

## THE INFLUENCE OF VARIOUS RISK FACTORS RELATED TO METABOLIC DISORDERS ON COGNITIVE FUNCTION IN THE ELDERLY GROUP

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### Abstract

Dementia is a condition characterized by significant impairment in at least one domain of cognition, including executive function, complex attention, language, learning, memory, perceptual-motor, or social cognition. Risk factors for vascular dementia include smoking, hyperlipidemia, hypertension, diabetes, atrial fibrillation, obesity, and lack of exercise. This study aims to examine the relationship between metabolic disorders and dementia in the elderly. The design of this research was cross-sectional at the Hana Nursing Home in January 2024, with inclusion criteria in the form of an elderly group of at least 60 years. The independent variables in this study were blood pressure, hemoglobin, hematocrit, body mass index, cholesterol, uric acid, and random blood sugar. The dependent variable in this study includes the Mini-Mental State Examination (MMSE) score. This study included 61 respondents who met the inclusion criteria. The results of the multiple linear regression statistical test (Backward LR) with 6 stages stated that body mass index (p-value: 0.001; B: 0.281) and hematocrit (p-value: 0.011; B: 0.528) played a significant role in decreasing the value MMSE. The conclusion of this study is that body mass index, and hematocrit are related to dementia. This research opens up insight into the importance of controlling body weight and body composition, especially in the elderly group to prevent decline in cognitive function in old age.

**Keywords:** Body Mass Index, Cholesterol, Dementia, Elderly, Hematocrit, MMSE.

### Introduction

Dementia is one of the greatest global health challenges of the 21st century. With increasing life expectancy in the world today, the number of people with dementia continues to increase, especially in low and middle-income countries (63% of all people with dementia).<sup>[1]</sup> According to Alzheimer's Disease International (ADI), around 47 million people had dementia in 2015, with the figure projected to increase to 76 million by 2030 and 135 million by 2050 due to the growing elderly population. There are 7.7 million new cases of dementia every year, or 1 new person every 4.1 seconds. The increase in prevalence of dementia was found to increase most in Asia at 46% every year.<sup>[2]</sup>

Dementia is a chronic neurodegenerative disorder characterized by progressive deterioration of cognitive function that affects daily life or social function. There are different types of dementia, with Alzheimer's disease being the most common, followed by vascular dementia and dementia with Lewy bodies. Mixed dementia with more than one cause may also occur. On the other hand, frontotemporal dementia and other disorders associated with dementia, such as brain injury, infections, and alcohol abuse, are less common.<sup>[1,3-5]</sup>

Dementia affects not only individuals with the condition, who lose their abilities gradually but also family and friends who need to address their needs, such as increased dependency and changes in behavior.<sup>[5]</sup> Despite the high prevalence and costs of dementia, the number of diagnoses of dementia patients and health services and integrated treatment of dementia patients still require improvement, especially in developing countries such as Indonesia. Data from the World Health Organization (WHO) shows that with education and proper management of dementia risk factors, 10-20% of dementia incidents can be prevented.<sup>[2,6]</sup> One of the current risk factors that is thought to play a major role in the occurrence of dementia is metabolic factors. Dementia will cause disturbances in cognition, behavior, and daily functional activities with severe consequences on physical, mental, and psychosocial aspects for the patient, family, and society. However, recognizing dementia cases at an early stage by the public and health workers is still a challenge at present. Besides that, diagnosed cases of dementia often receive inadequate management so that optimal quality of life is not achieved.<sup>[1]</sup> This study aims to identify the relationship between various risk factors such as blood pressure, body mass index, instant blood sugar, cholesterol, uric acid, and hemoglobin on Mini-Mental State Examination (MMSE) scores.

## **Material and Method**

This research design used a cross-sectional design, which was carried out at the Hana Nursing Home in January 2024. The sampling technique used in this research was total sampling. Inclusion criteria in this study included patients aged between 60 and 90 years. The exclusion criteria in this study were patients who were uncooperative and unwilling to be examined, as well as patients who could not read or write.

This research variables include independent variables and dependent variables. The independent variables in this study were body mass index (BMI), systolic and diastolic blood pressure, random blood sugar, total cholesterol levels, uric acid levels, hemoglobin and hematokrit levels. Body mass index values are measured using standard measurement methods using scales and microtoises that have been standardized and validated. Measurement of systolic and diastolic blood pressure values using applicable physical examination standards and validated tools. Temporary blood sugar values, total cholesterol levels, uric acid levels, hemoglobin and hematokrit levels are measured using capillary blood with a measuring instrument in the form of a standardized FORA-6 Plus Multi-Functional Monitoring System GD81.

