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To study the prevalence of mild cognitive impairment (MCI) and its subtypes in elderly person ≥ 60 years of age and to study the epidemiological aspect of MCI

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Abstract
Title: To study the prevalence of mild cognitive impairment (MCI) and its subtypes in elderly person ≥ 60 years of age and to study the epidemiological aspect of MCI.
Methods: It is a randomized urban population based study conducted in northwest part of India, Bikaner city. Kolkata cognitive test battery (based on consortium to establish a registry for Alzheimer's disease and Hindi mental state examination, HMSE) was used to evaluate 270 apparently non-demented subjects. CDR scale and GDS scale were used to exclude severe cognitive impairment and dementia respectively.
Results: The total prevalence of MCI was 19.26%, the prevalence of a MCI and multiple domains MCI was 7.78% and 11.48% respectively. The age group wise, sex wise and education group wise break up of prevalence rates of MCI types were not significant. People with memory complaint had a MCI and multiple domain MCI prevalence (20.45%) and (25%) respectively. In people without memory complaints prevalence of a MCI and multiple domains MCI were (5.31%) (9.37%). Prevalence of a MCI and multiple domain MCI in hypertensive elderly were (9.1%) and (14.05%) and the same thing in non-hypertensive were (6.71%) and (9.48%). Prevalence of aMCI in diabetic and non-diabetic elderly were (16.98%) and (5.52%). Multiple domains MCI was found among (20.75%) diabetics and (9.21%) non-diabetic. Mean scores, 10^{th} and 90^{th} percentile values of a MCI cases and multiple domains MCI cases in all cognitive domains were low and statistically significant when compared to normal control elderly.
Conclusion: Advancing age, low education level, hypertension, diabetes mellitus, chronic smoking, low socio–economic status were associated with higher prevalence of MCI in elderly. There was no significant difference in prevalence rates of MCI between sexes in our study.

Keywords: prevalence, mild cognitive impairment (MCI) epidemiological aspect,

Introduction

Improvements in health care over the past 50 years have extended average life expectancy, which has resulted in a substantial increase in the numbers of individuals over 60years of age. By the year 2020, more than 700 million people aged 60 years and older will be living in developing countries. Cognitive impairment and dementia are becoming increasingly prevalent because of these demographic changes.

Across the age continuum from middle to late life, cognitive functionary can remains normal, can decline into a state of mild cognitive impairment or can progress further to frank dementia [1]. Alzheimer's disease and other dementias are devastating conditions that create huge emotional, financial, and physical challenges for the person and his or her family. So, early diagnosis will facilitate planning to provide the necessary social support and therapeutic intervention to improve cognitive level. Clinically, MCI is defined as impairment in one or more cognitive domains (typically memory), or an overall mild decline across cognitive abilities that is greater than would be expected for an individual's age or education, but that is insufficient to interfere with social and occupational functioning, as is required for a dementia syndrome.

This condition has received several descriptions including mild cognitive impairment (MCI), incipient dementia, and isolated memory impairment [2]. At present, the term mild cognitive impairment and its acronym, MCI have been frequently used in studies on the pre-clinical phase of dementia [3]. Studies from developed countries have recorded that the prevalence rates of MCI or related disorders vary between 0.5 and 36% depending on the diagnostic criteria used as well as the demographic characteristics of the population studied [7-12]. People with MCI are three to four times more likely to develop Alzheimer's than those without such impairment. When they are followed longitudinally for few years have a high risk of progressing to dementia with annual conversion rate ranging from 6% to 25%.

Methods

The study was conducted within the municipal area of Bikaner. Bikaner is a city in the northwest of the state of Rajasthan in western India.The predominant ethnic group speaks Hindi and

marwadi languages. The municipal area of Bikaner has been divided into 55 wards based on geographic location and every 10th ward was selected. We included 5 largest wards of Bikaner city for our study. List of individual's ≥ 60 years of age was prepared using voter's id list. Individuals to be interviewed were selected by systematic random sampling method; every second individual from the list was selected. In this way, 336 individuals were included. The house to house survey was then conducted in selected households by the doctor. written consent was taken before interview.

