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Original Research

Association Between Components of Metabolic Syndrome and Cognitive Impairment among Middle-Aged and Elderly in Indonesia: A Nationwide Survey

HUBUNGAN ANTARA KOMPONEN SINDROM METABOLIK DAN GANGGUAN KOGNITIF PADA USIA PARUH BAYA DAN LANSIA DI INDONESIA: SURVEI SECARA NASIONAL

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Abstract: *Cognitive impairment is common among population worldwide which become an increasingly important health issue related with aging. Indonesia is one of low-middle income countries with reach the era of aging, as the population aged 60 years and over is 10.0% in 2020.The purpose of this study was to investigate associations between components of metabolic syndrome (MetS) and cognitive impairment among middle-aged and elderly Indonesians. Cognitively impaired was measured with the questionnaire derived from the instrument of telephone interview for cognitive status (TICS). Analysis of covariance was used to examine the differences and multivariate with logistic regression analysis of the odds of cognitive impairment. Setting on this study was using The Indonesia Family Life Survey (IFLS)-5 conducted in 2014-2015 with 1532 participants were placed into middle-aged and elderly. This study found that central obesity and dyslipidemia were less likely to have cognitive impairment among middle-aged and elderly. (OR adjusted for age and sex 0.67; 95% CI 0.37~1.20; p=0.175). In conclucion, central obesity and dyslipidemia were less likely to have cognitive impairment among middle-aged and elderly in Indonesia. Our findings suggest that middle-aged people should manage their waist circumference in order to prevent cognitive impairment as they age.*

Keywords: *metabolic syndrome, obesity, cognitive impairment, Indonesia, IFLS-5*

1. INTRODUCTION

Central obesity is one of components of metabolic syndrome (MetS) and a potential risk for cardiovascular diseases (CVDs). Over the past few decades, the prevalence of obesity has increased worldwide. Based on the National Health Survey of Indonesia (*Riskesdas*) data, obesity had reached 21.8% in that country (1). As one-third of adults are already overweight or obese, Indonesia is facing a healthcare challenge. The nutritional transformation theory suggests that economic growth, urbanization, and globalization contribute to increased intake of processed food and decreased physical activity, leading to higher prevalences of being overweight and suffering from non-communicable diseases (2).

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Indonesia is the fourth most populous country in the world with around 267 million individuals, and has the largest developed economy in Southeast Asia (3). The processes of urbanization and industrialization are developing rapidly, and these have contributed to changes in the infrastructure in Indonesia. More than half of the population now lives in urban areas, and urbanization is increasing at a rate of 2.3% every year. Economic development and urbanization are related to lifestyles, diets, and physical activities (PAs) (4,5). A previous study showed that the higher of prevalence obesity in Indonesia was due to increased consumption of meat and milk (6). Previous evidence from Indonesia and the Southeast Asian region showed that consumption of processed foods was significantly associated with consumption of meat, milk, and 'Western foods' among adults (7). Second, economic development and urbanization have also reduced PA levels and caused people to adopt more-sedentary lifestyles (8). Data on people with mild cognitive impairment (MCI) in Indonesia are still limited. In addition, no study has documented associations of central obesity with cognitive impairment in Indonesia.

Waist circumference (WC) is considered to be more precise than the body-mass index (BMI) and the most discriminating metabolic condition for the purpose of determining the likelihood of obesity-related comorbidities (9,10). The population of the elderly in the world in 2015 had reached 900.9 million and is expected to increase by more than 60% by 2030 to 1402.4 million (11). An elderly person is someone who has reached the age of 60 years and over, based on Law Indonesia number 13 of 1998 that is concerned with elderly welfare. Indonesia is among five countries with the largest population of elderly people in the world. Based on statistics from the 2015 Inter-Census Population Survey (SUPAS), the number of elderly is 21.7 million or 8.5%. Moreover, 11.6 million (52.8%) were women and 10.2 million (47.2%) were men (12). This indicates that Indonesia is one of the countries that will reach the era of ageing, when the population aged ≥60 years exceeds 7.0%. Changes in various systems in the body occur as a person gets older, and may include physical, psychological, and spiritual changes. One result of changes that occur in the elderly is cognitive impairment.

