ORIGINAL ARTICLE

Risk Factors Related to Mild Cognitive Impairment among Pre-Aging

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Background: Mild cognitive impairment (MCI) is a condition that represents a transitional stage between normal brain function and dementia. Prevalence of MCI increases in aging. Understanding the risk factors related to MCI in pre-aging people is essential for guiding the allocation of health resources and the development of relevant strategies for prevention.

Objective: To investigate the risk factors related to MCI among pre-aging.

Materials and Methods: In cross-sectional research, the 340 samples were a population aged 50 to 59 years with both cognitive impairment and normal cognition in Phitsanulok Province, using the multi-stage sampling method for selection. Questionnaires collected data and analyzed using binary logistic regression with a statistical significance 0.05.

Results: The results showed five risk factors affected the occurrence of MCI in the pre-aging with type 2 diabetes mellitus having the highest risk (adjusted OR 90.45, 95% CI 14.225 to 57.517), followed by hypertension (adj. OR 56.73, 95% CI 15.765 to 204.175), family history of dementia (adj. OR 36.36, 95% CI 3.742 to 353.422), dyslipidemia (adj. OR 13.73, 95% CI 3.443 to 54.764), and body mass index over 25 (adj. OR 4.12, 95% CI 1.204 to 14.132), respectively. These five factors predicted the incidence of MCI at 91.2% with statistical significance level of 0.05.

Conclusion: Occurrence of mild dementia in the pre-aging is predicted based on these five risk factors, type 2 diabetes, high blood pressure, family history of dementia, dyslipidemia, and body mass index over 25.

Keywords: Pre-aging; Logistic regression; Mild cognitive impairment; Predictive research; Risk factor

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Mild cognitive impairment (MCI) represents a transitional stage between normal brain function and dementia. Individuals with MCI may experience cognitive difficulties in various domains such as memory, decision-making, planning, visuospatial function, language use, concentration, and awareness of their surroundings[1], along with being evident in these cognitive function impairments during testing. However, these impairments do not typically result in significant loss of work or social functioning as seen in individuals with dementia. Compared to their peers of the same age and educational level, individuals with MCI tend to exhibit greater cognitive deficits[2,3]. Importantly, people diagnosed with MCI face a higher risk of progressing to dementia within five years[4]. They are three to five times more likely to develop dementia than the individuals without MCI[5,6], who have an estimated 5% to 16% risk of dementia per person per year[7], as opposed to the 16% to 44% chance for the general population[8,9]. Moreover, individuals with MCI have a mortality rate 2.17 times higher than the general population[10]. If left unaddressed and developed dementia, the burden of care costs becomes significantly higher than caring for individuals with other chronic diseases[11,12]. Therefore, it is crucial to implement preventive measures that target modifiable risk factors and provide timely assistance during the pre-dementia stage. The most effective approach is to intervene during the preclinical, prodromal, or MCI stages[13]. These include education initiatives, research studies, and innovation focusing on reduction of the incidence of dementia, especially in low- and middle-income countries[14]. Investing in such measures is worthwhile and aligns with the needs of these countries, where the burden of dementia is highest[14].

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The worldwide prevalence of MCI has been determined to be 15.56%[15]. In Thailand, the prevalence of MCI varies across different areas, ranging from 16.7%[16] to 47.1%[17], primarily among the elderly population. In the pre-elderly, the 50 to 59 years old, the prevalence of MCI was found to be 30.8%[18], indicating a high number of affected individuals. Additionally, in 2022, Thailand had the highest proportion of pre-elderly age group compared to other age groups in the country. This group represented 14.8% of the total population[19].

Therefore, it is essential to study the risk factors related to MCI during pre-aging. To use the present research results to plan for the prevention of MCI in the aging period in the future.

Materials and Methods

The Human Research Ethics Committee of Naresuan University approved the present research (IRB number P3-0116/2564).