The dependent variable in this study is cognitive function or dementia, which is measured using the Mini-Mental State Examination (MMSE), which has been validated in Indonesia. The classification of the degree of cognitive impairment from the MMSE questionnaire based on the Neurocognitive Study Group in 2015 is mild impairment if the MMSE is in the range of 21 – 26 points, moderate impairment if the MMSE is in the range of 15 – 20 points, moderately severe impairment if the MMSE is in the range of 10 – 14 points, and serious disturbances if the MMSE is in the range 0 – 9 points.<sup>[1]</sup> The statistical test technique used in this research is the Multiple Linear Regression method (Backward LR Method).

## Results

This study included 61 respondents who met the inclusion criteria with the characteristics of the respondents presented in Table 1

**Table 1. Demographic Characteristics and Disease History of Research Respondents**

Variable	N (%)
Gender	
Man	14 (23%)
Woman	47 (77%)
Education	
No School	5 (8,2%)
Elementary School	7 (11,5%)
Junior High School	8 (13,1%)
Senior High School	26 (42,6%)
Diploma	1 (1,6%)
Bachelor	14 (23,0%)
Wedding	
Not married yet	17 (27,9%)
Marry	39 (63,9%)
Divorced	5 (8,2%)
Disease History	
Diabetes	12 (19,7%)
Heart	8 (13,1%)
Lungs	1 (1,6%)
Strokes	3 (4,9%)
Joint	10 (16,4%)
Indigestion	9 (14,8%)
Hypertension	31 (50,8%)
Kidney	1 (1,6%)
Heart	1 (1,6%)
Asthma	1 (1,6%)
Gout	12 (19,7%)

Further investigation into the modeling of risk factors for hemoglobin, cholesterol, blood pressure, random blood sugar, body mass index, and uric acid on MMSE values was carried out using the Multiple Linear Regression method (Backward LR Method). This statistical test covers 6 stages, with the final result being only body mass index (p-value: 0.001; B: 0.281) and hematocrit (p-value: 0.011; B: 0.528), which significantly play an important role in decreasing the MMSE score. The risk magnitude of each research variable is presented in Table 2.

**Table 2. Influence of Risk Factors Related to Metabolic Disorders on Cognitive Function in the Elderly Group**

	Model	Unstandardized Coefficients		Standardized Coefficients	<i>t</i>	Sig.
		<i>B</i>	<i>Std. Error</i>	<i>Beta</i>		
1	(Constant)	-15.857	10.271		-1.544	.129
	Systolic Blood Pressure	.107	.059	.217	1.830	.073
	Diastolic Blood Pressure	-.094	.077	-.153	-1.220	.228
	Hemoglobin	.060	1.008	.013	.059	.953
	Hematocrit	.487	.400	.265	1.217	.229
	Random Blood Sugar	.035	.036	.111	.977	.333
	Cholesterol	.022	.015	.169	1.436	.157
	Uric Acid	.189	.576	.041	.328	.744
	Body Mass Index	.276	.082	.389	3.382	.001
2	(Constant)	-15.870	10.172		-1.560	.125
	Systolic Blood Pressure	.107	.058	.218	1.851	.070
	Diastolic Blood Pressure	-.094	.077	-.152	-1.230	.224
	Hematocrit	.508	.204	.276	2.492	.016
	Random Blood Sugar	.035	.036	.111	.985	.329
	Cholesterol	.022	.015	.170	1.451	.153
	Uric Acid	.188	.570	.041	.331	.742
	Body Mass Index	.275	.080	.388	3.424	.001
3	(Constant)	-15.627	10.061		-1.553	.126
	Systolic Blood Pressure	.107	.057	.218	1.869	.067
	Diastolic Blood Pressure	-.087	.073	-.141	-1.195	.237
	Hematocrit	.498	.200	.271	2.491	.016
	Random Blood Sugar	.037	.035	.117	1.061	.293
	Cholesterol	.024	.014	.184	1.705	.094
	Body Mass Index	.281	.078	.396	3.590	.001
4	(Constant)	-10.897	9.030		-1.207	.233
	Systolic Blood Pressure	.105	.057	.213	1.826	.073
	Diastolic Blood Pressure	-.102	.072	-.165	-1.419	.162
	Hematocrit	.515	.199	.280	2.582	.013
	Cholesterol	.026	.014	.202	1.892	.064
	Body Mass Index	.269	.077	.379	3.470	.001
5	(Constant)	-13.043	8.983		-1.452	.152
	Systolic Blood Pressure	.074	.054	.151	1.385	.172
	Hematocrit	.495	.201	.269	2.465	.017
	Cholesterol	.024	.014	.187	1.742	.087
	Body Mass Index	.264	.078	.372	3.376	.001
6	(Constant)	-6.049	7.489		-.808	.423
	Hematocrit	.528	.201	.287	2.627	.011
	Cholesterol	.026	.014	.197	1.829	.073
	Body Mass Index	.281	.078	.397	3.625	.001