Based on the National Health Survey of Indonesia in 2018 (13), the most prevalent diseases in the elderly are degenerative diseases, including hypertension, diabetes mellitus, heart disease, stroke, and other infectious diseases such as upper respiratory tract infections, diarrhea, and pneumonia. There is an increasing trend of people living with dementia due to enhanced numbers of cases with non-communicable diseases. Therefore, the aim of this study was to investigate associations between components of MetS and cognitive impairment among middle-aged and elderly Indonesians using data from the Indonesia Family Life Survey (IFLS)-5.

2. METHODS

2.1. *Study Design and Study Population*

This cross-sectional study was conducted in 2014 and 2015 using data from the IFLS. In short, the IFLS was conducted by the RAND Corporation in collaboration with Lembaga Demografi, University of Indonesia (Jakarta, Indonesia), University of California, Los Angeles (UCLA; Los Angeles, CA, USA), and the Center for Population and Policy Studies, University of Gadjah Mada (Yogyakarta, Indonesia). The institutional review board (IRB) processed an adequate and precise review of using the IFLS data with registration number s0064-06-01-

CR01, following IRB guidelines, and the study was approved by the RAND Corporation, the Indonesian Institute, and in particular, the Survey Meter Institute, which was given the task of working on the IFLS-5 study (14).
The total number of respondents in the IFLS dataset with cognitive data was 12,288 people aged from 0 to >80 years. Furthermore, complete data were collected relating to MetS components included anthropometric characteristics, and sociodemographic characteristics. Exclusion criteria were participants who had been diagnosed with cancer or a disability, or who were pregnant, to minimize the possibility of sampling bias. This study utilized a cohort of 1532 participants.

2.2. Components of MetS

This study used integrated IDF and AHA/NHLBI criteria to determine categories of MetS components (15), including (1) central obesity defined as a WC of ≥90 cm for men and ≥80 cm for women using Asian cutoff values; (2) hypertension as defined as systolic blood pressure (SBP) of ≥130 mmHg or diastolic blood pressure (DBP) of ≥85 mmHg; (3) diabetes treatment used as a substitute for insulin resistance (IR) due to a lack of data on fasting plasma glucose levels; and (4) cholesterol treatment used as a substitute for low high-density lipoprotein-cholesterol (HDL-C).

2.3. Cognitive Functioning

The assessment of cognitive function was based on items derived from the instrument Telephone Interview for Cognitive Status (TICS). This instrument was administrated by face-to-face interviews with respondents (14,16). Questions on the TICS include (1) the date, day, and year (9 points); (2) counting numbers (5 points); (3) recall of a 10-word list (10 points); (4) recall of a 10-word list (10 points); (5) question block (3 points); (6) counting down backwards (1 point); (7) animals repeated (1 point); and (8) drawing two overlapping pentagons (1 point). The standard score ranged 0∼40 points categorized into no cognitive impairment (24∼≤40 points); MCI (17∼≤23 points); and moderate cognitive impairment (≤17 points) (17).

2.4. Sociodemographics, BMI, PA, and Depression Status

Sociodemographic data were collected using a questionnaire from the IFLS-5 related to gender, age, education, marital status, smoking habits, ethnicity, BMI, physical activity, and depression status. We calculated BMI in kg/m^2 and adopted WHO criteria of BMI with Indonesian cut-off points as those with a BMI of <18.5 kg/m^2 were categorized as being underweight, 18.5∼25.0 kg/m^2 as having a normal weight, 25.1∼27.0 kg/m^2 as being pre-obese, and ≥27.0 kg/m^2 as being obese (18). Smoking habits were summarized into never (never smoked), current smoker (currently smoked), and former smoker (previously smoked but had stopped). Educational levels were categorized into low (<12 years of schooling) and high (≥12 years of schooling).

The depression status was defined using 10 self-reported items derived from the Center for Epidemiological Studies-Depression (CES-D) questionnaire (19,20). Answers to the 10 CES-D questions had four possible responses: “rarely or never” (≤1 day), “some days” (1 or 2 days), “occasionally” (3 or 4 days), and “most of the

time" (5 or 7 days). The score of each scale's answer was from zero ("rarely or never") to four ("most of the time"). We categorized having depressive symptoms as a score of ≥10 from sum of the answers which ranged 0~30 [20]. Categories of physical activity were based on the International Physical Activity Questionnaire (IPAQ) Physical activity short version for the last 7 days (IPAQ-S7S) (21). The scoring protocol was categorized as low, moderate, and high. Two self-reported questions assessed the PA volume as units of the metabolic equivalent of one task-hour per week (MET-h/wk) (22).

