CLINICAL PROFILE OF DEMENTIA IN YOUNGER PERSONS IN EASTERN INDIA

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ABSTRACT

Dementia is an increasingly recognized cause of morbidity and mortality in India and in other parts of the world, especially in the elderly population. There are very few reports about the causes of dementia in rural populations of eastern India. This was a retrospective study carried out using outpatient department records through the course of 2 years in a medical college in West Bengal. Cases which were diagnosed as dementia on the basis of the MMSE or Addenbrooke tests were included. Diagnosis of vascular dementia was done with the aid of DSM-IV. The diagnosis of FTD and DLB (Dementia with Lewy Bodies) were done on the basis of Lund-Manchester criteria and International Consensus Consortium Criteria respectively.The aim of this study is to delineate the clinical profile of dementia in patients attending a medical college outpatient department in eastern India. About one-fourth (93 out of 400) of the patients were of young onset. Women constituted about 1/3rd of the cases. With increasing age, the proportion of cases increased. The most common etiology was Alzheimer Disease (49%) followed by Frontotemporal Lobar Degeneration (20%) and vascular dementia (8%). Positive family history was found in less than 10% of cases. The decreased proportion of vascular dementia compared to frontotemporal lobar degeneration could be due to referral bias. Another 10% of cases had causes of dementia that could be considered as reversible. The study also showed that degenerative dementias were the most common cause of dementia even amongst young-onset patients. The limitations of this study include the lack of postmortem histopathological confirmation of the clinical diagnosis.

Keyword: - *Dementia , Alzheimer Disease, Vascular Dementia, Frontotemporal Lobar Degeneration, Dementia with Lewy Bodies, MMSE, cognitive impairment.*

1. INTRODUCTION

Dementia occurring below the age of 65 is defined as being of young-onset [1]. It is an increasingly recognized cause of mortality and morbidity in the young population. Economic consequences are severe because it affects them in their productive years. Several studies have been done of young-onset dementia and in the West it has been estimated that the prevalence is about 70 per hundred thousand population [2]. There is an exponential increase in cases of dementia as the age increases from 45 to 60 , one important study showed [3]. This is in line with the general observation all over the world that there is a rapid increase in the incidence of degenerative dementia with increasing age.The investigation and diagnosis of young-onset dementia is so important because there is a comparatively greater percentage of cases of treatable dementia in the young, which may warrant timely intervention leading to imporovement in the clinical condition of the patient. Despite this, almost all studies have shown that even in the young, degenerative causes account for the largest number of cases. Treatable causes include metabolic, infective, inflammatory and immunologic causes. Genetic causes such as Wilson disease [4], Fragile X syndrome, and several chromosomal defects [5] are important causes of dementia in the young are are potentially preventable by genetic counselling.

2. METHODS

This study was done in the Neurology outpatient department of Bankura Sammilani Medical College during the period March 2017 to July 2018. Some of the patients were referred from other departments, especially from Psychiatry, but most of the patients presented with other unrelated abnormalities which ultimately led to adiagnosis of dementia.History and the neuropsychologic examination were recorded in a semi-structured proforma. The following blood tests were done: complete blood count with erthrocyte sedimentation rate, serum cholesterol and triglycerides, creatinine, sodium, potassium, calcium, phosphorus, protein, glucose, bilirubin, alkaline phosphatase, thyroid hormones, alanine transaminase (ALT), aspartate transaminase (AST), VDRL (Venereal Diseases Research Laboratory) test, and HIV screening. Neuroimaging was done, mostly in the form of MRI, sometimes CT. In a few cases we were able to do SPECT (Single Photon Emission Computed Tomography). Neuropsychologic assessment was done using the Mini Mental Status Examination (MMSE) for the purposes of screening and then the Addenbrooke Cognitive Examination - Revised (ACE-R) was done for evaluation of the subdomains of orientation, attention, fluency, memory, language and visuospatial function.

