Clinical profile of young-onset dementia: A study from Eastern India


Department of Neurology, Bangur Institute of Neuroscience & Psychiatry, Kolkata; *Department of Neurology, North Bengal Medical College, Sushrutanagar, Darjeeling, India

Address correspondence to: Prof S K Das, Head, Department of Neurology, Bangur Institute of Neuroscience & Psychiatry, 52/1A Sambhunath Pandit Street, Kolkata 700025, West Bengal, India. E-mail: das_sk70@hotmail.com

Abstract

Young-onset dementia, defined as dementia occurring under the age of 65, is an increasingly recognized cause of morbidity and disability. There are few reports of the clinical profile of young-onset dementia from India. The objective of this study was to determine the clinical profile of patients attending a specialist cognitive disorders clinic in West Bengal. Almost one-fourth (94/379, 24.5%) of all the patients with dementia were of young onset. Women constituted about one-third of these cases. There was a gradual increase in the number of cases with increasing age. The most common etiologies were Alzheimer disease (33%), frontotemporal dementia (27%), and vascular dementia (20%). In contrast to other published studies of young-onset dementia, frontotemporal dementia was more common than vascular dementia. This could be due to referral bias. A positive family history was found in close to one-fifth of the patients. Close to 10% of the patients had reversible causes of dementia. Community based study is required to confirm the findings of this study.

INTRODUCTION

Young-onset dementia (YOD) is defined as dementia occurring in those below the age of 65 years and is being increasingly recognized as an important cause of medical, social and occupational disability. Since it affects patients during their more productive years of life, the economic consequences are severe. Studies of YOD have been recently done in a number of centers. In the West, it has been estimated that the prevalence of YOD in the community is between 67 and 81 per 100,000 people. One important study, by Harvey et al, made the observation that the proportion of cases diagnosed with dementia increased...
The primary focus in any study attempting to clarify the profile of YOD is to differentiate between the treatable and non-treatable causes and to give an indication of the frequency of reversible causes of dementia and pseudo-dementia. Though most studies have shown that degenerative dementias such as early onset Alzheimer’s disease and frontotemporal dementias are common even in this young age group, proportion of treatable causes of dementia is greater than older onset dementia. The treatable causes of YOD include metabolic, infective, inflammatory and immunological causes. Genetic causes, such as Huntington disease, Wilson’ disease, Hallervorden-Spatz disease, as well as chromosomal defects like trisomy 2, fragile X syndrome, are important causes of YOD, as they are potentially preventable by genetic counselling.

The present study aims to determine the clinical pattern of YOD, defined as dementia occurring below the age of 65 years, in patients attending a specialist clinic for cognitive disorders in a tertiary care neurological institute, West Bengal, Eastern India.

METHODS

This retrospective study was carried out in the Cognitive Disorder Clinic of the Bangur Institute of Neuroscience & Psychiatry, Kolkata, a tertiary referral public hospital. The period during which the data was collected was from January 2004 to January 2008. All subjects were referred from the general neurology clinic, psychiatry clinic and private specialists. The history, general and neurological examinations, including neuropsychological assessments was recorded in a semistructured proforma. Laboratory tests done were as follows: blood count including erythrocyte sedimentation rate, serum cholesterol, triglycerides, creatinine, urea, sodium, potassium, calcium, phosphorus, protein, glucose, bilirubin, alkaline phosphatase, alanine transaminase (AST) and aspartate transaminase (ALT), thyroid hormones, Venereal Diseases Research Laboratory (VDRL) test and HIV screening. Neuroimaging, in the form of computed tomography (CT) or magnetic resonance imaging (MRI), or both, and in some instances single photon emission computed tomography (SPECT) were performed. For neuropsychologic assessment, we used the Mini-Mental Status Examination (MMSE) for screening and the Addenbrooke Cognitive Examination – Revised (ACE-R) for detailed testing.

Diagnosis of Alzheimer disease (AD) and vascular dementia (VaD) were based on DSM-IV criteria. The diagnosis of frontotemporal dementia (FTD) and dementia with Lewy Bodies (DLB) was based on clinical and neuroimaging criteria (more specific and accepted criteria used?). 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 into six syndromes (multi-infarct dementia, single-infarct dementia in a strategic location, hypoperfusion, small-vessel disease with dementia, hemorrhagic dementia, and other mechanisms). In our study, the DSM-IV criteria for VaD were followed, due to the difficulty in further subclassifying the vascular-etiology causes. For patients with subjective 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.

