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Factors Associated with Mild Cognitive Impairment among Elderly Patients Attending Medical Clinics in Universiti Kebangsaan Malaysia Medical Centre

(Faktor-Faktor yang Berkaitan dengan Kecelaan Kognitif Ringan di Kalangan Pesakit Warga Tua yang Menghadiri Klinik-Klinik Perubatan di Pusat Perubatan Universiti Kebangsaan Malaysia)

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ABSTRACT

Mild cognitive impairment (MCI) is a common condition among the elderly and is believed to be a precursor to Alzheimer disease. This study aims to detect the prevalence of MCI and factors associated with it. A cross-sectional study was conducted on a group of elderly patients attending various medical clinics in Universiti Kebangsaan Malaysia Medical Centre (UKMMC) in 2010. Only patients aged 60 years and above, literate with no hearing or visual impairments were included. Screening instruments included the Mini Mental State Examination (MMSE) and a questionnaire on sociodemographic and clinical data. The cut-off points for MMSE for MCI was 21/30 to 28/30. The prevalence rate based on MMSE score for 'normal' and MCI were 35.3% and 64.7%, respectively. Most of the 346 patients (33.9%) had only one type of medical illness and on one type of medication. MCI was significantly associated with low educational achievement ($p<0.05$) and rheumatological diseases ($p= 0.05$). However, it is not associated with the number of medical illnesses suffered by patients and the number of medications prescribed. This study highlighted that MCI was a common condition among the elderly UKMMC Medical clinic attendees and was significantly associated with their low education level.

Keywords : Elderly; impairment; mild cognitive MCI; medical illness; MMSE

ABSTRAK

Kecelaan kognitif ringan (MCI) adalah satu keadaan yang sering terdapat di kalangan warga tua dan dipercayai adalah tanda awal penyakit Alzheimer. Kajian ini bertujuan untuk mengesan prevalen MCI dan faktor-faktor yang berkaitan dengannya. Satu kajian menggunakan kaedah keratan rentas telah dikendalikan di kalangan sekumpulan pesakit luar warga tua di klinik perubatan di Pusat Perubatan Universiti Kebangsaan Malaysia (PPUKM). Hanya pesakit yang berumur 60 tahun ke atas yang tiada penyakit Demensia, boleh membaca dan tiada kecacatan pendengaran serta penglihatan dimasukkan dalam kajian ini. Alat saringan terdiri daripada Mini Mental State Examination (MMSE) dan soal-selidik yang mengandungi data sosio-demografi dan data klinikal. Titik keratan untuk MCI menggunakan MMSE adalah 21/30 hingga 28/30. Kadar prevalen untuk gejala kognitif yang 'normal' dan MCI adalah masing-masing 35.3% dan 64.7%. Kebanyakan daripada 346 (33.9%) pesakit mempunyai hanya sejenis penyakit dan mengambil hanya sejenis ubatan. MCI dikaitkan secara signifikan dengan tahap pelajaran yang rendah ($p<0.05$) dan penyakit rheumatik ($p= 0.05$). Walau bagaimanapun, MCI tiada kaitan dengan bilangan penyakit dan bilangan ubatan yang diambil oleh pesakit. Kajian ini menunjukkan bahawa MCI adalah satu keadaan yang sering terdapat di kalangan warga tua pesakit luar klinik perubatan UKM dan ianya berkait secara signifikan dengan tahap pelajaran mereka yang rendah.

Kata kunci: Kecelaruan kognitif ringan; MCI; MMSE; penyakit perubatan; warga tua

INTRODUCTION

Cognitive impairment covers a wide variety of impaired brain functions in memory, judgement, language and attention. Cognition, like other bodily functions, decreases as a result of aging. However, cognitive changes as a result of diseases would usually affect social, functional or occupational abilities (Woodford & George 2007). Episodic memory, such as recall of experiences and events usually begins to decline in early adulthood. Immediate memory, ability to think and selective attention span also decline during the usual course of aging. However, knowledge and language abilities are preserved until late in life (Kester et al. 2002).