FTD, which was of great help in confirming the clinical impression. The National Institute of Neurological Disorders and Stroke (NINDS) and the Association Internationale pour la Recherche et l'Enseignement en Neurosciences (AIREN) have classified VaD [6] into six syndromes (multi-infarct dementia, single-infarct dementia in a strategic location, hypoperfusion, small-vessel disease with dementia, hemorrhagic dementia,and other mechanisms).17,18 In our study, the DSM-IV criteria for VaD[7] were followed, due to the difficulty in further sub-classify the causes of vascular- etiology. For patients with objective signs of memory impairment and other cognitive dysfunction as shown by assessment with standard neuropsychological tests but not fulfilling DSM-IV criteria for dementia, the categorization was 'cognitive impairment, not dementia.' Such patients were excluded from this study. Patients diagnosed to have pseudodementia and mild cognitive impairment (MCI) were also excluded in the study.

Table 1: Criteria for defining the different types of dementia

Alzheimer's disease - DSM-IV criteria
Vascular dementia - DSM-IV criteria, NINDS-AIREN criteria
Frontotemporal dementia - Lund-Manchester criteria*
Dementia with Lewy bodies - consensus guidelines of consortium on DLB international workshop**

*Lund-Manchester criteria for frontotemporal dementia [8]

1. Mandatory criteria: (i) Insidious onset and gradual progression; (ii) Early decline in social interpersonal conduct; (iii) Early impairment in regulation of personal conduct; (iv) Early emotional blunting; (v) Early loss of insight

2. Supportive diagnostic features include: (A) Behavioural disorder: decline in personal hygiene and grooming, mental rigidity and inflexibility, distractibility and impersistence, hyperorality and dietary change, utilization behavior; (B) Speech and language: altered speech output (aspontaneity and economy of speech, press of speech), stereotypy of speech, echolalia, perseveration, mutism; (C) Physical signs: primitive reflexes, incontinence, akinesia, rigidity, tremor, low/labile blood pressure; (D) Investigations: neuropsychology: impaired frontal lobe tests; no amnesia or perceptual deficits; EEG: normal on conventional EEG despite clinically-evident dementia; brain imaging: predominant frontal and/or anterior temporal abnormality)

**International consensus consortium criteria for dementia with Lewy bodies

1. Progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational function. Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression. Deficits on tests of attention and frontal-subcortical skills and visuospatial ability may be especially prominent.

2. Two of the following are required for a diagnosis of probable dementia with Lewy bodies: Fluctuating cognition with pronounced variations in attention and alertness, recurrent visual hallucinations which are typically well-formed and detailed, spontaneous motor features of parkinsonism.

3. Features supportive of the diagnosis are: Repeated falls, syncope or transient loss of consciousness, neuroleptic sensitivity, systematized delusions, hallucinations in other modalities.

3. RESULTS

There were a total of 400 patients with the diagnosis of dementia in the study period, of which 93 (24.5%) were YOD, i.e., with onset of their dementia before the age of 65 years. Thus, the YOD accounted for close to one-fourth of the dementia cases. The mean age of the YOD was 56.5 years (range 42 to 64). The mean duration of formal education was 11 years (range 3 to 20) . The mean duration of symptoms before presenting to the Clinic was 42.2 months (range 2 to 65). The mean MMSE score at the time of initial examination was 11.2 (range 4 to 17). There were more men than women among the YOD. The mean age of men was 56.3 years (range 39 to 64) and that of women was 59.5 years (range 43 to 64).

there was gradual increase in the cases with increasing age in both sexes. Table 2 lists the etiologies of the YOD. AD was the most frequent (49%), followed by FTD (20%), and VaD (8%). Huntington disease was more commonly seen in younger age groups. The risk factors for the 19 patients with vascular dementia were: hypertension (62.1%), smoking (34.7%), diabetes mellitus (12.5%), dyslipidemia (9.8 %), and alcoholism (3.5%). Table 3 lists the patients with positive family history according to various etiologies. Overall a positive family history was found in 16/93 (17.2%) of the patients.

As for the etiologies of the 10 patients with miscellaneous causes of dementia, they were 3 patients with neurocysticercosis, 3 patients each of hypothyroidism, central nervous system vasculitis, and one patient with progressive supranuclear palsy. Most of the etiological categories classified as 'miscellaneous' represent were reversible causes of dementia. On follow-up, the greatest clinical improvement (defined as improvement in two or more of the following domains: memory, fluency, naming, visuospatial abilities, and memory) was in patients with hypothyroidism and neurocysticercosis. In cases of central nervous system vasculitis, cognitive parameters improved significantly with initiation of glucocorticoid therapy. The multiple sclerosis patients, some of the patients stabilized with treatment but there was a general trend of stepwise deterioration corresponding with subsequent exacerbations of the disease. Vascular dementia cases, however, showed no improvement in any cognitive parameter, even after correction of modifiable vascular risk factors.

