Neurology Asia 2008; 13 : 103 – 108

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

Shankar P Nandi, *Atanu Biswas, Sandip Pal, Sagar Basu, Asit K Senapati, Shyamal K Das

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

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, an eastern state of India. 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 rising 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 commoner 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.[1] 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.[2-6] In the West, it has been estimated that the prevalence of YOD in the community is between 67 and 81 per 100,000 population.[7,8] One important study, by Harvey *et al*, made the observation that the proportion of cases diagnosed with dementia increased exponentially between ages 45 and 60.[1] 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 (AD) and frontotemporal dementias (FTD) 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.[9] 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, Wes 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,

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

calcium, phosphorus, protein, glucose, bilirubin, alkaline phosphatase, alanine transaminase (AST) and aspartate transaminase (AST), 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)[10] for screening and the Addenbrooke Cognitive Examination - Revised (ACE-R)[11,12] for further testing of cognitive subdomains (orientation, attention, memory, verbal fluency, language and visuospatial function).

Diagnosis of AD and vascular dementia (VaD) were based on DSM-IV[13] criteria. The diagnosis of FTD and dementia with Lewy bodies (DLB) was based Lund-Manchester criteria[14] and International consensus consortium criteria for dementia with Lewy bodies as in Table 1.[15] We were able to obtain SPECT images of a majority of the cases diagnosed clinically as FTD, which was of great help in confirming the clinical impression.[16] 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).[17,18] In our study, the DSM-IV criteria for VaD 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

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

*Lund-Manchester criteria for frontotemporal dementia

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.

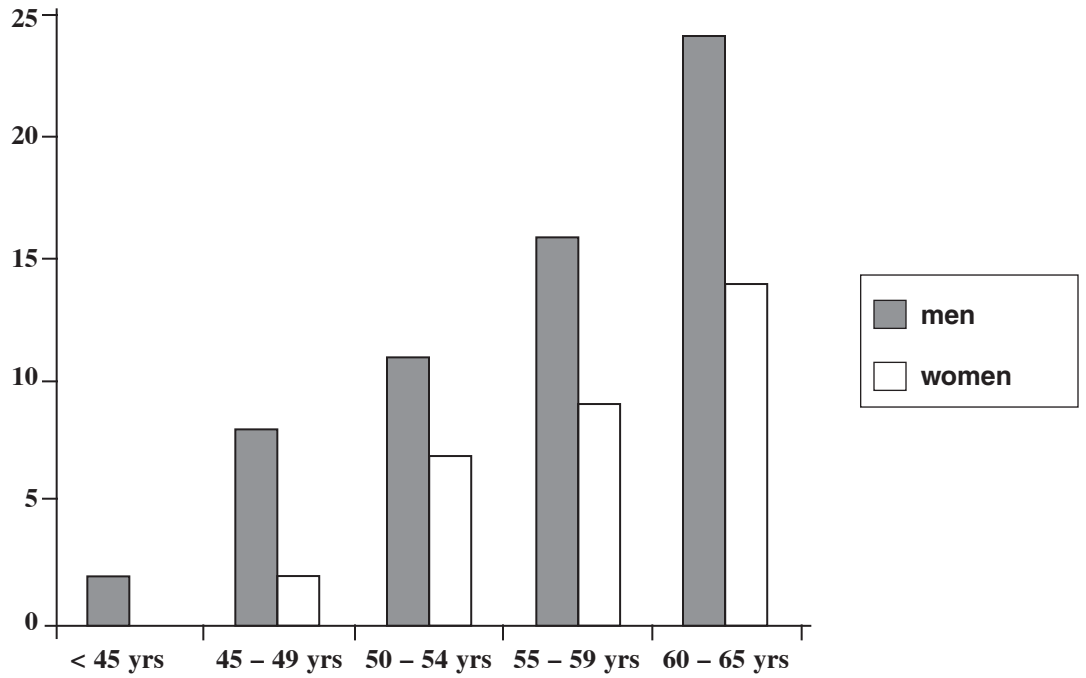

Figure 1. Age distribution by sex, of the young-onset dementia patients.

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 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 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 2 lists the etiologies of the YOD. As shown, AD was the most frequent (33%), followed by FTD (27%), and VaD (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 (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, 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. 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	31 (33%)
Frontotemporal dementia	25 (27%)
Vascular dementia	19 (20%)
Huntington disease	4 (4%)
Parkinson disease with dementia	4 (4%)
Miscellaneous	10 (11%)

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.[19] 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.[1,3-8] 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 4 studies[2,6,7,21] 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.[3,5,8,22,23] A community-based study in Japan 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 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. 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 general neurology clinic are usually investigated as stroke cases and tend to get referred to the Stroke Clinic rather than the Cognitive Clinic. This difference could be accounted for by differences in referral patterns, since many patients with VaD 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 important role of genetic factors in the pathogenesis. Genetic counseling is thus an important aspect of overall management.

As mentioned earlier, one of the objectives of

Table 3: The proportion of patients with positive family history according to etiology

Etiology	Positive family history
Alzheimer disease	7/31 (30%)
Frontotemporal dementia	4/25 (20%)
Vascular dementia	1/19 (5%)
Huntington disease	3/4 (75%)
Parkinson disease with dementia	1/4 (25%)
Miscellaneous	0/10 (0%)

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 with YOD, which has been reported by a number of studies in India.[25,26] 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.[27] VaD patients showed no improvement in any cognitive parameter, even after correction of modifiable vascular risk factors. This could be because the tissue damage was diffuse or permanent, more so than in demyelinating and inflammatory lesions.

