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Random blood glucose level as predictor of cognitive impairment in elderly

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ABSTRACT

BACKGROUND
Nutritional deficits have been linked to poor cognitive function and are highly prevalent in the elderly. Several factors associated with cognitive function have been studied, but the results were inconclusive. The objective of this study was to determine the relationship between blood glucose level and cognitive impairment in the elderly.

METHODS
A cross-sectional study was conducted and a total of 109 elderly were included in the study. Research subjects were selected using consecutive non-random sampling from the Tebet sub-district in South Jakarta. Random blood glucose level was assessed using glucose strips (Nesco). Cognitive function was measured with the Montreal Cognitive Assessment (MoCA) and Informant Questionnaire on Cognitive Decline in Elderly (IQCODE) questionnaire. The relationship between blood glucose levels and cognitive function was analyzed by means of multiple linear regression analysis.

RESULTS
The mean age of the elderly was 67.95 ± 6.42 years, length of formal education was 10.12 ± 5.88 years, and mean random blood glucose level was 137.41 ± 70.25 mg/dL. Multiple regression analysis showed that length of formal education (â= 0.769; p=0.000) and random blood glucose levels (â=0.016; p=0.014) were significantly associated with cognitive function.

CONCLUSION
Cognitive function is negatively affected by high blood glucose, thus random blood glucose level can be used to predict cognitive impairment.

Keywords: Random blood glucose level, cognitive impairment, elderly

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Kadar gula darah sewaktu sebagai prediktor gangguan fungsi kognitif pada lanjut usia

ABSTRAK

LATAR BELAKANG
Pada lanjut usia seringkali terjadi defisiensi nutrisi yang dapat mengakibatkan gangguan fungsi kognitif. Prevalensi gangguan fungsi kognitif pada lanjut usia sangat tinggi dan faktor yang dapat mempengaruhi fungsi kognitif adalah multifaktorial. Sejumlah penelitian tentang hubungan antara diabetes dan terjadnya gangguan kognitif pada lanjut usia masih belum konsisten. Penelitian ini bertujuan untuk menentukan adanya hubungan antara kadar gula darah sewaktu dalam darah dan gangguan fungsi kognitif pada lanjut usia.

METODE
Sebuah rancangan penelitian potong silang digunakan dengan mengikut sertakan 109 subjek lanjut usia. Sampel dipilih dengan menggunakan cara consecutive non-random *sampling di wilayah Kecamatan Tebet Jakarta Selatan. Kadar gula darah sewaktu diukur menggunakan alat pengukur gula darah dan strip glukosa (Nesco). Fungsi kognitif diperoleh dengan cara wawancara menggunakan kuesioner* Montreal Cognitive Assessment *(MoCA) dan* Informant Quessioner on Cognitive Decline in Elderly *(IQCODE). Data dianalisis mengunakan uji regresi linear ganda.*

HASIL
Rata-rata umur lansia besarnya 67,95 ± 6,42 tahun, lama pendidikan formal yang dialami besarnya 10,12 ± 5,88 tahun, dan kadar gula darah sewaktu 137,41 ± 70,25 mg/dL. Uji regresi linear ganda menunjukkan variabel yang berhubungan dengan fungsi kognitif adalah lama pendidikan (â=0,769; p=0,000) dan kadar gula darah sewaktu (â=0,016; p=0,014).

KESIMPULAN
Kadar gula darah yang semakin meningkat menurunkan fungsi kognitif pada lanjut usia. Lama pendidikan merupakan faktor yang tidak dapat diubah. Pengaturan kadar gula darah sangat diperlukan untuk mencegah terjadinya penurunan fungsi kognitif pada lanjut usia.

Kata kunci: *Kadar gula darah sewaktu, fungsi kognitif, lanjut usia*

INTRODUCTION

There is no agreement on a definition of old age, as there are too many opinions on what exactly constitutes old age (elderly). The definition of old age (elderly) according to the World Health Organization (WHO) includes middle age (between 45 and 59 years), elderly age (60-74 years), old age (75–90 years), and very old age (above 90 years). The currently accepted definition of old age in Indonesia is framed in the Law No. 13 of the year 1998 on older persons' welfare, stating that an elderly person is an individual aged 60 years and over.(1)

