Artikel Penelitian

THE VISCERAL FAT SIGNIFICANTLY ASSOCIATED WITH URIC ACID LEVELS AMONG THE ELDERLY AT HANA NURSING HOME

Ayleen Nathalie Jap[1], Shirly Gunawan[2*], Yohanes Firmansyah[3], Alexander Halim Santoso[4]
[1]Faculty of Medicine, Tarumanagara University, Jakarta, Indonesia
[2]Department of Pharmacology, Tarumanagara University, Jakarta, Indonesia
[3]Department of Physiology, Tarumanagara University, Jakarta, Indonesia
[4]Department of Nutrition, Tarumanagara University, Jakarta, Indonesia.

[*]Email: shirlyg@fk.untar.ac.id

Abstract

Visceral fat has a significant impact on metabolic health. Elevated visceral fat area could increase the risk of hyperuricemia, which may lead to further metabolic complications. The study aims to assess the relationship between uric acid levels and visceral fat accumulation and the subsequent effect on subcutaneous fat distribution in the trunk, arms, and legs among the elderly population. This study involved 61 elderly participants at Hana Nursing Home. Serum uric acid levels were measured using point-of-care testing (POCT). Body composition, including visceral and subcutaneous fat, was assessed using the Omron body composition monitor. Spearman correlation analysis evaluated the relationship between uric acid levels, visceral fat, and subcutaneous fat in different body regions, including the trunk, arms, and legs. This study has demonstrated a positive correlation between uric acid levels and visceral fat accumulation ($r = 0.285$, $p = 0.026$), subcutaneous fat in the trunk ($r = 0.804$, $p < 0.001$), arms ($r = 0.752$, $p < 0.001$), and legs ($r = 0.827$, $p < 0.001$), suggesting that having a high amount of visceral fat can be an indicator of having more subcutaneous fat as well.

***Kata kunci**: Elderly, Hyperuricemia, Subcutaneous fat, Uric acid, Visceral fat.*

INTRODUCTION

Uric acid is an organic fatty acid that results from the breakdown of purine nucleotides in circulation produced from xanthine by xanthine oxidase (Wang et al., 2024). Hyperuricemia is an abnormally high level of uric acid in the blood due to increased uric acid production or decreased excretion (Huang et al., 2024). Hyperuricemia increases the risk of multiple clinical conditions such as gout, hypertension, type 2 diabetes, stroke, chronic kidney disease, metabolic syndrome, atherosclerosis, and non-alcoholic liver disease, which impact the quality of life (Liu et al., 2024). Hyperuricemia is characterized by uric acid levels >6 mg/dL in women and >7 mg/dL in men (George et al., 2023). The incidence of gout is 1% -4% of the general population. According to the World Health Organization (WHO), the number of hyperuricemia sufferers increases every year worldwide. The prevalence of hyperuricemia in adults has increased significantly from 11.1% in 2015-2016 to 14% in 2018-2019 in China, with the highest incidence in men (Liu et al., 2024). Based on WHO data in the Non-Communicable Disease Country Profile in Indonesia, the prevalence of gout at the age of 55-64 is around 45%, at the age of 65-74 is around 51.9%, and at the age of >75 is around 54.8% (Yasin et al., 2023).

Adiposopathy or "sick fat" is a pathologic adipose tissue, anatomically and/or functionally, that disrupts adipose tissue's structural and functional integrity, which can later disrupt metabolic homeostasis. Adiposopathy may involve visceral and subcutaneous fat. Adipose tissue stores fuel that will produce hormones and immune factors. Visceral fat is the accumulation of fat in the abdominal cavity, which is more common in Asians than in Westerners. Visceral fat is a physical protection against mechanical intra-organ damage such as abdominal trauma (Bays, 2014). This fat is located around or inside internal organs such as the liver and intestines, which are influenced by epigenetic factors, race, aging, and hormonal changes. An increase in excessive visceral fat is associated with metabolic disorders (disorders of glucose, lipid, and uric acid metabolism) and high cardiovascular events. Obesity, especially visceral obesity, significantly increases hyperuricemia (Liu et al., 2024). The underlying mechanism is likely due to the excessive release of free fatty acids by visceral fat, which causes metabolic disorders, increases inflammation, and interferes with the kidney and liver management of uric acid, resulting in increased uric acid in the blood (Huang et al., 2019). Subcutaneous fat accumulates fat in the subcutaneous layer that protects the body from infection, such as superficial skin wounds (Bays, 2014). Excessive visceral fat causes an increase in subcutaneous fat, which may be linked to metabolic disorders (Smith et al., 2001).