2.5. *Statistical Analysis*

IBM SPSS Statistics version 21 (IBM, SPPS, Chicago, IL, USA) was used for all data analyses. Participants were separated into two groups of normal or no cognitive impairment and mild or severe cognitive impairment, categorized as having cognitive impairment. Analysis of differences in categorical variables used a Chi-squared test. Furthermore, a multivariate analysis to measure individual components of MetS by risk factors for cognitive impairment after controlling for covariates used a Binary logistic regression.

3. RESULTS

3.1. *Characteristics of Respondents*

In total, 1532 participants with complete data about their cognitive status and MetS were enrolled in the study. As to age categories included this study, 53.8% of participants were middle-aged and 46.2% were elderly. Table 1 shows the characteristics of respondents stratified into two age groups and cognitive impairment. There were significant differences in the proportions of middle-aged and elderly participants in terms of educational level and BMI with cognitive impairment (p<0.005 by a Chi-squared test).

3.2. *Associations between Components of MetS and Cognitive Impairment among Middle-aged and Elderly Indonesians*

Table 2 shows associations between components of MetS among middle-aged and elderly Indonesians stratified by cognitive impairment. Results show that the prevalence of central obesity was higher in middle-aged than elderly participants. Furthermore, more subjects in the middle-aged group were undergoing cholesterol treatment than in the elderly group. There were significant differences in central obesity, dyslipidemia (cholesterol treatment), and cognitive impairment among middle-aged and elderly Indonesians (p=0.05 by a Chi-squared test).

3.3. *MetS, Five MetS Components, and Odds of Cognitive Impairment*

Participants with central obesity in model 1 and model 2 were associated with cognitive impairment (both p<0.05; Table 4). Dyslipidemia was significantly associated with cognitive impairment in our analyses (odds ratio (OR) 0.47, 95% confidence interval (CI) 0.24-0.92, p=0.028). The presence of MetS was not significantly related to cognitive impairment (OR adjusted for age and sex 0.67; 95% CI 0.37-1.20; p=0.175; Table 5).

Table 1. Characteristics of respondents and cognitive impairment

Variables	All (*N*=1532)				*p**	Middle-aged (*N*=824)				*p**	Elderly (*N*=708)				*p**
	Cognitive impairment (N=1265)		Normal (N=267)			Cognitive impairment (N=659)		Normal (N=165)			Cognitive impairment (N=606)		Normal (N=102)		
	n	%	*n*	%		*n*	%	*n*	%		*n*	%	*n*	%	
Sex															
a. Male	675	83.1	137	16.9	0.542	324	79.4	84	20.6	0.689	351	86.9	53	13.1	0.261
b. Female	590	81.9	130	18.1		335	80.5	81	19.5		255	83.9	49	16.1	
Marital Status															
a. Single or never married	8	80	2	20	0.830	6	85.7	1	14.3	0.703	2	66.7	1	33.3	0.350
b. Married or once married	1257	82.6	265	17.4		653	79.9	164	20.1		604	85.7	101	14.3	
Educational level															
a. Low	1204	84.5	221	15.5	0.000	625	82.5	133	17.5	0.000	579	86.8	88	13.2	0.000
b. High	61	57	46	43		34	51.5	32	48.5		27	65.9	14	34.1	
Ethnicity															
a. Javanese	951	83.4	189	16.6	0.135	477	79.8	121	20.2	0.807	474	87.5	68	12.5	0.011
b. Non-Javanese	314	80.1	78	19.9		182	80.5	44	19.5		132	79.5	34	20.5	
Smoking status															
a. Never	1070	82.9	221	17.1	0.749	566	80.4	138	19.6	0.368	504	85.9	83	14.1	0.514
b. Former	36	80	9	20		15	68.2	7	31.8		21	91.3	2	8.7	
c. Current	159	81.1	37	18.9		78	79.6	20	20.4		81	82.7	17	17.3	
Body-mass index															
a. Underweight	182	87.9	25	12.1	0.001	61	81.3	14	18.7	0.055	121	91.7	11	8.3	0.030
b. Normal	723	83.7	141	16.3		361	81.5	82	18.5		362	86.0	59	14.0	
c. Pre-obese	169	82.4	36	17.6		105	84.0	20	16.0		64	80.0	16	20.0	
d. Obese	191	74.6	65	25.4		132	72.9	49	27.1		59	78.7	16	21.3	
Physical activity															
a. Low	477	82.1	104	17.9	0.892	255	80.4	62	19.6	0.881	222	84.1	42	15.9	0.679
b. Moderate	353	83.3	71	16.7		182	80.5	44	19.5		171	85.9	27	13.6	
c. High	435	82.5	92	17.5		222	79.0	59	21.0		213	86.6	33	13.4	
Depression															
a. No depression	778	82.6	164	17.4	0.981	413	80.5	100	19.5	0.625	365	85.1	64	14.9	0.631
b. Depression	487	82.5	103	17.5		246	79.1	65	20.9		241	86.4	38	13.6	

