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Study of Non-Genetic Risk Profile for Mild Cognitive Impairment in Elderly

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Abstract

Background: Identifying risk factors for mild cognitive impairment (MCI) in the elderly aids in early diagnosis and treatment of treatable risk factors, delaying progression to dementia. Relatively less studies have been conducted to predict cognitive disruption in late life. The objective of this study was to assess the non-genetic risk factors for MCI in the elderly population.

Methods: Subjects (N = 500) aged > 60 years were allocated into two groups, i.e., subjects with normal cognition (n = 340) or with MCI (n = 160), based on mini-mental status examination (MMSE score 23 - 26) were diagnosed to have MCI. Laboratory investigations were done to determine the risk factors for developing MCI.

Results: The prevalence of MCI was 32% in the elderly with male predominance. Mean glycated haemoglobin, random blood glucose, systolic blood pressure, thyroid-stimulating hormone, serum cholesterol, triglyceride, creatinine, and sodium levels were significantly higher in subjects with MCI as compared to subjects with normal cognition (P < 0.001). Logistic regression found that odds ratio for progressing to MCI was higher by 5.28 times in diabetics, 4.31 in hypertensives, 4.64 in subjects with ischaemic heart disease, 5.26 in subjects with renal disease, 4.46 in subjects with hypothyroidism, 4.31 in subjects with past history of cerebrovascular accident and 2.67 in subjects with vitamin B12 deficiency.

Conclusion: Non-genetic risk factors can be regarded as the potential markers of MCI. Hence, it is pertinent to evaluate the elderly for MCI, as risk factors that are reversible can be treated with proper intervention.

Keywords: Ageing, co-morbidity, dementia, diabetes mellitus, risk factors, blood pressure.

Introduction

Mild cognitive impairment (MCI), an intermediate state between cognition of normal aging and mild dementia, is a common clinical manifestation among elderly subjects[1]. MCI to dementia progression rates range from 5.4% to 11.7% each year[2]. MCI is a measurable cognitive problem that involves difficulties with memory, thought, language and judgment that is more than any age-related change that does not interfere with daily activities[3]. While dementia is an acquired deterioration that impairs the cognitive abilities and impacts the effective performance of daily activities[4].

The cause of MCI remains unknown; however, it is postulated that structural and functional alterations in the brain that occur due to cerebral hypoperfusion cause cognitive impairment[5]. It has also been reported that cardiovascular risk factors such as ischaemic heart disease (IHD), hypertension, diabetes mellitus (DM) and stroke (including cerebral infarction and cerebral haemorrhage) affect the cerebral perfusion, causing MCI and progression to dementia in the elderly[1]. Various screening tests, including Montreal Cognitive Assessment (MoCA), Mini-Mental State Examination (MMSE) or mini-cog are useful to measure the overall cognitive dysfunction, with varying specificities and sensitivities[6].

Although ample studies have reported the risk factors contributing to the shift from normal cognition to MCI[1], relatively lesser studies have been conducted to predict cognitive disruption particularly in late life, i.e., in the elderly. Identification of MCI, particularly in high-risk subjects is important as adequate preventable measures can be taken against the development of dementia to avoid functional deterioration[3]. Early intervention during the status of early pre-dementia also helps improve the quality of life of the patient[7]. This study thus intended to assess the non-genetic risk factors for MCI in the elderly.

Material and methods

This two-year (2013 - 2015) observational cross-sectional study was conducted on elderly subjects aged > 60 years (who had completed graduation), attending the outpatient department of medicine and neurology. Clinical diagnosis of MCI was based on Petersen's definition of MCI, which included the following – 1. Memory complaint, preferably

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corroborated by an informant. 2. Objective memory impairment (for age and education). 3. Preserved general cognitive function. 4. Intact activities of daily living. 5. Not demented[8].

Subjects who were diagnosed with dementia, hospitalised for acute illness or with neurological infections were excluded from the study. As depression was a common cause for pseudodementia/cognitive impairment, subjects with depression were excluded using the Geriatric Depression Scale (shorter version). Subjects aged > 60 years were regarded as elderly as per the Indian Council of Medical Research survey of the Indian geriatric population. Informed consent from the subjects and ethical approval from the Institutional Ethical Committee [STD-1/EC/13-14] was obtained before their participation in the study.

All subjects were allocated into two groups, i.e., subjects with normal cognition and subjects with MCI based on MMSE. Elderly subjects with MMSE score 23 - 26 were identified to have MCI. An experienced clinical psychologist performed the neuropsychological investigations.

Demographic data, general physical examination, complete clinical history of existing comorbidities with special emphasis on risk factors of the subjects, were recorded. Laboratory investigations including renal function, liver function, thyroid profile, serum vitamin B12, complete blood count, random blood sugar, HbA1c, lipid profile, serum electrolytes, HIV status, neuroimaging and electrocardiography were also performed. Collected data was analysed.