The increasing number of elderly people in Indonesia is unavoidable, concomitantly with the increase in life span. The population of elderly Indonesian persons is projected to increase between the years 1990-2025 by 414%, which is the highest in the world. A number of biological-physical, psychological, and social problems will appear in the elderly as a result of the aging process or degenerative diseases, concomitantly with the advancing age of these individuals.[2] According to the most recent census data from the year 2010, there are in Indonesia 18,037,009 elderly or approximately 7.59% of the total Indonesian population. In the Special Province of Jakarta (DKI Jakarta) there are 495,024 persons older than 60 years, or approximately 5.15% of the total population.[3]

In the elderly there are frequently nutritional deficiencies, particularly of micronutrients, and metabolic disorders (such as hyperlipidemia and type 2 diabetes mellitus), that are frequently associated with cognitive functional disorders that are very prevalent in the elderly.[4] A study showed that the prevalence of diabetes mellitus was 15.8%, and high blood glucose levels decreased quality of life of the elderly.[5] Several factors associated with cognitive function have been studied, among others diabetes mellitus, vascular disease, hypertension, and also individual characteristics and habits.[6,7]

In elderly persons with type 2 diabetes there is an accelerated decline of cognitive function, as has been demonstrated in several large population-based longitudinal studies,[8] but the factors involved have not been fully determined. It has been suggested by some investigators that hypertension may play an essential role,[9] but others have found associations with glycemic control.[10] Recently it was found that up to 80% of Alzheimer patients have type 2 diabetes or impaired fasting glucose.[11] The aim of the present study was to determine the risk factors (diabetes mellitus, hypertension, hyperlipidemia, nutritional status, and individual characteristics) associated with the occurrence of cognitive dysfunction in the elderly.

METHODS

Research design

An observational-analytical study using a cross-sectional design approach was conducted at the Tebet subdistrict, South Jakarta, from September to October 2011.

Study subjects

Elderly persons aged $\geq$60 years, who were cooperative and capable of communication, constituted the subjects of this study. Exclusion criteria were elderly with severe chronic disease (e.g. stroke), and severe disabilities that could prevent them from participating. The subjects were selected by consecutive non-random sampling of patients attending the Primary Health Center (*Puskesmas*) of Tebet subdistrict, South Jakarta.

Data collection

Data on the characteristics of the subjects, comprising age, gender, marital status, number of children, educational level, occupation, income, smoking, alcohol consumption, past history of illness, were collected by means of questionnaire-based interviews.

Laboratory investigations

Capillary blood samples were collected by the finger-prick method from the left third finger for determination of blood glucose and cholesterol concentrations. Cholesterol concentrations, expressed in mg/dL, were determined by means of a total blood cholesterol meter and cholesterol strips (Nesco). Random blood glucose concentrations, also expressed in mg/dL, were determined using a blood glucose meter and glucose strips (Nesco).

Measurements of blood pressure, body weight and height

Systolic and diastolic blood pressures were measured by means of a sphygmomanometer with the subjects seated in front of the examiner and the manchette around the right upper arm, using a Littman stethoscope applied to the cubital region, with the first and fifth Korotkoff sounds denoting systolic and diastolic pressures, respectively. Both systolic and diastolic pressures were expressed in millimeters of mercury (mmHg).

Subjects were weighed without footwear using Tanita weighing scales and weight was expressed in kilograms (kg) to the nearest decimal. Knee height of the subjects was measured with the subjects in the sitting position without footwear, using a wooden knee height meter and was expressed in centimeters (cm) to the nearest decimal. The height of the subjects was obtained from knee height by means of the following mathematical equation. For men: height = 64.65 + 1.87 x knee height (cm); for women: height = 53.80 + 2.10 knee height (cm) – 0.09 x age (years).[12] Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). For Asian populations BMI is categorized as underweight (<18.5 kg/m^2), normal weight (18.5 – 23.0 kg/m^2), overweight (23.0 – 27.5 kg/m^2), and obese ($\geq$27.6 kg/m^2).[13]

Cognitive function

Cognitive function is a person's way of thinking and how a person's intrapsychical functions prepares him or her to react to external reality and is measured by means of the Montreal Cognitive Assesment (MoCA) questionnaire and the Informant Questionnaire on Cognitive Decline in Elderly (IQCODE). The MoCA questionnaire evaluates short term memory (5 points), visuospatial ability (4 points), executive function (4 points), attention, memory, and concentration (6 points), language ability (5 points) and orientation (6 points).[14] The MoCA is a useful screening tool for the detection of mild dementia and mild cognitive impairment. The IQCODE questionnaire consists of 16 everyday life situations where a person has to use memory and intelligence. Each situation is evaluated by the respondents' nearest family members regarding changes in the last 10 years, using the scale of "far better", "somewhat better", "not much changed", "somewhat worse" and "far more worse".[15] Based on the IQCODE instrument, a score between 3.3 and 3.6 is the cuttoff for determining early cognitive impairment. The IQCODE is a reliable informant questionnaire that is unaffected by education or language.[16] MoCA scores range from 1-30, while IQCODE scores are in the range 1.0 – 5.0.

