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Clinical Presentation of Alzheimer Disease (ad): a hospital based observational study.

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Abstract:

Introduction: Alzheimer's disease (AD) is a neurodegenerative illness that manifests itself clinically and pathologically.

Objective: To identify the various patterns of Alzheimer's disease (AD) in adults.

Methodology: A hospital based observational study was conducted in the Department of Neurology Jinnah Postgraduate Medical Centre (JPMC) Karachi, Pakistan from May 2018 to November 2019. Cases with complaint of memory impairment and/or cognitive impairment, with or without behavioral changes were included in the study. Acute delirious state uremia / hepatic encephalopathy hypo / hyperglycemia and hypo / hyponatremia were excluded diagnosis. The main outcome measures were clinical patterns of AD with age and sex distribution, affective disorder with cognitive impairment (Pseudo dementia) and affective disorder without cognitive impairment.

Results: A sample of 51 cases (36 males and 15 females) with memory impairment was included. Age's between 25-85years (mean 57years). Out of 51 cases 44 had probable /possible Alzheimer's disease (AD) 03 had affective disorder with cognitive impairment (pseudo dementia), 04 patients had affective disorder without cognitive impairment. Among probable / possible cases of AD 23 (52.27%) had multi infarct dementia (having history of past cerebrovascular disease), same statistics among Parkinson's patient's i.e. diagnosis was Parkinson's disease with memory impairment were 18 (40.90%) followed by alcoholic dementia in 03 (6.8%). There was no definite Alzheimer's disease case in this study.

Conclusion: Vascular dementia not the definite Alzheimer's disease is the commonest memory impairment type presentation in our study. Among Parkinson's disease patient's dementia was found quite high in our study.

Keywords: Alzheimer's disease (AD), Vascular dementia (MID), Parkinson's disease (PD), Cognition, Memory .

Introduction:

Alzheimer's disease (AD) is a neurodegenerative illness that manifests itself clinically and pathologically. Alzheimer's disease has a wide range of causes, including mutations in chromosomes 21, 14, and 1, as well as unknown pathogenic factors.¹ Differences in age of onset, rate of advancement, pattern of neuro-

psychological deficits, and incidence of non-cognitive neuropsychiatric symptoms are all frequent clinical variants. There are currently no biological indicators known for AD that allow preclinical identification or conclusive premorbid detection, except in rare examples of recognizable mutations in pre-symptomatic patients.²

Alzheimer's disease is the most frequent cause of dementia, accounting for more than two-thirds of all cases, according to most studies.³ The origin, clinical manifestations, and pathophysiology of Alzheimer's disease are all different. Because of this variability, correct diagnosis is more challenging.⁴ Correct diagnosis is critical for furthering Alzheimer's research, administering treatment, and identifying non-AD causes of dementia. There are no established biomarkers for Alzheimer's disease, but standardized clinical criteria have increased diagnosis accuracy to above 85 percent.⁵ The commencement is delayed and the progression is hidden. The aphasia advances to fluent aphasia with word replacement or aphasia with comprehension difficulties, and the language disorder may be an early component.⁶ Early on in Alzheimer's disease, recent memory and the ability to learn new information are both compromised. Apraxia (reduced capacity to perform motor activities despite intact motor function) and agnosia are two other prevalent disorders in cortical function (inability to comprehend the written word). Patients with Alzheimer's disease are frequently unaware of their memory impairments.^{7,8} Delusions and hallucinations are widespread and can happen to anyone.^{9,10}

Alzheimer's disease is a major public health issue. The annual cost of Alzheimer's disease, the most common form of dementia, is projected to be \$335 billion in the United States.¹¹ The International Classification of Diseases 10th Edition (ICD-10), Diagnostic and Statistical Manual of Mental Disorders 4th Edition (DSM-IV), and National Neurological and Communication DSM-IV are three widely used standards-based AD diagnostic methodologies. There is substantial overlap in structural and functional characteristics of AD and vascular dementia (VaD). Distinguishing between AD and VaD has proven difficult given the overlap in the symptoms. Differentiation of other dementias from AD is important in order to implement an appropriate treatment plan, including providing prognostic information and counseling to patients and their families.¹²⁻¹⁴

AD is a public health problem of enormous magnitude with serious social and economic implications for the society. In Pakistan there have been few studies focusing on AD, particularly with reference to the role of cholinesterase inhibitors and estrogen replacement therapy in its treatment.¹⁵ For the past few decades,

among Pakistani aging of the population has increased leading to changes in the prevalence of AD and its associated risk factors. The data regarding epidemiology and etiology of AD in Pakistan are lacking. This study aims at identifying the clinical presentation of AD in the local population.

