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Correlation of Uric Acid Levels with Lipid Profile among MCU Patients

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ABSTRACT

Introduction: *Uric acid (C5H4N4O3) is a product of purine degradation and can act as a pro-oxidant substance because of the formation of ROS through the enzymatic activity of xanthine oxidase. Previous research has shown that uric acid can affect lipid metabolism in the body.* ***Purpose:*** *This study aims to explore the relationship between lipid profiles in MCU patients and uric acid levels. This study employs a cross-sectional design, and we will analyze the data using linear regression.* ***Methods:*** *This study is an observational analytic study without intervention, using a cross-sectional study design. The research data came from secondary data, especially the medical records of MCU patients. Researchers selected the study sample using a random sampling technique. The study uses 86 secondary data samples.* ***Results:*** *Linear regression analysis reveals a significant positive correlation between uric acid and triglycerides (p-value < 0.001 and r = 0.464), total cholesterol (p-value = 0.018 and r = 0.255), and LDL (p-value = 0.011 and r = 0.273). A significant negative correlation exists between uric acid levels and HDL (p-value < 0.001 and r = 0.477). Increased uric acid levels are associated with higher levels of TG, TC, and LDL, as well as a decrease in HDL levels. The average levels of LDL and total cholesterol are 140.27 mg/dl and 206.66 mg/dl, respectively, which are at the high threshold, while all other variables are within normal limits.* ***Conclusion:*** *This study concludes that uric acid levels and lipid profile levels are significantly related.*

1. Introduction

Non-Communicable disease (NCDs) are degenerative conditions caused by modifiable and non-modifiable risk factor.[1] Early detection through health checks is still an appropriate strategy for controlling NCDs. Blood chemistry tests can be performed to measure uric acid levels and lipid profiles. The test results can also show an increase or decrease in both parameters, causing metabolic disorders in a person. The relationship between uric acid levels and lipid profile needs to be recognized, as it can be useful in treatment management and patient education.

The prevalence of hyperuricemia in developing and high-income countries has increased in recent years. Global burden disease shows that the prevalence of hyperuricemia in Indonesia reached 18%.[18] The non-communicable disease Risk Factor Collaboration (NCD-RisC) study on the global distribution of dyslipidemia found that Indonesia ranked fifth in the increase of non-HDL-C levels over the past four decades from 1980 to 2018.[19]

Uric acid is the end product of the purine breakdown process. Excessive increase in uric acid production and imbalance in its excretion are the chief causes of hyperuricemia (men >7.2 mg/dL, women >6.0 mg/dL).[20] The enzymatic activity of xanthine oxidase has the potential to produce ROS (Reactive Oxygen Species), which can facilitate inflammation at the cellular level through the signaling of pro-inflammatory cytokine NF-κB and increase the expression of biomarkers for inflammation.[3] Lu W et al.[4] conducted experimental research in 2015 using rats given uric acid has shown the results of dyslipidemia and glucose intolerance mediated by neuroendocrine changes through the NF-κB signaling pathway. Inflammation also reduces the ability of HDL in reverse

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cholesterol transport and prevents LDL oxidation.[2] Some research results also show differences in the effect of uric acid levels on changes in lipid profile levels. Research conducted by Yudha et al.[6] in 2023 showed an insignificant correlation between uric acid levels and HDL, while research by Bayu et al.[5] in 2023 showed an insignificant correlation between uric acid levels and triglycerides. Based on previously developed theories and differences in some research results, this study aims to determine the relationship between uric acid levels and lipid profiles in patients undergoing medical check-ups (MCU). This study's results can help patients manage diseases related to uric acid and lipid profile changes. Furthermore, these results encourage health workers to provide more holistic health education, preventing complications and improving quality of life.

