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Original Article

Incidence and Risk Factors of Subjective Memory Complaints in Women in Central Bogor City, Indonesia

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ABSTRACT

Background/Purpose: Subjective Memory Complaints (SMC) is one of the earliest symptoms that can develop into dementia. Women have a higher risk of dementia than men. The purpose of this study was to investigate the incidence and risk factors of SMC in women.

Methods: A prospective cohort study design conducted in 2,668 women over 25 years old in Central Bogor City, Indonesia (2 years follow up between 2014-2017). Data was collected through interviews, physical examination, and blood tests.

Results: In this study, the mean age was 47.4±9.7 years and the incidence rate within 2 years of observation was 377 per 1000 women. Multivariate analysis showed older age (OR=1.47; 95% CI: 1.07-2.03), coronary heart disease (OR=1.55; 95% CI: 1.09-2.21), presence of migraine (OR=1.58; 95% CI: 1.22-2.06), as a risk factor for SMC.

Conclusion: SMC incidence rate within 2 years of observation was 377 per 1,000 women population in Central Bogor City. Age, presence of migraines and coronary heart disease were risk factors for subjective memory complaints in women.

1. INTRODUCTION

A elderly life expectancy in Indonesia grows to 69 years in men and 73 years in women by 2016,[1] it is estimated that degenerative diseases, such as cognitive impairment and dementia, will increase. Subjective Memory Complaints (SMC) are known to predict the occurrence of dementia.[2-4] Several studies have shown an increased risk of developing Alzheimer's dementia (AD) among individuals with SMC.[5,6] Longitudinal studies over an 8 year period suggest that the presence of SMC at the onset of AD predicts a faster decline in episodic memory tests (immediate and delayed verbal memory skills).[7] This suggests the role of SMC may affect the decline of other cognitive domains.

Several studies exploring the relationship between gender and cognition have implied that women are more likely to experience cognitive decline than

men.[8,9] Women not only have a higher risk of AD than men of the same age,[10-13] but also a faster decline in line with increased age and greater cognitive impairment than men.[14-16] This is supported by a study by *Lin KA, et al.* which showed that women had faster progressivity than men on a cognitive assessment scale.[17] In the other findings, studies by *Pradono J and Müller-Gerards, et al.* showed that the proportion of women with SMC was higher than men.[18,19] In their study, *Müller-Gerards, et al.* found that men have a lower level of amyloid deposits than women, however, women were found to have superior verbal learning skills.[19] A study by *Wang, et al.* stated that the role of gender towards cognition only occurs in specific cognitive domains.[20] Physical abilities affect how men perceive themselves in memory self-assessments; men with greater physical health tend to overestimate their memory whereas women with poor health and depression tend to underestimate their recall abilities.[21]

Women over 65 years of age with SMC are known to have a heightened risk of cognitive impairments compared to women without SMC, and the risk of impairment increases with age.[22] Prospective studies have shown that SMC in women increases the rate of MCIs after 5 years.[19] Consequently, this study aims to investigate the risk factors for SMC in women.

2. METHODS

A prospective cohort study was conducted by the Center for Research and Development of Public Health Efforts, Ministry of Health Republic of Indonesia in 2014-2015 in Central Bogor City. The subjects of the study were women who did not have SMC and mental disorders on baseline data from 2014-2015 (2,668 subjects). Subjects were followed up in two years.

Subjects were categorized as having SMC based on interviews through the question "Are you considered forgetful by others (family, friends, etc)?". Mental disorders were identified using the Self-Reporting Questionnaire (SRQ-20).[23] Data collection was done through interviews, measurements, and blood laboratory tests. Data included sociodemographic information (age, marital status, education, and occupation), behavioral risk factors such as smoking habits, sodium intake, hormonal contraceptive and hormone replacement use, and vascular risk factors comprising of history of heart disease, hypertension, diabetes, coronary heart disease, obesity and central obesity. Blood laboratory tests were performed to asses fasting plasma glucose, two-hour postprandial glucose, and lipid profiles of the subjects.[24-31] Analysis was done using the SPSS 16 program. Logistic regression was carried out to determine risk factors associated with SMC by controlling other variables. Logistic regression analysis was performed by observing the dependent variable (SMC) among study participants after a two-year interval.

This study was approved by the Health Research Ethics Committee, the Health Research and Development Agency of the Ministry of Health of the Republic of Indonesia (Number : LB.02.015/5.2/KE.143/2014). Informed consent after thorough explanation was sought from all prospective subjects in writing and signed before interviews, measurements and examinations.

