Journal of Society Medicine
Research & Review Articles on Diseases
Journal of Society Medicine. 2023; 2(7)

Relationship between Homeostatic Model Assessment for Insulin Resistance and Waist Hip Ratio with Cognitive Function in Type 2 Diabetes Mellitus

Oriza Novita[1*], Fasihah Irfani Fitri[2], Haflin Soraya Hutagalung[2]
[1] *Resident in Department of Neurology, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia*
[2] *Lecturer in the Department of Neurology, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia*

***Corresponding Author**: Fasihah Irfani Fitri, E-mail: fasihah.irfani@usu.ac.id

ARTICLE INFO

Article history:
Received
28 May 2023

Revised
06 June 2023

Accepted
31 July 2023

Manuscript ID:
JSOCMED-280523-27-1

Checked for Plagiarism: Yes

Language Editor:
Rebecca

Editor-Chief:
Prof. Aznan Lelo, PhD

ABSTRACT

Introduction: Cognitive impairment is a common complication of Type 2 Diabetes Mellitus (T2DM) in which the underlying mechanism are insulin resistance and associated central obesity. Homeostatic model assessment of insulin resistance (HOMA-IR) and waist-hip ratio (WHR) have been used as markers for insulin resistance and central obesity, respectively, but their direct association with cognition remains unclear. This study was conducted to determine the relationship between HOMA-IR and WHR with cognitive function in T2DM patients.

Method: This was a correlative analytic study with a cross sectional design involving T2DM pateints. The HOMA-IR was assessed based on blood laboratory results, the WHR was measured by dividing circumference of the waist by the circumference of the hips and cognitive function was assessed using the Montreal Cognitive Assessment Indonesian Version (MoCA-INA).

Results: **:** There were 56 patients included in the study. There was no significant relationship between HOMA-IR and cognitive function in T2DM patients (p=0.276; r=0.148). There was also no significant relationship between WHR and cognitive function (p = 0.499; r = 0.092).

Conclusion: The HOMA-IR and WHR were not correlated with cognitive function in T2DM.

Keywords

HOMA-IR, cognitive, MoCA-Ina,WHR

How to cite: Novita O, Fitri FI, Hutagalung HS. Relationship between Homeostatic Model Assessment for Insulin Resistance and Waist Hip Ratio with Cognitive Function in Type 2 Diabetes Mellitus. *Journal of Society Medicine*. 2023; 2(7): 219-226. **DOI: https://doi.org/10.47353/jsocmed.v2i7.60**

INTRODUCTION

Type 2 diabetes mellitus is a group of metabolic diseases characterized by relative insulin deficiency and insulin resistance, and obesity and physical inactivity are the main risk factors for this disease. The prevalence of type 2 diabetes is increasing in developing and developed countries due to changes in socioeconomic factors and increasing unhealthy living habits. The International Diabetes Federation (IDF) in 2017 estimated that as many as 451 million people in the world suffer from DM. By 2045, this number is expected to increase to 693 million if effective prevention measures are not taken.[1]

One of the chronic complications of type 2 DM can involve the brain and nervous system. Type 2 DM is associated with decreased cognitive function, and patients often complain of worsening memory and attention and more brain imaging abnormalities than non-diabetic patients. Decreased cognitive function in type 2 DM patients can be in the form of mild cognitive impairment, Alzheimer's disease, vascular dementia, and various other forms of dementia as assessed by neuropsychological tests.[2]

Various mechanisms are thought to play a role in cognitive function decline in type 2 DM patients, namely atherosclerosis, microvascular dysfunction, oxidative stress, and especially insulin resistance. Research on Alzheimer's dementia shows that this failure is related to several mechanisms, namely insulin

resistance, insulin growth factor (IGF) signaling, the inflammatory response, oxidative stress, the glycogen synthase kinase 3 (GSK3) signaling mechanism, the formation of amyloid beta (A) and neurofibrillary tangles, and regulation of acetylcholinesterase activation.[3]