2. Methods

This study is an observational analytic study without intervention, using a cross-sectional study design. The research data came from secondary data, especially the medical records of MCU patients. Researchers selected the study sample using a random sampling technique. They randomized patient medical record numbers using Microsoft Excel's "=RAND()" function, selecting 86 samples. The sample data were MCU patients at the Klinik X Jakarta Pusat from January 22 to December 2023 who met the inclusion and exclusion criteria. Inclusion criteria are MCU patients aged 18 – 60 years old with complete MCU data, while exclusion criteria are patients who routinely use drugs that reduce uric acid and lipid levels. We analyzed the research samples using the BMI SPSS 26 program. The Kolmogorov-Smirnov test assessed data normality. Univariate analysis was performed to determine the characteristic of the samples tested. Bivariate analysis used linear regression test to determine the correlation between uric acid level variables and lipid profile variables. The Health Research Ethics Committee of the Faculty of Medicine, Tarumanagara University, granted ethical clearance, and we conducted the data collection process according to applicable regulations and ethical rules.

3. Results

We analyzed data on uric acid, triglyceride, total cholesterol, HDL, and LDL levels using the Kolmogorov-Smirnov method (p-value > 0.05) indicated a normal distribution of the study data. Therefore, measurements of data centering and distribution were made using the mean and standard deviation.

Table 1.
Subject Characteristics

Variabel	Categorical	Numerical		
	Frequency (%)	Mean (SD)	Min	Max
Gender				
Men	55 (63,2%)			
Women	31 (35,6%)			
Age		44,43 (10,118)	26	55
Uric Acid		6,25 (1,57)	3,0	10,3
Uric acid (men)		7 (1,29)	3,6	10,3
Uric Acid (women)		4,9 (1,06)	3,0	8,2
Lipid Profile				
Triglycerides		138,89 (72)	36	313
Total cholesterol		206,66 (37,71)	116	304
HDL		49,29 (11,87)	31	90
LDL		140,27 (34,54)	63	219

Of the total 86 MCU patient samples, the number of male patients outnumbered female patients by 55%. The age range of patients was between 22 to 56 years old with an average age of 44.43 years old. This can indicate that the majority of people who do medical checks-up are men at a productive age. In terms of the variables studied, it was found that the average total cholesterol and LDL levels were at the high threshold, namely total cholesterol of 206.66 mg/dL and LDL of 140.27 mg/dL. The average uric acid level in men was higher than in women, at 7 mg/dL. Meanwhile, the average levels of other variables were within normal limits.