The evaluation of the subjects included collecting information on age, sex, literacy level, religion, occupation, family income, addictions (smoking, chewing tobacco, alcohol, drugs), and any deterioration of memory over period of six month preceding the test as noted by family members or the subject. Behavioral functions, language and orientation difficulties, past history of medical/neurological disorders (hypothyroidism, epilepsy, stroke, hypertension, diabetes, loss of consciousness, abnormal movements, disturbed sensation, weakness, head injury, chronic medication use), and psychiatric illnesses (schizophrenia, depression, mania, mental retardation) as well as relevant family history were also probed. A general physical and neurological examination was also carried out. Bio chemical evaluation included CBC, blood sugar, complete lipid profile, serum creatinine, and thyroid function test. Radiological investigation used was CT scan head. A structured proforma was used to capture all information. HMMSE score was applied to screen for dementia. Persons with score ≤ 20 on HMMSE were excluded from the further evaluation. CDR score was used to confirm and stage the cognitive status. Geriatric depression scale was applied to detect the presence of depression and to assess the activities of daily living. Information was verified from at least one close family member or a reliable informant staying with the subject. 66 subjects were excluded in this way from the further study. The excluded individuals were as follows: refused cognitive evaluation (female 22 and male 3), hearing and visual problem (females 3 and males 2), CVA (females 4 and males 2), seizure disorder (female 1 and males 2), head injury (females 1 and male 1), parkinsonism (female 1 and male 1), hypothyroidism (females 2), depression (females 5 and male 2), severe cognitive impairment and dementia (females 7 and males 3), acutely ill (females 3 and male 1). Hence, 270 participants ≥ 60 years, apparently non–demented were included for the detailed cognitive test. Kolkata cognitive test battery [4]. consisted of category-based verbal fluency tests (fruits and animals), a 15-item version of the object-naming test (based on the visual presentation of the objects), mental state examination, calculation tests, visuoconstru- ctional ability (which included circle, diamond, overlapping rectangles, and box), and a set of memory tests (immediate memory, delayed memory, and recognition of a 10- item wordlist). We administered the available kolkata cognitive test battery with little modification under the guidance of our neurologist and geropsychiatrist. We removed fruits naming and memory recognition test items from the original kolkata cognitive battery.

We defined amnestic MCI as follows : 1 objective memory impairment as evidenced by scores of 1.5 SD below normative values; 2) those subjects who had no self-reported memory complaints but showed objective memory impairment based on analysis of the neuropsychological data; 3) essentially preserved other general cognitive function; 4) largely intact functional activities; For the MCI multiple domain type, we defined as deficits evidenced by scores of 1.5 SD below normative values in multiple (more than one) areas of cognitive functioning with or without memory impairment.

Data were analyzed using SPSS version 10. The normative data have been presented in the form of mean (±SD), 10th and 90th percentile scores. The 10th percentile score was taken as the operational cut-off point for identifying the cognitively impaired section of the population. The 90th percentile score on the GDS assessment (11 in our case) was taken as the cut-off point for identifying participants with significant depression.

Results

The total study population was 270 elderly persons living in an urban community. There were 189 males (70%) and 81 females (30%). The proportion of female elderly was around half of the male population (Male: Female ratio = 2.3:1). The mean age of study population was 67.53± 5.81 years. The mean ages of male and female were 68.38 ± 6.08 & 65.56± 4.61 years respectively. The maximum number of persons were in 60-64 year age group (36%) and minimum number of persons were in >75years age group (13%). The numbers of females were less compared to males in all age groups. In >75 year age group, female constituted only 1.4 %. The mean year of education of overall study population was 6.92± 5.4. In male and female, mean year of education were 7.52±5.25 and 6.55 ± 5.58. (Table 1)

The overall distribution of tests scores with mean value (± SD), Median, Range and both 10th & 90th Percentile are shown. The maximum scores of individual tests have also been shown. (Table 2)

In the study population, 16.30% (4.80% female & 11.50%male) complained of memory decline while the remaining 83.70% (25.20% female & 58.50% male) didn't complain of memory decline (table 4).

