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Relationship Between Serum Uric Acid Levels And Triglyceride Glucose (TyG) Index In Young Adults

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Abstrak

Background: Hyperuricemia is positively associated with insulin resistance. Triglyceride-glucose (TyG) index has been developed as test for insulin resistance. Insulin resistance predisposes to several metabolic disorders, including hyperglycemia, hypertension, and dyslipidemia, all of which are closely associated with diabetes, atherosclerosis, and cardiovascular disease. This study aims to assess the relationship between serum uric acid levels and insulin resistance as measured by the TyG index in young adults.

Methods: This was an observational with a cross-sectional study method, conducted on internal medicine residents of Hasanuddin University, Makassar. The statistical tests used were the Kolmogorov-Smirnov test to assess data normality, the Mann-Whitney test, the Spearman correlation test, and the multiple linear regression test.

Results: In this study, it was found that significant positive correlation between serum uric acid levels and the TyG Index, where the higher uric acid levels, the higher the TyG Index value ($p<0.001$). Mean TyG Index was found higher in hyperuricemia (8.64) compared to normal serum uric acid levels (8.09) ($p<0.001$), a significant relationship between hyperuricemia and a high TyG Index.

Conclusion: The results obtained a significant positive correlation between serum uric acid levels and insulin resistance measured by the TyG Index in young adults.

Keywords: Uric acid, Hyperuricemia, insulin resistance, TyG index

INTRODUCTION

Uric acid is the end product of purine metabolism, which primarily comprises the breakdown of nucleic acids as well as other purine compounds in cells and food through the action of enzymes.(1) This compound is widely considered a redox agent, acting as an antioxidant and prooxidant under certain conditions conditions.(2) Different factors have been reported to

affect serum uric acid levels, namely internal and external factors, including renal and extrarenal excretion, genetics, as well as diet. [(1)] Hyperuricemia is a condition characterized by increased serum uric acid levels, which is often diagnosed in 5-30% of the general population.[(3)] Hyperuricemia is known to be associated with the development of various diseases, including insulin resistance playing an important pathological role. [(1,2)]

Insulin resistance is a condition caused by decreased cellular sensitivity to insulin and is a cardinal feature of the metabolic syndrome.[(4)] The condition predisposes to several metabolic disorders, including hyperglycemia, hypertension, and dyslipidemia, all of which are closely associated with diabetes, atherosclerosis, and cardiovascular disease.[(5,6)] The gold standard test for insulin resistance is the hyperinsulinemic-euglycemic clamp (HEC), but it has been shown to have various limitations, such as high costs and invasive nature. Consequently, a surrogate triglyceride-glucose (TyG) index has been developed as an effective alternative.[(7)] The TyG index, calculated using fasting blood glucose (FBG) and triglyceride (TG) levels, is considered a reliable and relatively simple diagnostic method.[(8)] Fasting blood glucose and TG levels are routine biochemical tests performed in primary care. [(9)]

Hyperuricemia is positively associated with insulin resistance.[(7)] The mechanisms by which uric acid contributes to the development of insulin resistance include inflammation, oxidative stress, and endothelial dysfunction.[(2)] Elevated serum uric acid may contribute to the condition by reducing nitric oxide (NO) bioavailability and causing oxidative stress on mitochondria.[(1,10)] Oxidative stress in adipose tissue is a significant risk factor for insulin resistance because it decreases sensitivity in adipose tissue.[(10)] In addition, oxidative stress caused by reactive oxygen species (ROS) can cause damage to cellular components, including proteins, and disrupt insulin signaling pathways.[(2)] Soluble uric acid can also cause increased ROS formation and inhibit insulin-induced glucose uptake in H9c2 and primary cardiomyocytes.[(10,11)] Uric acid has been potential to directly interfere with insulin receptors and downstream signaling molecules, leading to impaired glucose uptake and metabolism.[(2)] Inflammation is an important factor in the insulin resistance-hyperuricemia relationship. Serum uric acid can affect insulin signaling and induce resistance under the action of inflammatory factors.[(12)] Endothelial dysfunction can also lead to decreased NO production, which reduces blood flow to insulin-sensitive tissues, further exacerbating the condition.[(2)] Therefore, this study

aims to assess the relationship between serum uric acid levels and insulin resistance as measured by the TyG index in young adults.