RESULTS

There were a total of 379 patients (273 men and 106 women) 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 03 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 12.6 (range 4 to 17). There were more men than women among the YOD, 61/93 (65%) and 32/93 (35%) respectively. The mean age of men was 57.3 years (range 39 to 64) and that of women was 54.5 years (range 43 to 64).

Figure 1 shows the age distribution by sex of the YOD patients. As shown, there was gradual increase in the cases with increasing age in both sexes. Table 1 lists the etiologies of the YOD. As shown, Alzheimer’s disease was the most frequent (33%), followed by frontotemporal dementia (27%), and vascular dementia (20%). 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 in 3.5%. Table 2 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, 2 patients each of hypothyroidism, central nervous system vasculitis, multiple sclerosis, 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. 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 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.

DISCUSSION

A number of studies throughout the world have shown that the prevalence of YOD is lower than that in older age groups. Our study shows, similarly, that only about one quarter of patients attending the specialist Cognitive Disorder Clinic had onset before the age of 65. At least four studies have shown that the frequency increases between the ages of 45 and 60, which is similar to the finding in our study. Our study shows a predominance of men in YOD which is also similar to previous studies. Almost all studies of YOD, as in our study, have shown Alzheimer disease as the most common etiology, with the exception of a Japanese study. (The study by Ikeda is for prevalence of dementia in those age >65?) Most studies have shown vascular dementia as the next most common etiology but in our study frontotemporal dementia was the next most common, with vascular dementia occupying the third place. This difference could be accounted for by differences in referral patterns, since many patients with vascular dementia were managed in the general neurology 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.

Our study also demonstrated that close to a fifth of our patients has positive family history, suggesting the importance role of genetic factors in the pathogenesis. Genetic counseling is thus an important aspect of overall management. Before the age of 50, it is FTD and neither VaD nor AD which is the most common cause. (Is this the result of your study, or you are quoting some other studies? If it is your study result, it should be stated in result section. If you are quoting other studies, please give the reference)

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 disease in India. But we did not have many patients with extensive neurocysticercosis 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. Vascular dementia patient showed no improvement in any cognitive parameter, even after correction of modifiable vascular risk factors. This could be because the tissue damage is diffuse or permanent, more so than in demyelinating and inflammatory lesions.

There were certain limitations in this study. The study was done on clinical criteria alone and there was no histopathological confirmation of the diagnoses. 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 frontal lobe dementia.

There are a number of clinical implications that can be drawn from this study. Even amongst persons under the age of 65 years, degenerative dementia remains the commonest cause. Hence clinicians should be aware of the possibility of Alzheimer disease in evaluation of dementia in middle age patients. About one-quarter of the YOD cases were due to frontotemporal dementia. These patients present with prominent behavioral symptom 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.
REFERENCES


Figure 1. Age distribution by sex, of the young-onset dementia patients.

Table 1: The distribution of patients according to etiology (N=93)

<table>
<thead>
<tr>
<th>Etiology</th>
<th>No. of patients</th>
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<tr>
<td>Alzheimer disease</td>
<td>31 (33%)</td>
</tr>
<tr>
<td>Frontotemporal dementia</td>
<td>25 (27%)</td>
</tr>
<tr>
<td>Vascular dementia</td>
<td>19 (20%)</td>
</tr>
<tr>
<td>Etiology</td>
<td>Positive family history</td>
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<tr>
<td>--------------------------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>Alzheimer disease</td>
<td>7/31 (30%)</td>
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<tr>
<td>Frontotemporal dementia</td>
<td>4/25 (20%)</td>
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<tr>
<td>Vascular dementia</td>
<td>1/19 (5%)</td>
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<tr>
<td>Huntington disease</td>
<td>3/4 (100%?75%)</td>
</tr>
<tr>
<td>Parkinson disease with dementia</td>
<td>1/4 (30%?25%)</td>
</tr>
</tbody>
</table>

Table 2: The proportion of patients with positive family history according to etiology