Methodology:

This observational prospective study on patients presenting with memory impairment conducted at the Department of Neurology, Jinnah Postgraduate Medical Centre (JPMC) Karachi. Adult patients of more than 18 years of age presenting with multiple cognitive deficits with a score of 23 or less out of 30 on folstein Mini-Mental State Examination (MMSE) were included in the study. Patients with acute delirious state, electrolyte abnormalities (hyponatremia & hypernatremia), hypoglycemia or hyperglycemia, hepatic encephalopathy and patients with uremic encephalopathy were excluded. After addressing the ethical issues (consent, confidentiality) all patients enrolled in the study were undergo a detailed history including history of presenting illness, past history, family history drug history and through physical and neurological examination. The folstein Mini-Mental State Examination translated into the vernacular, was used to assess the mental status. Blood tests, neuro-imaging, CSF examination and an EEG in selected patients, were done to record the details. A short assessment of affective disorder was made on following parameter: Emotional instability/desire to weep, sense of worthlessness of life, palpitation, psychomotor retardation, elation/overactivity, sleep disturbance (early part/late, part/loss of fresh full sleep), Fearfulness. For screening of the dementia patients, we have a modified form of Mini Mental State Examination, which we label as Culture Relevant and Literacy Independent Cognition Test (CR-LICT). The changes in the questionnaire were mandatory because in Pakistan we have different psychosocial and cultural aspects and literacy rate 33.5% 140, of the literate persons, has received education less than metric, even lower in the elderly and in rural population.

The cases fulfilling the inclusion criteria were evaluated clinically grouped as follows: Non-treatable dementias like senile or presenile dementia of Alzheimer's type, Treatable dementias like hydrocephalus, multi-infarct dementia, myxedema, chronic subdural hema-

toma and brain tumor, Pseudodementia like psychiatric disorders fulfilling the study criteria (e.g. depression with memory impairment). After clinical evaluation the relevant laboratory were carried out they were subject to the compliance of the patient (and also the availability of the tests). Blood CP, ESR, Urea, Blood sugar, Thyroid Scan, Urine D/R and CSF & CT brain, were done to support the clinical diagnosis.

The results were tabulated and analyzed using SPSS-19 (Statistical package for social sciences version 19). Discrete variables like Gender, impaired memory, Impairment of other cognitive domains, past History of diseases, motor examination, planters, etc. were expressed by frequencies & percentages whereas age, pulse, blood pressure, laboratory investigations & MMSE were presented in mean & SD. Chi square test for discrete variables and Independent t test for continuous variable was used to see the significance relation b/w male & female respectively. Numerical variables are expressed as mean \pm SD, while categorical variables are expressed as frequency (percent). The statistical software tool SPSS version 19 was used to complete all calculations, and a p value of < 0.05 considered statistically significant.

Results:

In this In this hospital-based observational study we enrolled 51 patients to identify the underlying pattern of presentation with multiple cognitive deficits. All patients as per the inclusion criteria have memory impairment problem presented at the Memory Clinic run once in a week; their age varied between 25-85 years (mean 57 years). Out of these were 36 (70.6%) males and 15 (29.4%) females.

Out of 51 cases 44 had probable /possible Alzheimer's disease (AD). 03 patients with features of affective disorder scored low on cognitive assessment and were given the diagnosis of pseudo dementia, 04 patients had affective disorder without low score on cognitive assessment. Age had direct relationship with probable /possible Alzheimer's disease (AD). All 86% (n=44) of patients with probable /possible Alzheimer's disease (AD) were above 50 years, while those with others cognitive impairment i.e., pseudo dementia (14%, n=07) were below the age of 50 years, difference was statistically significant ($p < 0.01$). Considering the frequency distribution of patients with probable/ possible Alzheimer's disease

(n=44) most patients were between the age 50-85 years with equal number in each decade. Discerning the individual diagnosis among the patients with probable/ possible Alzheimer's disease (AD), 23 (52.27%) had multi-infarct dementia (having history of past cerebrovascular disease), 18 (40.90%) had Parkinson's disease, followed by alcoholic dementia in 03 (6.8%). There was no definite Alzheimer's disease case in this study.

Out of 51 patients 37 (72.5%) having language problem; 25 (69.4%) were males and 12 (80%) were females. We found issues related to motor activity in 38 (74.5%) patients; 30(83.3%) were males and 8 (53.3%) were females giving a p-value of 0.442. Out of 51 patients 32 (62.7%) having sleep problem; 22 (61.1%) were males and out of 36 and 10(66.7%) were females. We identified 31 patients (60.8%) with behavioral problems; males were 21/36 (58.3%) and female were 10/15 (66.7%). Incontinence issues was found in 17 patients (33.3%) in which out of 36 males were 11 (30.6%). Among 15 females 6 (40%) have incontinence problems. Patients with issues in their activity of daily living were 46 (90.2%) while activity of daily living impaired in 86.1% of males i.e., 31 and all (100%) females.