As shown in table 3, the overall prevalence rate of MCI was 19.26%.The prevalence rate of aMCI was 7.78% and that of multiple domains MCI was 11.48%. The prevalence rates of aMCI in male & female were 7.40% & 8.64% and that of multiple domains MCI were 11% & 12.60% respectively. The prevalence rates of both types of MCI were more in female on compare to male. However, Sex wise break up of prevalence rates of MCI was not significant (P>0.05). The prevalence of aMCI was lowest in 60-64 year age group (2.06%) and highest in >75years age group (14.29%). The prevalence rates of multiple domains MCI across age spectrum ranged from 6.19% to 25.71% being lowest in 60-64 year age group and highest in >75years age group. Age group and sex wise break up of prevalence rates of MCI types was not significant (P>0.05). The prevalence rates of multiple domains MCI was in decreasing trend as the level of education attained by the elderly people and being highest in Illiterate (23.80 %) and lowest in graduates (1.47%). The prevalence rate of aMCI was uneven across educational groups being highest in persons with primary education (11.76%) and lowest in graduates (3.23%). (Table 3)

The prevalence rates of multiple domains MCI was more than aMCI in illiterate, primary and secondary educated groups; but was lower in graduates. The prevalence rate of aMCI (3.23%) was more than multiple domains MCI (1.47%) in graduates (table 3).

The prevalence rates of aMCI and multiple domains MCI in persons with memory complaint were 20.45% & 25.00% and that in persons without memory complaints were 5.31% &

9.73%. Prevalence rates of both types of MCI was statistically significant on comparison between persons with and with out memory complaint. (Table 4)

Mean scores, 10th & 90th Percentile values of multiple domain MCI cases in all cognitive domains were low and statistically significant on comparison with normal control elderly (P value < 0.001). (Table 5)

There was high prevalence of multi domains MCI and aMCI in elderly with lower socio economic class. There was no difference in prevalence rate of MCI in middle and upper class elderly people (table 6). Prevalence of aMCI was more common chronic smokers (10.71%) than nonsmokers (6.45%), but was not significant (P>0.05). In case of multiple domains MCI, prevalence rates were equal. The Prevalence rate of aMCI & multiple domains MCI in hypertensive elderly were 9.1% & 14.05% and the same things in non-hypertensive elderly were 6.71% and 9.48% (p value > 0.05%) (table 6). The prevalence rates of aMCI in diabetic & non-diabetic elderly are 16.98% & 5.52% and it is statistically significant (p value <0.01). The prevalence of multi domain MCI in diabetic & non-diabetic elderly are 20.75% & 9.21% and it is also significant (p value <0.05) (table 6).

Discussion

In epidemiologic studies, the term MCI has been used to describe a subject with a cognitive impairment, due to any etiology, who may improve, remain stable, or progress to a fully demented state [7, 8]. MCI is essentially an evolving concept in which different criteria have been proposed and modified with time. Research on MCI has mostly evaluated the amnestic type [9, 10]. and in some cases the multiple domain type [11, 12]. We used the modified Petersen criteria in defining the amnestic variety.

Studies from developed countries have recorded that the prevalence rates of MCI or related disorders vary between 0.5 and 36% depending on the diagnostic criteria used as well as the demographic characteristics of the population studied [13, 16]. The prevalence rate of MCI in our study was well with in the reported range.

Artero *et al.* [15]. obtained prevalence rate of MCI using MCI-R criteria. The MCI-R prevalence was found to be 16.6% using revised criteria. A significantly better prediction of transition to dementia was obtained with MCI-R than with the previous MCI criteria.

The Canadian Study of Health and Aging [16]. reported an estimated prevalence rate of 16.8% for cognitive impairment in general and 5.3% for circumscribed memory impairment. The overall prevalence rate of MCI and prevalence rate of aMCI in our study were near to the Canadian Study of Health and Aging prevalence rate.

In the present study, prevalence rates of both types of MCI were increasing trend as age advances across the age spectrum. An increase in prevalence of MCI with age was also found in other studies [17, 19]. A general decline with age was found in one study[20] but others found no significant influence of age on the frequency of mild cognitive impairment [19, 21].

Frisoni *et al*. [21]. defined mild cognitive impairment as a score 1 SD below the mean of age- and education- specific norms on the MMSE, and reported a prevalence rate of 15% for their study sample, aged 75–95 years. The prevalence of MCI was not different across age and education strata. In our study, prevalence rate of MCI was affected by age and education.

According to Unverzagt *et al*. [19]. the overall rate of cognitive impairment among community dwelling elderly was 23.4%. Age-specific rates indicate increasing prevalence with increasing age: 19.2% for ages 65 to 74 years, 27.6% for ages 75 to 84 years, and 38.0% for ages 85 years. Our study also showed similar increasing prevalence rate as age advances.

The prevalence rates of both types of MCI were high in female on compared to male. However, Sex wise break up of prevalence rates of MCI was not significant (P>0.05). In our study males are more in number than females. The possible reasons were religious and social customs, traditional females refused for interrogation.