Statistical analysis

SPSS v17 was used to analyse the data. All the quantitative parameters such as age and MMSE were expressed as mean ± SD and tested with the Mann-Whitney U test. Qualitative variables were expressed as proportions and tested with a chi-square test of significance. Independent factors involved in the development of MCI were assessed using logistic regression analysis. Multinomial logistic regression analysis determined the variables that influence the conversion of MCI to dementia.

Results

Of the total 500 elderly subjects, 340 (68%) had normal cognition and 160 (32%) were diagnosed with MCI. The prevalence of MCI was 32% in the elderly with male predominance in either group. Mean age and body mass index significantly differed in both groups (P < 0.001). Most subjects identified with MCI also had anaemia (93.1%), followed by DM (40.6%) and hypertension (33.1%) while most subjects with normal cognition were anaemic (68.8%; Table I).

Table I: Demographic, comorbidity, and neuropsychological profile in the study subjects.

Variables	Normal cognition, n = 340	MCI, n = 160	P value
Age	68 ± 5.61	67.46 ± 4.76	< 0.001**
Male/Female	222/118	122/38	
BMI (kg/m^2)	22.54 ± 1.06	23.28 ± 1.55	< 0.001**
Co-morbidities			
Diabetes mellitus	39 (11.5%)	65 (40.6%)	< 0.001**
Hypertension	36 (10.6%)	53 (33.1%)	< 0.001**
Ischaemic heart disease	18 (5.3%)	33 (20.6%)	< 0.001**
Cerebrovascular accident	20 (5.9%)	34 (20.3%)	< 0.001**
Hypothyroidism	29 (8.5%)	47 (29.4%)	< 0.001**
Renal disease	10 (2.9%)	22 (13.8%)	< 0.001**
Anaemia	234 (68.8%)	149 (93.1%)	< 0.001**
Vitamin B12 Deficiency	22 (6.4%)	25 (15.6%)	0.0018
Hypercholesterolaemia	7 (2%)	23 (14.3%)	< 0.001**
Hypertriglyceridaemia	14 (4.1%)	46 (28.7%)	< 0.001**
Renal dysfunction	9 (2.6%)	22 (13.7%)	< 0.001**
Hyponatremia	44 (12.9%)	39 (24.3%)	0.002*
Smoking	68	25	0.29
Alcohol consumption	77	31	0.48
Neuropsychological assessment			
MMSE	27.64 ± 0.60	24.70 ± 0.82	< 0.001**

***Highly significant; *Significant; MCI, Mild cognitive impairment.*

Mean systolic blood pressure (SBP), cholesterol, HbA1c in diabetics, random blood glucose, thyroid-stimulating hormone, serum creatinine levels were higher in subjects with MCI as compared to subjects with normal cognition. (P < 0.001; Table II).

Table II: Laboratory investigations in the study subjects.

Variables	Normal cognition#	MCI#	P value
Haemoglobin	12 ± 0.8	11.3 ± 0.9	< 0.001**
Random blood glucose	140 ± 29	180 ± 44	< 0.001**
HbA1c (glycated haemoglobin)	6.0 ± 0.3	6.5 ± 0.7	< 0.001**
Systolic blood pressure	136 ± 6.68	141 ± 6.99	< 0.001**
Diastolic blood pressure	80 ± 7.98	81 ± 10.72	0.29
Thyroid stimulating hormone	2.72 ± 1.07	3.42 ± 1.67	< 0.001**
Serum creatinine	0.90 ± 0.20	1.11 ± 0.46	< 0.001**
Cholesterol	140 ± 18	164 ± 28	< 0.001**
Triglycerides	112 ± 25	144 ± 48	< 0.001**
Serum sodium	136.8 ± 1.5	135.8 ± 2.3	< 0.001**
Serum albumin	3.5 ± 0.4	3.3 ± 0.2	0.64

*#Data presented in mean ± SD; **Highly significant; MCI: Mild cognitive impairment.*

Multinomial logistic regression analysis found that DM, hypertension, IHD, hypothyroidism, cerebrovascular accident, vitamin B12 deficiency and renal disease were significant predictors in the conversion to MCI among elderly patients. The odds of conversion to MCI was higher by 5.28 times in diabetics, 4.31 in hypertensives, 4.64 in subjects with IHD, 5.26 renal disease subjects, 4.46 hypothyroid subjects, 4.31 in subjects with history of CVA and 2.67 in vitamin B12 deficiency subjects (Table III).

Table III: Risk factors that influence the development of mild cognitive impairment in the elderly patients.

Variables	Odds ratio, 95% confidence interval
Diabetes mellitus**	5.28 (3.33 - 8.35)
Hypertension**	4.31 (2.67 - 6.97)
Ischaemic heart disease**	4.64 (2.52 - 8.55)
Cerebrovascular accident**	4.31 (2.39 - 7.78)
Hypothyroidism**	4.46 (2.67 - 7.43)
Renal disease**	5.26 (2.42 - 11.40)
Vitamin B12 deficiency**	2.67 (1.45 - 4.91)

***Highly significant.*

Discussion

Several modifiable risk factors for MCI and dementia have been reported, and a proper search for these risk profiles in the elderly is the need of the hour. Although not all MCIs progress to frank dementia; identification of risk profiles aid in early prognosis and in the formulation and modulation of prevention strategies in the elderly population.

