Clinical profile of early-onset dementia from a geriatric clinic in South India

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ABSTRACT

Background: Early-onset dementia (EOD) defined as dementia with clinical onset before the age of 65 years, has estimated proportion ranging up to 45.3%. Although EOD leads to severe psychosocial consequences that affect people in their latter part of working age, the literature from India is limited. Objective: The aim of this study is to investigate the profile of patients with EOD attending Geriatric Clinic and Services, National Institute of Mental Health and Neurosciences, Bengaluru, Karnataka, India. Materials and Methodology: All records of patients attending the Geriatric Clinic and Services, diagnosed with EOD between January 2017 and June 2018 with their details pertaining to sociodemographic, clinical, risk factors, and behavioral problems were examined. Results: Of the 320 patients with cognitive complaints seen during the period of 18 months, 108 (33.75%) patients had a diagnosis of EOD. The mean age at onset of illness was 55.38 (Standard deviation - 6.53) years (range - 34–65 years). Of these 58 (53.6%) patients found to have Alzheimer’s dementia (AD), 31 (28.7%) have fronto-temporal dementia (FTD), 6 (5.5%) have vascular dementia (VaD), 3 (2.7%) patients have Parkinson’s disease-related dementia, and 6 (5.5%) have unspecified dementia. Discussion: During the 18 months, the EOD patients constituted one-third of all dementia patients visiting Geriatric Clinic. Degenerative etiology was the main diagnostic cluster. The most common type was AD, similar to senile type of dementia, was followed by FTD and VaD. The study showed a delay of 3.18 years in seeking consultation. Conclusion: EODs seems to have higher degenerative etiology and with higher associated behavioral and psychological symptoms. There is a need for setting up specialized memory clinics.

Key words: Degenerative condition, dementia, disability, early-onset dementia

INTRODUCTION

Dementia is a neuropsychiatric condition with progressive cognitive decline leading to dependency for basic activities of daily living (ADL).[4] Increase in life expectancy and medical advances lead to demographic changes in India with considerable increase in elderly population. As per the Dementia India report, 2010, there are 3.7 million dementia patients and this number is expected to increase exponentially in the near future leading to a major public health problem.[2] Dementia is considered a condition usually affecting patients above the age of 65 years with risk doubling every 5 years.[3] Although less common, dementing process can start before 65 years and rarely, it can start even below the age of 45 years.

The dementing illness in people with onset before the age of 65 years is referred to as early-onset dementia (EOD).[4] Various studies utilized different age cutoffs to study presenile dementia. Presenile dementia is a term which was used to define the same condition, but it is no longer used now.[5] Young-onset dementia is another term which is used synonymously with EOD.[6] There has also been subclassification of presenile dementia into EOD (45–65 years) and YOD (17–45 years) based on estimated age at onset.[7]

The proportion of EOD from clinic-based samples across regions range from 7.3% to 44%.[8,9] A study from the eastern part of India by Nandi et al. reported that one-fourth of...
dementia cases seen in cognitive specialty had early onset. Another study from a memory clinic in south India reported that EOD constituted 49.9% of all dementia cases. EOD unlike late-onset dementia is heterogeneous condition with diverse etiology. Degenerative conditions still constitutes the major proportion in terms of etiology in EOD. Other conditions such as infectious diseases, autoimmune conditions, recurrent seizures, head trauma, substance use, and vitamin deficiency contribute to a smaller proportion. Among the etiological conditions, similar to late onset, Alzheimer’s dementia (AD) is the most common phenotype in EOD patients.

EODs are unique in many aspects compared to late-onset dementia. EOD’s neurobiology provides insights into the underlying etiology, risk factors, and genetic factors about late-onset dementia. It also provides opportunity to test new therapeutic agents as EOD often presents as pure phenotypes. From psychosocial perspective, EOD has significant impact as it affects working age group. EOD leads to the loss of earning member, financial crisis, caregiver burden, and medical costs. Another pertinent thing in people with EOD, there is often delay in diagnosis or misdiagnosis as another condition. This might be due to atypical presentation or prodrome of psychiatric features preceding the cognitive decline. Despite its importance there is dearth of literature on EOD, especially from India. Hence, we took on this study with an objective to look into the prevalence, sociodemographic features, clinical profile, and the management of patients with EOD presenting to our clinic.