Limited subcutaneous fat storage in the elderly may result in an energy overflow in the form of increased free fatty acid transport in the blood, resulting in increased accumulation of pericardial, perivascular, visceral fat, lipotoxicity, and fat infiltration into nonadipose organs such as the liver, muscles, pancreas, heart, and kidneys (Bays, 2014). This condition may lead to metabolic dysfunction, disrupting glucose, lipid, and uric acid metabolism, increasing the risk of hyperuricemia. The aim of this study was to determine the relationship between visceral fat distribution and uric acid metabolism in the elderly elderly (Liu et al., 2024).

METHODS

This study used a cross-sectional design to investigate the relationship between visceral fat, subcutaneous fat, and hyperuricemia in the elderly. This study is ideal for analyzing the relationship between variables without being bound by a specific period. This study was conducted at Hana Nursing Home in February 2024. The total number of respondents involved in this study was 61 elderly who lived at Hana Nursing Home. Total sampling techniques were used in this study. The inclusion criterion in this study is elderly aged 51 – 90 years old, living in Hana nursing home, willing to be respondents by filling out and signing the consent form. Exclusion criteria in this study were having acute or infectious diseases that could affect metabolism and uric acid levels, suffering from chronic diseases such as kidney failure, liver disease, or metabolic conditions that affect uric acid levels, and taking medications that affect uric acid levels.

Uric acid was measured using Point-of-Care Testing (POCT), which provides results in mg/dL. Blood samples for measuring uric acid levels were taken in the morning from respondents who had fasted for at least 8 hours. Blood was taken from the tip of finger by being pricked with a needle, and blood which came out from peripheral blood vessels were dropped into a strip test. The strip was then inserted into a uric acid meter. Result from the device was then recorded in the form.

Visceral and subcutaneous fat were measured using the body composition analysing device Omron HBF-375 Body Fat Monitor. Participants with a history of using pacemakers, and who had any metal implanted in the body were not allowed for measuring. Eligible participants were then asked for their body height and age. Those data were then typed into the device. Before measuring, participants were asked to remove their shoes and sandals including soaks, and then climbed on the device. Participants were then asked to pull the electrode grip, stand straight, raised both arms to shoulder height, and hold the electrode grip until the device finished measuring.

Measurement results, including demographic data, were recorded into the analysing application. Data were then analysed using the Statistical Package for the Social Sciences (SPSS) version 26 from IBM Corporation. Univariate data were presented in %, mean ± SD if the data were distributed normally, and median if the data were distributed abdnormally. Bivariate data were analysed using Spearman correlation. The confidence limit was set at 95%.

RESULT AND DISCUSSION

This research was conducted with the approval of the Human Research Ethics Committee of Tarumanagara University, Institute for Research and Community Service No. 013-UTHREC/UNTAR/VI/2024. This study involved 61 elderly who had met the inclusion criteria. Demographic data were presented in Table 1. In this study, most respondents were female (77%), and were in the age range of 51-90 years with an average age of 75.97 years. The average uric acid was 5.76 mg/dL, visceral fat 5.27%, subcutaneous fat on the trunk 16.74%, subcutaneous fat on the arms 29.09%, and subcutaneous fat on the legs 23.53%. (Table 1)

