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Correlation between Urea Creatinine Ratio (UCR) and lipid profile in COVID-19 patients

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ABSTRACT

Background: SARS-CoV-2, as the leading cause of COVID-19 disease, can cause kidney disorders characterized by the presence of hematuria, increased creatinine, and other kidney pathological conditions. Since a 24-hour urine examination as the gold standard for urea examination has several weaknesses, it is necessary to carry out an alternative examination method especially, the Urea Creatinine Ratio (UCR). This study evaluates the correlation between UCR and lipid profile in COVID-19 patients.

Methods: A descriptive-analytical design with a cross-sectional approach is applied. COVID-19 patients with positive PCR were examined for UCR, Total Cholesterol, Triglycerides, HDL, and LDL. The assessment was based on clinical chemistry analysis using an automatic analyzer. We perform a normality test using Shapiro-Wilk. The Pearson correlation test is used to see a correlation between variables. The study was conducted at Siloam Hospital in April-August 2021. Data were analyzed using SPSS version 20 for Windows.

Results: There was no significant difference between UCR and the other variables based on the statistical analysis test ($p>0.05$). There was no significant correlation between UCR and cholesterol total ($p= 0.230$), UCR and Triglyceride ($p= 0.680$, UCR and HDL ($p=0.970$) and UCR and LDL ($p= 0.190$).

Conclusion: There is no significant correlation between UCR and lipid profile in COVID-19 patients

Keywords: UCR, Cholesterol Total, Triglycerides, HDL, LDL.
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INTRODUCTION

In the last two decades, the world has had to deal with the outbreaks of Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV), Middle East Respiratory Syndrome (MERS-CoV), and Corona Virus Disease 2019 (COVID-19). Most SARS-CoV-2 infected patients show mild symptoms manifested in generalized respiratory distress. However, the infection ends in death in most cases due to multi-organ complications.[1,2]

Several studies have reported changes in lipid profile associated with COVID-19.[2,3] Lipids to form the structural foundations of cellular and viral membranes as well as hence play an important role in lung biology and the pathophysiology of viral disease.[4] Viruses target lipid syn-thesis and signal modification of host cells to generate lipids for their envelopes.[5] The lipid profiles include Total Cholesterol (TC), High-Density Lipoprotein Cholesterol (HDL-C), Low-Density Lipoprotein Cholesterol (LDL-C) and Triacylglycerol (TG).[6] Lipids are crucial in the infection process, as they are important structural components of cellular and subcellular organellar membranes. Membrane lipid components participate in the regulation of transmembrane molecular trafficking, including infectious materials such as viruses.[7]

There is a strong correlation between COVID-19 and renal impairment, partly due to increased baseline renal viral load, systemic inflammation, or both. SARS-CoV-2 can penetrate cells through two receptors; Angiotensin-Converting Enzyme 2 (ACE2) and Transmembrane Protease Serine 2 (TMPRSS2). ACE2 receptors are massively displayed in proximal tubular epithelial cells and podocytes.[8]

Renal impairment is a progressive and irreversible kidney function disorder that causes uremia. Kidney function will decrease with age and inflammation. Decreased kidney function can occur mild, moderate, and severe.[9] There are no signs and symptoms in the early stages of decline in kidney function, so it is necessary to check the urea creatinine ratio as an early marker of chronic kidney disease. Both urea and serum creatinine have advantages and disadvantages in assessing glomerular filtration function; therefore, we can use the urea to creatinine ratio (UCR) to determine kidney failure. The UCR level was obtained from calculating of urea level divided by creatinine level.[10]

The spectrum of lipid disorders in renal impairment is usually characterized by high triglycerides and reduced High-Density Lipoprotein (HDL), associated with normal or slightly reduced Low-Density Lipoprotein (LDL)-cholesterol. This dyslipidemia is associated with an increased risk for atherosclerotic

cardiovascular disease.[11] In this study, we wanted to see how the UCR correlates with lipid profiles in COVID-19 patients.