In previous studies, it was stated that there are several factors that affect the decline in cognitive function in DM, such as plaque in atherosclerosis, microvascular disease, or secondary factors such as age or aging, genetic factors and co-morbidities, and the duration of diabetes, blood glucose levels, and obesity, and poor glycemic control, all of which can negatively affect cognitive function in DM patients. Several previous studies have also investigated the role of insulin resistance in the development of cognitive impairment in type 2 DM patients.[4-7] The HbA1c level is a standardized glycemic control marker that can describe the state of glycemic control in the previous 9-12 weeks. This examination has been widely used and is trusted for assessing poor glycemic control, which is characterized by HbA1c levels > 6.5%.[8] Homeostatic model assessment of insulin resistance (HOMA-IR) is a simple and affordable method of assessing insulin resistance.[9] A low HOMA-IR indicates high insulin sensitivity, while a high HOMA-IR indicates high insulin resistance.[10,11] Apart from HOMA-IR, there are other parameters that can also describe insulin resistance, namely the waist-hip ratio (WHR).[12] One study showed that higher WHR could increase the risk of cognitive impairment among elderly with BMI >25.3 kg/m2.[13] We aimed to determine the association between these markers of insulin resistance with cognitive impairment in type 2 DM patients.

METHOD

This study was an analytic-correlative with a cross-sectional design, with primary data sources taken consecutively from all type 2 DM patients in the neurology polyclinic, the endocrine polyclinic, and the integrated inpatient unit at Haji Adam Malik General Hospital Medan from May to November 2022. The number of subjects required after calculation was 56 patients.

The inclusion criteria were type 2 DM patients, aged 40-60 years, had minimal education of 12 years, had HbA1C level of less than 8%, duration of DM less than 10 years, and was able to read, write in and speak Bahasa Indonesia fluently. The exclusion criteria were patients with central nervous system (CNS) lesions such as stroke, tumor, infection; patients with aphasia and/or major psychiatric disorders. All subjects gave consent to participate in this research by signing the research informed consent sheet. HOMA-IR was calculated multiplying fasting plasma insulin (FPI) by fasting plasma glucose (FPG), then dividing by the constant 22.5, i.e. HOMA-IR=(FPI×FPG)/22.5.[9,10] Waist-to-hip ratio was measured measured by dividing circumference of the waist by the circumference of the hips.[13]

Cognitive function was assessed by Indonesian version of the Montreal Cognitive Assessment (MoCA-Ina). The MoCA-INA has been developed and validated in Indonesia and has been found to be useful as a brief cognitive tool in various clinical settings. The MoCA-Ina test consists of 30 questions and assesses 8 cognitive domains, namely visuospatial/executive, naming, memory, delayed memory, attention, language, abstraction, and orientation. The MoCA-Ina test scores range from 0 to 30, with higher scores indicating better cognitive function and lower scores indicating worse cognitive function. A score of 26 or above was considered normal.[14-15] This study was approved by the Clinical Research Ethics Committee of Faculty of Medicine, Universitas Sumatera Utara.

Data from this study were analyzed statistically using the SPSS for Windows computer program (Statistics Products and Science Services) version 22.0. Univariate analysis was used to describe the demographic data. Numerical variables were presented by displaying the number and frequency, mean and standard deviation, where appropriate. Bivariate analysis was used to determine the relationship between waist-hip ratio and HOMA-IR with cognitive function by using the Pearson or Spearmen correlation tests based on the normality distribution of the data.