Study design

The present predictive research aimed to investigate risk factors affecting MCI in pre-aging, the aged 50 to 59 years old group.

Participants (sample size)

Study population and setting

The present study population comprised 100,363 people aged 50 to 59 years in three districts and nine sub-districts of Phitsanulok Province. The sample size was determined with a ratio of 1:20. The present study included 20 observational variables. Initially, the total sample consisted of 400 individuals. However, data collection was affected due to the COVID-19 outbreak, resulting in only 340 individuals being included. This represented 85% of the original sample. The researchers evaluated the results using the Montreal Cognitive Assessment (MoCA) test[20], whereby a total test score greater than or equal to 25 indicated the normal group and a score below 25 indicated the MCI group. To select samples from both groups, the researchers employed a multi-stage random sampling method.

The inclusion criteria were being aged between 50 and 59 years, living in the three sub-district areas in Phitsanulok Province, and willing to participate in the program voluntarily and provide written consent. The exclusion criteria were acute illness while answering the questionnaire and withdrawing from the research before completing the questionnaire.

Research instrument

The instruments for data collection were the MoCA Thai version 01 updated August 2011 developed by Ziad Nasreddine and translated into Thai by Solapath Hemaranroj[20], and a questionnaire for risk factors affecting MCI in pre-elderly developed by the researchers.

This questionnaire's content validity was checked by five experts, a geriatrician specializing in dementia, a family physician, a nurse specializing in dementia, and two nurse instructors specializing in dementia and geriatric research. This questionnaire had IOC values between 0.6 to 1.0., and Cronbach's alpha value of 0.8.

The questionnaire for risk factors affecting MCI in pre-elderly were divided into three parts as follows, part 1) personal factors including gender, marital status, education level, and occupation, part 2) Illness factors for 11 items with 0 for no and 1 for yes, and part 3) five health behavior factors for 16 items, in which response options for this part were divided into four levels, utilizing a rating scale with 0 for not practiced, 1 for rarely practiced, 2 for sometimes practiced, and 3 for routine practice. The MCI condition is an outcome variable (Y).

Data collection

Data was collected at health clinics located near the residences of the participants in the target area. The researchers introduced themselves and provided a comprehensive explanation of the study's objectives, procedures, and duration of data collection. The participants were informed about the research and allowed to make an informed decision before signing the consent form. Cognition was assessed using the MoCA scale, which allowed for the classification of participants into normal and MCI groups.

The data was collected between September 2021 and January 2023. The researcher provided a face mask to prevent COVID-19 for participants.

Data analysis

The researchers analyzed the data obtained from the questionnaire with a statistical package. The general characteristics of the sample were described using descriptive statistics, including frequency, percentage, mean, standard, minimum, and maximum values. The risk factors for MCI were analyzed using binary logistic regression analysis [IBM SPSS Statistics, version 26.0 (IBM Corp., Armonk, NY, USA)]. The statistical significance was set at 0.05.

Table 1. Number and percentage of subjects with a medical history

Medical history		Number	Percent
1	Having a family member with dementia	15	4.4
2	Having high blood pressure >130/85 mmHg or receiving antihypertensives	162	47.5
3	Having a cerebrovascular disease (hemorrhage, ischemic, transient ischemic attack)	10	2.9
4	Having had a serious brain accident	2	0.6
5	Having heart disease	12	3.5
6	Having type 2 diabetes (not insulin dependent)	134	39.3
7	Having hearing impairment	21	6.2
8	Having obstructive sleep apnea (indicated by snoring and the need to wake up to breathe while sleeping, as reported by people in their surroundings)	46	13.5
9	Having depression or receiving antidepressants	6	1.8
10	Having body mass index (BMI) over 25 [BMI is calculated from body weight (kg)/height (m^2)]	165	48.4
11	Having hyperlipidemia or receiving hypolipidemic agents	199	58.4