Table 2.
Characteristic of Lipid and Uric Acid Profile of Patients

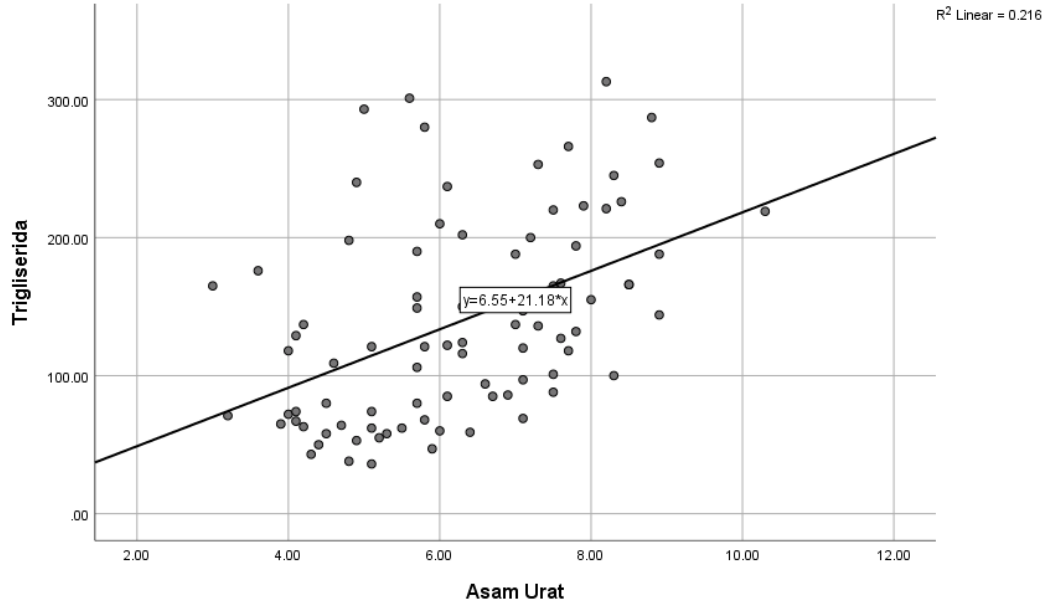
Variables	Level(mg/dl)	n(%)
Triglycerides		
Optimal	<150	52(60,5%)
Borderline high	150-199	15(17,4%)
High	200-499	19(22,1%)
Very high	>500	0
Total Cholesterol		
Desirable	<200	36(41,9%)
Borderline high	200-239	35(40,7%)
High	>240	15(17,4%)
High density lipoprotein (HDL)		
Low	<40	17(19,8%)
Optimal	40-59	52(60,5%)
High	>60	17(19,8%)
Low density lipoprotein (LDL)		
Optimal	<100	6(7%)
Near optimal	100-129	31(36%)
Borderline high	130-159	26(30,2%)
High	160-189	17(19,8%)
Very high	>190	6(7%)
Uric acid (women)		
Low	<2.6	0
Normal	2.6-6	29(93,5%)
High	>6	2(6,5%)
Uric Acid (men)		
Low	<3.5	0
Normal	3.5-7.2	30(54,5%)
High	>7.2	25(45,5%)

The results of the sample data mapping showed that the majority of medical check-up patients had lipid profile levels within normal limits. 52 patients (60.5%) had triglyceride levels within optimal limits. 36 patients (41.9%) had total cholesterol levels within desirable limits. 52 patients (60.5%) had HDL levels within optimal limits. 31 patients (36%) had LDL levels in the near optimal category. Uric acid levels in women tended to be distributed within normal limits, with 29 patients (93.5%). The distribution of uric acid levels in men showed that the majority of patients had normal uric acid levels, namely 30 patients (54.5%).

Linear Regression Test

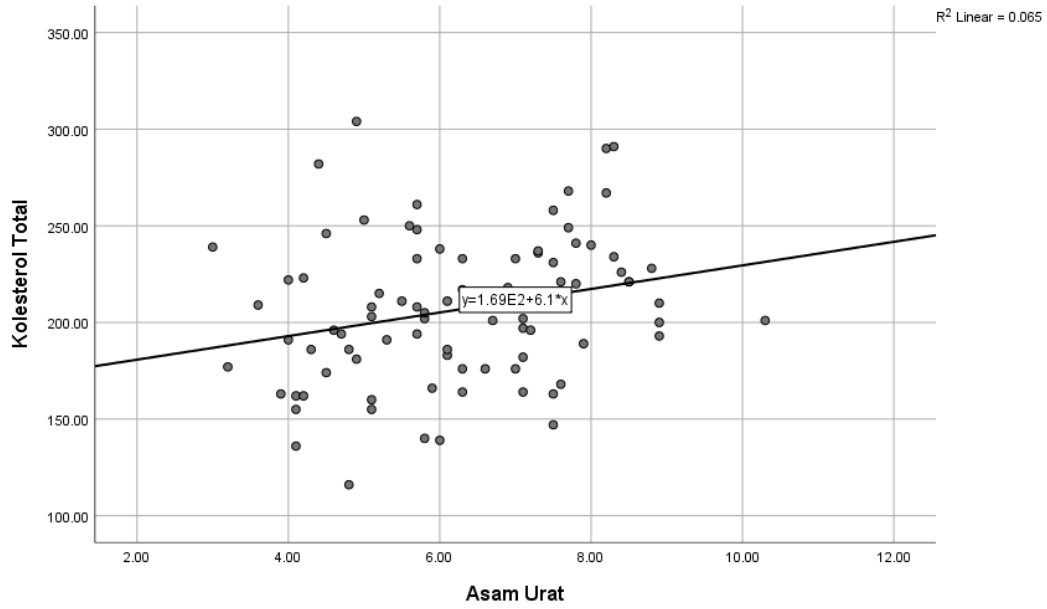
The results of the linear regression test showed a significant correlation between uric acid levels and each lipid profile component with a p-value <0.05. Uric acid levels with triglycerides have a positive correlation with a moderate degree (r = 0.464). Uric acid levels with total cholesterol have a positive correlation with a weak degree (r = 0.255). HDL and uric acid levels showed a moderate negative correlation (r = -0.477). A weak positive correlation (r = 0.273) exists between uric acid levels and LDL. We can also present this correlation graphically using a linear regression equation