There were several terms to describe the intermediate stage between normal ageing and dementia. Benign senescence forgetfulness was used to describe memory impairment as a variant of normal ageing (Kral 1962). However, more recent data have challenged this concept which advocates identifying people with poor memory

and following them up as longitudinal studies have shown that 20-100% of people with memory impairment develop Alzheimer disease (Ritchie & Touchon 2000).

Mild cognitive impairment (MCI) is considered to be the transitional stage between normal aging and Alzheimer disease or the preclinical stage which precedes mild dementia as evidenced by the presence of widespread amyloid plaques and neurofibrillary tangles in the neocortex of those with MCI and mild dementia, but not normal aging (Morris & Price 2001). Various criteria have been used in the definition and diagnosis of MCI in prospective studies. Often MCI is commonly referred to as the amnestic type which requires a subjective complaint of memory loss, impairment on a memory test after correction for age and education, preserved general cognitive functioning, intact activities of daily living, and absence of dementia (Petersen et al. 1999). Another common MCI definition is that of Age-Associated Memory Impairment (AAMI) which requires a subjective complaint of memory impairment, a score on a memory test one standard deviation below the mean performance of healthy young adults, adequate intellectual functioning, absence of dementia or other diseases that may contribute to the memory impairment. This concept describes memory changes in ageing as a manifestation of normal cognition (Crook et al. 1986). Recently, the term, 'age-associated cognitive decline' (AACD) has been proposed by individuals of the International Psychogeriatric Association to refer to multiple cognitive domains presumed to decline in normal ageing (Levy 1994). The term, 'cognitive impairment no dementia' (CIND), has been coined by the Canadian Study of Health and Aging to characterize intermediate cognitive function of insufficient severity to constitute dementia (Graham et al. 1997). This concept has been rather heterogeneous with regard to its inclusion of a variety of types of cognitive dysfunction, but more recently has been refined further to correspond more closely to MCI (Fisk et al. 2003).

Petersen et al. (2004a, 2004b) proposed three different MCI subtypes (Amnestic; Multiple-Domain; and Single Non-Memory Domain MCI) to describe possible subtypes of cognitive impairment and their possible differing etiologies and outcomes. These were later redivided to include two major subgroups (amnestic and nonamnestic MCI), with further subdivisions within each (single- and multiple-domain). MCI has now been recognized as a clinical entity on its own, no more as part of normal ageing. However, there is still no agreement on a single set of criteria for MCI. In general, the concept of MCI refers to "a group of individuals who have some cognitive impairment but of insufficient severity to constitute dementia" (Petersen 2004b). The typical MCI patient is a person with memory impairment beyond what is considered to be normal for age, and other relatively intact cognitive domains.

The exact cause of MCI is unknown but it is believed to be a heterogenous condition of numerous causes. Memory impairment may be due to underlying depression, neuroticism, anxiety, fatigue, stress, chronic pain, sleep disorder, substance abuse, adverse effects of medications or serious medical conditions (Ellison 2008). Old age is a known risk factor for development of Alzheimer disease as well as other dementias. Currently, an average Malaysian man is expected to live up to 71 years of age and a Malaysian woman up to 77.1 years of age. Those aged 65 and above comprised of 4.7% of the whole population and this figure is expected to rise up to 13% by 2025 (Rosdinom et al. 2011).

Besides age, cognitive impairment among the elderly has been found to be significantly associated with gender, ethnicity, marital status and levels of education (Sherina et al. 2004). Evidences have shown that persons with MCI are at high risk for dementia, more so in the presence of comorbid medical conditions (Oscar et al. 2007). Infectious diseases such as influenza and pneumonia have been replaced by chronic medical illnesses such as diabetes mellitus, hypertension and heart disease.