Table 2. Factors affecting mild cognitive impairment among pre-aging analyzed by binary logistic regression (n=340)

Variable	R	Wald	Crude OR	95% CI for OR		p-value	Adjusted OR	95% CI for OR		p-value
				Lower	Upper			Lower	Upper	
Having type 2 diabetes (reference: not having type 2 diabetes)	4.505	22.782	223.277	53.230	936.539	<0.001*	90.45	14.225	575.178	<0.001*
Having high blood pressure >130/85 mmHg or receiving an antihypertensive drug (reference: hypertension >130/85)	4.038	38.202	14.038	59.467	339.465	<0.001*	56.73	15.765	204.175	<0.001*
Having a family member with dementia (reference: no family history of dementia)	3.594	9.594	6.745	1.509	30.156	<0.001*	36.36	3.742	353.422	0.002*
Having dyslipidemia or receiving hypolipidemic agents (reference: no dyslipidemia or receiving hypolipidemic agents)	2.620	13.774	56.102	27.801	113.213	<0.001*	13.73	3.443	54.764	<0.001*
Having body mass index (BMI) over 25 (reference: BMI <25)	1.583	5.087	13.398	7.944	22.595	0.009*	4.12	1.204	14.132	0.024*
Constant	5.199, Pseudo R^2=0.912, p<0.005*									

CI=confidence interval; OR=odds ratio

* p<0.05, statistical significance

Results

Demographic data

In the present study, the majority of the samples were female, accounting for 79.8% of the total participants, followed by males at 20.2%. The age distribution showed that the late pre-elderly group, aged 55 to 59 years, had the highest representation at 51%, followed by the early pre-elderly group at 49%. The mean age of the sample was 54.7 years (SD 2.7), with the youngest participant being 50 and the oldest being 59 years old. Regarding education, the highest proportion of participants, at 79.8%, had completed secondary school, followed by 20.5% completed elementary school. A small percentage, or 2.6%, had obtained a diploma or an equivalent qualification. The majority of participants were married, accounting for 67.7%, followed by single individuals 18.2%, while separated individuals accounted for 1.2%. The most common occupation among the sample group was in the labor sector, 24.9%, followed by trade or personal business at 22.6%, and the least common occupation was government employment, at 4.1% (Table 1).

From Table 2, the results show five risk factors affecting the occurrence of MCI in the pre-aging. They were type 2 diabetes mellitus with the highest risk (adjusted odds ratio [OR] 90.45, 95% confidence interval [CI] 14.225 to 57.517), followed by hypertension (adj. OR 56.73, 95% CI 15.765 to 204.175), family history of dementia (adj. OR 36.36, 95% CI 3.742 to 353.422), dyslipidemia (adj. OR 13.73, 95% CI 3.443 to 54.764), and body mass index (BMI) over 25 (adj. OR 4.12, 95% CI 1.204 to 14.132), respectively. Those five factors predicted the occurrence of MCI at 91.2% at the statistical significance level of 0.05.

Discussion

The researchers discussed the research results

based on the risk of the variables as follows:

1. Individuals with type 2 diabetes faced a 90.45-fold higher risk of developing MCI in the pre-aging age group compared to the normal group. Specifically, had a greater likelihood of experiencing cognitive impairment compared to those without the condition. It is consistent with the previous study[21] which also demonstrated a 2.8-fold. The exact mechanism through which diabetes, particularly type 2, increases the risk of MCI is still unknown. However, the MCI is associated with hyperglycemia, deficiencies in insulin pathways, oxidative stress, neuroinflammation, and mitochondrial dysfunction[22]. The higher values found in the present study may be attributed to the presence of other co-morbid conditions in the sample, as well as the diminution in sample size caused by the COVID-19 outbreak.