Figure 1.
Correlation Graph of Uric Acid and Triglyceride levels



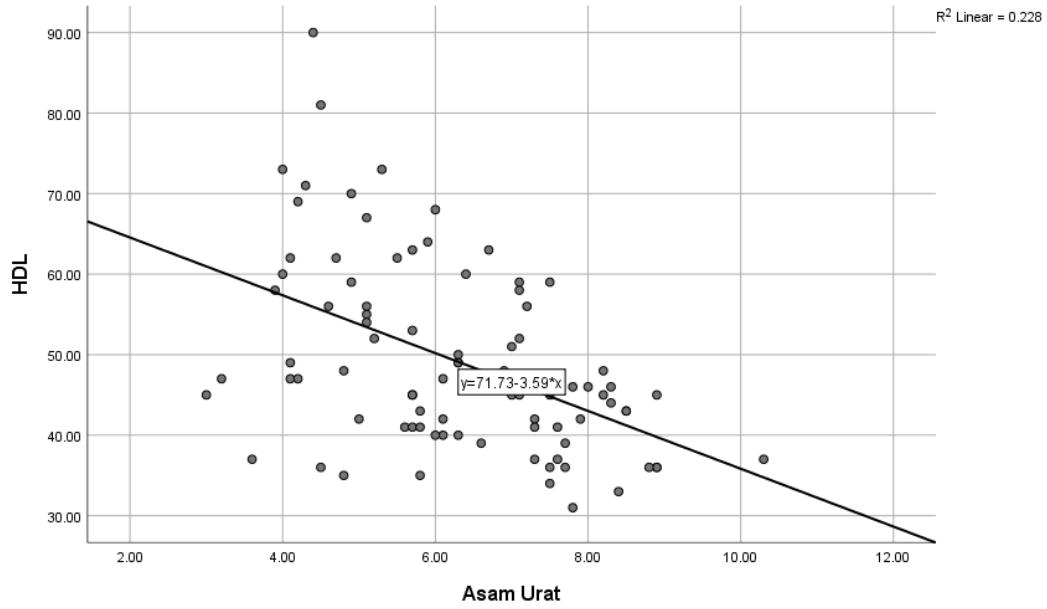
The regression equation between uric acid and triglyceride levels is y = 6.547 + 21.176x. The regression coefficient has a positive value of 21.176, this means that each increase in uric acid levels by 1 mg/dL will be accompanied by an increase in triglyceride levels by 21.176.