MATERIALS AND METHODOLOGY

The current study was conducted in the National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru, Karnataka, India. The design adopted for the study was retrospective and had approval from the Institutional Ethics Committee. The sample for the study was patients seeking treatment from Geriatric Clinic and the management of patients with EOD presenting to our clinic. The neuropsychiatry evaluation in geriatric psychiatry. The neuropsychiatry evaluation in our clinic was as described in our earlier report by Bharath et al. The age of most patients was confirmed through the valid Government-issued identity certificate/cards with information on date of birth. In minority of cases where there was discrepancy, age estimation was done through collateral information, using personal life events and historical dates. This was a valid and simple way of age estimation in India. The exclusion criteria included patients with cognitive deficits primarily due to traumatic brain injury, referred cases with cognitive impairment secondary for psychiatric evaluation. Data collected were analyzed using descriptive statistics such as mean, standard deviation (SD), median, frequency, and percentages to describe the data distribution.

RESULTS

Of the total 320 patients with cognitive concerns seen in the past 18 months (2017–2018) in the facility, 108 (33.7%) patients had a diagnosis of EOD. The mean age of the patients at presentation was 58.54 (SD - 6.54) years (range - 36–68). The mean age of onset of dementia in our sample was 55.38 (SD - 6.53). The number of men was 58 and women were 50. The average number of years of education was 9.87 (SD - 5.42) years. Among these patients, 100 were married and 8 were either single/separated/widowed. The mean duration of illness prior to consultation was 1.18 (SD - 2.35) years. The mean HMSE score of the patients was 14.99 (SD - 8.77) (median: 8.77, range: 0–30) and mean EASI score 7.13 (SD - 3.34) (median: 7.0, range: 0–12). There was positive family history of dementing illness in 23.1% of sample.

Vascular risk factors such as hypertension and diabetes mellitus were present in 35.2%. Vitamin B12 deficiency and hypothyroidism that are potentially known to cause cognitive deficits were found in 9.3% and 10.2%, respectively. However, these patients were subsequently treated and none reverted back to normal. These patients were finally diagnosed to have degenerative dementing conditions [Table 1]. The percentage of patients below the age of 45 years was 7.4%, 45–49 years was 10.1%, 50–54 years was 19.4%, 55–59 years was 35.18%, and 60–64 years was 27.8% [Table 1]. The most common phenotype was AD (53.6%), followed by behaviour variant of frontotemporal dementia (FTD) (23.13%). Vascular dementia (VaD) (5.6%) and language variant FTD (4.6%). Minority of patients were diagnosed with FTD-Parkinson’s disease (PD) (2.8%), diffuse Lewy body disease (DLBD) (2.7%), corticobasal degeneration (0.9%), mixed etiology (2.8%), and unspecified dementia (5.6%) [Figure 1]. Regarding the severity of dementia 52 (48.1%) were in mild stage, 37 (34.3%) were in moderate stage, and 19 (17.6%) were in severe stage [Table 2]. The common dementia phenotypes as per age group are shown in Table 3.

We found 69 (63.9%) of these EOD patients were brought for the first comprehensive evaluation (no prior consultation with any doctor for cognitive symptoms). Among the remaining EOD patients, 39 (36.1%) were either referred or came for the second opinion. There were few predominant reasons for consultation found in the study. Thirteen EOD patients were brought predominantly for cognitive
### Table 1: Profile of the sample