This study looks into the prevalence of MCI among local elderly patients with medical illnesses in Universiti Kebangsaan Malaysia Medical Centre (UKMMC) and to determine factors that are associated with MCI. Early detection of MCI is important as prompt treatment can delay the progression of MCI to dementia.

Material and Methods

This descriptive, cross-sectional study was carried out on 357 elderly patients aged 60 and above who were attending the Medical and Nephrology Clinics at UKMMC in March until May 2010. They included 'old' as well as newly-referred patients to the clinics and selection was made by the convenient sampling method. Only patients with MCI, defined as experiencing mild cognitive deficits which were not severe enough to warrant a diagnosis of dementia, and gave consent were included in this study. Patients already diagnosed as having Dementia, based on DSM IV-R, by the neurologists or psychiatrists were excluded from this study. Patients who were detected to have moderate or severe cognitive impairment at the time of screening, as well as those with severe hearing or visual defects were also excluded. Patients who were newly suspected of having dementia were then referred to the memory clinic in UKMMC for further assessment and treatment. The sample size of 357 was calculated based on the formula used to estimate a population proportion with specified absolute precision (Lwanga & Lemeshow 1991). The prevalence of 36.1% for MCI used in the formula was based on an earlier study among elderly patients in a general hospital (Bickel et al. 2006).

There are 2 major medical clinics in UKMMC comprising of different disciplines, which are being run on different days by their respective specialists and medical officers. Medical Clinic 1 consists of Cardiology, Dermatology, Gastroenterology and Respiratory units while Medical Clinic 2 consists of Endocrinology, Neurology, Hematology and Rheumatology units. The Nephrology clinic is opened daily, handling patients with renal diseases and systemic lupus erythematosus (SLE).

Instruments used in this study were the validated English and Malay versions of the Mini Mental State Examination (MMSE) (Folstein et al. 1975) and a sociodemographic data questionnaire. The MMSE has the advantages of being brief, easy to administer and has a high inter-rater reliability. In this study, the severity of cognitive impairment was classified as normal (29-30/30), mild (21-28) and moderate/severe (<20/30) (Chenders 2009). MCI is defined as impairment in delayed recall of verbal material, non-verbal material, or both, with a total score of 21-28/30 on the MMSE.

The sociodemographic questionnaire collected data on age, gender, race, marital status, educational level, occupational status and living arrangement. Clinical data on the types of illness and number of medications received by patients were also included in this questionnaire. These data were obtained from the patients and wherever possible, verified by the clinic notes. The study data were analyzed using the Statistical Package for Social Sciences (SPSS) version 17. This study had been approved by the UKMMC Ethical Committee (UKM 1.5.3.5/224/FF-326-2009).

RESULTS

Three hundred and forty six (346) subjects out of the 357 selected fulfilled the inclusion and exclusion criteria for

TABLE 1. Sociodemographic data of patients (N=346)

		N	(%)
Age (years)	60 – 64	111	(32.1)
	65 – 69	113	(32.7)
	70 – 74	78	(22.5)
	75 – 79	30	(8.7)
	80 – 84	12	(3.5)
	85 – 89	2	(0.6)
Gender	Male	177	(51.2)
	Female	169	(48.8)
Race	Malay	186	(53.8)
	Chinese	142	(41.0)
	Indian	12	(3.5)
	Others	6	(1.7)
Marital Status	Married	339	(98.0)
	Single	7	(2.0)
Educational Level	Never go to school	32	(9.2)
	Primary school	127	(36.7)
	Secondary school	146	(42.2)
	College & University	41	(11.8)
Occupational Status	Employed	29	(8.4)
	Retired / Unemployed	317	(91.6)
Living Arrangement	Living alone	17	(4.9)
	Living with family members	329	(95.1)