Table 1. Characteristics of Respondents

Parameter	N (%)	Mean (SD)	Med (Min-Max)
Age	61 (100)	75.97 (8.03)	76 (51-90)
Gender			
Male	14 (23)		
Female	47 (77)		
Uric Acid Level		5.76 (1.6)	5.30 (3.3-11.6)
Uric Acid Level – Male			
Normal	11 (18)		
High	3 (4.9)		
Uric Acid Level – Female			
Normal	34 (55.7)		
High	13 (21.3)		
Visceral Fat		5.27 (5.79)	4.50 (0-23.5)
Normal	52 (85.2)		
High	5 (8.2)		
Very High	4 (6.6)		
Subcutaneous Fat			
Trunk		16.74 (13.01)	22.70 (0-34.6)
Arms		29.09 (22.94)	39.90 (0-59)
Legs		23.53 (18.25)	31.40 (0-50.5)

Spearman correlation analysis showed a weak correlation between visceral fat and uric acid, as indicated by a correlation coefficient (r) of 0.285 and a p-value of 0.026. (Table 2)

Table 2. Correlation between Visceral Fat and Uric Acid Level

Parameter			Uric Acid Level	Visceral Fat
Spearman's rho	**Uric Acid Level**	Correlation Coefficient	1.000	0.285
		Sig. (2-tailed)	.	0.026
	Visceral Fat	Correlation Coefficient	0.285	1.000
		Sig. (2-tailed)	0.026	.

Analysis of the correlation between visceral fat and subcutaneous fat obtained significant results and a strong correlation. Proven through the results of the body correlation coefficient (r) 0.804 and p-value <0.001, in the arms obtained a correlation coefficient (r) 0.752 and p-value <0.001, and in the legs the correlation coefficient (r) 0.827 and p-value <0.001. This result shows that increased visceral fat increases the percentage of subcutaneous fat in the body, arms, and legs in the elderly, which plays a role in hyperuricemia. (Table 3).

Table 3. Correlation between Visceral Fat and Subcutaneous Fat

Parameter			Visceral Fat	Subcutaneous Fat Trunk	Subcutaneous Fat Arms	Subcutaneous Fat Legs
Spearman's rho	**Visceral Fat**	Correlation Coefficient	1.000	0.804	0.752	0.827
		Sig. (2-tailed)	.	<0.001	<0.001	<0.001

Increased visceral fat is associated with increased uric acid. Excessive visceral fat that causes obesity will have an impact on insulin resistance. Accumulation of visceral fat will cause direct damage to insulin receptors through excessive free fatty acids in the portal vein (Hikita et al., 2007). Due to excessive visceral fat percentage, insulin resistance is the most essential process that will cause hyperuricemia. This condition can be the result of reduced GAPDH activity. GAPDH is an enzyme that plays a role in the synthesis of uric acid in the purine metabolism pathway, the activity of which is regulated by insulin. If insulin resistance occurs, it will reduce the enzyme's activity and increase uric acid production because insulin cannot regulate GAPDH to function properly, as GAPDH, which should play a role in the glycolysis process, will decrease. This condition will disrupt cell energy metabolism related to the accumulation of free fatty acids due to lipogenesis and impaired glucose regulation. These free fatty acids will increase purine synthesis, resulting in hyperuricemia (Panlu et al., 2024).

Hyperinsulinemia and insulin resistance in obese patients can directly affect the kidneys. Insulin has a mild diuretic effect while increasing sodium reabsorption in the renal tubules. Hyperinsulinemia and insulin resistance will reduce the kidney's ability to clear uric acid, thereby increasing its levels in the blood (S. Li et al., 2023). In addition, insulin resistance or hyperuricemia can increase uric acid reabsorption in the renal tubules, thereby decreasing urinary uric acid excretion and increasing its concentration in plasma (Z. Li et al., 2022).

Furthermore, uric acid will promote citrate to be converted into acetyl-CoA for de novo lipogenesis in hepatocytes, increasing free fatty acids. Increased free fatty acids will be converted into triglycerides and cause visceral fat accumulation and obesity (Tao et al., 2023). Likewise, visceral fat will increase free fatty acid levels that play a role in de novo purine synthesis, thereby increasing uric acid. Increased uric acid affects increased visceral fat and vice versa. To control hyperuricemia, it is crucial to understand that weight loss is the key, not anti-hyperuricemic drugs. However, it should be noted that hyperuricemia can also occur in people with normal weight or even underweight because it is related to fat distribution. Therefore, it is important to provide lifestyle interventions before giving treatment (S. Li et al., 2023).