MATERIALS AND METHODS:

Patient population

This was an observational with a cross-sectional study method, conducted on internal medicine residents of Hasanuddin University Makassar in February 2023 until the minimum sample size of 85 individuals was met. Samples are individuals who match all criteria for inclusion. This research was approved by the Ethics Committee for Biomedical Research on Humans, Faculty of Medicine, Hasanuddin University, Makassar, South Sulawesi, Indonesia. Based on recommendation letter Number: 223/ UN4.6.4.5.31/ PP36/ 2024, with protocol number: UH24030180.

Inclusion criteria

The Inclusion criteria were an age range of 18 to 40 years, not suffering from diabetes mellitus, being willing to participate in the study, and signing an informed consent.

Clinical data and sample collection

Sampling was carried out by consecutive sampling. Anamnesis was carried out on all study participants. Furthermore, body weight, height, and waist circumference were measured to determine obesity based on body mass index (BMI) and waist circumference (WC). Obesity based on BMI was calculated using the formula = Body weight (kg)/height $(m)^2$ with a limit of ≥ 25 for the obesity category in Asian adults according to WHO. Waist circumference using a circular measurement in the middle of the lower ribs and iliac crest with the participant standing and measured at the end of expiration where males obesity when WC ≥ 90 cm and females were determined obese when WC ≥ 80 cm.

A total of 3 ml blood samples were obtained from the vein in the fossa cubiti region and placed into a citrate tube where the participants were asked to fast for 8 to 12 hours beforehand. Chemical methods were used to examine blood samples for uric acid levels, FBG, and TG. Hyperuricemia was characterized by serum uric acid levels > 6.8 mg/dl. Insulin resistance was

evaluated using the TyG index calculated as = Ln [TG (mg/dl) × FBG (mg/dl)/2], with a cutoff value of 8.8 in males and 8.7 in females.

Statistical analysis

Data analysis was carried out using SPSS version 25. The statistical analysis performed was calculation of descriptive statistics and frequency distribution, The statistical tests were the Kolmogorov-Smirnov test to assess data normality, the Mann-Whitney test, the Spearman's correlation test, the multiple linear regression test, and the results of statistical test were significant if the p value <0.05.

RESULTS:

Study population

This study comprised 97 participants consisting of 48 females and 49 males. In addition, those with and without comorbidities were 12.4% and 87.6%, respectively. The participants had an average TG level of 100.5±57.8 mg/dl, an average FBG level of 88.4±7.8 mg/dl, an average TyG index of 8.26±0.54, an average BMI of 26.6±4.8 kg/m^2 with obese participants based on BMI 59.8%, meanwhile, for non-obese participants based on a BMI of 40.2%, an average waist circumference (WC) of 92.3±12.0 cm with obese waist circumference of 77.3% and non-obese waist circumference of 22.7%, and an average uric acid level of 5.8±1.7 mg/dl with hyperuricemia 30.9% and normal uric acid levels 69.1% (Table 1).

Variables	**n**	**%**	**Min**	**Maxs**	**Mean**	**SD**
Sex						
Female	48	49.5				
Male	49	50.5				
Comorbid						
Yes	12	12.4				
No	85	87.6				
Obesity (BMI)			18.7	49.2	26.6	4.8
Obese	58	59.8				
Non obese	39	40.2				
Obesity (WC)			63.0	130.0	92.3	12.0
Obese	75	77.3				
Non obese	22	22.7				
Hyperuricemia			1.8	10.4	5.8	1.7
Yes	30	30.9				
No	67	69.1				
TG			29	326	100.5	57.8
FBG			72	117	88.4	7.8
TyG index			7.09	9.63	8.26	0.54

Table 1 Subjects characteristics

BMI: *body mass index, WC: waist circumference,* TG: *triglyceride,* FBG: *fasting blood glucose,* TyG index: *tryglyceride glucose index*

The relationship between serum uric acid levels and TyG index

In this study, the relationship between serum uric acid levels and TyG index was tested using Spearman's correlation test.