2. Having high blood pressure, greater than 130 over 85 mmHg, or receiving antihypertensives was associated with a 56.73-fold higher risk of developing MCI in the pre- aging group compared to the normal group. Hypertension results in cerebrovascular structural and functional alterations, disruption in the renin-angiotensin system's function, inflammation, and oxidative stress. Such hypertension-induced alterations may compromise brain health by predisposing the brain to white matter damage and cerebral small vessel disease, brain atrophy, cerebral macro- and micro-bleeds, brain ischemia or hypoxia, and deposition of pathologic proteins in the brain. All of the aforementioned brain lesions have been shown to negatively affect cognitive function[23]. In line with the research conducted in China, hypertension was found to be a significant risk factor for MCI (OR 1.62, 95% CI 1.34 to 2.35, $p<0.001$), and MCI is more common in individuals with hypertension. Additionally, in less developed regions, hypertension stands alone as a risk factor for MCI[24]. The higher values found in the present study compared to the previous studies may be attributed to the presence of other co-morbid conditions in the sample, as well as the reduction in sample size caused by the COVID-19 outbreak.

3. Individuals with a family history of dementia were found to have a 36.36-fold higher risk of developing MCI in the pre-elderly age group compared to the normal group. This is consistent with the previous study that a person with a family history of dementia (RR 3.228)[25]. APOE and rs101644112 are associated with MCI (OR 1.323)[26] as well as the presence of cortical thickness and left hemisphere hippocampus regions associated with similar to those found in Alzheimer's[27]. The higher values found in the present study may be attributed to the presence of other co-morbid conditions in the sample, as well as the diminution in sample size caused by the COVID-19 outbreak. Blood tests should be studied to find genetic material related to dementia, as well as information about the family history of dementia in the future.

4. Having dyslipidemia or receiving hypo-lipidemic agents is associated with a 13.73-fold higher risk of cognitive impairment in the pre-aging group compared to the normal group. Research has shown that having high levels of cholesterol in midlife can increase the likelihood of developing MCI (the effect size 2.01, 95% CI of 1.19 to 2.84). Conversely, having high-density lipoprotein levels was found to be associated with a lower incidence of MCI (the effect size was 0.39, 95% CI of 0.22 to 0.70)[28]. The present study showed a higher risk of MCI among participants compared to the previous studies in the elderly population. This may be due to co-existing medical conditions and smaller study sizes caused by the COVID-19 outbreak.

5. Individuals with BMI over 25 (adj. OR 4.12) face a 5-fold higher risk of developing MCI in the pre-aging group compared to the normal group. According to the present research, there is a correlation between BMI and an increased incidence of MCI in older adults (adj. OR 2.08, 95% CI 1.26 to 3.44), women (adj. OR 2.06, 95% C 1.35 to 3.12), and older adults (adj. OR 3.20, 95% CI 1.34 to 7.45). Among older women, this effect was still statistically significant (adj. OR 3.38, 95% CI 1.69 to 6.73). Compared to the normal BMI group, older men in the increased BMI group had a greater risk of MCI (adj. OR 2.32, 95% CI 1.17 to 4.61)[29].

Limitation

The present research was conducted during the COVID-19 pandemic. As a result, the number of volunteers willing to participate was less than the calculated sample number affecting the 95% CI value.

Conclusion

The agency responsible for monitoring the health status of the population should closely and continuously monitor the performance of the brain in the pre-elderly population, particularly considering the risk factors affecting MCI across all five variables. It is important to develop and implement preventive policies addressing the presence of these risk factors, starting from early adulthood, to achieve maximum

effectiveness in preventing MCI, which can lead to dementia.

What is already known on this topic?

MCI population has a higher risk of dementia than normal people. MCI is between normal brain and dementia. There is no complete cognitive assessment tool that can assess all components of cognition.

What does this study add?

There are risk factors for cognitive impairment among pre-aging. Each risk factor can predict the likelihood of MCI. Pre-aging populations should be monitored for MCI as well as older adults.

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Conflicts of interest

The authors declare no conflict of interest.

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