Mild cognitive impairment: Profile of a cohort from a private sector memory clinic

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Abstract

Background: Private hospital memory clinics might see a different clientele than university or academic institutes due to referral biases. **Objective:** To characterize the profile of patients with mild cognitive impairment (MCI) from a private sector memory clinic. **Materials and Methods:** MCI was diagnosed according to revised clinical criteria of Petersen *et al*. For a subset of patients with MCI medial temporal atrophy and cerebral small vessel disease (white matter lesions and lacunes) were rated on magnetic resonance imaging (MRI) scans and analyzed for their contribution towards cognitive impairment. **Results:** Subjects with MCI formed one-third (113/371) of this memory clinic sample from a private hospital. MCI could be effectively diagnosed and subtyped using a brief cognitive scale (Concise Cognitive Test (CONCOG)). The amnestic MCI (single and multiple domains) subtype comprised the majority of cases with MCI. In a subsample of 33 patients, lacunar infarcts were more common than white matter lesions and hippocampal atrophy and were inversely associated with verbal fluency. **Conclusions:** MCI may be more commonly encountered in private hospital settings probably due to early referrals. It is possible to diagnose and subtype MCI using a brief cognitive instrument such as the CONCOG. In this sample, lacunar infarcts were more commonly encountered than medial temporal atrophy in such patients.

Key Words

Brief cognitive scale, mild cognitive impairment, private hospital

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Introduction

Mild cognitive impairment (MCI) represents the intermediate stage between normal ageing and dementia. Patients diagnosed with MCI have cognitive impairment in excess of that expected for age and some limitation in complex functional activities, but do not warrant a diagnosis of dementia.[1] In a substantial percentage of subjects, MCI is the pre-dementia stage. It has been estimated to affect 15-25% of community dwelling elderly over the age of 65 years and carries a higher risk of functional dependence and excess mortality in those affected.[2] The various causes of MCI include neurodegenerative diseases, such as Alzheimer's disease, cerebrovascular disease, major psychiatric illnesses like depression, and other systemic causes.[1,2]

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MCI has been subtyped on whether memory functions are affected and if one or multiple domains of cognitive functioning are affected. Similar to the multifarious etiology, the prognoses of MCI subtypes also vary. Roughly similar numbers of patients with MCI decline cognitively and functionally to be later diagnosed with dementia or improve/remain stable.[3,4] The strongest predictors of decline to dementia have been the presence of hippocampal atrophy on neuroimaging and greater cognitive and functional impairment at baseline.[5]

Descriptive studies of cohorts of MCI patients outside of North America and Europe are few. A few studies from Japan, Korea, Taiwan, and India have described the features of MCI subjects recruited from memory clinics or from epidemiological studies.[6-9] The results have been broadly similar to those from other studies. Although all these have come from university-affiliated hospitals or institutes, no study on MCI has been reported from a private hospital setting where the patient population might be different. In this article, we intend to describe the clinical profile of patients with MCI being followed-up at a private hospital in Sri Lanka.

Materials and Methods

Subjects

All subjects were consecutive patients seen at the memory clinic of our hospital, which is a tertiary care, multispecialty, non-teaching hospital in Colombo. They were either self-referred or health professional referred to the clinic for evaluation of memory complaints. The study was approved by the hospital ethics review committee, and all subjects gave written informed consent. The study period was from January 2006 to January 2013.

Clinical assessments

All subjects were evaluated in a standard fashion that included history, neurological examination, cognitive assessment using the Concise Cognitive Test (CONCOG),[10] and functional assessment using locally developed activities of daily living (ADL) scale.

The CONCOG has items screening for the following cognitive domains: Orientation to time (3 points), language (7 points), verbal episodic memory (8 points), visuospatial skills (4 points), and semantic verbal fluency (8 points). The language item includes naming of seven body parts. The memory item includes learning, delayed free recall, and multiple choice recognition of four unrelated words. Category verbal fluency (animals per minute) was chosen as the executive function item. The visuospatial domain includes copying of two simple diagrams (flower and diamond within a square). The total possible score on the CONCOG is 30.