| Domain                          | Frequency (%) |
|--------------------------------|---------------|
| Total patients with cognitive concerns | 320           |
| Number of EOD                   | 108 (33.7)    |
| Age at presentation (years), mean (SD) | 58.54 (6.54) |
| Age of onset of dementia (years) |                |
| Mean (SD)                       | 55.38 (6.53)  |
| Median (range)                  | 57 (34-63)    |
| Men                             | 58 (53.7)     |
| Women                           | 50 (46.3)     |
| Married                         | 100 (92.6)    |
| Single/widowed/separated         | 8 (7.4)       |
| Years of education, mean (SD)    | 1.87 (5.42)   |
| Duration of illness (prior to consultation), mean (SD) | 3.18 (2.35) |
| HMSE                            |               |
| Mean (SD)                       | 14.99 (8.77)  |
| Median (range)                  | 8.77 (0-30)   |
| EASI                            |               |
| Mean (SD)                       | 7.13 (3.34)   |
| Median (range)                  | 7.0 (0-12)    |
| Family history of dementia      | 23 (21.3)     |
| Past history of psychiatry illness | 6 (5.6)     |
| Vascular risk factors (HTN, DM) | 38 (35.2)     |
| Vitamin B12 deficiency          | 10 (9.3)      |
| Hypothyroidism                  | 11 (10.2)     |
| Age-wise distribution of EOD    |               |
| < 44                            | 8 (7.4)       |
| 45-49                           | 11 (10.1)     |
| 50-54                           | 21 (19.4)     |
| 55-59                           | 38 (35.18)    |
| 60-64                           | 30 (27.8)     |
| Psychotropic details            |               |
| AChEI                           |               |
| Donepezil                       | 65            |
| Rivastigmine                    | 4             |
| Galantamine                     | 1             |
| Total                           | 70 (64.8)     |
| Memantine                       | 43 (39.8)     |
| Antidepressants                 | 51 (47.3)     |
| Benzodiazepines                 | 20 (18.5)     |
| Antipsychotics                  | 42 (42)       |

HMSE: Hindi mental status examination, EASI: Everyday ability scale for Indians, HTN: Hypertension, DM: Diabetes mellitus, EOD: Early-onset dementia, SD: Standard deviation, AChEI: Acetylcholinesterase inhibitors

### Table 2: Diagnosis-wise distribution of early-onset dementia

| Dementia phenotype                          | Frequency (%) |
|---------------------------------------------|---------------|
| AD                                          | 58 (53.6)     |
| AD                                          | 57 (52.7)     |
| AD variant                                  | 1 (0.9)       |
| FTD                                         | 31 (28.7)     |
| FTD-FTD                                     | 23 (21.3)     |
| Language variant-FTD                        | 5 (4.6)       |
| FTD-PD                                      | 3 (2.8)       |
| VaD                                         | 6 (5.6)       |
| Diffuse Lewy body dementia and PD            | 3 (2.7)       |
| Corticobasal degeneration (CBD)              | 1 (0.9)       |
| Mixed etiology (AD + TBI, AD + vascular)     | 3 (2.8)       |
| Unspecified dementia (no subtyping was done) | 6 (5.6)       |

TBI: Traumatic brain injury, AD: Alzheimer’s dementia, VaD: Vascular dementia, FTD: Fronto-temporal dementia, PD: Parkinson’s disease, Bv-FTD: Behavioral variant-FTD

### DISCUSSION

In our study, the EOD formed nearly 34% of the persons attending with complaints of cognitive impairment in those 18 months period, is a substantive number. The current geriatric psychiatry unit takes referral of any patient with mental health and cognitive decline above 60 years of age and below the age of 60 years if they predominantly are related to cognitive decline.

Literature on dementia in people below 65 years of age is sparse compared to late-onset dementia. Population-based studies conducted in US, Japan, and Italy estimated EOD prevalence as 42.3–98.1/100,000 persons.[21-23] Proportion of EOD in specialized memory clinics ranged from 7.3% in Japan to 44% in Greece.[24,25] A study done from the eastern part of India by Nandi et al. reported that 24.5% of dementia patients in their clinic were below 65 years of age.[10] The proportion of EOD in our study sample is 33.7% which falls within the range of previous studies by Nandi et al., Yokota et al., Papageorgiou et al., McMurtray et al., Shinagawa et al., Picard et al., and Croisile et al. as shown in Table 5.[10,24-29] The mean age of patients at presentation in our study was 58.54 years, which is a little higher than previous study reports (51.5–56.5 years)[24,26,28] but comparable to study by Nandi et al. (56.5 years).[10]