Another study reported that the cytokine storm induced by COVID-19 also triggers low urea creatinine. This can increase the risk of death, and the phenomenon, which is common in the stage of viral infection, can be used as an independent predictor of disease progression. A meta-analysis also showed that serum creatinine levels 133 mol/L are correlated with COVID-19 severity. This hypothesis is in line with the finding showing that a decrease in the glomerular filtration rate and an increase in the creatinine-urea ratio strongly correlate with the risk of hospitalization and is correlated with the incidence of death.[12]

A previous study using the Urea Creatinine Ratio (UCR) method has a very good correlation with 24-hour urine protein levels (r=0.830; p=<0.001), adequate inspection facilities (autoanalyzer facilities) that this examination is still rarely carried out. An alternative method for measuring urinary frequency, blood sugar levels, and cholesterol is the measurement of urea levels with a dipstick.[13] The strip-dip method is faster, cheaper, easier to do, and reliable. Examination results can be read manually or semi-automatically. In the study, it is found that reading with the instrument will increase the sensitivity of the examination by 12%.[13]

METHODS

This quantitative research took the sample at Siloam Hospital Semarang City using a cross-sectional approach. The examination of urea creatinine ratio (UCR), cholesterol total, triglycerides, HDL, and LDL levels was performed at Siloam Laboratory using Roche Cobas C-111 chemical analyzer. The COVID-19 examination through isothermal PCR was conducted at the Siloam Hospital laboratory installation in Semarang for April-August 2021.

The study sample was patients diagnosed with COVID-19 by consecutive sampling methods and confirmed by isothermal polymerase chain reaction examination. The study sample signed informed consent to participate in the study and was willing to examine lipid profiles. The normality test was assessed using Shapiro-Wilk, followed by the Pearson correlation test. A p-value less than 0.05 is considered statistically significant. The data display uses a scattergram to see the relationship between the two variables. Data were analyzed using SPSS version 20 for Windows.

RESULTS

23 patients meet the criteria and are willing to participate in the study at Siloam Hospital, Semarang. The sample consists of 20 males and 3 females. Urea levels had an average of 20.74 ± 8.46 mg/dL, and creatinine levels were 0.87±0.27 mg/dL. UCR is calculated by dividing the variable urea by creatinine. UCR has a mean of 24.15±7.90 with a median value of 23.89, a minimum value of 13.33, and a maximum value of 42.22 (Table 1).

Lipid profile examination was performed on patients fasting 8 hours. Cholesterol levels had an average of 187.78±33.13 mg/dL; HDL levels had an average of 40.21 ± 8.55 mg/dL; LDL examination had a mean of 125.39±31.60 mg/dL. Triglycerides have an average level of 127.56±62.64 mg/dL (Table 1).

Based on Table 2, it can be concluded that there was no significant correlation between UCR (urea creatinine ratio) and Total Cholesterol, HDL (High-Density Lipoprotein), LDL (Low-Density Lipoprotein) and Triglycerides (p>0.05) (Table 2 and Figure 1).

DISCUSSION

According to the recent findings, it can be concluded that there is no correlation between UCR, total cholesterol, High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL), and triglycerides which can be seen from the correlation value of more than 0.05. This result is similar with the research conducted by Fauziah et al., the journal of clinical pathology at Universitas Muhammadiyah Yogyakarta (UMY), which stated that there was no relationship between Urea Creatinine Ratio (UCR) and High-Density Lipoprotein (Low-Densitynsity Lipoprotein (LDL).[14]

The mechanism thought to play a role in this increase in total cholesterol values is excessive lipoprotein production because of low plasma urea concentrations, low plasma oncotic pressure, and impaired catabolism of apolipoprotein B and VLDL chylomicrons.[15] Low urea values occur due to increased reabsorption and catabolism of urea by the proximal tubule. When the intake increases, the glomerular

Table 1. Baseline characteristic of respondents

Variable	Total (N=23)	Mean±SD	Median (Min–Max)	p
Gender, n (%)				
Male	20 (87.0%)			
Female	3 (13.0%)			
Age (years)		42.00±13.90	41 (23–72)	0.140
Ureum (mg/dL)		20.74±8.46	19 (10–43)	0.030
Creatinine (mg/dL)		0.87±0.27	0.90 (0.40–1.80)	0.000*
UCR		24.15±7.90	23.89 (13.33–42.22)	0.270
Cholesterol (mg/dL)		187.78±33.13	184 (123–258)	0.990
HDL (mg/dL)		40.21±8.55	38 (28–57)	0.170
LDL (mg/dL)		125.39±31.60	127 (67–194)	0.990
Triglyceride (mg/dL)		127.56±62.64	120 (43 – 301)	0.100