The overall prevalence (32%) of MCI among the elderly in our study was quite similar to the prevalence reported in the community-based study by Mohan *et al*[9] (26.6%). We found advancing age to be an independent risk factor for developing MCI. Hussin *et al*[10], also revealed in their study that the MCI group was significantly older (69.2 ± 5.9 years vs. 68.1 ± 5.8 years; $P < 0.05$) than the group without MCI. Most subjects identified with MCI in this study also had history of DM, hypertension, cerebrovascular accident, ischaemic heart disease, renal disease and hypothyroidism. This is in agreement with previous studies[11,12] that identified DM and stroke to be the significant risk factors in the development of MCI. Another study revealed cerebrovascular and cardiovascular risk factors were involved in developing MCI[13]. A retrospective study reported that low vitamin B12 levels did not affect the cognitive functions[14]. Similarly, in this study, vitamin B12 deficiency was only seen in 15.6% of the subjects with MCI, which might be due to coincidence.

It has been reported that cardiovascular risk factors such as mean SBP, cholesterol, triglycerides, HbA1c, serum creatinine, random blood glucose, thyroid-stimulating hormone are the mediating progressors of cognitive impairment in the elderly population[15]. Although the pathogenesis involved is unclear, it is hypothesized that the haemodynamic phenomenon that is disrupted in the presence of cardiovascular risk factors via diverse pathways causes cerebral hypoperfusion and affects the cognitive status in the elderly population[16]. Similarly, in this study, the MCI group reported more comorbid conditions compared to the normal cognition group. The observations in this study were corroborated well with other studies[17-22].

A community-based cohort study conducted among elderly subjects, including Blacks and Whites, reported that change in body mass index significantly declined the cognition, especially episodic and semantic memory, irrespective of the race[17]. A study conducted among non-insulin dependent type 2 diabetic subjects showed that the reduction in HbA1c levels was associated with better cognitive functions in elderly subjects[18]. Contrarily, other studies[19,20] showed no significant correlation between HbA1c and cognitive impairment among diabetics. Similar to our study, a population-based study reported that elevated SBP significantly influences progression to MCI[21]. In contrast, a population-based longitudinal study revealed that elevated diastolic blood pressure independently influences the cognitive function.

A population-based study from Chicago (USA) showed that impaired kidney function rapidly declined the cognitive function in the elderly[22]. A population-based cohort study conducted among women in Denmark reported that cognitive impairment was higher in elderly women who were physically inactive, with high cholesterol levels and with history of depression[23]. A population-based cohort study from Minnesota (USA) reported that neither clinical nor subclinical hypothyroidism was associated with MCI[24]. A large prospective community-based cohort study showed that among elderly subjects, anaemia could accelerate the risk of developing dementia[25]. A community-dwelling study in the older population revealed that lowered extracellular sodium levels contribute to cognitive decline via brain senescence, caused due to the release of oxidative stress markers[26].

This study suggests that the probability of developing MCI in elderly patients is significantly higher among subjects with DM, hypertension, IHD, hypothyroidism, renal disease, vitamin B12 deficiency and with history of CVA. A study by Mohan *et al*[9] in Kerala (India) found that history of lack of balance while walking (adjusted OR: 2.75; CI: 1.46 - 5.17), depression (adjusted OR: 2.17; CI: 1.21 - 3.89), anxiety (adjusted OR: 2.22; CI: 1.21 - 4.05) and alcohol consumption

(adjusted OR: 1.99; CI: 1.02 - 3.86) were significant factors that lead to development of MCI. A community-based study by Su *et al*[27] revealed advancing age, education status, absence of religious attendance and history of stroke to be significant predictors of MCI in older individuals.

In this study, non-genetic risk profiles among elderly subjects revealed that risk factors were similar for both MCI and dementia. It is desirable to ascertain the risk factors in the elderly to possibly prevent high-risk progression of MCI to dementia. Since this is a cross-sectional study limited to risk profile, follow-up of subjects for rectification of correctable risk factors was not performed, therefore prognostication was not possible. All subjects in our study were graduates and may not represent the worldwide population, hence the findings cannot be generalised. Therefore, the study should be replicated in diverse cohorts to validate our findings.

Conclusion

Overall, the study emphasizes that 32% of the elders had MCI. Since MCI is known to convert into full-fledged dementia, it is pertinent to evaluate the elderly for MCI, even though they may be asymptomatic, since risk factors that are reversible can be halted by treatment with appropriate strategies. This constitutes an important preventive strategy against the advancement to dementia, which creates both a physical and an economic burden.

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