The Functional Abilities Scale is a six-item screener of instrumental ADL with a maximum score of 12 with higher scores representing better function. The six instrumental ADL assessed are safely keeping/locating personal belongings, medication intake, money management, travel outside of home, using the telephone, and watching/following newspapers or television.

Subjects were screened for depression using the Patient Health Questionnaire-2, but the presence of depression was not used to exclude subjects in the present study.

Most patients underwent neuroimaging (computed tomography (CT) scanning or magnetic resonance imaging (MRI)) and blood work—thyroid-stimulating hormone (TSH) and serum vitamin B12 assays. Other investigations were done on an as needed basis. Neuropsychological testing was used sparingly.

MCI diagnostic criteria

MCI was diagnosed according to revised criteria.[11] These criteria are as follows:

1. Cognitive complaints coming from the patient or their family
2. Impairment in memory or other cognitivedomains evidenced by clinical evaluation
3. No or minimal impairment in instrumental ADL
4. Absence of dementia.

The aforementioned MCI criteria were operationalized as follows: Cognitive impairment was defined as CONCOG scores < 23, which correspond to 7th percentile (or 1.5 standard deviation (SD) less than norms) scores on normative sampling; functional impairment was defined as more than one item of the instrumental ADL (IADL) scale having scores < 2 (the maximum for each IADL item). Dementia was diagnosed as cognitive + functional impairment; whereas, only cognitive impairment was diagnosed as MCI. All neurological, cognitive, functional, and neuroimaging assessments were made on the first visit by the author himself as part of the routine information collected for each patient.

Neuroimaging assessment

For a subset of 33 patients who had complete MRI data, we analyzed the presence of hippocampal atrophy and cerebral small vessel disease and their contribution to cognitive impairment. We rated hippocampal atrophy on T1-weighted/inversion recovery coronal images on a 4-point scale, which was a slight modification of the more widely used Scheltens scale[12] for visual rating of medial temporal atrophy. The scale used here marked hippocampal atrophy as 0 = none, 1 = mild, 2 = moderate, and 3 = severe. Cerebral small vessel disease (white matter lesions and lacunar infarcts) was rated on axial fluid attenuated inversion recovery (FLAIR) images. White matter hyperintensity (WMH) severity was graded semiquantitativelyaccording to the modified Fazekas rating scale: 0 = absence of WMH; 1 = punctate foci below 10 mm, areas of grouped lesions must be smaller than 20 mm in diameter; 2 = single lesions between 10 and 20 mm, areas of "grouped" lesions more than 20 mm in any diameter; and 3 = large confluence of foci, single lesions of more than 20 mm in diameter.[13]

Statistical analyses

Significant differences in the mean test scores of the three groups—subjective memory complaints (SMCs), MCI, and dementia were evaluated using one-way analysis of variance (ANOVA) with Scheffe's post hoc test for pair wise comparisons. Multiple linear regression and correlational analyses were used to assess the impact of neuroimaging parameters on cognitive function in a subgroup. All tests were done using Statistical Package for Social Sciences (SPSS) version 16.0 and Medcalc version 11.[14] Significance was set at $P < 0.05$, and all analyses were two-tailed.

Results

A total of 113 subjects of a total of 371 fulfilled inclusion criteria and have been included in the present study. The mean age of the MCI group was 68.1 years and there were 80 males and 33 females. Mean age was significantly greater in the dementia group than in the other two groups, which did not differ from each other. ADL scores were not significantly different between the SMCs and MCI groups but the mild dementia group had significantly lower scores than the other two groups Table 1.

We next compared the CONCOG total and subscale scores between the three groups—SMCs, MCI, and mild dementia (CONCOG > 15). All scores were significantly lower in the dementia group compared with the other two groups. On comparing the SMCs and MCI groups except for orientation and copying domains, the MCI group had significantly lower scores on all other subscales (naming, verbal fluency, and recall) [Table 1].