*Shapiro-Wilk: Statistically significant if p-value less than 0.05

Table 2. Correlation between UCR and lipid profile parameter

Variable	r	p
Cholesterol	0.013	0.23
HDL	0.121	0.97
LDL	0.089	0.19
Triglyceride	0.075	0.68

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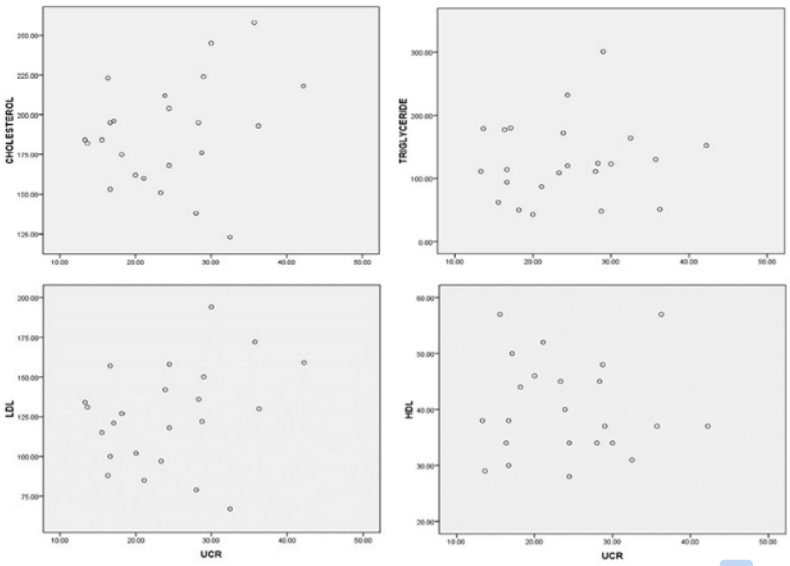

Figure 1. Graphic correlation between UCR/UACR and Lipid profile parameter (A. Total Cholesterol; B. Triglyceride; C. HDL; D. LDL)

pressure will increase, increasing the amount of protein that passes into the urine. The greater the value of total blood cholesterol, the smaller the patient's urea value. Vice versa, the smaller the total blood cholesterol value, the greater the patient's urea value. The results were similar to Karim S et al., showing that as many as 70% of patients experienced low urea and 30% of patients experienced a severe decrease in urea.[16]

Research conducted by Shandilya A et al., in 2018 at a hospital in India stated that there was a significant increase in total cholesterol and triglycerides and a significant decrease in urea and serum globulins in patients with nephrotic syndrome, but there was no correlation with urea.[17] Another study conducted by Watuseke AE et al. is also in line with this study which stated that there was a correlation between urea and triglycerides butt found no correlation between urea and triglycerides.[18] In women, triglycerides are generally lower than in men. But at menopause, women's triglycerides tend to increase and cause the incidence of coronary disease in women to increase as well. Consumption of alcohol, saturated fatty acids, carbohydrates, and high calories can increase triglycerides. Uncontrolled obesity and diabetes are the most common causes of high triglyceride levels.[18] High triglyceride levels occur when a person eats many foods containing carbohydrates or high sugar levels. The risk of heart disease will increase along with a person's high triglyceride levels. It is possible that the high triglyceride levels in some respondents were caused by obesity and diabetes. However, the researchers did not measure the respondents' BMI and blood sugar levels. This is due to the limitations of the types of examinations given to respondents, which only measure triglyceride levels.[18]