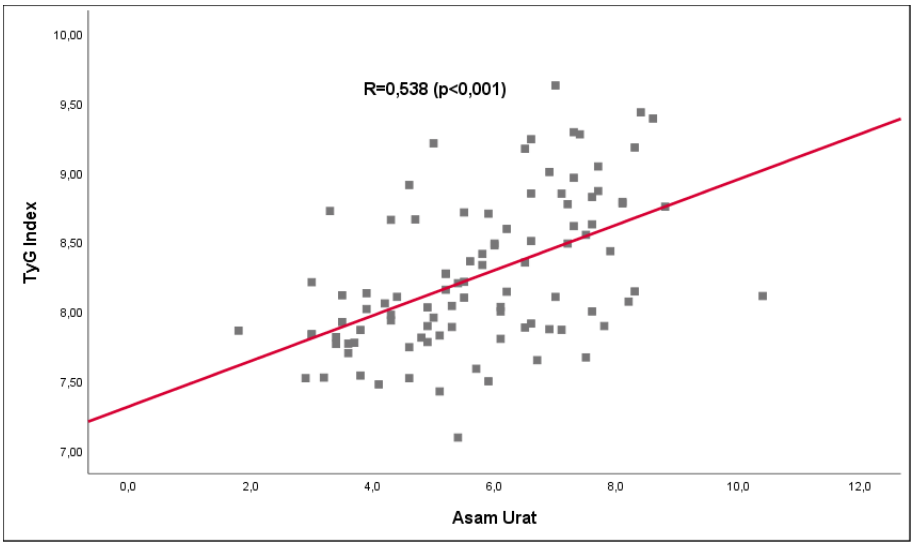

Figure 1. Correlation of Uric Acid with TyG Index

Figure 1 showed that there was a significant positive correlation between serum uric acid levels and the TyG Index, where the higher uric acid levels, the higher the TyG Index value ($p<0.001$). According to the R-value, the close relationship between serum uric acid levels and the TyG Index value was included in the strong category ($R>0.500$).

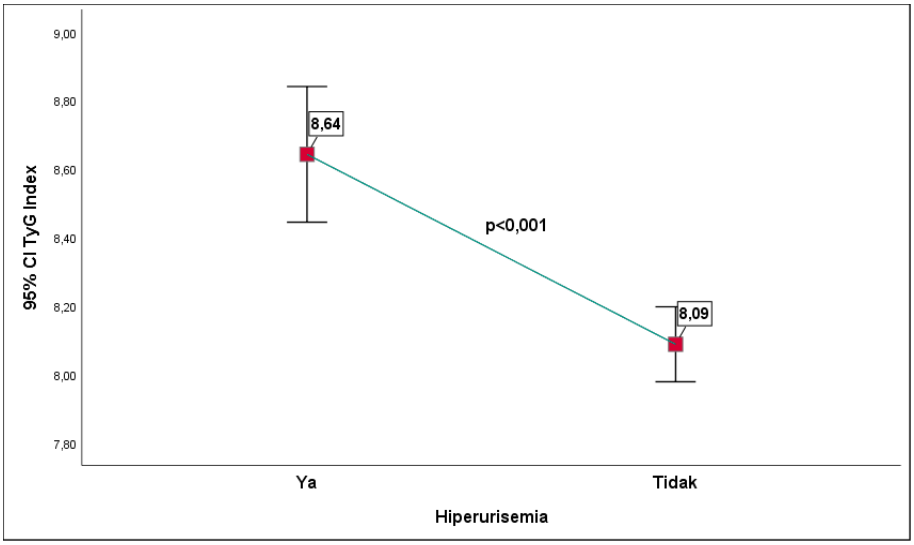

Figure 2. Comparison of TyG Index according to Hyperuricemia

Figure 2 showed that Mean TyG Index was found higher in hyperuricemia (8.64) compared to normal serum uric acid levels (8.09). The results of statistical tests showed that the difference was significant ($p<0.001$). This showed a significant relationship between hyperuricemia and a high TyG Index.

The role of confounding factors on TyG index

A comparative test of the TyG Index value between each category of confounding factors was conducted to assess the role of confounding factors on the TyG Index value in this study. The comparison results were as follows (Table 2).

Table 2 Comparison of TyG Index Values by Confounding Factors

Variable	**n**	**TyG index**		**p**
		Mean	**SD**	
Sex				**0.021**
Female	48	8.13	0.45	
Male	49	8.39	0.59	
Comorbid				0.618
Yes	12	8.37	0.67	
No	85	8.24	0.52	
Obesity (BMI)				**0.000**
Obese	58	8.42	0.53	
Non obese	39	8.02	0.46	
Obesity (WC)				**0.002**
Obese	75	8.34	0.53	
Non obese	22	7.97	0.46	

Independent-t-test

BMI: *body mass index, WC: waist circumference,* TyG index: *tryglyceride glucose index*

Based on Table 2, the mean TyG Index was found to vary significantly by gender (p 0.021), obesity was based on BMI (p 0.000), and obesity was based on WC (p 0.002). This showed a significant relationship between sex and obesity according to BMI and WC with the TyG Index value. Based on these results, to determine the relationship between serum uric acid levels and the TyG Index value, it was necessary to control the impact of sex, obesity based on BMI, and obesity based on WC.