Ethical clearance

Ethical clearance was issued by the Commission on Research Ethics of the Faculty of Medicine, Trisakti University and all subjects were asked to give written informed consent.

Data analysis

The computer software program used for data analysis was the SPSS version 15.0. Data are presented as proportions (%) and mean ± SD. Simple linear regression analysis was used to determine the presence of an association betwen independent variables and cognitive function variables. To determine independent variables with the highest impact on cognitive functions of the elderly, multiple linear regression analysis was used. The level of significance used in this study was 0.05.

RESULTS

A total of 109 subjects participated in this study, consisting of 98 (89.9%) females and 11 (10.1%) males, with a mean age of 67.95 ± 6.42 years. The mean level of education (indicated by length of formal education) was 10.12 ± 5.88 years. Most of the subjects, totalling 60 (56.9%) were widowers/widows. Only 11 (10.1%) of the subjects were smokers, and 2 (1.8%) regularly consumed alcohol. A total of 36 (33.0%) subjects had a history of diabetes mellitus and 54 (49.5%) had hypertension.

Mean random blood glucose level was 137.41 ± 70.25 mg/dL, and mean blood cholesterol level was 68.13 ± 48.69 mg/dL. Mean cognitive function as measured by the MoCA and IQCODE instruments was 19.01 ± 6.21 and 3.69 ± 0.39, respectively. Mean BMI of the participants was 22.84 ± 4.21 kg/m^2 (Table 1).

The results of simple linear regression analysis showed that educational level, random blood glucose level, and BMI were significantly

Table 1. Distribution of several important variables in the elderly (n= 109)

Variables	Mean ± SD
MoCA*	19.01 ± 6.21
IQCODE@	3.69 ± 0.39
Random blood glucose level (mg/dL)	137.41 ± 70.25
Total cholesterol level (mg/dL)	168.13 ± 48.69
Blood pressure (mmHg)	
Systolic	135.18 ± 20.50
Diastolic	82.94 ± 11.81
Body mass index (kg/m^2)	22.84 ± 4.21

*MoCA=Montreal Cognitive Assesment; @IQCODE= Informant Questionnaire on Cognitive Decline in Elderly

associated with cognitive function, with regression coefficient values of 0.703 (95% CI 0.552 – 0.854), -0.044 (95% CI -0.053 – -0.035), -0.019 (95% CI -0.036 – -0.003), 0.001 (95% CI 0.000 – 0.002), 0.421 (95% Confidence Interval 0.150 – 0.693) and -0.026 – -0.009), respectively (Table 2). These three variables with a significant association with cognitive function, were input into a multiple linear regression model.

The level of education of the elderly subjects and random blood glucose level were significantly associated with cognitive function. It is apparent from Table 3 that educational level (Beta = 0.652 for both MoCA and IQCODE) and random blood glucose (Beta = - 0.118 for MoCA and Beta = 0.181 for IQCODE) were of influence for cognitive function. Higher educational level had the greatest positive influence on cognitive function. In contrast, increased random blood glucose level had a lowering effect on cognitive function of the elderly. Low IQCODE and high MoCA scores both signify better cognitive function (Table 3).