Previous studies stated a significant negative correlation between cholesterol and urea, triglycerides and urea, and between Low-Density Lipoprotein (LDL) and urea.[18,19] This hyperlipidemia arises due to low levels of urea in the blood. The low urea state stimulates the liver cells to make as much urea as possible so that along with this urea synthesis, the liver cells will also make lipoproteins. This decreased fat degradation is related to the reduced lipoprotein lipase activity so that the levels of circulating free fatty acids in the serum increase. Lipoprotein lipase is an enzyme that catalyzes the reduction of fat in the blood causes a decrease in the clearance of fat in the blood. Increased lipoprotein synthesis and decreased fat degradation will lead to hyperlipidemia.[19] A previous study also stated that there was a significant increase in total cholesterol, HDL, LDL, and triglycerides and a significant decreased in urea and serum globulins in patients with nephrotic syndrome.[17]

The small number of samples in this study accompanied by consecutive sample selection (non-randomized) is a limitation of the results of this study to be generalized to a wide population. So, further studies with greater sample size as well as total sampling approach is recommended to clarify the recent findings.

CONCLUSION

Total Cholesterol, HDL, LDL, and triglyceride variables were not significant to UCR. Further research is recommended with a larger sample and other COVID biomarker variables. Cholesterol, HDL, LDL, and Triglycerides with UCR are affected by various causes, concerning the significance. For that, we have to think about its application in the management of COVID-19.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the manuscript.

ETHICS CONSIDERATION

Ethics approval has been obtained from the ethics committee of Medical Faculty, Universitas Diponegoro, Semarang, Indonesia, with number 324/EC/KEPK/FK-UNDIP/IX/2021 prior to the study being conducted.

FUNDING

The government-funded this research through research development and application.

AUTHOR CONTRIBUTIONS

IKS: take data, process data, discuss discussions; US: take care of EC, take data, process data and discuss; and AS: process data. All authors and co-authors agree to submit the manuscript.

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GENERAL COMMENTS

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RUBRIC: SHORT ANSWER

CLAIM/FOCUS

State a clear claim/topic sentence and stay focused on supporting it.

MEETS EXPECTATIONS	A precise claim/topic sentence based on the topic and/or source(s) is present. The response maintains a strong focus on developing the claim/topic sentence, thoroughly addressing the demands of the task.
APPROACHES EXPECTATIONS	A claim/topic sentence based on the topic and/or source(s) is present, but it may not completely address the demands of the task, or the response does not maintain focus on developing it.
DOESN'T MEET EXPECTATIONS	The claim/topic sentence is vague, unclear, or missing, and the response does not address the demands of the task.

SUPPORT/EVID

Provide evidence and explain how it supports the claim/topic sentence.

MEETS EXPECTATIONS	The response includes sufficient, appropriate evidence to support the claim/topic sentence. Reasoning and understanding of the topic and/or source(s) are demonstrated by thorough explanations of the relationship between claims and support.
APPROACHES EXPECTATIONS	The response presents some evidence to support the claim/topic sentence, but it may be insufficient or inappropriate. Some reasoning and understanding of the topic and/or source(s) are demonstrated, but attempts to explain the relationship between claims and support are inadequate.
DOESN'T MEET EXPECTATIONS	Evidence is general or largely absent, and explanation of the relationship between claims and support is minimal.

ORGANIZATION

Present ideas in a logical structure that shows the relationships between ideas.

MEETS EXPECTATIONS	An effective organizational structure enhances the reader's understanding of the information. The relationships between ideas are made clear with effective transitional phrases.
APPROACHES EXPECTATIONS	An organizational structure is evident, but may not be fully developed or appropriate. Transitional phrases may be used but the relationships between ideas are somewhat unclear.
DOESN'T MEET EXPECTATIONS	An organizational structure is largely absent and the relationships between ideas are unclear.

LANGUAGE

Communicate ideas using formal language and vocabulary specific to the topic.

MEETS EXPECTATIONS	The response has an established, formal style that is maintained throughout. Varied sentence structure, precise language, and domain-specific vocabulary are used to communicate ideas effectively. The response may stray from an objective tone at times, or have some errors that do not interfere with meaning.
APPROACHES EXPECTATIONS	The response attempts a formal style that may not be maintained throughout. Sentence structure is somewhat varied and some precise language and/or domain-specific vocabulary are used. The response contains some errors that may interfere with meaning.
DOESN'T MEET EXPECTATIONS	The response does not establish a formal style and and ideas are unclear at times. There is little variety in sentence structure and language is general throughout. The response contains several errors that interfere with meaning.