TABLE 2. Clinical data and MMSE scores of patients

		N	(%)
Number of medical illnesses	1	120	(34.7)
	2	99	(28.6)
	3	93	(26.9)
	4	19	(5.5)
	5	10	(2.9)
	6	5	(1.4)
Number of medications	0	16	(4.6)
	1	106	(30.6)
	2	83	(24.0)
	3	57	(16.5)
	4	29	(8.4)
	5	21	(6.1)
	6	18	(5.2)
	More than 7	16	(4.6)
Type of diseases	Cardiovascular	215	(62.1)
	Endocrinology	204	(57.1)
	Rheumatology	51	(14.3)
	Nephrology	46	(13.3)
	Gastroenterology	39	(11.3)
	Neurology	24	(6.9)
	Respiratory	23	(6.6)
	Dermatology	10	(2.9)
	Hematology	2	(0.6)
MMSE scores	29 – 30	112	(34.2)
	21 – 28	224	(64.7)
	≤20	11	(3.1)

TABLE 3. Socio-demographical data with MCI

		MMSE		Statistical Result	
		≥ 21/30, ≤28/30 (MCI)	≥29/30 (Normal)	X^2 value	P value
		N (%)	N (%)		
**Age	60 – 69	142 (41.0)	82 (23.7)	0.505	0.497
	70 – 79	71 (20.5)	37 (10.7)		
	80 - 89	11 (3.2)	3 (0.9)		
Gender	Male	115 (33.2)	62 (17.4)	0.009	0.926
	Female	109 (31.5)	60 (16.8)		
**Race	Malay	125 (36.1)	61(17.6)	1.070	0.301
	Non-Malay	99 (28.6)	61 (17.6)		
**Educational Level	Low Education	123 (35.5)	36 (10.4)	20.521	0.000
	High Education	101 (29.2)	86 (24.9)		
Marital Status	Married	220 (63.6)	119 (34.4)		0.701*
	Single	4 (1.2)	3 (0.9)		
Occupational Status	Employed	16 (4.6)	13 (3.8)	1.269	0.260
	Retired / Unemployed	208 (60.1)	109 (31.5)		
Living Arrangement	Living alone	9 (2.6)	8 (2.3)	1.090	0.269
	Living with family members	215 (62.1)	114 (32.9)		

Note: Chi-Square tests were used except for those with * (Fisher Exact test).

Test was significant at $p < 0.05$.

**Age, race and educational level were collapsed into two categories

the study. The remaining 11 had MMSE scores of 20/30 and below, suggestive of probable moderately severe dementia. Their age ranged between 60 and 87 years (67.9 ±5.8 years). Majority of them were within the age group of 65 to 69 years old (32.3%), male (51.2%), Malays (52.8%) and still married (98.0%). Most of them were already retired or unemployed (91.6%), and had at least a secondary school level of education (42.2%). Almost 95% of the respondents were living with family members (spouses or children) at the time of study (Table1).

The number of medical illnesses ranged from 1 to 6 different types of illnesses (2.18 ±1.14). Most of the respondents had only 1 illness (34.7%) and the number of illnesses was inversely proportional with the percentage of patients. The number of medications that each patient took ranged from 0 to 10 types (2.62 ±1.98) but majority of respondents (30.6%) were prescribed only 1 type of medication. Medical illnesses were grouped according to their respective clinics. Majority of the respondents were diagnosed with cardiovascular (62.1%) and endocrinological (57.1%) disorders (Table 2).

The data was analysed using the Chi-square and Fisher Exact tests for categorical variables. Table 3 shows that the only significant relationship among the sociodemographic factors was between MCI and educational level ($p<0.05$). Patients with low educational achievement had a high likelihood of having MCI and those with a higher level of education were more likely to be 'normal'. The number of medical illnesses and number of medications prescribed did not show any significant relationship with MCI (Table 4). The categories or types of medical illnesses among patients also did not show any significant association with MCI, except for rheumatological diseases ($p=0.043$) (Fig. 1).

