive activities, Life time principal occupation and physical activity.

Table II. Biomarkers are of two categories

Biomarkers of Aβ-plaque deposition

a. CSF Aβ42 - Low cocentration corelates with AD.5
b. Amyloid PET scan- Uses pittsburgh compound (pib) which binds to fibrillary Aβ and corelates with AD.6

Both are valid biomakers of brain Aβ plaque.7
Biomarkers of Neurodegeneration

a. CSF Tau - Increased conectration corelates with presence fo Neurofibrillary tangles.8
b. FDG PET scan - Shows a specific pattern of decreased glucose uptake in - Lateral temporo parietal and posterior cingulate distribution.7
c. MRI- Provides supporting evidence for diagnosis of AD such as - Hippocampal atrophy, in addition to posterior predominant cortical atrophy.

RESULTS

In our study 47 patients were of late onset Alzheimer's disease (i.e. symptoms begins after 65 years) and 3 patients were of early onset Alzheimer's disease (i.e. symptoms begins before 65 years). Mean age of patients was approximately 81 years. Age wise distribution is shown in table III.

Females outnumbered males as 30 patients were females in comparison 20 male patients. Family history of Alzheimer's disease was found in 3 patients, but clear cut autosomal dominant

inheritance pattern was lacking.

Diabetes Mellitus is well defined risk factor for Alzheimer's disease. 5 patients in our study were found to have diabetes mellitus. Head injury in past was found to be associated with Alzheimer's disease.10 We had 3 patients of Alzheimer's disease with past history of head injury.

Educational level of patients is shown in table III. Among 50 patients, 26 had education upto primary school, 14 had education upto secondary school and 10 had education upto graduate and above that. So, the people having lower educational level were more common.

Life time principal occupation was divided into two broad categories as given below in table III.

Table III. Age , Education level and life time principal occupation of patients

(a) Age wise distribution	Early onset	<65 years	3
	Late onset	65-74 years	8
		75-84 years	16
		>85 years	23
(b) Education level	Upto primary		26
	Upto secondary		14
	Graduate and above		10
(c) Life time Principal occupation	Lower Employment Grade	House keepers, Farmers, non-intellectual workers, elementary occupationers	38
	Higher Employment Grade	Legislators, government adminstrators, businiss executives ans managers	12

Thus , we see that those having lower employment grade(house keeper's, farmers, non intellectual workers, elementary occupationers) were more than those having higher employment grade (Legislators, Government adminstrators, businesh executives and managers)

Participation in physical activity was evaluated and we found that those participating in physical activities such jogging, walking, etcs were less(19 patients) than those living sedentary life (31 patients).

When involvement in cognitive stimulating activities was asked, we found that only 10 patients were involved in cognitive stimulating activities reading newspaper and magazines, etc,

DISSCUSSION

Advanced age and sex are the two most important non modifiable risk factor for dementia including Alzheimer's disease. Mean age of onset of dementia in our study was approximately 81 years. Matching results were found in French study, where mean age of onset of dementia was 82.3 years.[11]

Prevalence of early onset Alzheimer's disease is 5%.[12] Our result matches it as 6% of our patients had early onset and 94% had late onset Alzheimer's disease.

Females are at greater risk of developing Alzheimer's disease in study by Jessiaca L Podcasy etal.[13] Our study supports this as 60% of patients were females. Women at greater risk had been correlated to postmenopausal estrogen decline.[14] Therefore use of Hormone replacement therapy is suggested to prevent Alzheimer's disease.

According to study in past majority of Alzheimer's disease is sporadic(>95%).[15] We found similar results as 94% were sporadic and 6% were familial. In addition to the e^4 allele of the apolipoprotein E gene (APOE-4), the major know genetic risk factor, a family history of Alzheimer's disease also increase risk to develop the disease.

In our study all 3 patients with family history of first degree relatives were of early onset. Our study result is supported by result of Li and co-workers, whose study concluded that early onset Alzheimer's disease patients were more likely to have relatives with disease.[16]

Diabetes is a important risk factor for Alzheimer's disease. In a study adjusted for age, sex and education level, those with diabetes had a 65% increased risk of developing Alzheimer's disease.[17] 10% of patients in our study were having diabetes. Screening for Alzheimer's disease is suggested in diabetic patients, specially in older age group.

Head injury may be important etiological factor in Alzheimer's disease. Data from study on head injury, suggest increased expression of β-APP in head injury patient that can lead to deposition of β-Amyloid protein and initiation of an Alzheimer's disease.[18]6% patients were having head injury in past. It is another important non modifiable risk factors.

Each year of formal education modifies Alzheimer's disease pathology and level of cognitive function.[19] Our study favours this as most patients (52%)did not had education above primary level.

Study in America found that life time principal occupation is associated with risk of Alzheimer's disease.[20] Another study found inverse a relationship between employment grade and risk of cognitive decline.[21] Similar results were found in our study as 76% patients were having lower employment grade, such as housekeepers, elementary occupationers.

Benefits of physical exercise on the brain and general wellness are well recognized. Data suggests the relevance of integrating physical exercise in the prevention and cure of Alzheimer's disease.[22] Our study supports this as 62% of patients had sedentary lifestyle.

Frequent participation in cognitive stimulating activities (reading newspaper and books etc.) is associated with reduced risk of Alzheimer's disease.[23] Lesser i.e. 10 patients (i.e. only 20%) were involved in cognitive stimulating activities in our study.

Alzheimer's disease should be actively searched in old age people, specially those having positive family history, diabetes mellitus and Head injury. Providing hormone replacement therapy in females, improving educational level and employment grade would help in reducing risk of Alzheimer's disease. Engaging people in physical exercise and cognitive stimulating activity would decrease chances of future Alzheimer's disease.

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