This could be due to the setting of our study which is a geriatric psychiatry clinic predominantly catering to patients older than 60 years. As shown in Table 1, the prevalence of EOD increases with increasing age in keeping with previous studies.[11,13,14] Male preponderance was seen in our study (M: F = 1.16) similar to reports with gender ratios ranging from 1.12 to 1.9.[11,12] The mean years of education in our sample was lower (8.87 years) than that reported by Nandi et al.[10] (11 years) indicating lower cognitive reserve in our sample. It also leads to higher impairment and more challenges during cognitive assessment. The most common phenotype in our study was AD followed by FTD. This was similar to study by Alladi et al.
et al., with AD as the most common phenotype, but the second most common phenotype was FTD.\[11\]

The mean duration of illness before presentation was comparable to previous studies.\[10\] The mean HMSE score of 14.99 indicates that majority performed below the 10th percentile cutoff of 19 at presentation. A mean EASI score of 7 out of possible 12 indicates significant disability at presentation, reflecting the degree of care required for these patients. Nearly a quarter of our patients had positive family history which was higher than previous report of 17% from Nandi et al. study.\[10\] Preventable and modifiable risk factors were present in 54.7% indicating more aggressive screening for vascular, endocrine, and dietary risk factors.

The investigative work-up for people with early-onset cognitive impairment includes blood investigation (complete blood counts, electrolytes, thyroid function tests, Vitamin B12 levels, ESR, liver function, and renal function tests), STD profile, CSF studies, autoimmune profile, brain imaging, and electroencephalogram.\[10\] This was evident from larger study from Sweden which found that majority of patients with EOD underwent extensive diagnostic evaluation and multiple specialist consultations compared to late-onset dementia.\[13\] In our clinic, we recommend most of these investigations for people with EOD, but depending on their affordability, patient families consent for only important investigations. As clinician, we help the patient families in choosing the most relevant investigation depending on the history and differential diagnosis.

Various studies reported on different etiologies in EOD. These range from neurodegenerative, infective, metabolic, endocrine, and traumatic. The proportion of AD ranged from 17% to 38.8% in EOD samples.\[11,16-18,20\] In contrast, we found much higher AD prevalence accounting for 53.6% in our sample. FTD accounted for 28.7%, which is similar to 27% in Nandi et al. study\[10\] from India and Papageorgiou et al. study\[25\] from Greece but much higher than studies.

### Table 3: Age-wise distribution of diagnosis

| Age group (years) | Commonest phenotype of dementia | 2nd most common |
|-------------------|---------------------------------|-----------------|
| <49              | FTD                            | AD              |
| 50-54            | FTD                            | AD              |
| 55-59            | AD                             | FTD             |
| 60-64            | Alzheimer’s dementia           | FTD             |

AD: Alzheimer’s dementia, FTD: Fronto-temporal dementia

### Table 4: Behavioral and psychological symptom symptoms in early-onset dementia patients

| Domain                  | Frequency (%) |
|-------------------------|---------------|
| Agitation               | 19 (17.6)     |
| Apathy                  | 18 (16.7)     |
| Aggression/irritability | 20 (18.5)     |
| Depressive symptoms     | 24 (22.3)     |
| Psychotic symptoms      | 19 (17.6)     |
| Wandering               | 4 (3.8)       |
| Decreased sleep         | 25 (23.1)     |
| Repetitive, ritualistic behaviours | 7 (6.5)     |
| Disinhibition           | 6 (5.6)       |