Table 2. Simple linear regression between age, educational level, blood glucose level, total cholesterol, blood pressure, body mass index and cognitive function (n=109)

Variables	MoCA@		IQCODE#	
	B*	p	B*	p
Age	-0.182	0.051	0.011	0.050
Educational level	0.795	0.000	-0.050	0.000
Blood glucose level	-0.019	0.021	0.001	0.021
Total cholesterol level	0.010	0.439	0.000	0.436
Systolic blood pressure	-0.055	0.059	0.003	0.058
Diastolic blood pressure	-0.012	0.061	0.001	0.841
Body mass index	0.421	0.003	-0.026	0.003

*B=regression coefficient; @ MoCA=Montreal Cognitive Assesment; # IQCODE=Informant Questionnaire on Cognitive Decline in Elderly

Table 3. Multiple linear regression between educational level, blood glucose level, body mass index, and cognitive function

	MoCA@			IQCODE#		
	B*	Beta**	p	B*	Beta**	p
Educational level	0.769	0.652	0.000	-0.048	-0.652	0.000
Random blood glucose	-0.016	-0.118	0.014	0.001	0.181	0.013
Body mass index	0.036	0.024	0.777	- 0.021	-0.023	0.777

*B=regression coefficient; **Beta=standardized regression coefficient; @MoCA=Montreal Cognitive Assesment; #IQCODE=Informant Questionnaire on Cognitive Decline in Elderly

DISCUSSION

This study involving elderly subjects showed that educational level and random blood glucose level were significantly associated with cognitive function. Of these two variables, it is only the random blood glucose level that may be modified to improve cognitive function of the elderly. Essentially similar results were found in two large population-based data sets in Sweden, using a random sample from the population aged 35–85 years, where an increase in plasma glucose was associated with impairment in episodic memory in women. This could be explained by a negative effect on the hippocampus caused by the raised plasma glucose levels.[17] Glucose increases the risk of atherosclerosis, thereby increasing the risk of vascular dementia. Hyperglycemia is often coupled to other metabolic abnormalities that could be linked to cognitive impairment.[18]

Regarding the well-known sex differences in memory, there are several studies suggesting a major role for glucose levels. According to Awad et al.[19] improving metabolic control in diabetic patients has been reported to improve cognitive function. Differing results were found in the study conducted by Euser et al, indicating that increased blood glucose level was not associated with impaired cognitive function in elderly persons without diabetes.[20] However, the Nurse Health Study reported that increased insulin concentration was associated with decreased cognitive function in nondiabetic female elderly.[21]

These differing study results indicate the need for further studies on the relationship between glucose metabolism and cognitive function in the elderly. There are several biological mechanisms that are possibly involved in the metabolism of amyloid B, such as accumulation of advanced glycation end products and acceleration of cerebrovascular disease.

In addition to vascular pathways, several possible pathophysiologic mechanisms, including hyperglycemia, insulin resistance, oxidative stress, advanced glycation end products, and inflammatory cytokines, may explain the effect of glucose deregulation on dementia risk. Therefore, an increased risk of developing dementia resulting from diabetes can be expected in people with mild cognitive impairment.[22]

The results of our study showed that BMI was not associated with impaired cognitive function in the elderly. A cohort study on subjects aged $\geq$70 years with diabetes also showed that BMI was not associated with impaired cognitive function in the elderly.[16] A population-based cross-sectional study in Singapore among older adults aged 55 and above showed that low BMI by itself was not significantly associated with poor cognitive performance, but low BMI with chronic comorbidity (OR 1.73; 95% CI 1.02–2.95) was independently associated with poor cognitive performance.[23] Results of the relationship between high BMI or obesity and cognitive status are also inconsistent,[24,25] but most studies suggested that low BMI was related to dementia risk.[26,27]

In our study two instruments were used to assess cognitive function in the elderly, namely IQCODE and MoCA, because one study has demonstrated that the use of two instruments is capable of providing better information than the use of one instrument only.[28] The information obtained may increase the accuracy of screening and diagnosis. There are numerous tests that have been studied for their efficacy in assessing individuals for the presence of cognitive impairment. At this time there is no one test that is clearly better than all of the others. There are two test-related criteria that must be considered when evaluating the accuracy of a test, sensitivity and specificity. Variation in the specificity and sensitivity of a test can have a substantial impact on the cost of a screening test.[29]

In spite of the above, our study has several limitations that should be noted. First, we used random blood glucose to measure the blood glucose levels, which might result in an attenuation of the associations. Second, as there are no specific recommended tools to diagnose cognitive dysfunction, the operationalization of the criteria may differ slightly from those in other studies. Third, our study was of cross-sectional design and thus cannot demonstrate the presence of a causal relationship between random blood glucose level and impaired cognitive function in the elderly.

CONCLUSIONS

Elevated blood glucose level is associated with cognitive impairment in older people. Longer duration of education increases the cognitve performance of older people. Our findings underline the importance of regularly monitoring the serum blood glucose levels to reduce the risk of cognitive impairment in the elderly.

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