RESULT

From May 2022 to November 2022, type 2 diabetes mellitus patients visited the neurology polyclinic, the endocrine polyclinic, and the inpatient room at H. Adam Malik General Hospital Medan. All subjects met the inclusion and exclusion criteria. Based on the characteristics of the 56 research subjects, it was found that the lowest age of the research subjects was 41 years and the highest was at the age of 60, with an age range of 40–50 years for 14 subjects (25%), an age range of 50–60 years for 39 subjects (69,6%), and an age range of 60–70 years for 3 subjects (5.4%). The sex of the research subjects consisted of 30 male subjects (53.6%) and 26 female subjects (46.4%). The highest educational level of research subjects was high school, with 35 subjects (62.5%); the most common occupations were housewives with 21 subjects (37.5%). The most ethnic groups sequentially are Batak with 37 people (66.1%), Javanese with 9 people (16.1%), Karo with 8 people (14.3%), and Malay with 2 people (3.6%). Descriptive data shows that the longest time to suffer from type 2 DM is 2 years, and the highest is 10 years. The mean HOMA-IR was 1.7±0.89. The average waist-hip ratio is 0.9 ±0.03. The MoCA-INA average is 24±2.1. The demographic characteristics of the research subjects are detailed in Table 1.

Table 1. Demographic Characteristics of Research Subjects

Characteristics	Average	n (56)	Percentage (%)
Age, average (years)	41-60**		
• 40 - <50 years		14	25
• 50 - <60 years		39	69.6
• 60 - <70 years		3	5.4
Gender			
• Male		30	53.6
• Female		26	46.4
Education			
• Senior High School		35	62.5
• Diploma		2	3.6
• Bachelor		19	33.9
Ethnic			
• Batak		37	66.1
• Javanese		9	16.1
• Karo		8	14.3
• Malay		2	3.6
Occupation			
• Housewives		21	37.5
• Entrepreneur		18	32.1
• Private Employee		8	14.3
• Civil Servant		6	10.7
• Retired		3	5.4
Diabetic Drugs			
• Oral		42	75
• Insulin		14	25
Duration Of Diabetes	2-10**		
Moca-INA *score*	24±2.1*		
HOMA IR	1.7±0.9*		
WHR	0.9±0.03*		

Table 2 shows the relationship between HOMA-IR and cognitive function as assessed by the MoCA-Ina score in type 2 DM patients. Using the Pearson correlation test, there was no significant relationship between HOMA-IR and cognitive function of type 2 DM patients (r=0.148, p=0.276)

Table 2. Relationship between HOMA-IR and cognitive function in type 2 DM patients

	MoCA-Ina Score
HOMA-IR	r=0,148 p=0,276 n=56

Noted: Pearson's Correlation Test

Table 3 shows the relationship between waist-hip ratio and cognitive function in type 2 DM patients as measured by the MoCA-Ina. The Pearson correlation test showed that there was no significant relationship between WHR and cognitive function with a value (r=0.092, p=0.499).

Table 3. The relationship between WHR and cognitive function in type 2 DM patients

	MoCA-Ina Score
WHR	r=0,092 p=0,499 n=56

Noted: Pearson's Correlation Test

DISCUSSION

Based on the characteristics of the 56 research subjects, the lowest age was 41 years and the highest was 60 years, with the highest age range in the 50–60 years range for 39 subjects (69.6%). The highest age group was also found to be almost the same as the results of the data from Riskesdas 2018, namely the age group of 55–64 years (6.29%).[16] The results of this study are relevant to previous research conducted by Tambunan et al. in 2021, which stated the average age of type DM patients was largest age group at 51–60 years (60%).[17] Trisnawati et al. explained in a 2013 study that there was a relationship between age and fasting blood sugar levels, with age 45 years being the most risk factor for increasing blood sugar levels. This is because aging can reduce insulin sensitivity, which can affect blood glucose levels, and thus increase the incidence of type 2 diabetes.[18]

There were 30 male subjects (53.6%) in the study compared to 26 female subjects (46.4%). According to a 2019 study by Sastrawan et al., the proportion of men and women with type 2 diabetes at H. Adam Malik General Hospital Medan was the same.[5] This research is in line with research by Lalithambika et al. in 2019 which showed that out of 70 research subjects, 57 (81.4%) were male.[19]

The characteristics of the education level of the research subjects that were most common in this study were high school students with 35 subjects (62.5%). The results of this study are in line with previous research conducted by Sastrawan et al. in 2019, where the education level of the most patients was high school (30%).[5] The occupational status of the most subjects was housewife, with 21 subjects (37.5%). This study is consistent with a 2017 study by Purwoningsih and Purnama, which found that housewives held 36% of all jobs.[20] According to Riskesdas 2013, it was found that the highest proportion of DM sufferers was in the non-working group.[16]