DISCUSSION

In this study, the prevalence of MCI among the elderly medically ill patients was 64.7 %. The only factor significantly associated with MCI was the elderly patients' level of education. Results showed significant association ($p<0.05$) between lower level of education and MCI which was consistent with previous studies which showed that low level of education tended to be associated with higher prevalence of cognitive impairment. It is believed that intellectual activities can be protective against cognitive impairment (Chenderes et al. 2009) and that lifetime intellectual enrichment has the ability of lessening the effect of brain disease on cognition, withstanding more severe neuropathology before the emergence of MCI or dementia (Krister et al. 2009).

It is known that increasing age leads to declining cognitive functions (Salthouse 2006). However, in this

TABLE 4. Number of medical illnesses and number of medications with MCI

		MMSE		Statistical Result	
		≥21/30, ≤28/30 (MCI)	≥29/30 (Normal)	X^2 value	*p* value
		N (%)	N (%)		
Number of Medical Illnesses	≤1	78 (22.5)	42 (12.1)	0.005	0.941
	> 1	146 (42.2)	80 (23.1)		
Number of Medications	≤ 1	78 (22.5)	44 (12.7)	0.054	0.815
	> 1	146 (42.2)	78 (22.5)		

Note: Chi-square tests were used. The test was significant at $p< 0.05$.

study on elderly clinic attendees, age was not significantly associated with MCI (p=0.477). This could be due to the fact that almost 2/3 (64.8%) of them were in the relatively 'young' age group of 60-69 years old and were still healthy with relatively intact cognitive functions. MCI was also not significantly associated with their gender and marital status. Both genders had equal chances of becoming mildly impaired in their cognitive functioning (p=0.926). A study by Krister et al. (2009) showed that marital status was one of the factors that could affect cognitive functions in the elderly. A person who was living with a partner was less likely to have cognitive impairment as compared to others, which implied that certain social and cognitive challenges in the relationship might help to reduce the occurrence of cognitive impairment. However in this study, marital status was not a significant factor and it did not really affect the outcome of MCI, probably because almost all of the respondents were still married.

The level of education was one of the factors that could influence the impairment of cognitive functions. Results of this study showed significant association (p<0.05) between lower level of education and MCI which was consistent with previous studies which showed that low level of education was associated with higher prevalence of having more severe cognitive impairment (Norlinah et al. 2009). There seemed to be no significant association (p=0.260) between occupational status and cognitive impairment, despite some studies revealing that employment has effect on cognition. A study on persons with schizophrenia showed that those with more severe positive and negative symptoms and unemployed had almost all domains of their cognitive functioning affected (Mc Gurk & Mueser 2003). The insignificant findings may be due to the fact that retired or unemployed elderly patients, despite having some forms of medical illness, were still actively involved in leisure or social activities, for example, reading or playing *Mahjong* which entails high cognitive effort that helps to stimulate mental capacity. A study has shown that regular leisure activity entailing high cognitive effort or social interaction is associated with better cognitive ability (Singh-Manoux et al. 2003). Unfotunately, patients' previous types of occupation and leisure activities or hobbies which could be related to their premobid cognitive functioning were not explored in this study.

This study revealed that there was no significant association (p=0.269) between living arrangement and cognitive impairment. Although a study had suggested that the psychological well-being of older people living in hostels was better than that of older people living alone, the psychological well-being of older people living with their family was no different from that of older people living alone (Ng et al. 2006). The insignificant association found in this study could be explained by the better accessibility to social services nowadays despite them living by themselves and their own personal preference against staying with their children.

Results showed that there was no significant association between races (p=0.301) and MCI despite there were more Malays than non-Malays having MCI. This finding was in accordance with that of a study done among the Chinese and Malay elderly population in Singapore which reported that the prevalence of dementia among the Malays (4.7%) was higher than the Chinese (2.3%) (Kua 1993). Most of them had medical illnesses such as hypertension, hyperlipidemia and diabetes mellitus which might contribute to neuropathological cerebral changes. One study showed that as high as 60% of dementia cases in Malaysia were reported to have such chronic illnesses (Ng & Tan 2006).