Table 2. Associations between components of metabolic syndrome (MetS) and cognitive impairment

Component of MetS	All (*N*=1532)				*p**	Middle-aged (*N*=824)				*p**	Elderly (*N*=708)				*p**
	Cognitive impairment (N=1265)		Normal (N=267)			Cognitive impairment (N=659)		Normal (N=165)			Cognitive impairment (N=606)		Normal (N=102)		
	n	%	*n*	%		*n*	%	*n*	%		*n*	%	*n*	%	
Central obesity	566	44.7	140	52.4	0.026	324	49.2	90	54.5	0.251	242	39.9	50	49.0	0.106
High blood pressure	1143	90.4	236	88.4	0.389	592	89.8	144	87.3	0.417	551	90.9	92	90.2	0.960
High glucose	51	4.0	15	5.6	0.320	27	4.1	8	4.8	0.832	24	4.0	7	6.9	0.287
Dyslipidemia	30	2.4	13	4.9	0.041	19	2.9	6	3.6	0.802	11	1.8	7	6.9	0.008

*p, p-value comparison between components of MetS and cognitive function variables with $p<0.05$ level of significance was determined by Chi-squared (χ^2) test.

Table 4. Multivariate logistic regression of components of metabolic syndrome (MetS) associated with cognitive impairment

MetS and components	Total (*N*=1532)				Middle-aged (*N*=824)		Elderly (*N*=708)			
	Model 1§		Model 2[a]		Model 1§		Model 1§		Model 2[b]	
	OR (95% CI)	*p**	OR (95% CI)	*p**	OR (95% CI)	*p**	OR (95% CI)	*p**	OR (95% CI)	*p**
Metabolic syndrome										
Normal MetS	1.00		-	-	1.00	-	1.00	-	-	-
MetS	0.67 (0.37-1.20)	0.175	-	-	0.93 (0.42-2.08)	0.871	0.41 (0.16-1.02)	0.056	-	-
Central Obesity										
Normal	1.00		1.00		1.00		1.00		-	-
Central obesity	0.73 (0.56-0.95)	0.022	0.72 (0.53-0.97)	0.035	0.80 (0.57-1.13)	0.806	0.69 (0.45-1.05)	0.086	-	-
High Blood Pressure										
Normal	1.00		-	-	1.00	-	1.00		-	-
High blood pressure	1.23 (0.81-1.87)	0.331	-	-	1.28 (0.76-2.17)	0.342	1.08 (0.53-2.21)	0.814	-	-
High glucose										
Normal	1.00		-	-	1.00		1.00		-	-
High glucose	0.70 (0.39-1.27)	0.248	-	-	0.83 (0.37-1.88)	0.669	0.56 (0.23-1.33)	0.191	-	-
Dyslipidemia										
Normal	1.00		1.00		1.00		1.00		1.00	
Dyslipidemia	0.47 (0.24-0.92)	0.028	0.48 (0.24-0.94)	0.034	0.78 (0.30-2.00)	0.615	0.25 (0.09-0.66)	0.005	0.29 (0.10-0.83)	0.021

CI, confidence interval; OR, odds ratio. MetS, metabolic syndrome; OR, odd ratio; CI, confident interval.
§: Model unadjusted model (associated each exposure variable with cognitive impairment). [a]: Model adjusted with age, sex, central obesity and dyslipidemia.
[b]: Model adjusted with sex and dyslipidemia. *p, p-value comparison between independent variables (MetS and components) and cognitive impairment with significantly $p<0.05$ using binary logistic regression.