The largest ethnic group in this study is the Batak ethnic group, with 37 people (66.1%). This is consistent with Tambunan et al.'s research from 2021, in which the Batak tribe has the most subjects with 38 persons (77%).[17] According to the 2019 Literature Review, 56.6% of the Batak tribe suffers from type 2 diabetes.[5] A family history of diabetes mellitus and the habit of consuming alcohol made the majority of Batak people suffering from type 2 DM more likely to prefer to eat and have bad eating habits such as consuming foods high in carbohydrates and fats and consuming less fiber, which can cause prolonged hyperglycemia, obesity, and eventually diabetes mellitus.[20,21]

In this study, based on statistical analysis of the Pearson correlation test on 56 subjects with type 2 DM, it was found that there was no significant relationship between HOMA-IR and the cognitive function of patients with type 2 DM, with a value of $p = 0.27$ ($p > 0.05$) and a value of $r = 0.148$. This research is in line with Kong et al.'s 2018 study, which reported that there was no significant relationship between HOMA-IR and cognitive function.[22] In Zhao et al.'s 2019 study, it was concluded that there was no significant

relationship between the MoCA score and the HOMA IR ($p > 0.05$).[23] Muthiah et al.'s 2019 study said that type 2 DM subjects with regular therapy and good glycemic control of HbA1c values showed no decline in cognitive function.[24]

According to Preetam et al.'s 2022 study, older people with longer DM duration and higher HbA1c levels had higher cognitive impairment with a correlation of MoCA scores (p 0.001).[25] This difference might be due to differences in the population, where in several previous studies the results of a correlation between HOMA-IR and cognitive function were carried out without age restrictions, in other words, on subjects with an older age, while in this study the age was limited to between 40 and 60 years. Increasing age can cause a decrease in cognitive function. Brain degeneration causes a decrease in gray matter volume in the prefrontal cortex and white matter volume in the frontal lobe and corpus callosum, which has an impact on cognition.[26] The age factor has been widely studied and is a risk factor for dementia, where the risk of developing dementia increases significantly with increasing age, namely 2-fold every 5 years in individuals over 65 years, and 50% of individuals over 85 years experience dementia.[27]

Furthermore, in this study, there were limitations on HbA1c values, whereas most studies with related results only evaluated patients with type 2 DM without any restrictions on HbA1c values. Uncontrolled type 2 DM is associated with a decrease in executive function, and this is largely due to the presence of hyperglycemia.[28] Hyperglycemia can cause impaired cognitive function through mechanisms such as the formation of glycation end products, inflammation, and microvascular disease.[29,30] Long-term hyperglycemia can cause thickening of the basement membrane of the cerebral vascular muscles, reduce cerebral blood circulation, and directly damage neurons. Studies have confirmed that reduced cerebral blood flow hinders the brain's ability to perceive, process, and integrate information and ultimately leads to learning disorders and memory impairment.[2]

In this study, based on statistical analysis of the Pearson correlation test on 56 subjects with type 2 DM, it was found that there was no significant relationship between WHR and cognitive function with a value of $p = 0.499$ ($p > 0.05$) and a value of $r = 0.092$. This research is in line with Ma et al.'s 2020 study, where no correlation was found between WHR and cognitive function.[31] Singh-Manoux et al.'s 2018 study also stated that there was no relationship between increased RLPP and the risk of mild cognitive impairment or dementia.[32] This is in contrast to the findings of Yerrapragada et al. in 2019, who found that RLPP was significantly associated with impaired cognitive function in type 2 diabetes patients.[33] In subjects aged 60 years, a high waist-hip ratio was also associated with decreased cognitive function. Increased RLPP increases the risk of cognitive function decline in elderly patients with type 2 DM.[34,35]