DISCUSSION

This study showed a significant positive correlation between serum uric acid levels and the TyG Index, where the higher the uric acid levels, the higher the TyG Index value ($p < 0.001$). The mean TyG Index was higher in hyperuricemia (8.64) compared to normal serum uric acid levels (8.09). The results of statistical tests showed a significant difference ($p < 0.001$). In a previous study by Malene et al(2021) in Brazil, participants with insulin resistance calculated by the TyG index showed high serum uric acid levels.[13] Another study by Jia Zheng(2021) et al involving 5,727 participants in Peking, China, found that higher initial values of this uric acid were associated with higher follow-up TyG values.[10] Subsequently, a study by Sethapong Lertsakulbunlue et al.,(2024) on 231,386 Thai Army personnel, showed the prevalence of hyperuricemia increased with increasing TyG index quartiles.[7] Feitosa RS et al.(20233) analyzed women from northeastern Brazil and found that the TyG index was significantly higher in the hyperuricemic population than the non-hyperuricemic population, showing that hyperuricemia was a risk factor for insulin resistance.[1] Eswar Krishnan et al(2012) analyzed young adults aged 18-35 years in America who were followed for 15 years, showing the use of serum uric acid levels as a simple indicator to assess the occurrence of insulin resistance, prediabetes, and type 2 diabetes in the future. Moreover, Krishnan et al(2012) showed that those with hyperuricemia were 1.36 times more likely to exhibit insulin resistance than those without hyperuricemia.[4] Uric acid could directly interfere with insulin receptors and downstream signaling molecules, leading to impaired glucose absorption as well as metabolism. The inflammatory response triggered by relative hyperuricemia could interfere with insulin signal and induce insulin resistance.[1,2,11] In addition, insulin resistance could cause inflammation and indirectly increase hyperuricemia.[12] Oxidative stress caused by ROS caused oxidative damage to cellular components, including proteins, disrupted insulin signaling pathways, and contributed to insulin resistance. Endothelial dysfunction led to decreased production of NO which reduced blood flow to insulin-sensitive tissues, further exacerbating insulin resistance.[1,2] In addition, increased serum uric acid concentrations were shown to reduce NO levels.[4]

The mean TyG Index was found to vary significantly by sex (p 0.021), obesity was based on BMI (p 0.000), and obesity was based on WC (p 0.002). This showed a significant relationship between sex and obesity according to BMI and WC with the TyG Index value. Based on these results, to determine the relationship between serum uric acid levels and the TyG Index

value, it was necessary to control the impact of sex, obesity based on BMI, and obesity based on WC.

In adults and children, males tended to exhibit a higher level compared to females. This difference was likely due to the different roles of sex hormones and higher muscle mass in males. Testosterone, which was present at higher levels in males, was shown to increase serum uric acid production and decrease its excretion. In addition, estrogen, which was dominant in females, had a uricosuric effect, promoting uric acid excretion from the body. These hormonal differences contributed to higher uric acid levels in males. Furthermore, skeletal muscle mass and strength played a role in serum uric acid metabolism. Skeletal muscle was the major site of purine metabolism, and higher muscle mass in males, leading to increased purine turnover and uric acid production which combined with higher testosterone levels. This contributed to higher serum uric acid levels in males.[(1)] Moreover, differences in dietary habits, transportation modes, and physical activity between males and females could be potential factors affecting the prevalence of hyperuricemia.[(12)]

In the study of Sethapong Lertsakulbunlue et al.,(2024) obesity based on BMI was found to have a modifying effect on the correlation between TyG index and serum uric acid (P-interaction <0.001). Adipose tissue was known to release proinflammatory cytokines that were shown to worsen insulin resistance. However, the increased insulin resistance observed among obese participants could potentially attenuate the relationship between TyG index and serum uric acid, specifically in females who had a higher percentage of adipose tissue than males. Preadipocytes in visceral fat showed a lower adipogenic capacity than preadipocytes in subcutaneous fat.[(7)] Leptin, a hormone whose secretion was directly related to the degree of adiposity, induced oxidative stress in endothelial cells, increasing uric acid concentrations. Moreover, leptin and insulin resistance could reduce renal uric acid excretion, contributing to increased and altered metabolic.[(13)]