4. DISCUSSION

We found that individual components of MetS including central obesity and dyslipidemia (cholesterol treatment) were independently associated with cognitive impairment among middle-aged and elderly Indonesians. These results differed from those of previous studies (23-26), which reported that elevated triglycerides and high blood pressure were significantly associated with cognitive impairment. In the current study, we demonstrated that cognitive impairment among middle-aged and elderly Indonesians was affected by components of MetS, age, sex, sociodemographic variables.

Prolonged obesity in adults may lead to the development of atherosclerosis during middle age (27). Some researchers suggested that the risk of MetS increases after middle age, because MetS affects the aging process as it progresses, and the risk of MetS increases as well as the risk of CVDs (28,29). Management of MetS in persons of all age groups is required. Because the aging process is accelerated during this middle-aged period, control needs to focus on preventing CVDs and MetS (30). The progression of obesity in middle age predicts the occurrence of moderate cognitive decline at a later age following adjustment for natural cognitive ageing (24,31).

Interestingly, we found that central obesity was less closely associated with cognitive impairment. Otherwise, central obesity was concluded to be a protective factor. This

finding is similar to that of previous studies, particularly for participants who are obese (32-34). Many studies of neurodegeneration found that greater weight or BMI in dementia patients with Alzheimer's disease (AD) was associated with an increased volume of the medial cortex, which is associated with improved cognitive scores (35). The potential mechanisms of the association of being overweight with cognitive impairment are not immediately apparent. Two alternative mechanisms might explain the beneficial impacts of being overweight on cognitive impairment in the elderly. First, leptin is predominantly secreted by adipose tissues and can affect higher cognitive function, then it was shown to enhance learning and memory output in mice by controlling hippocampal synaptic plasticity and amyloid β-processing (36-38). Second, elderly people who are overweight have a lower chance of mortality than those underweight or average-weight individuals. Thus, relative to being of average weight or underweight in later life, being overweight tends to suggest a better health condition. In contrast, a higher BMI in the middle-aged group is associated with cardiovascular and metabolic risk factors related to increased risks of cognitive impairment (39).

Central obesity is a component of MetS, which also includes IR, hyperglycemia, dyslipidemia, and hypertension (40). We found that dyslipidemia or cholesterol treatment was less likely to be associated with cognitive impairment especially in the elderly category. However, another study found that central obesity was not related to cognitive function, because central nervous system alterations related to motor function, metabolism, and fatigue might be affected by frailty (24,41). In addition, there were no significant associations of cognitive impairment and other individual components of MetS, including high blood sugar (diabetes treatment). A previous study also reported a lack of significant associations of cognitive impairment with various individual components, but together they posed a significant negative impact on cognitive function (42). In this study, age might have been a confounder in the associations between components of MetS. Age-related changes in body fat distribution might not be reflected in simple anthropometric measures such body weight and WC (43,44).

In our study, there are several important strengths. First, this is the first report on cognitive impairment among Indonesian population. These results can be early detection to prevent cognitive impairment progress to dementia among middle-aged and elderly Indonesian as changing the modifiable risk factors. Second, we used a large number of participants and our data were nationwide survey, so that these results can be used as a reference because it representative of the Indonesian population. Nevertheless, we have limitations in our study. First, due to a cross-sectional design study may not fully assess the cause-effect relationship cannot be drawn. Second, we measure obesity used waist circumference as a single parameter. Previous study showed that using waist circumference as a single marker is considered poor indicator of cardio metabolic health because obesity in the elderly need adjusted for body composition which consist of body mass (skeletal muscle mass, fat mass, and fat-free mass). In the future, prospective cohort design studies using the IFLS wave 4 (2000) to IFLS wave 5 (2014/2015) are needed.

5. CONCLUSION

In conclusion, our study showed that central obesity and dyslipidemia were positively associated with cognitive impairment among middle-aged and elderly Indonesians Our conclusion is helpful in better identifying Indonesian population those who may

be a higher risk for cognitive impairment and reemphasize the importance of early detection in the middle-aged group to manage the risk factors including components MetS and lifestyle. However, the mechanisms underlying of these results require further investigations in a longitudinal study.

CONFLICTS OF INTEREST

The authors declare that there were no conflicts of interest in this study.

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