Berbegal et al. in 2022 found that there was a relationship between waist-to-hip ratio and the memory function domain, short-term memory ($p = 0.04$) and working memory ($p = 0.03$).Visceral fat is a risk factor for insulin resistance, which can cause dysfunction in the hippocampus, which is an area of the brain that regulates memory processes.[36] Obesity is a state of chronic inflammation that is associated with brain aging. Inflammation is also implicated in the development of type 2 diabetes and insulin resistance, which affects the transport of insulin and glucose across the blood-brain barrier. Obesity also affects cholesterol metabolism, which has an impact on insulin resistance, which has implications for glucose hypometabolism that precedes the occurrence of dementia.[37] Central obesity is also associated with cerebral atrophy and white matter, where inflammatory factors are thought to be associated with changes in cognitive function.[38,39]

This research has limitations, namely that it is a cross-sectional study where the examination of cognitive function is only carried out once, so it cannot assess cognitive changes as in a prospective cohort study. In addition, we suggest that education is needed to prevent cognitive function decline by controlling type 2 DM disease, namely by taking regular medication in order to achieve good glycemic control. Second, further research can be longitudinal in nature such as a prospective cohort so that the assessment of cognitive function can be carried out more than once so that the factors that influence cognitive function in type 2 DM patients can be studied further.

CONCLUSION

This study found no significant relationship between HOMA-IR and WHR and cognitive function in type 2 DM patients. The findings of this study emphasize the fact that there are many factors that contribute to cognitive impairment in DM patients, other than insulin resistance that were studied.

DECLARATIONS

Ethics approval and consent to participate. Permission for this study was obtained from the Ethics Committee of Universitas Sumatera Utara and Haji Adam Malik General Hospital.

CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

FUNDING

This research has received no external funding.

COMPETING INTERESTS

In this study, we declare that there are no conflicts of interest.

AUTHORS' CONTRIBUTIONS

All authors significantly contribute to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas. Contribute to drafting, revising, or critically reviewing the article. Approved the final version to be published, agreed on the journal to be submitted, and agreed to be accountable for all aspects of the work.

ACKNOWLEDGMENTS

We would like to thank all staff at the endocrinology clinic and neurology clinic at Haji Adam Malik General Hospital Medan and all patients that participated in our study.

REFERENCE

1. Lin X, Xu Y, Pan X, Xu J, Ding Y, Sun X, et al. Global, regional, and national burden and trend of diabetes in 195 countries and territories: an analysis from 1990 to 2025. Scientific Reports. 2020;10:1-11.
2. Sun L, Diao X, Gang X, Lv Y, Zhao X, Yang S, et al. Risk Factors for Cognitive Impairment in Paitents with Type 2 Diabetes. Journal of Diabetes Research. 2020:1-10.
3. Damanik J, Yunir E. Type 2 Diabetes Mellitus and Cognitive Impairment. Acta Med Indones - Indones J Intern Med. 2021;53(2):213-20
4. Tsalissavrina I, Tritisari KP, Handayani D, Kusumastuty I, Arietiningsih AD, Armetristi F. Hubungan Lama Terdiagnosa Diabetes dan Kadar Glukosa Darah Dengan Fungsi Kognitif Penderita Diabetes Tipe 2 Di Jawa Timur. Jurnal AcTion. 2018;3(1):28–33.
5. Sastrawan MG, Sjahrir H, Iqbal KM. Hubungan Kadar Hemoglobin Terglikasi (HbA1c) dengan Working Memory pada Pasien Diabetes Melitus Tipe-2 dan Prediabetes. Repository USU. 2018.
6. Oktavia AI, Isnuwardana R, Rotinsulu DJ. Faktor-Faktor yang Mempengaruhi Fungsi Kognitif pada Pasien Diabetes Mellitus Tipe 2 di RSUD Abdul Wahab Sjahranie Samarinda. Universitas Mulawarman Samarinda. 2014.
7. Duron E, Olivier H. Vascular risk factor, cognitive decline and dementia. Vasc Health Risk Manag. 2008;4(2): 369-81
8. Paputungan SR, Sanusi H. Peranan Pemeriksaan Hemoglobin A1c pada Pengelolaan Diabetes Melitus. Cermin Dunia Kedokteran. 2014;41(9):650-55.