Figure 2.
Correlation Graph of Uric Acid and Total Cholesterol Levels



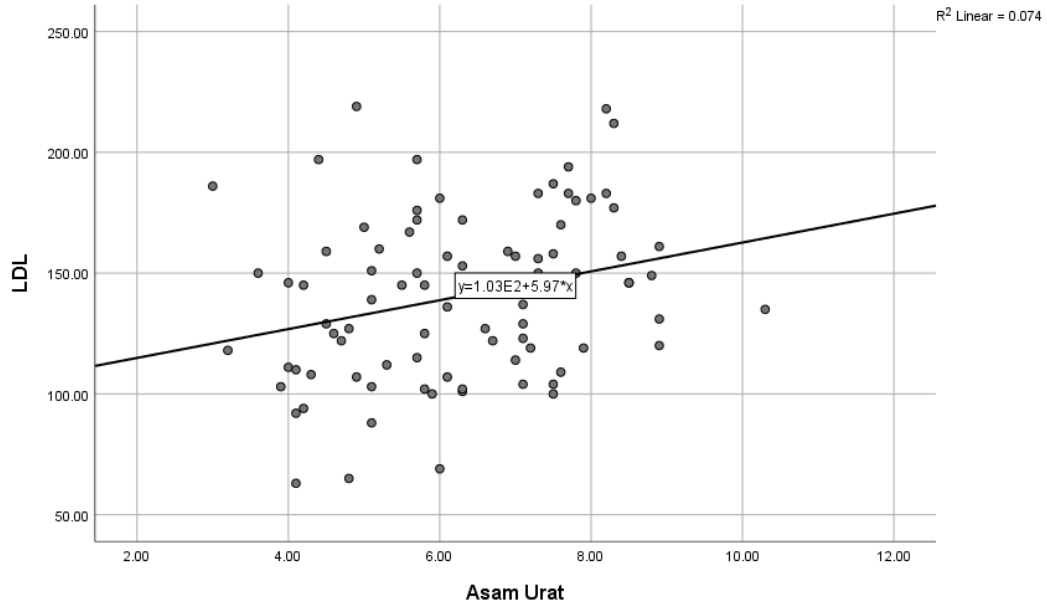
The regression equation between uric acid and total cholesterol levels is y = 168.554 + 6.097x. The regression coefficient has a positive value of 6.097, this means that each increase in uric acid levels by 1 mg/dL will be accompanied by an increase in total cholesterol levels by 6.097.

Figure 3.
Correlation Graph of Uric Acid and HDL Levels



The regression equation between uric acid and HDL is y = 71.730 - 3.590x. The regression coefficient has a negative value of 3.590, this means that each increase in uric acid levels by 1 mg/dL will be accompanied by a decrease in HDL levels by 3.590.

Figure 4.
Correlation Graph of Uric Acid and LDL Levels



The regression equation between uric acid and LDL levels is y = 102.962 + 5.971x. The regression coefficient has a positive value of 5.971, this means that each decrease in uric acid levels by 1 mg/dL will be accompanied by an increase in LDL levels by 5.971.

4. Discussion

The results indicated that women had an average uric acid level of 4.9 mg/dL and men had 7 mg/dL. Uric acid levels in women are lower than men. Estrogen hormones can suppress the activity of GLUT9/SLC2A9 transporters in the renal tubules, thereby reducing uric acid reabsorption and increasing its excretion in the urine.[7] High uric acid levels tend to have patients with an age range of 50-55. The results of this study show an increase in uric acid levels with age. This is relevant to the study conducted by Suwanchatchai *et al.*[8] in 2023 which used samples with middle age and older, that the prevalence of hyperuricemia reached 30.9% and was found more in men. A cohort study in 2022 conducted by Tsai MK *et al.*[9] in the period 2007 - 2017 of 1,899 patients also showed that a decrease in total testosterone levels (<400 ng/dL) in men with advanced age can increase the risk of hyperuricemia.

The results of the study indicate an influence on increasing uric acid levels on increasing triglyceride levels. This study is in line with the findings of Zheng *et al.*[10] in their cohort study that examined the relationship between these two variables in 1461 patients for 8 years. Patients with higher uric acid levels had a tendency to develop hypertriglyceridemia compared to patients with lower uric acid levels. A known mechanism in the effect of uric acid on triglycerides is that high uric acid levels can inhibit hepatic lipase enzymes, thereby reducing the breakdown of triglycerides. Elevated uric acid levels also lead to increased oxidative stress in the mitochondria. This induces apoptotic activity and mitochondrial dysfunction, so that the release of citrate into the cytosol will initiate lipogenesis and triglyceride synthesis.[11]

The results indicate the influence of uric acid levels on increasing total cholesterol levels. Previous studies also found a significant correlation. Research in Bangladesh in 2019 by Ali *et al.*[13]in Bangladesh using 280 samples examined the relationship between the two variables with a p-value <0.001.[13] This is also relevant to similar research conducted by Chen *et al.*[12] in China with 8,642 adult samples showing similar results.