The Leipzig Longitudinal Study of the Aged (LEILA75+) [22]. a population-based study of the epidemiology of dementia and mild cognitive impairment (Riedel-Heller *et al.* 2001) revealed no difference in prevalence rates between men and women. Furthermore, Finnish and German studies found no gender difference in the prevalence of AACD and MCI [22, 23]. Like the study by Ha¨nninen *et al*. [23]. we found no gender difference in the prevalence of mild cognitive impairment.

Some studies did not find different prevalence rates of CIND or MCI in men and women [16, 24]. whereas others reported a higher prevalence of AAMI and AACD in men [20, 23]. or CIND in women. However, higher prevalence rates for men [20]. and women [18]. have been reported.

In our study the prevalence rate of aMCI was uneven across educational groups being highest in persons with primary education (11.76%) and lowest in graduates (3.23%). In eastern Finland, Palmer *et al*. [24]. found decreasing trend in prevalence rates of MCI, from 0–5 years of formal education (13.3%) to ≥ 9 years (3.0%). Kivipelto *et al*. [24]. reported higher prevalence rates of MCI for those with low education levels.

Jennifer *et al*. [10]. revealed frequency of amnestic MCI of 5.0%. Other subtypes of MCI ranged in frequency from 2.1% to 6.2%; MCDM (multiple cognitive domain with memory impairment) 6.2%, MCDN (multiple cognitive domain without memory impairment) 5.9% and noticed higher prevalence of MCI in persons >75years and individuals with fewer than 9 years of schooling. The prevalence rate of MCI was slightly higher in our study compared to Jennifer J *et al*. and other results of our study were also similar to their study.

Das *et al*. [25]. reported 14.89% of overall prevalence of MCI based on neuropsychological testing. Prevalence of the amnestic type was 6.04% and that of the multiple domain type was 8.85%. Adjusted for age, education and gender, the amnestic type was more common among men and the multiple domain type among women with advancement of age. Rates differed considerably with educational attainment. The number of cases with multi domain MCI was proportionately higher than the amnestic variety in the lower or no education category. We also found the similar results in our study.

The prevalence rate of aMCI multiple domains MCI in hypertensive elderly were 9.1% & 14.05% and the same thing in non-hypertensive elderly were 6.71% & 9.48% in our study. Reitz *et al*. [125]. in 2007 conducted a study to explore whether hypertension was associated with the risk of mild cognitive impairment (MCI) in prospective community–based cohort followed up for a mean of 4.7 years. They found that hypertension was related to a higher risk of MCI. The association seemed to be stronger with the non–amnestive than the amnestive type of MCI in the elderly. In our study also, there was high prevalence of multi domains MCI in hypertensive

elderly. Our findings were comparable with findings of Reitz *et al*. [125].

The prevalence rates of aMCI in diabetic & non-diabetic elderly were 16.98% & 5.52% and it was statistically significant (p value <0.01). The prevalence of multi domain MCI in diabetic & non-diabetic elderly was 20.75% & 9.21% and was also significant (p value < 0.05).

Luchsinger *et al*. [129]. studied relation between diabetes and MCI. They reported the incident rate of aMCI 47.9% and 52.1% of non-amnestic MCI. The prevalence rates of MCI in diabetic elderly in our study were well with in the prevalence rates of Luchsinger *et al*.

Table 1: Distribution of study population by sex, age and education

	n	Mean age (SD)	Mean years of education (SD)
Total participants	270	67.53±5.80	6.92±5.4
Male	189	68.38±6.08	7.52±5.25
Female	81	65.56±4.61	6.55±5.58
Age groups			
60-64	97	61.97±1.45	7.51±5.56
65-69	79	66.63±1.33	6.88±5.52
70-74	59	71.23±1.33	6.74±5.27
>75	35	78.74±3.43	6.52±4.91
Education groups			
Illiterate	63	67.86±6.40	0±0
Primary	68	67.59±5.96	4.55±0.65
Secondary	77	67.66±5.17	9.79±1.11
Graduation & above	62	66.98±5.61	14.47±1.43

Table 2: Normative data: distribution of tests score on Kolkata cognitive battery applied to study population aged >60years. N=270