9. Wallace TM, Levy JC, Matthews DR (2004) Use and abuse of HOMA modeling. Diabetes Care 27: 1487–1495.
10. Lee CH, Shih AZL, Woo YC, Fong CHY, Leung OY, Janus E, et al. Optimal Cut-Offs of Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) to Identify Dysglycemia and Type 2 Diabetes Mellitus: A 15-Year Prospective Study in Chinese. PloS ONE. 2016;11(9):1-11
11. Lestari AAW. Resistensi Insulin: Definisi, Mekanisme dan Pemeriksaan Laboratoriumnya. 2011.
12. Yang XY, Shao MJ, Zhou Q, Xia Y and Zou HQ. Association of waist-to-hip ratio with insulin resistance in non-diabetic normal-weight individuals: a crosssectional study. Journal of Southern Medical University. 2017;37(11):p.1540-44
13. Zhang T, Yan R, Chen Q, Ying X, Zhai Y, Li F, Wang X, He F, Ye C, Lin J. Body mass index, waist-to-hip ratio and cognitive function among Chinese elderly: a cross-sectional study. BMJ Open. 2018 Oct 18;8(10):e022055.
14. Husein N, Silvia L, Yetty R dkk. Uji Validitas dan Reabilitas Montreal Cognitive Assessment Versi Indonesia (MoCA-Ina) Untuk Skrining Gangguan Fungsi Kognitif. Neurona Neuro Sains. 2010;27(4):15–22.
15. Nasreddine ZS, Phillips NA, Bedirian V, Charbonneau S, Whitehead V, Collin I, et al. The Montreal Cognitive Assessment, MoCA:a brief screening tool for mild cognitive impairment. J Am Geriatr Soc. 2005;53
16. Riset Kesehatan Dasar (RISKESDAS). Badan Penelitian dan Pengembangan Kesehatan Kementerian Kesehatan Republik Indonesia (Balitbangkes Kemenkes) 2013. Jakarta. 2018.
17. Tambunan LPS, Ritarwan K, Pujiastuti RA. Hubungan Antara Easy Sleep Apnea Predictor (ESAP) Dengan Risiko Obstructive Sleep Apnea Dan Gangguan Fungsi Kognitif Pada Pasien Diabetes Melitus Tipe2. Repository USU. 2021.
18. Trisnawati SK, Setyorogo S. Faktor Risiko Kejadian Diabetes Melitus Tipe II di Puskesmas Kecamatan Cengkareng Jakarta Barat Tahun 2012. Jurnal Ilmiah Kesehatan. 2013; 5(1):6–11.
19. Lalithambika CV, Arun CS, Saraswathy LA, Bhaskaran R. Cognitive Impairment and its Association with Glycemic Control in Type 2 Diabetes Mellitus Patients. Indian J Endocrinol Metab. 2019;23(3):353-6
20. Purwoningsih E, Purnama M. Perbandingan Faktor Perilaku Suku Batak dan Melayu Terhadap Kejadian Diabetes Melitus Tipe 2 di RSUD Dr. Tengku Mansyur Tanjung Balai. Ibnu Sina Biomedika. 2017;1(2):1-15
21. Tambunan LPS, Sjahrir H, Arina CA. The Difference of Stroke Risk Factor between Bataknese and Non Bataknese at H. Adam Malik General Hospital Medan. Indonesian Journal of Medicine. 2019;4(2):122-34.
22. Kong SH, Park YJ, Lee JY, Cho N, Moon MK. Insulin Resistance is Associated with Cognitive Decline Among Older Koreans with Normal Baseline Cognitive Function: A Prospective Community-Based Cohort Study. Scientific Reports. 2018:1-9
23. Zhao H, Wu C, Zhang X, Wang L, Sun J, Zhuge F. Insulin Resistance Is a Risk Factor for Mild Cognitive Impairment in Elderly Adults with T2DM. Open Life Sci. 2019;14:255-61.
24. Muthiah S, Kanagamuthu R, Mohanraj S, Lakshmi KN. Assessment of memory and cognitive functions in controlled and uncontrolled Type 2 diabetes mellitus patients. National Journal of Physiology, Pharmacy and Pharmacology. 2019;9(2):140-45
25. Preetam K, Chandrashekar NKT, Krishnappa R. Evaluation of Neurocognitive Disorder in Patients with Type 2 Diabetes Mellitus. International Journal of Nutrition, Pharmacology, Neurological Diseases. 2022:247-52
26. Murman D. The Impact of age on cognition. Pubmed Central Journal. 2015; 36(3):111-21.
27. Perhimpunan Dokter Spesialis Saraf Indonesia. Panduan Nasional Praktik Klinik Diagnosis dan Penatalaksanaan Demensia. Jakarta: Perdossi; 2015.