We subdivided the MCI patients into four groups based on the individual domains (language, visuospatial, executive, and episodic memory domains) affected singly or in combination. The largest subgroup was the single domain amnestic subtype, followed by the multiple domain amnestic subtype and single domain nonamnestic subtype in that order. The commonest nonamnestic cognitive domain impaired was the executive domain as measured by the verbal fluency subscale on the CONCOG. The language domain was the second most common nonamnestic domain impaired followed by visuospatial skills domain. Overall amnestic MCI (single or multiple domain subtypes) was almost twice as common as nonamnestic MCI. The distribution of scores on the CONCOG and its domains for the four subtypes of MCI are shown in table. As expected, the amnestic subtypes had lowest memory scores; whereas, the nonamnestic subgroups had lowest naming, copying, and verbal fluency scores among the four subtypes [Table 2].

In a subset of 33 patients, we measured hippocampal atrophy, white matter lesions, and lacunar infarcts on the MRI brain images. None of these 33 patients had infarcts elsewhere or significant atrophy of other cortical areas. These patients had a lower mean age (65.6 years) than subjects whose MRI was not analyzed, but had comparable mean CONCOG scores (20.8). Six patients had moderate to severe hippocampal atrophy, 15 patients had lacunar infarcts, and six had moderate to severe white matter lesions. We also calculated the effect of the presence of these structural alterations on cognitive function (CONCOG total and verbal fluency and memory subscales). Linear regression analyses in this regard revealed that the only significant association was between lacunes and executive function as measured by the semantic verbal fluency subscale where an inverse association was noted [Table 3].

Discussion

This study of MCI from a private sector memory clinic showed that subjects with MCI accounted for nearly one-third of all referrals for evaluation. MCI could be effectively diagnosed and subtyped with a brief cognitive assessment tool—the CONCOG. Using this brief scale, we could clearly separate subjects with MCI from those with normal cognition and mild dementia. MCI affecting the memory domain (singly or in combination) was more common than nonamnestic MCI. Among the neuroimaging correlates, only lacunar infarcts correlated significantly with cognition being inversely associated with scores on a semantic verbal fluency test.

The strengths of this study are:

(a) The use of brief instruments that can be easily applied in the clinic/office,
(b) Inclusion of MCI subjects due to both neurodegenerative disease and cerebrovascular disease, and
(c) Neuroimaging with MRI and systematic visual assessment of hippocampal atrophy and cerebral small vessel disease using validated scales in a subset of patients.

The relatively large number of MCI subjects in this memory clinic cohort compared to patients with dementia can possibly be due to the fact that patients with memory complaints might present early to a private hospital. This observation needs to be interpreted in light of the fact that for every patient with dementia in the community there are two persons with a pre-dementia state,[15] but clinic-based studies do not report

Table 1: Baseline characteristics

	SMC *N* = 58	MCI *N* = 113	Mild dementia *N* = 49
Age (years)	65.4	68.1	69.6 *#
Education (years)	13.2	11.7	10.4 #
CONCOG total	25 (1.7)	20.6 (1.9)	17.4 (1.8) *#
Orientation	2.7 (0.6)	2.6 (0.7)	1.9 (0.8) #
Naming	6.7 (0.6)	6.2 (1.0)@	6.0 (1.0) *#
Copying	3.98 (0.2)	3.77 (0.5)	3.3 (1.0) #
Verbal fluency	5.2 (1.3)	3.8 (1.4)@	3.0 (1.4) *#
Memory	6.4 (1.2)	4.3 (2.2)@	3.3 (2.0) *#
ADL scale	10.0 (1.93)	9.7 (1.7)	7.75 (0.95) #

SMC = Subjective memory complaints, MCI = Mild cognitive impairment, CONCOG = Concise Cognitive Test, ADL scale = Activities of daily livingscale, *$P < 0.05$ for MCI versus dementia,#$P < 0.05$ for SMC versus dementia,@$P < 0.05$ for SMC versus MCI