Cognitive tests	Max Score	Range	Mean (SD)	Median	10th Percentile	90th Percentile
HMMSE	30	19-30	27.29±2.40	28.00	24	30.0
Verbal fluency (VF)	16	3-16	10.96±2.63	11.00	7.1	14.0
Object Naming (ON)	15	12-15	14.49±0.74	15.00	14.0	15.0
Calculation (Cal)	5	0-5	4.72±0.66	5.00	4.0	5.0
Immediate Memory recall (IMR)	22	5-22	14.14±3.34	14.00	10.00	19.0
Delayed Memory (DM)	8	0-8	4.39±1.46	4.00	2.00	6.0
Visio constructional ability (VCA)	13	3-13	10.31±2.50	11.00	6.00	13.0

Table 3: Age, educational groups &Sex wise prevalence of MCI and its subtype

Age groups	Sex	N	aMCI			Multiple domain MCI		
			n	PR %	P value	n	PR %	P value
60-64 years	Male	59	02	3.39%	>0.05	2	3.39%	>0.05
	Female	38	00	0.00%		4	10.53%	
65-69 years	Male	57	04	7.02%	>0.05	5	8.77%	>0.05
	Female	22	02	9.09%		2	9.09%	
70-74 years	Male	43	05	11.63%	>0.05	6	13.95%	>0.05
	Female	16	03	18.75%		3	18.75%	
>75 years	Male	32	05	15.63%	>0.05	8	25.00%	>0.05
	Female	03	00	0.00%		1	33.33%	
Education groups								
Illiterate	Male	47	05	18.52%	>0.05	10	21.28%	>0.05
	Female	16	01	6.25%		05	31.25%	
Primary	Male	43	04	9.30%	>0.05	05	11.63%	>0.05
	Female	25	04	16.00%		05	20.00%	
Secondary	Male	53	04	7.55%	>0.05	05	9.43%	>0.05
	Female	24	01	4.17%		00	0.00%	
Graduate	Male	46	01	2.17%	>0.05	01	2.17%	>0.05
	Female	16	01	6.25%		00	0.00%	
Total		270	21	7.78%		31	11.48%	

Table 4: Prevalence of MCI and it's subtype in memory complaint wise

Risk Factor	N	aMCI			Multiple domain MCI		
		n	PR %	P value	n	PR %	P value
Memory +ve	44	9	20.45%	<0.001	11	25.00%	<0.001
Memory–ve	226	12	5.31%		22	9.73%	

Table 5: Comparison of test score on Kolkata cognitive battery applied between Controls and MCI

Cognitive tests	Controls		aMCI		Multiple MCI		Control Vs aMCI	Control Vs MultipleMCI
	Mean SD	10^{th} 90^{th} Per	Mean SD	10^{th} -90^{th} per	Mean SD	10^{th} -90^{th} per		
HMMSE	27.97± 1.66	26-30	25.80± 1.47	24-28.6	23.61± 1.80	21-26	<0.001	<0.001
Verbal fluency	11.48± 2.30	8-14	8.00± 2.52	5.2-12	6.96± 1.66	5.2-10	<0.001	<0.001
Object Naming	14.64± 0.54	14-15	14.09± 0.88	13-15	13.38± 0.91	12-14.8	<0.001	<0.001
Calculation	4.84± 0.39	4-5	4.42± 0.87	3-5	3.87± 1.17	2.2-5	<0.001	<0.001
IMR	14.79± 2.90	11-19	9.14± 1.62	7-11	9.70± 2.68	7-13	<0.001	<0.001
Delayed Memory	4.67± 1.23	3-6	1.85± 0.47	1.2-2	2.25± 1.15	1-4	<0.001	<0.001
V. C. A	10.86± 1.97	8-13	7.38± 2.47	3.2-10.8	5.00± 1.09	4-6	<0.001	<0.001

Table 6: The prevalence of multi domain MCI in different groups

Economic Status	N	aMCI			Multiple domain MCI		
		N	PR%	p value	N	PR%	p value
Lower class	146	07	4.80%	–	19	13%	–
Middle class	107	12	11.20%	–	10	9.3%	–
Upper class	17	02	11.76%	–	02	11.76%	–
Smoking							
Chronic smoker	84	9	10.71%	>0.05%	10	11.90%	>0.05%
non-smoker	186	12	6.45%		21	11.29%	
Hypertension							
HTN	121	11	9.1%	>0.05%	17	14.05%	>0.05%
No HTN	149	10	06.71%		14	9.40%	
Diabetes							
DM	53	09	16.98%	<0.01%	11	20.75%	<0.05%
No DM	217	12	5.52%		20	9.21%	

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