a. Dependent Variable: Mini-Mental State Examination (MMSE) Results

## Discussion

Dementia is a condition characterized by significant impairment in at least one domain of cognition, including executive function, complex attention, language, learning, memory, perceptual-motor, or social cognition. One of the dementias that most often causes cognitive impairment is vascular dementia.<sup>[7]</sup> Risk factors for vascular dementia include smoking, hyperlipidemia, hypertension, diabetes, atrial fibrillation, obesity, and lack of exercise. Atherosclerosis in large arteries can cause infarction and thromboembolism, usually causing gradual cognitive and functional decline.<sup>[8]</sup>

Hypertension is a major risk factor for damage to target organs, including the brain.<sup>[9,10]</sup> Hypertension causes changes in the structure of cerebral arteries, hypertrophy, and endothelial damage, which will impact the disruption of the blood circulation system in the brain and disrupt cerebrovascular regulation, which causes neuropathological abnormalities such as microinfarctions, microhemorrhages, cerebral infarctions, and brain atrophy, resulting in decreased cognitive function.<sup>[11]</sup> In this study, no significant relationship was found between systolic blood pressure and decreased cognitive function ( $p$ -value  $> 0,05$ ). At the same time, there was no significant relationship between diastolic blood pressure ( $p$ -value  $> 0,05$ ). Sierra et al. found that persons with untreated hypertension have reduced cognition.<sup>[12]</sup> However, a study conducted by Shang et al. in a population in China showed that systolic, diastolic, and mean blood pressure were associated with cognitive decline.<sup>[13]</sup>

Random blood sugar (RBS) is a blood sugar examination carried out at a certain time. The state of hyperglycemia, such as in people living with diabetes, poor glycemic control causes a decrease in blood flow to the brain. As a result, the resulting change in osmotic pressure causes excessive production of reactive oxygen species (ROS). The antioxidant capacity of the brain is found to be low so when ROS production exceeds the antioxidant response capacity, neuronal damage occurs with decreased function. Hyperglycemia also causes vascular damage, which results in the buildup of ROS and proinflammatory cytokines.<sup>[14]</sup> In this study, there was no significant relationship between random blood sugar and the incidence of dementia ( $p$ -value  $> 0,05$ ). This is not in line with research conducted by Smolina et al. that there is a strong relationship between increased blood sugar levels and vascular dementia.<sup>[15]</sup> A study by Chatterjee et al. also showed that increased blood sugar can increase the risk of vascular dementia by 2.5 times.<sup>[16]</sup>

Body Mass Index (BMI) is an anthropometric measurement carried out to determine a person's nutritional status. BMI classification according to WHO based on Asia Pacific is categorized into underweight (BMI  $18.5 \text{ kg/m}^2$ ), Normal (BMI  $18.5 - 22.9 \text{ kg/m}^2$ ), Overweight (BMI  $23 - 24.9 \text{ kg/m}^2$ ), and obesity (BMI  $\geq 25 \text{ kg/m}^2$ ).<sup>[17]</sup> Obesity and Overweight can be defined as excessive accumulation of adipose tissue. This fatty tissue can release immune and metabolic mediators that can cross the blood-brain barrier and cause neuroinflammation, which ultimately triggers neuronal dysfunction. This will cause cognitive impairment and, ultimately, dementia.<sup>[18]</sup> Being overweight and obese, which is characterized by a high BMI, can increase the risk of dementia through vascular disorders, such as atherosclerosis, vascular endothelial dysfunction, vascular stiffness, and blood-brain barrier disorders. In this study, it was found that BMI had a significant relationship with the incidence of dementia ( $p$ -value  $0.001$ ). A study by Garcia et al. also showed that high BMI was significantly associated with the incidence of vascular dementia.<sup>[19]</sup> Research conducted by Zeki et al. also showed similar results that high BMI in early adulthood (aged 20-49 years) and middle adulthood was indirectly related to a higher incidence of dementia.<sup>[20]</sup> According to research conducted by Li et al., a high BMI in middle adulthood (40-49 years) is associated with a higher increased risk of dementia, but not at age  $\geq 70$  years.<sup>[21]</sup> This suggests that low BMI or underweight in old age is a risk factor for dementia and brain atrophy. However, interpretation of the results of this study requires caution because low BMI in the elderly may be due to a decrease in muscle mass, not fat mass, and weight loss may be a preclinical marker for dementia 6-10 years before clinical diagnosis.<sup>[22]</sup> However, according to Wang et al., the sarcopenic obesity group and the obesity group, respectively, increased the risk of cognitive impairment by 2.5