This study revealed that there was no significant association (p=0.941) between the number of medical illness and MCI. A study by Feil et al. (2003), showed no significant interactions between cognitive impairment and each chronic medical illness on the mortality rate. This might be due to the fact that most respondents had strong awareness towards their health and were compliant with their medications. Among the various chronic medical diseases, only rheumatological diseases revealed

a significant association ($p<0.05$) with MCI (Figure 1). An autoimmune response may be the most likely explanation for this finding. It is likely that the central nervous system is preferentially targeted by antibodies of the rheumatological disorders which may lead to cognitive impairment. In SLE, it has been proven that antiphospholipid (aPL) antibodies played a role in the development of cognitive dysfunction (Harrison et al. 2006). The common use of steroidal agents in the treatment of rheumatological diseases could also affect cognitive functions directly or indirectly.

Polypharmacy is often associated with side effects, drug-drug interactions and poor compliance among patients. However, there was no significant association ($p=0.815$) between the number of medications prescribed to patients and MCI in this study.

The strength of this study is in the favourable sample size of 346 patients and equal distribution of male and female respondents for comparison, as well as the fair distribution of elderly respondents from different ethnic groups. However, there were also a few limitations in this study. Patients were selected through convenient sampling method and then assessed for MCI even though they had no subjective complaints of memory problem. This over inclusiveness could have contributed to the high prevalence of MCI in this sample. Ideally, only patients with complaints of memory impairment should be screened for MCI and recruited into this study. By definition, amnestic MCI is a condition that lies between normal aging and dementia. Patients can be relatively normal but may show deficits in their memory (Peterson et al. 1999). For others, there may be deficits in their motor performances (Kluger et al. 2008).

Another limitation was that the number of patients was not equally distributed in the different medical clinics and there was difficulty in categorizing patients according to the different types of diseases and types of medications prescribed. For example, a patient with thyrotoxicosis seen at the Endocrine clinic could also be suffering from hypertension and ischemic heart disease. Many patients had multiple medical illnesses which required different clinic follow-ups and some patients were on various types of treatment at any one time, including renal dialysis. There were also patients who were ill-informed or unsure of their current condition or diagnosis due to either lack of information given by their doctors or some were still awaiting confirmatory results of their blood or radiological tests. The wide heterogeneity in diagnoses, number and types of medication as well as severity of illness are confounding factors which could have inevitably affected the outcome of this study.

There is no clear-cut definition of mild cognitive impairment when using the MMSE as different cut-off points have been adopted in many studies. Probably, a more narrow cut-off points of 25 or 26 on the MMSE instead of 21 might be able to detect MCI more accurately. A better screening instrument with high specificity and sensitivity, such as the Montreal Cognitive Assessment (MOCA) (Naseriddine et al. 2005) should have been validated and used in this study. In a validation study of Montreal Cognitive Assessment (MoCA) for detection of MCI and dementia, using a cut-off point of 26 on the MMSE as comparison, MoCA had a sensitivity of 83% to detect MCI as compared to 17% by MMSE (Tasha et al. 2007). There is still lack of validated screening instruments for the detection of MCI and dementia among our local population. It is hoped that a more methodologically sound prospective study be conducted among the population of Malaysia in the near future to determine the prevalence of MCI in the community and its conversion rate to early dementia.

The findings in these UKMMC patients are also not reflective of MCI among the elderly in the community as this study was conducted among the medically ill elderly in an urban, tertiary level teaching hospital. Nevertheless, despite its various limitations, this study is optimistic in triggering more future research on MCI or dementia in the country.

Conclusion

The prevalence of MCI among elderly medical outpatients in UKMMC is high. However, it was not significantly associated with the numbers of illnesses of the patients nor the medications prescribed. There was a significant association between patients' level of education with MCI whereby patients and lower educational level tend to have a higher risk of getting MCI. In addition, there was also a significant association between rheumatological diseases and MCI, in which they have a higher likelihood of getting MCI as compared to other medical conditions.

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