Studies have shown that subcutaneous fat stored under the skin correlates weaker with increased uric acid levels than visceral fat (Hikita et al., 2007). Thus, individuals with high total fat levels, especially visceral fat, show higher subcutaneous fat levels, increasing uric acid levels through systemic inflammation and insulin resistance. Subcutaneous fat contributes to systemic inflammation by releasing pro-inflammatory cytokines such as TNF-α and IL-6. These cytokines will increase oxidative stress and stimulate uric acid production as the body's response to cell damage (Zhang et al., 2022).

The location of subcutaneous fat, especially the trunk area, appears to contribute more to increasing uric acid than those in arms and legs. Subcutaneous fat in the trunk area is usually more metabolically active than in the arms or legs. So, it is associated with releasing pro-inflammatory cytokines that contribute to systemic inflammation and insulin resistance. This inflammation increases uric acid levels indirectly by increasing oxidative stress. In addition, excess subcutaneous fat in the trunk is associated with central obesity, a major sign of metabolic syndrome and a significant factor in hyperuricemia and gout. Subcutaneous fat accumulation in the trunk area towards central obesity occurs due to the interaction between hormonal regulation, metabolic pathways, and environmental factors. Fat accumulation in the trunk is influenced by cortisol, insulin, and sex hormones. Increased cortisol encourages fat accumulation in the abdominal area, while insulin resistance, often found in metabolic syndrome, results in more fat storage in the abdominal area due to impaired lipid metabolism. In addition, changes in sex hormones, such as decreased testosterone levels in men and estrogen in postmenopausal women, are associated with fat redistribution in the body's trunk area, which worsens central obesity (Neeland et al., 2013). Subcutaneous fat in the legs generally releases less pro-inflammatory cytokines, so it can be considered a "safer" storage place. At the same time, excess fat in the arms is also associated with systemic inflammation, especially in individuals with high total body fat. However, this contribution is likely smaller than the fat in the trunk (Cuccio & Franzini, 2016; Hinojosa-Moscoso et al., 2023; Zhang et al., 2022).

The relationship between visceral and subcutaneous fat with uric acid is essential, especially in older adults who often experience metabolism and body composition changes. Uric acid is closely related to visceral fat because releasing pro-inflammatory cytokines and free fatty acids into the portal circulation will interfere with kidney function and disrupt the balance of uric acid, resulting in decreased excretion capacity and increased production capacity. Subcutaneous fat, although it has lower metabolic activity, still affects uric acid levels through systemic inflammation pathways. Excess subcutaneous fat can worsen insulin resistance, reducing renal excretion of uric acid. Although the impact is weaker than visceral fat, it contributes to the overall burden of adiposity-related metabolic dysfunction (Tao et al., 2023). In older adults, age-related changes in fat distribution will be associated with decreased kidney function, worsening the impact of visceral and subcutaneous fat on uric acid metabolism. So, it is important to conduct interventions that focus on reducing visceral and subcutaneous fat to manage hyperuricemia and prevent complications such as gout and cardiovascular disease (Bertoli et al., 2016).

CONCLUSION

This study shows a significant relationship between the percentage of visceral fat and and uric acid levels in the elderly group. Although subcutaneous fat has a weak correlation, individuals with excess visceral fat show more subcutaneous fat. Thus, this study provides significant insight into the fact that a proactive approach to reducing visceral and subcutaneous fat levels in older adults will also reduce uric acid levels.

This study has several limitations. It used a cross-sectional design, so it cannot ascertain whether fat causes an increase in uric acid or vice versa. In addition, it focused exclusively on the elderly population in the exact location, so it does not reflect the diversity of the population, either older people in general or the wider population. This study also did not consider other variables affecting uric acid levels or the percentage of visceral and subcutaneous fat percentage.