times or 2.1 times. As we age, there is a loss of muscle mass and function, accompanied by excessive fat accumulation, known as sarcopenic obesity.<sup>[23]</sup>

Uric acid is a waste product in the blood that is produced through the process of breaking down (catabolism) of purine compounds. The upper limit for uric acid levels in men is 7 mg/dl, while in women, it is 6 mg/dl. An increase in uric acid levels above normal is called hyperuricemia. Uric acid exerts neuroprotective effects by repairing protein and DNA damage induced by free radicals. In addition, uric acid has been shown to increase the activity of antioxidant enzymes (e.g., superoxide dismutase). The brain is highly susceptible to oxidative stress, and dysfunction of antioxidant properties has been reported to contribute to neurodegenerative diseases. In this study, there was no significant relationship between uric acid and the incidence of dementia (p-value > 0,05). However, a study conducted by Engel et al. showed significant results in reducing the incidence of dementia in adults with hyperuricemia, whether they had been treated with anti-hyperuricemia or not.<sup>[24]</sup> The same research results were also stated by Du et al. that high uric acid levels would reduce the risk of dementia significantly, confirming the hypothesis of the role of uric acid as a neuroprotective.<sup>[25]</sup>

High cholesterol levels in the blood are related to the incidence of dementia because it is a risk factor for vascular disease, forming plaque in the blood vessels (atherosclerosis), which causes cognitive decline through cerebral embolism or hypoperfusion to the brain. Hypercholesterolemia can cause extracellular deposition of amyloid protein (A $\beta$ ), which inhibits the synaptic connections of neurons in the brain and increases the risk of dementia. In this study, there was no significant relationship between cholesterol and the incidence of dementia (p-value > 0,05). A review by Vazquez et al. showed that cholesterol in middle adulthood had a stronger correlation with the risk of dementia later in life than in late adulthood. Research conducted by Iwagami et al. also showed that there was a significant relationship between cholesterol and the incidence of dementia in middle adulthood (<65 years) with a follow-up of >10 years.<sup>[26,27]</sup>

Hemoglobin is a protein in the blood that functions to bind oxygen. Normal hemoglobin levels in men are 14-18 g/dl and in women 12-16 g/dl. Hematocrit measures the volume of red blood cells compared to the total volume of blood (red blood cells and plasma). Normal hematocrit levels in men are 40-54%, and in women are 36-48%. Both hemoglobin and hematocrit are included in whole blood components, so if there is a decrease in these levels, it is categorized as anemia. As is known, the oxygen supply to the brain mainly comes from oxygen carried by red blood cells (RBC). A decrease in the number of RBCs can cause hypoxia, which can promote A $\beta$  production and neurodegeneration in the brain, thereby impacting brain function, including cognitive function.<sup>[28,29]</sup> In this study, there was no significant relationship between hemoglobin levels (p-value 0.144) and hematocrit (p-value 0.033) with dementia. This does not agree with Wolters et al., who found that high or low hemoglobin levels were closely related to an increased risk of dementia.<sup>[30]</sup> According to research conducted by Hong et al., anemia is associated with a 2 times increased risk of dementia within 3 years.<sup>[31]</sup> According to a study conducted by Chen et al., the red blood cell (RBC) count was significantly lower in Alzheimer's disease patients, and patients with mild dementia had higher RBC counts than patients with severe dementia.<sup>[29]</sup> Research by Qiang et al. also stated that the hematocrit percentage is closely related to the risk of dementia.<sup>[32]</sup>

## Conclusion

Dementia is a condition of cognitive decline in the elderly caused by various factors. This study explains that body mass index (BMI) and hematocrit are significant and strong factors that trigger the incidence of dementia. On the other hand, various other factors indirectly contribute to the incidence of dementia, such as blood pressure, metabolic syndrome, age, and many other risk factors. This research

opens up insight into the importance of controlling body weight and body composition, especially in the elderly group, to prevent a decline in cognitive function in old age.

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