Table 2: The distribution of patients according to etiology (N=93)

Etiology	No. of patients
Alzheimer disease	45 (49%)
Frontotemporal dementia	18 (20%)
Vascular dementia	07(8%)
Huntington disease	2 (2%)
Parkinson disease with dementia	3 (3%)
Miscellaneous	16 (18%)

4. DISCUSSION

Accurate diagnosis of YOD is important, since the YOD subjects may have predominant cognitive deficits than memory loss and many patients often presents with neuropsychiatric features. A study however identified greater role of neurologist in identifying YOD cases.20 A number of studies throughout the world have shown that the prevalence of YOD is lower than that in older age groups [9.10] Our study shows, similarly, that only about one quarter of patients attending the OPD had onset before the age of 65. Some studies[11,12] have shown that the frequency increases between the ages of 45 and 60, which correlates with the present study. Our study also shows a predominance of men in YOD which is also similar to previous studies.7,8 Almost all studies of YOD, as in our study, have shown AD as the most common etiology A community-based study[13] showed an increased prevalence of VaD in persons aged >65.24 This is in accordance with a general pattern observed in all studies: that of AD being the most common cause of dementia across all age -groups, FTD being relatively commoner [14] in younger age -groups (although still less common than VaD), and VaD relatively more common in older age-groups. Most studies have shown VaD as the next most common etiology in YOD cases [15]. In contrast, in our study, while the largest number of cases in all age-groups was AD, the second largest group was FTD. One interesting finding of our study was that before the age of 50, it was FTD and neither VaD nor AD was the most common cause. One factor that could be responsible for this finding was that VaD cases in this age-group presenting to the medicine department are usually investigated as stroke cases and tendnot to get referred to Neurology. This difference could be accounted for by differences in referral patterns, since many patients with VaD were managed in the general medicine clinic, as the dementia is often overshadowed by other problems like motor or sensory deficit. Community based study is required to confirm the findings of this study.

Close to a fifth of the patients had a positive family history of dementia, This suggests the need of genetic counselling in young-onset dementia [16]. As mentioned earlier, one of the objectives of this study was to assess the long term outcome in patients with potentially reversible etiology. As mentioned earlier, the greatest improvement was seen in hypothyroidism and neurocysticercosis. Neurocysticercosis is a common neurological disease in India. But we did not have many patients with extensive neurocysticercosis [17] with YOD, which has been reported by a number of studies in India. One of the studies showed that with anticysticidal treatment and meticulous control of seizures, there was notable improvement in cognitive functioning, although some deficits in constructional ability and calculation persist. VaD patients showed no improvement in any cognitive parameter, even after correction of modifiable vascular risk factors. This could be because the tissue damange in vascular dementia is more permanent and irreversible than in inflammatory demyelinating cases [18].

Etiology	Positive family history	
Alzheimer disease	3/31	(10%)
Frontotemporal dementia	10/25	(40%)
Vascular dementia	10/19	(53%)
Huntington disease	3/4	(75%)
Parkinson disease with dementia	1/4	(25%)
Miscellaneous	0/10	(0%)

There were certain limitations in this study. The diagnosis was based on clinical and imaging criteria and there was no histopathological confirmation of the diagnosis. The estimate of the number of subjects with YOD may be lower because the time of onset of dementia in some patients could not be ascertained and they were not included as YOD

cases. MMSE was used to screen the patients in the outpatient clinics. It could have missed early frontal lobe dysfunction, and thus underestimated the number of patients with FTD.

5. CONCLUSIONS

In conclusion, even amongst persons under the age of 65 years, degenerative dementia remains the commonest cause. Hence clinicians should be aware of the possibility of AD in evaluation of dementia in middle age patients. About one-quarter of the YOD cases were due to FTD. These patients present with prominent behavioral symptoms, that might be misdiagnosed as primary psychiatric disorder. Moreover, a positive family history is present amongst a significant proportion across all groups, indicating the need to take a careful family history. Family history may be a valuable clue for making a diagnosis, and in genetic counseling.

6. REFERENCES

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