Further research is highly recommended using a longitudinal study design to explore the cause-and-effect relationship or an intervention study to evaluate the impact of interventions on uric acid levels. In addition, it is important to conduct it in a more diverse and larger group to increase statistical power and generalizability of findings.

ACKNOWLEDGMENT

The authors would like to thank Hana Nursing Home for providing the opportunity, support, and facilities as a place for this research.

REFERENCES

Bays, H. (2014). Central obesity as a clinical marker of adiposopathy; increased visceral adiposity as a surrogate marker for global fat dysfunction. In *Current opinion in endocrinology, diabetes, and obesity* (Vol. 21, Issue 5, pp. 345–351). https://doi.org/10.1097/MED.0000000000000093

Bertoli, S., Leone, A., Vignati, L., Spadafranca, A., Bedogni, G., Vanzulli, A., Rodeschini, E., & Battezzati, A. (2016). Metabolic correlates of subcutaneous and visceral abdominal fat measured by ultrasonography: A comparison with waist circumference. *Nutrition Journal*, *15*(1). https://doi.org/10.1186/s12937-015-0120-2

Cuccio, G., & Franzini, M. (2016). Oxygen-ozone therapy in the treatment of adipose tissue diseases. *Ozone Therapy*, *1*(2), 25. https://doi.org/10.4081/OZONE.2016.6270

George, C., Leslie, S. W., & Minter, D. A. (2023). Hyperuricemia. *Urology at a Glance*, 107–109. https://doi.org/10.1007/978-3-642-54859-8_23

Hikita, M., Ohno, I., Mori, Y., Ichida, K., Yokose, T., & Hosoya, T. (2007). Relationship between hyperuricemia and body fat distribution. *Internal Medicine*, *46*(17), 1353–1358. https://doi.org/10.2169/internalmedicine.46.0045

Hikita, M., Ohno, I., Mori, Y., Ichida, K., Yokose, T., & Hosoya, T. (2007). Relationship between hyperuricemia and body fat distribution. *Internal Medicine*, *46*(17), 1353–1358. https://doi.org/10.2169/internalmedicine.46.0045

Hinojosa-Moscoso, A., Motger-Albertí, A., De la Calle-Vargas, E., Martí-Navas, M., Biarnés, C., Arnoriaga-Rodríguez, M., Blasco, G., Puig, J., Luque-Córdoba, D., Priego-Capote, F., Moreno-Navarrete, J. M., & Fernández-Real, J. M. (2023). The Longitudinal Changes in Subcutaneous Abdominal Tissue and Visceral Adipose Tissue Volumetries Are Associated with Iron Status. *International Journal of Molecular Sciences*, *24*(5), 4750. https://doi.org/10.3390/IJMS24054750

Huang, X., Jiang, X., Wang, L., Chen, L., Wu, Y., Gao, P., & Hua, F. (2019). Visceral adipose accumulation increased the risk of hyperuricemia among middle-aged and elderly adults: a population-based study. *Journal of Translational Medicine*, *17*(1), 341. https://doi.org/10.1186/S12967-019-2074-1

Huang, X., Zhong, Z., He, J., Them, S., Chen, M., Liu, A., Tan, H., Wen, S., & Deng, J. (2024). Association between Visceral Adiposity Index and Hyperuricemia among Steelworkers: The Moderating Effects of Drinking Tea. *Nutrients* , *16*(18). https://doi.org/10.3390/nu16183221

Li, S., Feng, L., Sun, X., Ding, J., & Zhou, W. (2023). Association between serum uric acid and measures of adiposity in Chinese adults: a cross-sectional study. *BMJ Open*, *13*(5), e072317. https://doi.org/10.1136/BMJOPEN-2023-072317

Li, S., Feng, L., Sun, X., Ding, J., & Zhou, W. (2023). Association between serum uric acid and measures of adiposity in Chinese adults: a cross-sectional study. *BMJ Open*, *13*(5), e072317. https://doi.org/10.1136/BMJOPEN-2023-072317