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.

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.

REFERENCES

1. Harvey RJ, Skelton-Robinson M, Rossor MN. The prevalence and causes of dementia in people under the age of 65 years. *J Neurol Neurosurg Psychiatry* 2003; 74:1206-9.
2. Harvey RJ, Rossor MN, Skelton-Robinson M, *et al*. Young onset dementia: epidemiology, clinical symptoms, family burden, support and outcome. London: Dementia Research Group, 1998.
3. Shinagawa S, Ikeda M, Toyota Y, Matsumoto T, Matsumoto N, Mori T, *et al*. Frequency and clinical characteristics of early-onset dementia in consecutive patients in a memory clinic. *Dement Geriatr Cogn Disord* 2007; 24:42-7.
4. Newens AJ, Forster DP, Kay DW. Clinically diagnosed presenile dementia of the Alzheimer type in the Northern Health Region: ascertainment, prevalence, incidence and survival. *Psychol Med* 1993; 23:631-44.
5. Woodburn KJ, Johnstone EC. Early-onset dementia in Lothian, Scotland: an analysis of clinical features and patterns of decline. *Health Bull (Edinb)* 1999; 57:384-92.
6. Bottino CM, Azevedo D Jr, Tatsch M, Hototian SR, Moscoso MA, Folquitto J, *et al*. Estimate of Dementia Prevalence in a Community Sample from São Paulo, Brazil. *Dement Geriatr Cogn Disord* 2008; 26:291-9.
7. Jorm AF, Korten AE, Henderson AS. The prevalence of dementia: a quantitative integration of the literature. *Acta Psychiatr Scand* 1987; 76:465-79.
8. Elberling TV, Stokholm J, Hogh P, Waldemar, G.Diagnostic profile of young and middle-aged memory clinic patients. *Neurology* 2002; 59:1259-62.
9. McMurtray A, Clark DG, Christine D, Mendez MF. Early-onset dementia: frequency and causes compared to late-onset dementia. *Dement Geriatr Cogn Disord* 2006; 21:59-64.
10. Folstein, M., Folstein, S. and McHughs, P. The "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research* 1975; 12:189-98.
11. Mathuranath PS, P. J. Nestor, G. E. Berrios, W. Rakowicz, J. R.Hodges . A brief cognitive test battery to differentiate Alzheimer's disease and frontotemporal dementia. *Neurology* 2000; 55:1613-20.
12. Mioshi E, Dawson K, Mitchell J, Arnold R, Hodges JR. The Addenbrooke's Cognitive Examination Revised (ACE-R): a brief cognitive test battery for dementia screening. *International Journal of Geriatric Psychiatry* 2006; 21:1078-85.
13. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 4th ed (DSM-IV). Washington DC: American Psychiatric Association, 1994
14. Varma AR, Adams W, Lloyd JJ, *et al*. Diagnostic patterns of regional atrophy on MRI and regional cerebral blood flow change on SPECT in young onset patients with Alzheimer's disease, frontotemporal dementia and vascular dementia. *Acta Neurol Scand* 2002; 105:261-9.
15. The Lund and Manchester Groups. Clinical and neuropathological criteria for frontotemporal dementia. *J Neurol Neurosurg Psychiatry* 1994; 57:416-8.
16. McKeith IG, Galasko D, Kosaka K, Perry EK, Dickson DW, Hansen LA. Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): Report of the consortium on DLB international workshop. *Neurology* 1996; 47:1113-24.
17. Erkinjuntti T. Clinical criteria for vascular dementia: the NINDS-AIREN criteria. *Dementia* 1994; 5:189-92.
18. Roman GC, Tatemichi TK, Erkinjuntti T. Vascular

dementia: diagnostic criteria for research studies. Report of the NINDS/ AIREN International Workshop. *Neurology* 1993; 43:250-60.
19. Allen H, Baldwin B. The referral, investigation and diagnosis of presenile dementia: Two services compared. *International Journal of Geriatric Psychiatry* 1995; 10:185-90.
20. Mendez MF. The accurate diagnosis of early-onset dementia. *International Journal of Psychiatry in Medicine* 2006; 36:401-2.
21. Hofman A, Rocca WA, Brayne C, Breteler MM, Clarke M, Cooper B, *et al*. The prevalence of dementia in Europe: a collaborative study of 1980-1990 findings. Eurodem Prevalence Research Group. *Int J Epidemiol* 1991; 20:736-48.
22. McGonigal G, Thomas B, McQuade C, Starr JM, MacLennan WJ, Whalley LJ. Epidemiology of Alzheimer's presenile dementia in Scotland, 1974-88. *BMJ* 1993; 306:680-3.
23. Treves T, Korczyn ADK, Zilber N, *et al*. Presenile dementia in Israel. *Arch Neurol* 1986; 43:26-9.
24. Ikeda M, Hokoishi K, Maki N. Increased prevalence of vascular dementia in Japan: a community-based epidemiological study. *Neurology* 2001; 57:839-44.
25. Varma A, Gaur KJ. The clinical spectrum of neurocysticercosis in the Uttaranchal region. *J Assoc Physicians India* 2002; 50:1398-400.
26. Biswas A, Prasad A, Anand KS. Cysticercal dementia. *J Assoc Physicians India* 1998; 46:569.
27. Ramirez-Bermudez J, Higuera J, Sosa AL, Lopez-Meza E, Lopez-Gomez M, Corona T. Is dementia reversible in patients with neurocysticercosis? *J Neurol Neurosurg Psychiatry* 2005; 76:1164-6.