### Table 5: Prevalence studies on early onset dementia

| Author, Year | Country | Setting | Type of study | EOD/total dementia | Percentage | Commonest phenotypes (%) |
|--------------|---------|---------|---------------|--------------------|------------|--------------------------|
| Yokota et al., 2005 McMurtray et al., 2006 | Okayama, Japan Los Angeles, USA | Outpatient clinic Memory center | Retrospective | 34/464 | 7.3 | AD (49.1) |
|             |         |         |               | 278/1683 | 30 | VaD (29) |
| Shinagawa et al., 2007 | Ehime, Japan | Memory clinic | Retrospective | 185/861 | 27.7 | AD (55.4) |
|             |         |         | (referrals from generalists, geriatricians and neuropsychiatrists) | | | |
| Nandi et al., 2008 | West Bengal, India Athens, Greece | Specialized clinic | Retrospective | 94/379 | 24.5 | AD (33) |
| Papageorgiou et al., 2009 |          |         | (referrals from neurologists and psychiatrists) | 114/260 | 44 | AD (27.2) |
| Ikejima et al., 2009 | Japan | Hospital-based (population estimates were made) | 2 step postal survey | 617 EOD patient | Prevalence estimates - 42.3 per lac | VaD (42.5) |
| Picard et al., 2011 | Amiens, Lille, France Rouen, France | Cohort of 3 memory clinics Memory clinic | Retrospective (referrals) | 811/3473 | 23.5 | AD (22.3) |
| Alladi et al., 2011 | Amiens, Lille, France Rouen, France | Cohort of 3 memory clinics Memory clinic | Retrospective (referrals) | 347 dementia patients | EOD constituted 49.9 | AD commonest phenotype followed by VaD |
| Croisile et al., 2012 | Lyons, France | Memory clinic | Retrospective (referrals) | 91/746 | 12.2 | MCI (18.7) |
| Harvey et al., 2003 | UK | Population estimates derived from large catchment area | Multistage survey | 185 EOD patient | Prevalence estimates - 54 per lac | AD (34) |
| Borroni et al., 2011 | Italy | Population estimates | Retrospective from tertiary care memory clinic (for 10 years) | 175 EOD | Prevalence estimates - 55.1 per lac | FTLD (29.6) |

EOD: Early onset dementia, AD: Alzheimer’s dementia, VaD: Vascular dementia, MCI: Mild cognitive impairment, FTLD: Fronto-temporal lobar degeneration
from USA, UK, Japan, and France (3%-15.9%). The variable prevalence of FTD could be explained by study setting, source of sample, and geographical region. FTD owing to the behavioral symptoms at the onset are more likely to visit psychiatric clinics. The proportion of VaD (5.6%) and DLBD and PD dementia (2.7%) is remarkably low. This could be due to the most of VaD and DLBD patients were either seen/referred to neurologist in our facility. Mixed and unspecified etiology accounted for <10% in our study indicating that in most cases efforts were made to reach a consensus diagnosis.

More than half (51.9%) of the patients presented beyond mild stage that indicates lack of awareness and possible lack of access to health care. Around 2/3rd of the patients (63.9%) presented for the first evaluation to our tertiary care center indicating the lack of geriatric/cognitive disorder specialists in the peripheral setting.

BPSD, the usual reason for a psychiatric consultation were present in 81.4% in our sample. There are very little data on BPSD in EOD from previous studies. Reports on BPSD from Indian studies on late-onset dementia vary based on the type of dementia studied, setting, and the assessment method. As per 10/66 study, 70% have BPSD, with depression being the most common disorder. Comparison between the Late-onset AD and Early-onset AD in terms of neuropsychiatry symptoms by Ferreira et al., found no difference. In our study, depression is the second-most common BPSD after sleep disturbances. Apathy, aggression, agitation, and psychotic symptoms account for 16%-18% each indicating the need for psychiatric evaluation and management. This was also reflected in the psychotropic usage with nearly half the patients receiving either antipsychotic or antidepressant or both. These values might not be comparable to community-based or neurology clinic samples indicating that full picture of dementia can only be obtained by including samples from both neurology and psychiatry clinics. However, the prescription practice is similar to our earlier study on dementia patients with donepezil being the most common AChEI and quetiapine being the most common antipsychotic drug.

Dementia leads to significant disability and decreased life span. The mean age at onset of dementia in sample was 55.38 years. Assuming the average retirement age to be 60 years (most states) in India, there is a mean 4.62 years loss of productive life in terms of employment and income. The average reported life span of EOD was 6.08 years.