Li, Z., Gao, L., Zhong, X., Feng, G., Huang, F., & Xia, S. (2022). Association of Visceral Fat Area and Hyperuricemia in Non-Obese US Adults: A Cross-Sectional Study. *Nutrients*, *14*(19). https://doi.org/10.3390/nu14193992

Liu, Y., Zhao, W., Liu, X., Jiang, H., Wu, Y., Luo, L., & Gao, Z. (2024). Identifying reliable obesity indices for hyperuricemia among middle-aged and elderly populations: a longitudinal study. *Lipids in Health and Disease* , *23*(1). https://doi.org/10.1186/s12944-024-02296-6

Neeland, I. J., Ayers, C. R., Rohatgi, A. K., Turer, A. T., Berry, J. D., Das, S. R., Vega, G. L., Khera, A., McGuire, D. K., Grundy, S. M., & De Lemos, J. A. (2013). Associations of visceral and abdominal subcutaneous adipose tissue with markers of cardiac and metabolic risk in obese adults. *Obesity (Silver Spring, Md.)*, *21*(9), E439. https://doi.org/10.1002/OBY.20135

Panlu, K., Zhou, Z., Huang, L., Ge, L., Wen, C., & Lv, H. (2024). Associations between obesity and hyperuricemia combing mendelian randomization with network pharmacology. *Heliyon*, *10*(6). https://doi.org/10.1016/j.heliyon.2024.e27074

Smith, S. R., Lovejoy, J. C., Greenway, F., Ryan, D., De Jonge, L., De La Bretonne, J., Volafova, J., & Bray, G. A. (2001). Contributions of total body fat, abdominal subcutaneous adipose tissue compartments, and visceral adipose tissue to the metabolic complications of obesity. *Metabolism: Clinical and Experimental*, *50*(4), 425–435. https://doi.org/10.1053/meta.2001.21693

Tao, M., Liu, J., Chen, X., Wang, Q., He, M., Chen, W., Wang, C., & Zhang, L. (2023). Correlation between serum uric acid and body fat distribution in patients with MAFLD. *BMC Endocrine Disorders*, *23*(1), 204. https://doi.org/10.1186/S12902-023-01447-7

Tao, M., Liu, J., Chen, X., Wang, Q., He, M., Chen, W., Wang, C., & Zhang, L. (2023). Correlation between serum uric acid and body fat distribution in patients with MAFLD. *BMC Endocrine Disorders*, *23*(1). https://doi.org/10.1186/s12902-023-01447-7

Wang, Y., Xu, Y., Hu, T., Xiao, Y., Wang, Y., Ma, X., Yu, H., & Bao, Y. (2024). Associations of Serum Uric Acid to High-Density Lipoprotein Cholesterol Ratio with Trunk Fat Mass and Visceral Fat Accumulation. *Diabetes, Metabolic Syndrome and Obesity*, *17*, 121–129. https://doi.org/10.2147/DMSO.S444142

Yasin, L., Febriyona, R., & Sudirman, A. (2023). *Pengaruh Air Rebusan Kumis Kucing terhadap Penurunan Asam Urat di Desa Manawa Kecamatan Patilanggio*.

Zhang, Y., Cai, M., Dilimulati, D., Lin, Z., Sun, H., Cui, R., Fei, H., Gao, X., Zeng, Q., Shao, X., Zhang, M., & Qu, S. (2022a). Correlation Between Serum Uric Acid and Body Fat Distribution in Patients With Polycystic Ovary Syndrome. *Frontiers in Endocrinology*, *12*. https://doi.org/10.3389/fendo.2021.782808

Zhang, Y., Cai, M., Dilimulati, D., Lin, Z., Sun, H., Cui, R., Fei, H., Gao, X., Zeng, Q., Shao, X., Zhang, M., & Qu, S. (2022b). Correlation Between Serum Uric Acid and Body Fat Distribution in Patients With Polycystic Ovary Syndrome. *Frontiers in Endocrinology*, *12*, 782808. https://doi.org/10.3389/FENDO.2021.782808