Out of 51 patients 19 patients (37.3%) onset of symptoms was acute while in 32 (62.7%) patients onset was insidious. It was observed that 14 (38.9%) males having acute onset of symptoms while 22 (61.1%) have insidious while 5 (33.3%) females have acute and 10 (66.7%) have insidious onset of symptoms. Among 36 males, 24 (47.1%) patients reported progression of their symptoms; 18(50.0%) have gradual while 18(50.0%) have stepwise progression of symptoms. Among 15 females; 6(40%) have gradual and 9 (60%) have stepwise progression of symptoms.

Among all 13 (25.5%) patients having past history of diabetes mellitus; 10(27.8%) were males and three females. 17 (33.3%) patients were known hypertensive. Again male (n=12,33.3%) outnumber female (n=5, 33.3%). Out of 51 patients nine (17.6%) were smokers and 11 patients (21.1%) were using alcohol and other substance abuse. Cerebrovascular disease was found in 13(25.5%) patients among them 8 (22.2%) out of 36 were males and 5 (33.3%) out of 15 were female. We found 18 patients out of the 51 patients were the known case of Parkinson's disease.

Among all family history of dementia identified in 7 cases; 5 males and 2 females. Out of 51 patients 21 patients had CT scan brain done; in 17 cases atrophy was reported while in 4 patients no any atrophic changes were reported. While two had single infarction lesion 11 had multiple infarcts and rest 8 CT Scan had no infarct changes.

Table-1: Demographic and Clinical Characteristics of Patients With Alzheimer Disease (AD) (n=51)

Variables	Minimum	Maximum	Mean ± SD
Age (years)	25	85	57.4 ±13.9
Pulse	60	100	73.11 ±8.3
SBP	110	170	124.8 ±20.5
DBP	70	110	80.1 ±14.2
FBS	56	221	118.1 ±37.6
Hb	9.8	15.4	12.7 ±1.1
ESR	3	80	23.7 ±13.4
Urea	9	55	30.2 ±10.4
Creatinine	0.6	1.5	0.9 ±0.2
T3	1.03	5.4	2.4 ±0.7
T4	0.5	7.1	1.4 ±1.2
TSH	0.8	9.1	3.1±1.9
Time Orientation	0	5	3.1 ±1.8
Registration	0	3	1.7 ±1.3
Attention and Calculation	0	5	1.4 ±1.7
Recall	0	3	1.4 ±1.4
Language	0	9	4.5 ±3.2
Mini Mental Score Examination	0	30	15.3 ±10.36

Figure 1: Comorbidities in Patients with Alzheimer Disease (AD)

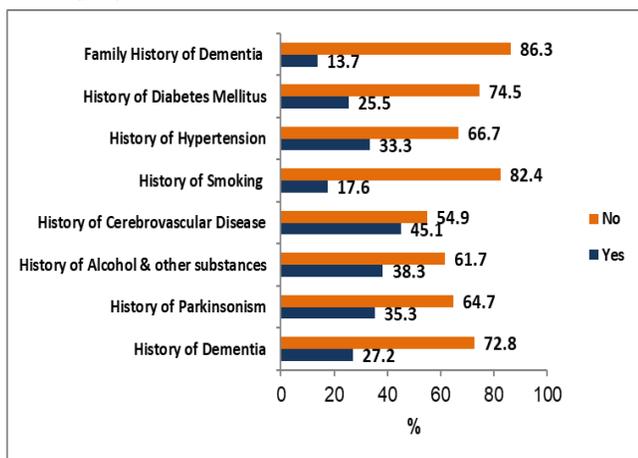


Table 2: Clinical Presentation of Alzheimer Disease (AD)

Impairment of Other Cognitive Domain	n		%
	Yes	No	
Language	37	14	72.5
	14	37	27.5
Motor Active	38	13	74.5
	13	38	25.5
Sleep	32	19	62.7
	19	32	37.3
Behavior	31	20	60.8
	20	31	39.2
Incontinence	17	34	33.3
	34	17	66.7
Activity of Daily Living	46	5	90.2
	5	46	9.8
Onset of Symptoms	19	32	37.3
	32	19	62.7
Progression of Symptoms	24	27	47.1
	27	24	52.9

Discussion:

Alzheimer’s disease (AD) is the 6th major cause of death, when incidence compared to age group of the highest rate, contribute 0.70% of total deaths per 100,000 per year, with prevalence of 3% of men and women ages 65 to 74 have AD, and nearly half of those aged 85 and older may have the disease, it is under reported from developing world.¹⁶⁻¹⁸ It is estimated that by year 2025, 44% of the elderly (aged 65 and above) of the world will be residing in five countries; China, India, Indonesia, Pakistan, and Bangladesh will be having AD.¹⁹ It is expected with this enormous increase in number of the elderly; the gerontological and geriatric problems including dementia will rise in this part of the world. Thus by 2040, if growth in the older population continues, 71% of 81.1millions dementia cases will be in the developing world.²⁰

According to a study from Singapore²¹, focusing epidemiology of dementia, the prevalence of Alzheimer's disease (AD) among Chinese males was 1.1 percent and 1.8 percent among Chinese women. Malay males and women pay 1.2 percent and 1.5 percent in taxes, respectively. In a Nigerian community survey (subject = 2494), 28 dementia patients were recognized as having Alzheimer's disease, with 18 of them having the condition (64.3 percent) of which 16 may suffer from AD. All of the individuals are over the age of 65. The

age of the subjects in the research of the prevalence of dementia and Alzheimer's disease in two groups of people with the same ethnic background but significantly diverse settings was > 65 years. That instance, the age-adjusted prevalence of dementia (2.29%) and Alzheimer's disease (1.41%) among Nigerian Africans and African-Americans in Nigeria (Ibadan) is scientifically lower than the Indianapolis sample, and the individuals simply live in the neighborhood (8.24 percent and 6.24 percent, respectively). The prevalence of dementia in Indians was 33.6 per 1000 people. The most frequent type of dementia was Alzheimer's (54 percent), followed by vascular dementia (39%). Among Ethiopian Africans (150) the senile dementia was uncommon. The histological hallmark of AD and aging is found significantly in white Americans than in Black Americans. In Israel, the prevalence of dementia of the Alzheimer type (DAT) is high in Arab community in Wadi area. The frequency of dementia subtypes of Alzheimer's disease was 2.2 in an Egyptian study, with multi-infarct dementia at 0.95, mixed dementia at 0.55, and secondary dementia at 0.45. The prevalence of dementia in Japan is comparable to that of other nations, but Alzheimer's disease is uncommon, vascular dementia is more common. While the studies from Europe shows prevalence of Alzheimer's disease ranges from 15.1 to 153 per 100,000 of the population.²²⁻²⁴ In present study (n= 51 cases) the age range varied between 25-85 years with mean age of 57 years. The lower age limit of 25 year was kept to identify other causes of dementia in Pakistan if exist. Out of total sample 36 (70.6%) were male and 15 (29.4%) were females. The lower number for females may be due to selection bias as this was a hospital-based study. In present study the clinical diagnosis was grouped into probable / possible Alzheimer's disease, affective disorder with cognitive impairment and affective disorder without cognitive impairment. In this study (n=51) the actual number in the above labeled group was 44(86%), 03(06%) and 04 (08%) respectively. Those without cognitive impairment or affective disorder but with memory complaint were probably having preoccupation of their mind for example due to increased workload, for them a detailed interview including psychological evaluation is required which was not possible in the present study. In Nigerian

study 4.4% had impairment of cognition, out of these 0.6% were found to be suffering from depressive disorders, and there was no case of Alzheimer's disease.²²

In this study more than one third of the patients with probable / possible Alzheimer's disease were above the 50 years, this is in agreement to many prevalence and incidence studies from western as well as eastern worlds.¹¹ Multi infarct dementia (MID) was the commonest presentation in this study being n=23 (52.27%), besides this we have dementia in Parkinson's disease patients n=18 (40.90%) followed by alcoholic dementia n=03 (6.8%). Patients with Parkinson's disease (PD) are at a high risk of dementia by definition, in a recent research, the annual incidence rate has been as high as 10%, with a prevalence rate of 20-30% has been reported²²; this is in sharp contrast to present study where Parkinson's dementia identified in 18 (40.90%). The studies from Japan and Singapore have also reported the lower rates of Alzheimer's disease.²¹ Comparing the MID v/ s non-MID (dementia and affective disorder with memory complaint), age was the single non-modifiable risk factor and hypertension was the single modifiable risk factor for the MID. Hypertension is reported to be significant risk factor for MID and age is reported to increase the risk of stroke in general population.²⁵ In the present study CT were possible in 21 cases only because of the financial constraints. Many population-based studies are clinical based for the same reason.

Conclusion:

Vascular dementia, not the definite Alzheimer's disease, is the commonest cause of memory impairment in current study. Hypertension is the single modifiable risk factor for possible / probable Alzheimer's disease. Among Parkinson's disease patient's dementia was quite high in our study. The study is in accordance to the population-based studies from developing countries and future studies can be planned to assess the outcome of treatable cases of AD.

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