Table 2: Scores on the CONCOG and subscales for the different MCI subtypes

MCI Subtype		CONCOG	Naming	Copying	Verbal fluency	Recall
SDA (*N* = 42)	Mean	21.26	6.64	3.88	4.79	3.40
	SD	1.99	0.62	0.33	1.26	1.95
SDNA (*N* = 26)	Mean	20.92	6.16	3.64	3.08	5.44
	SD	1.71	1.28	0.70	0.95	2.18
MDA (*N* = 37)	Mean	19.78	6.03	3.78	3.22	4.08
	SD	1.77	0.96	0.53	0.95	1.71
MDNA (*N* = 8)	Mean	20.63	5.25	3.50	2.50	6.63
	SD	1.19	1.28	0.76	0.76	1.30

CONCOG = Concise Cognitive Test, SDA = Single domain amnestic, SDNA = Single domain nonamnestic, MDA = Multiple domain amnestic, MDNA = Multiple domain nonamnestic, SD = Standard deviation

Table 3: Regression analyses of MRI parameters

	CONCOG		Verbal fluency		Memory	
	Regression coefficient (β)	Correlation coefficient (ρ)	Regression coefficient	Correlation coefficient	Regression coefficient	Correlation coefficient
WMLs	0.160	0.110	0.076	−0.041	0.073	0.120
Lacunes	−0.151	−0.120	−0.372*	−0.353	0.148	0.159
HA	−0.065	−0.002	−0.141	−0.101	0.057	0.078

CONCOG = Concise Cognitive Test, WMLs = White matter lesions, HA = Hippocampal atrophy, MRI = Magnetic resonance imaging.*$P < 0.05$

this phenomenon because many patients with MCI might not come to evaluation in large university-based memory clinics.[16]

There have only been a few clinic-based studies that have used short cognitive assessments in diagnosing and subtyping MCI. These various instruments include the Alzheimer's Disease Assessment Scale, Cognitive Abilities Screening Instrument, Short Test of Mental Status, and the Montreal Cognitive Assessment.[6,17-20] All the a forementioned studies have demonstrated important and easily identifiable differences in various cognitive domains between patients with MCI and those with normal cognition even while using short scales of cognitive impairment. The results of the present study are consistent with these showing that memory, verbal fluency, and naming are easily applicable tasks that can unmask even the earliest deficits seen in MCI.

Amnestic MCI (single or multiple domains) was the commonest MCI subtype encountered in this study that is similar to other community-based prevalence studies.[7,21] In addition, we also found that multiple domain amnestic-type MCI was almost as frequent as single domain amnestic MCI. This further lends support to the current practice of not defining MCI as amnestic only as was originally done by Petersen *et al*., and Petersen and Negash.[1,11] The finding of executive function being the commonest non-memory domain to be affected in MCI is also in accordance with other studies.[22,23] The nonamnestic multiple domain subtype MCI patients had lower scores than other subtypes on naming and verbal fluency domains, but not in the copying domain.

Though hippocampal atrophy and cerebrovascular disease (particularly subcortical cerebral small vessel disease) have been well-recognized as the most common correlates of cognitive impairment,[24] in the present study only lacunar infarcts had a significant correlation with any cognitive domain (executive functioning as measured by semantic verbal fluency). We are unable to explain this single positive association and posit that it might have been due to the small size of subjects with complete MRI data.

A further limitation of this study is the absence of neuropsychological data. The diagnostic process in this study closely approximates that seen in most memory clinics outside of academic settings. We also do not have sufficient follow-up data on all subjects to determine the conversion rate of MCI to dementia. We hope to present that data in a future publication.

Conclusions

Subjects with MCI formed one-third of this memory clinic sample from a private hospital. MCI could be effectively diagnosed and subtyped using a brief cognitive assessment in this sample. Memory and verbal fluency subscales showed impairments most frequently. The amnestic MCI subtype comprised the majority of cases with MCI. In this sample, lacunar infarcts were inversely associated with verbal fluency; whereas, hippocampal atrophy was not significantly associated with impairment in any cognitive domain.

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