The results also indicate the influence of uric acid levels on HDL levels negatively, where an increase in HDL levels will be followed by a decrease in uric acid levels. Research by Ali *et al.*[13] in Bangladesh using 280 samples showed significant results also negatively with a p-value <0.001. The significance is reinforced by the findings of Moriyama K[14] in 2018 that hyperuricemia will make the levels of HDL particles with larger sizes decrease in number. Larger HDL, such as HDL 1 and HDL 2 are more effective at carrying cholesterol back into the liver to be metabolized, so a decrease in HDL levels can increase the incidence of atherosclerosis and other cardiovascular diseases.[14]

The results also indicate the influence of uric acid levels on increasing LDL levels. Research by Lim S *et al.*[15] in Korea in 2020 using 8,127 samples has shown positive significance with a p-value <0.001. A 5-year cohort study by Kuwabara *et al.*[16] in Japan in 2018 also showed significant results between uric acid levels and LDL levels. The mechanism underlying the relationship between uric acid and LDL is not fully known. A possible process is that uric acid has a role in inhibiting lipoprotein lipase, thereby increasing LDL levels.

There are differences in the results of the current study with several other studies. Research by Bayu *et al.*[5] produced an insignificant relationship between uric acid and triglyceride variables with a p-value = 0.124. Another study by Yudha *et al.*[6] also showed an insignificant relationship between uric acid variables and HDL with a p-value = 0.054. Differences in the population used in the study can cause this difference. The composition of a population will affect the characteristics of each sample used. The study reviewed the relationship between the two variables in a sample of patients with certain diseases, while this study used a sample of MCU patients who tended to be healthy or did not have certain diseases. It is also expected to bring results that can be more broadly generalized to the general population.

The correlation in this study has a degree that is almost equivalent to the research conducted by Ali *et al.*[13] in Bangladesh. The resulting correlation of the variables of uric acid levels and lipid profiles in these studies has a weak degree on average.The difference in the level of correlation produced can be due to the number of samples in the study being more than the number of samples in this study.

Another study conducted in India in 2013 by Sarmah D[17] showed a strong degree of correlation between uric acid variables and lipid profiles. The r value in the study can reach 0.79 to 0.88. Sample selection can cause the difference in the magnitude of the resulting correlation in Indian studies using participants who all have hyperuricemia.

This study has several limitations. The secondary data of this study partly had incomplete data regarding the history of consumption of lipid and uric acid lowering drugs which could affect the status of uric acid levels and lipid profiles in patients. Additionally, we need further analysis of uric acid's relationship with other metabolic syndrome criteria to reveal a more comprehensive correlation in metabolic disorders.

5. Conclusion

Based on the findings of this study, it can be concluded that there is a significant relationship between uric acid levels and lipid profile levels. The average total cholesterol and LDL cholesterol levels of the patients were 206.66 mg/dL and 140.27 mg/dL, respectively, both of which were in the near optimal category, while the other variables were within normal limits. Uric acid levels showed positive significant correlations with triglycerides (*p-value* < 0.001, r = 0.464), total cholesterol (*p-value* = 0.018, r = 0.255), and LDL (*p-value* = 0.011, r = 0.273). Increased uric acid levels have the potential to increase triglyceride, total cholesterol, and LDL levels. Uric acid levels showed a significant negative correlation with HDL (*p-value* < 0.001, r = 0.477). Increased uric acid levels have the potential to reduce HDL levels. Future studies should add variables related to metabolic syndrome criteria to gain a more comprehensive understanding of metabolic disorders.

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