3. RESULTS

The incidence rate of SMC in two years observation was 377 cases (14.1%) per 1,000 women in Central Bogor City, with a mean age of 47.4±9.7 years. More than half of the subjects had a mid-level education (47.6%), were overweight (59.9%), suffered from central obesity (74.2%), high LDL levels (82.1%) and high total cholesterol (54.3%). Nearly two-thirds of respondents used hormonal contraceptives (72%) and a small proportion (2.5%) used hormone replacement (Table 1).

Bivariate analysis of new SMC cases among women within the two-year monitoring period portrayed significant covariates; the women were found to be older, of low educational status, unemployed, divorced, and being paid less than minimum wage (p <0.05). Behavioral and biological factors associated with SMC were moderate physical activity, hormonal contraceptive use, and hypertriglyceridemia. Moreover, hypertension, coronary heart disease, stroke, and migraine are morbidity risks that were also found to affect SMC (Table1). Adjusting for age and education, the risk factors of SMC in women during 2 years of monitoring were found to be migraine and coronary heart disease (Table 2).

4. DISCUSSION

Our findings show that increasing age is associated with a high incidence of SMC, this is consistent with some studies.[32-34] Concurrent with our findings, Holmen et al. found that a majority of memory complaints increased with age, along with cases that occurred in the younger population. Around 30% of women aged 30-49 stated that they "sometimes had problems remember dates, names, plans, days ago", and more than 50% of women experience those difficulties above the age of 60.[35]

Rickenbach, et al. conducted a study to compare the predictors of objective performance with greater perceived decline, they found that younger participants were more likely to rate their memory as worse compared to others their age. The finding that age positively predicted self-rated memory indicates that older adults, more so than younger adults,

Table 1. Demographic characteristics, health status and risk behavior of SMC in women.

Variables	n total (%)	SCC			
		Yes (%)	No (%)	*p*	OR (95% CI)
Age					
≥60 years	316 (11.8)	63 (19.9)	253 (80.1)	0.002	1.616 (1.197-2.183)
<60 years	2,352 (88.2)	314 (13.4)	2,038 (86.6)		
Education					
Low	376 (14.1)	67 (17.8)	309 (82.2)	0.001	
Medium	1,270 (47.6)	197 (15.5)	1,073 (84.5)		1.180 (1.153-1.692)
High	1,022 (38.3)	113 (11.1)	909 (88.9)		1.744 (1.256-2.423)
Marital status					
Not married	79 (3.0)	6 (7.6)	73 (92.4)	0.049	
Married	2,283 (85.6)	317 (13.9)	1,966 (86.1)		0.384 (0.159-0.927)
Divorce	306 (11.5)	54 (17.6)	252 (82.4)		0.752 (0.548-1.033)
Working status					
Not working	865 (32.4)	91 (10.5)	774 (89.5)	0.000	
House wife/retirment	1,148 (43.0)	169 (14.7)	979 (85.3)		0.541 (0.402-0.726)
Work	655 (24.6)	117 (17.9)	538 (82.1)		0.794 (0.613-1.028)
Economic status					
≥minimum wage	89 (3.9)	8 (9.0)	81 (91.0)	0.051	0.488 (0.234-1.017)
<minimum wage	2,191 (96.1)	369 (16.8)	1,822 (83.2)		
Smoking					
Heavy smokers	20 (0.8)	5 (25.0)	15 (75.0)	0.343	
Light smokers	88 (3.3)	11 (12.5)	77 (87.5)		2.333 (0.733-5.614)
Not smoker	2,536 (95.9)	358 (14.1)	2,178 (85.9)		2.028 (0.733-5.614)
Overweight					
Yes	1,345 (59.9)	220 (16.4)	1,125 (83.6)	0.697	0.956 (0.763-1.199)
No	901 (40.1)	153 (17.0)	748 (83.0)		
Central obesity					
Yes	1,654 (74.2)	274 (16.6)	1,380 (83.4)	0.980	1.003 (0.777-1.295)
No	575 (25.8)	95 (16.5)	480 (83.5)		
Hormonal contraceptive					
Yes	1,634 (72.0)	284 (16.3)	1,455 (83.7)	0.054	1.300 (0.995- 1.697)
No	635 (28.0)	93 (10.0)	836 (90.0)		
Hormone replacement					
Yes	57 (2.5)	12 (21.1)	45 (78.9)	0.583	1.375 (0.409-1.653)
No	2,197 (97.5)	357 (16.2)	1,840 (83.8)		
Intake salt					
≥2,000 mg	886 (33.2)	87 (14.1)	531 (85.9)	0.081	1.223 (0 975-1.534)
<2,000 mg	1,782 (66.8)	290 (17.5)	1,371 (82.5)		
Total cholesterol					
High	1,449 (54.3)	211 (17.3)	1,010 (82.7)	0.339	1.115 (0.892-1.396)
Normal	1,219 (45.7)	162 (15.8)	865 (84.2)		
HDL					
Low	870 (32.6)	125 (17.1)	607 (82.9)	0.668	1.053 (0.832-1.333)
Normal	1,789 (67.4)	248 (16.4)	1,268 (83.6)		
LDL					
High	2,190 (82.1)	304 (16.5)	1,541(83.5)	0.753	0.955 (0.717-1.272)
Normal	478 (17.9)	69 (17.1)	334 (82.9)		
Triglyceride					
High	507 (19.0)	84 (19.7)	342 (80.3)	0.054	1.303 (0.995-1.706)
Normal	2,161 (81.0)	289 (15.9)	1,533 (84.1)		