Studies on AD reported that early-onset AD has heritability ranging from 96% to 100% compared to 69.8% in late-onset AD. The heritability is majorly due to autosomal recessive gene and to minor extent due to autosomal dominant, X-linked and mitochondrial genes. Studies on Apo E allele in AD reported that proportion of APOE2 found to be more frequently found among Early-onset AD (18%) compared to Late-onset AD (10%). Whereas the frequency of ApoE4 was more among Late-onset AD. In contrast to the above study previous study from our center did not find any difference in frequency of ApoE4 with regard to age of onset in AD. Studies have reported usefulness of genetic testing as a part of investigative work up in EOD with unclear phenotype. The lifetime risk of AD is 10%-12% and it doubles if there is positive history in a first-degree relative. It is likely that families with EOD and those with positive history of dementia will be more apprehensive of developing dementia. There will also be request for screening and genetic testing for unaffected relatives from these families. One-third of people with cognitive decline had EOD and in that 23.1% had a positive family history. In this scenario, there is need to develop services including genetic counseling and genetic testing in selective patients. There are guidelines that are recommended for genetic counseling for these families/patient caregivers.

To summarize, we found that nearly one-third of patients with cognitive disorders has early onset presenting to geriatric psychiatric services. Till now, there are only two epidemiological studies from India last been 2011. These studies were done in specialised memory clinic. From an epidemiological point of view, our study is probably first coming from a geriatric psychiatric setup. In terms of clinical significance, our study has shown there was significant delay in seeking treatment even among EOD patients. Another important finding from a psychiatrist’s point of view which was not investigated in previous studies was BPSD in EOD patients. Nearly 80% of patients in our study have BPSD symptoms stressing the need for specialized geriatric psychiatric clinics for the management of these symptoms [Table 6].

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### Table 6: Main finding in the study

| Key findings                                | Frequency (percent) | Mean (SD) |
|---------------------------------------------|--------------------|-----------|
| Proportion of EOD (%)                       | 108 (33.7)         |
| Commonest phenotypes (%)                   | 58 (53.6)          |
| AD                                          | 31 (28.7)          |
| Duration of illness prior to consultation (years), mean (SD) | 3.18 (2.35)       |
| Advanced stage of dementia (%)             | 56 (51.8)          |
| Patient with BPSD (%)                      | 85 (79.6)          |

BPSD: Behavioral and psychological symptom, AD: Alzheimer's dementia, EOD: Early-onset dementia, FTD: Fronto-temporal dementia

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**Figure 1:** Bar diagram showing proportion of subtypes of dementia in our sample
Strengths of the study

Diagnosis of dementia was given as per the existing system wherein, all patients are seen by specialist psychiatrists specialized in managing dementia. DSM 5 criteria and standardized scales were used for diagnosis and staging the severity of dementia. Patients who did not complete minimum standard evaluation were excluded from the study.

Limitations of the study

Patients who are primarily seen by a neurologist and seen in the Geriatric clinic briefly were not included in the study. Patients with suspected infectious etiology, autoimmune, tumors, and traumatic brain injury were usually referred to neurology/neurosurgery by general medical officer who did initial screening. This limits patients with these etiology and thus kind of phenotype presenting to our clinic.

Implications

This study highlights the need for dedicated memory clinics catering to all age groups where both psychiatric and neurology services can be availed. This review also shed light on the challenges ahead in terms of service delivery and long term care in people with EOD in India. Preventable and modifiable risk factors were present in 54.7% showing that early detection and intervention at general physician/primary health center will either prevent or delay the onset of dementia. Two-thirds of sample presented in moderate and severe stage in our sample. There is misconceptions among general public about dementia as disorder of late-life which needs to be addressed. There is a need to increase awareness among general physicians to pick up the early signs and symptoms of dementia in young and middle age patients. There also need to increase the liaison between cognitive disorders clinics, neuropsychiatric clinics, geriatric clinics, and psychiatric facilities to provide comprehensive care for these patients. Models of care from other nations for people with EOD need to be studied in our setting.

CONCLUSION

Dementia should not be considered a disease of late life, various studies reported on dementing illness starting very well in middle age. EOD constitutes a significant proportion among people with dementia. EOD presenting to geriatric psychiatry clinics are slightly different from neurology and memory clinics with respect to their subtypes with higher degenerative etiology and with higher BPSD. There was a delay of 3.18 years in seeking consultation, and two-thirds of cases come beyond the mild stage of dementia. There is a need to increase awareness among public as well as among general physicians for early identification and appropriate referral. There is a need for setting up specialised memory clinics to screen and assess persons with cognitive decline, especially in the working-age group.

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Conflicts of interest

There are no conflicts of interest.

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