In a previous study by Jia Zheng et al.,(2021) higher baseline waist circumference was significantly associated with serum uric acid levels and TyG index at follow-up. It was widely known that poor dietary habits and sedentary lifestyles, along with increasing social pressure, were shown to have a higher correlation with the occurrence of insulin resistance. Waist circumference was a simple and reliable measure of central obesity. This study showed that waist circumference could be used as an indicator to assess insulin secretion.[(10)]

CONCLUSIONS

In conclusion, the results obtained a significant positive correlation between serum uric acid levels and insulin resistance measured by the TyG Index in young adults, where the higher the uric acid levels, the higher the TyG Index value. This study suggested screening for insulin resistance could use the TyG index in young adults patients with hyperuricemia.

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REFERENCES

1. Zhao Q, Zhang M, Chu Y, Ban B. Association between serum uric acid and triglyceride-glucose index in children and adolescents with short stature. *Sci Rep*. 2023 *13*(1). Doi: 10.1038/s41598-023-40972-2
2. Anaizi N. The Impact of Uric Acid on Human Health: Beyond Gout and Kidney Stones. *Ibnosina J Med Biomed Sci*. 2023; *15*(03), 110–116. Doi: 10.1055/s-0043-1770929
3. Lohsoonthorn V, Dhanamun B, Williams M. Prevalence of Hyperuricemia and its Relationship with Metabolic Syndrome in Thai Adults Receiving Annual Health Exams. *Arc Med Res*. 2006; *37*(7), 883–889. Doi: 10.1016/j.arcmed.2006.03.008
4. Krishnan E, Pandya B, Chung L, Hariri A, Dabbous O. Hyperuricemia in young adults and risk of insulin resistance, prediabetes, and diabetes: a 15-year follow-up study. *Am J Epidemiol*. 2012; *176*(2), 108–116. Doi: 10.1093/aje/kws002
5. Moon S, Park J, Ahn Y. The Cut-off Values of Triglycerides and Glucose Index for Metabolic Syndrome in American and Korean Adolescents. *J.Korean Med Sci*. 2017; *32*(3), 427–433. Doi: 10.3346/jkms. 2017.32.3.427
6. Unger G, Benozzi S, Perruzza F, et al. Triglycerides and glucose index: A useful indicator of insulin resistance. *Endocrinol Nutr*. 2014; 61(10): 533-540.
7. Lertsakulbunlue S, Sangkool T, Bhuriveth V, et al. Associations of triglyceride-glucose index with hyperuricemia among Royal Thai Army personnel. *BMC Endocr Disord*. 2024; *24*(1). Doi: 10.1186/s12902-024-01542-3

8. Jiang M, Li X, Wu H, et al. Triglyceride-Glucose Index for the Diagnosis of Metabolic Syndrome: A Cross-Sectional Study of 298,652 Individuals Receiving a Health Check-Up in China. *Int J Endocrinol*. *2022*, 1-9. Doi: 10.1155/2022/3583603
9. Sánchez-García A, Rodríguez-Gutiérrez R, Mancillas-Adame L, et al. Diagnostic Accuracy of the Triglyceride and Glucose Index for Insulin Resistance: A Systematic Review. *Int J Endocrinol*, *2020*, 1-7. Doi: 10.1155/2020/4678526
10. Zheng J, Jiang M, Xie Y. Influence of uric acid on the correlation between waist circumference and triglyceride glucose index: an analysis from CHARLS. *Lipids Health Dis*.2021; *20*(1). Doi: 10.1186/s1 2944-021-01474-0
11. Yu W, Cheng J. Uric Acid and Cardiovascular Disease: An Update From Molecular Mechanism to Clinical Perspective. *Front Pharmacol*.2020 (11), 1-13. Doi: 10.3389/fphar.2020.582680
12. Luo Y, Hao J, He X, et al. Association Between Triglyceride-Glucose Index and Serum Uric Acid Levels: A Biochemical Study on Anthropometry in Non-Obese Type 2 Diabetes Mellitus Patients. *Diabet Metab Synd Ob*.2022; *15*, 3447–3458. Doi: 10.2147/DMSO.S387961
13. Sodré M, Ferreira A, Ferreira A, et al. Relationship between serum concentrations of uric acid, insulin resistance and metabolic alterations in adolescents. *J Bras Patol Med Lab.* 2021, *57*, 1–7. Doi: 10.5935/1676-2444.20210020