Table 1. Demographic characteristics, health status and risk behavior of SMC in women (continued.)

Variables	n total (%)	SCC			
		Yes (%)	No (%)	*p*	OR (95% CI)
Fasting glucose plasma					
High	406 (15.2)	67 (16.5)	339 (83.5)	0.136	1.244 (0.933-1.660)
Normal	2,262 (84.8)	310 (13.7)	1,952 (86.3)		
Blood sugar after 2 hrs					
High	223 (8.4)	35 (15.7)	188 (84.3)	0.484	1.145 (0.784-1.671)
Normal	2,445 (91.6)	342 (14.0)	2,103 (86.0)		
Hypertension					
Yes	1,940 (72.7)	257 (13.2)	1,683 (86.8)	0.033	0.777 (0.613-1.028)
No	728 (27.3)	120 (16.5)	608 (83.5)		
Coronary heart disease					
Yes	229 (8.6)	47 (23.9)	150 (76.1)	0.004	1.664 (1.175-2.358)
No	2,439 (91.4)	330 (15.8)	1,753 (84.2)		
Diabetes					
Yes	328 (12.3)	59 (15.6)	318 (84.4)	0.378	1.145 (0.847-1.549)
No	2,340 (87.7)	317 (13.9)	1,957 (86.1)		
Stroke					
Yes	75 (97.2)	16 (25.4)	47 (74.6)	0.055	1.750 (0.982-3.121)
No	2,593 (97.2)	361(16.3)	1,856 (83.7)		
Migraine					
Yes	504 (18.9)	95 (22.1)	335 (77.9)	0.001	1.577 (1.215-2.046)
No	2,164 (81.1)	282 (13.1)	1,882 (86.9)		

Table 2. The predictors of incidence of SMC in women during 2 years of monitoring.

Variables	B	*p*	Odds Ratio Adjusted	95% CI	
				Lower	Upper
Age	0.388	0.017	1.474	1.072	2.025
Education		0.018			
	-0.076	0.635	0.927	0.678	1.267
	-0.403	0.020	0.668	0.476	0.939
Coronary Heart disease	0.438	0.016	1.549	1.085	2.213
Migraine	0.460	0.001	1.584	1.217	2.061

assume their memory is better than that of their age-matched peers. Studies conducted by *Jessen F, et al.* found that 30 percent of the elderly with no objective cognitive disorder and with no disorder in their daily activities claimed that they had "difficulties in recent memory and the difficulties in remembering where the goods were stored."[21]

Age is often associated with the presence of cognitive performance disorder.[36] In subpopulations of women over 65 years with SMC, the risk of cognitive impairments increases by 3 fold in 18 years and continues to increase alongside aging and duration of follow-up.[22] On the contrary, a study performed by Schultz among middle-aged adults concluded that no association was found between age and SMC.[37]

The findings of our study suggest that migraines are a risk factor for SMC. This is supported by several previous studies that have reported the occurrence of migraines among patients with SMC.[38,39] In a study by *Gil-Gouveia, et al.* comprising of 165 migraine patients, 89.7% described cognitive symptoms during the headache phase of a migraine attack. On average, 2-3 symptoms were reported per patient uninfluenced by demographic or disease-related variables. The most commonly occurring spontaneous symptoms were related to executive functions such as poor ability to concentrate (37%), difficulty in reasoning (25%), and thinking (23%).[40] Cognitive performance decreases during migraine attacks, especially in regards to speed of reading and processing, verbal memory, executive function, calculation, orientation and learning, hence bolstering patients' subjective complaints.[40,41] Findings regarding migraine and cognitive impairment are often inconsistent. In a study by *Martins, et al.*, migraine subjects reportedly performed worse in a test regarding attention compared to controls, whereas non-migraine subjects presented with more intrusions and worse discriminability in memory recognition along with lower performance on semantic memory tests.[42] Conversely, another study reported that migraineurs attained higher mean MMSE scores and global cognition compared to non-migraineurs. This difference was particularly marked for migraineurs with auras. Migraineurs performed better on tests

of executive function and fine motor skills amongst specific cognitive domains. The difference in MMSE scores between migraineurs and non-migraineurs was greater in women than in men, whereas the difference in global cognition was similar among both genders.[43]