28. Geijselaers SLC, Sep SJS, Claessens D, Schram MT, van Boxtel MPJ, Henry RMA, et al. The role of hyperglycemia, insulin resistance, and blood pressure in diabetes-associated differences in cognitive performance-the maastricht study. Care.Diabetesjournal.org. 2017;40(11):1537-47.
29. Vlassara H, Palace MR. Diabetes and advanced glycation endproducts. J Intern Med. 2002;251(2):87-101.
30. Yaffe K, Kanaya A, Lindquist K, Simonsick EM, Harris T, Shorr RI, Tylavsky FA, et al. The metabolic syndrome, inflammation, and risk of cognitive decline. JAMA. 2004;292(18):2237-42.
31. Ma W, Zhang H, Wu N , Liu Y , Han P , Wang P, et al. Relationship between obesity-related anthropometric indicators and cognitive function in Chinese suburb-dwelling older adults. PLoS ONE. 2020;10(40):1-14
32. Singh-Manoux A, Dugravot A, Shipley M, Brunnerb EJ, Elbaza A, Sabiaa S, et al. Obesity trajectories and risk of dementia: 28 years of follow-up in the Whitehall II Study. Alzheimers Dement. 2018;14(2):178-86.
33. Yerrapragada DB, Rao CR, Karunakaran K, Lee HSE. Cognitive Dysfunction Among Adults With Type 2 Diabetes Mellitus in Karnataka, India. Ochsner Journal. 2019;19(3):227-34.
34. Zhen YF, Liu XY, Li YK, Fang H, Cassidy RM, Zhang XY. Association of Brain-Derived Neurotrophic Factor With Cognitive Function: An Investigation of Sex Differences in Patients With Type 2 Diabetes. Psychosomatic Medicine. 2019;81(6):488-94
35. Ntlholang O, McCarroll K, Laird E, Molloy AM, Ward M, McNulty H, et al. The relationship between adiposity and cognitive function in a large community-dwelling population: data from the Trinity Ulster Department of Agriculture (TUDA) ageing cohort study. British Journal of Nutrition. 2018;120:517-27.
36. Berbegal M, Tomé M, SanSegundo MS, Martí AZ, Sánchez JA. Memory Function Performance Individuals Classified as Overweight, Obese and Normal Weight. Frontiers. 2022.1-11
37. Septyaningrum N, Martini S. Lingkar Perut Mempunyai Hubungan Paling Kuat Dengan Kadar Gula Darah. Jurnal Berkala Epidemiologi. 2014;2(1):48-58
38. Debette S, Seshadri S, Beiser A, Au R, Himali JJ, Palumbo C, et al. Midlife vascular risk factor exposure accelerates structural brain aging and cognitive decline. Neurology. 2011;77:461-8.
39. Tinta I, Sumarni. Hubungan Obesitas Sentral Dengan Memori Jangka Pendek Mahasiswa Fakultas Kedokteran Universitas Tadulako. Healthy Tadulako Journal. 2019;5(3):1-5