In accordance with our findings, a study has reported weakening of cognitive performance during migraine attacks wherein the cognitive dysfunction experienced is related to the duration and frequency of a migraine attack.[41] A study by *Karen, et al.* resulted in similar findings in which patients with chronic migraine were found to have cognitive deficits in multiple tasks, regardless of the presence of comorbidities or the use of medications. Continuation of migraines was found to be the only relevant factor affecting poorer performance in the Montreal Cognitive Assessment, Verbal Fluency, Clock Drawing and Stroop tests.[44] A study by *Lee, et al.* stated that migraineurs with Subjective Cognitive Decline (SCD) reported higher headache pain intensity and headache impact as well as greater prevalence of anxiety, depression, reduced quality of sleep, and shorter sleep duration during weekdays compared to migraineurs without SCD.[45]

Results from our study illustrate the presence of a relationship between coronary heart disease (CHD) with incidences of SMC. Several studies have found correlations between CHD and SMC after coronary artery bypass grafting (CABG). *Salnes, et al.* reported that the frequency of self-reported memory symptoms 3 and 12 months after baseline is significantly higher among CABG patients than control patients with comparable risk factors for coronary and cerebrovascular disease, The frequency of self-reported changes in memory, personality, and reading at 3 months was significantly higher among CABG patients than among nonsurgical controls.[46] Another study reported that at early (3-month or 1-year) follow-up, subjective memory complaints were reported more often by the CABG than the nonsurgical group (45.5% vs. 17.0%, p <0.0001).[47]

Several studies have shown that the relationship between CHD and cognitive impairment remains unclear and have resulted in conflicting outcomes. A study by *Jackson TI, et al.* showed a significant association between cognitive impairment complaints with CHD events and some other vascular risk factors.[48] Supported by a prospective cohort study of a meta-analysis showing a 45% increased risk of dementia, cognitive impairment was associated with the incidence of CHD.[49] Yet several other studies have shown no significant association between CHD events with dementia and other cognitive impairments.[50-52] Similarly, our study did not find a relationship between SMC and other vascular conditions such as hypertension, diabetes, stroke, central obesity, overweight, and lipid profile abnormalities. Other studies have supported our findings. A study by *Jorm, et al.* likewise reported that that diabetes, heart troubles and a history of strokes were not associated with memory complaints.[53] *Stewart R, et al.* also found that subjective memory impairments (SMI) could not be explained by vascular diseases/risks such as hypertension, cholesterol, and triglyceride levels.[54]

Our study did not find a relationship between sodium intake, marital status, smoking habits, and hormone use with regards to SMC. A study by *Rush, et al.* found that lower sodium intake was associated with poorer performance on Trails B and MMSE, and after controlling individual characteristics, the associations did not differ by sex.[55] However, results from our study differ from a study conducted by *Maki, et al.* wherein they reported some evidence for a beneficial effect of estrogen alone on verbal memory in younger naturally post-menopausal women and more consistent evidence from small-n studies of surgically post-menopausal women.[56] A study by *Chen, et al.* found that the interaction between physical activity and smoking was associated with the risk of SMC; among respondents who exercised more, smokers were 1.8 times more likely to have SMI than non-smokers but among those who exercised less, smoking did not have a significant association with SMI.[57] Our study showed no relation between SMC and marital status. Conversely, a meta-analysis study involving 15 studies with a total of 812,047 subjects showed that the risk of dementia was higher in subjects with single-life status (RR=1.42; CI: 1.07-1.90) and subjects with divorce status (RR=1.20; CI: 1.02-1.41) when compared to subjects with marital status. On the other hand, no relationship between divorce (life) with the incidence of dementia was found.[58]

The limitation of this study is the absence of further cognitive examination on subjects with SMC. Furthermore, this study does not account for the duration of illness and history of surgeries for medical conditions that may cause an increased risk of SMC. In the conclusion, in a population of women, the incidence rate of SMC within 2 years of observation is 377 per 1,000. Older age, history of migraine and coronary heart disease are risk factors for subjective memory complaints.

CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this paper.

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