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Association between Triglyceride Serum Levels and Glomerular Filtration Rate (eGFR) in Patients with Chronic Renal Failure at Jemursari Islamic Hospital Surabaya, Indonesia

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Abstract

Chronic Renal Failure (CRF) is a progressive and irreversible decrease in kidney function. One risk factor that affects the progression of CRF is dyslipidemia due to abnormalities of lipid metabolisms. Dyslipidemia is characterized by the increase level of total cholesterol, LDL cholesterol, triglycerides, and a decrease in HDL cholesterol level. eGFR is a parameter for assessing the excretion function, by calculating the amount of filtrate produced by the renal glomerulus. This study aims to determine the relationship between serum triglyceride levels with eGFR in patient suffering from CRF at Jemursari Islamic Hospital Surabaya. This type of research is descriptive experimental with cross–sectional design. The study population was the patients with CRF. The primary data in this study was the results of examination of serum triglyceride levels in patients with CRF. The secondary data (serum creatinine levels, body weight, age, and sex) was obtained from medical records of CRF patients in February 2019. As much as 12% of patients were in the 40–50 years old category, 36% of patients were 51–60 years old, 44% of patients were 61–70 years old, and 8% of patients were 71–80 years old. 72% of patients were male. The mean triglyceride level was 146.68 mg/dL and the average eGFR was 19.86 mL/min/1.73m^2. The relationships between triglyceride levels and eGFR was carried out by the Spearman–rho test where r value was –0.442 and ρ value was 0.027. It was concluded that there was a significant negative correlation between serum triglyceride levels and eGFR in patients with CRF.

Keywords

Chronic renal failure, triglycerides, eGFR, GPO–PAP

INTRODUCTION

Renal failure is a condition in which the kidney decrease the function, so the kidneys are unable to maintain body homeostasis. In general, there are 2 types of kidney failure, namely chronic renal failure and acute renal failure. Acute renal failure is a condition in which the kidneys suddenly stop functioning entirely or almost entirely but may still be able to return to normal kidney function in a short time. Meanwhile, chronic renal failure is a condition in which there is a progressive damage to the function of many nephrons that have an effect on reducing the kidney function. Both of those categories produce specific renal failure which results in renal blood vessels, glomerulus, tubules, interstitial kidneys, and parts of the urinary tract outside the kidney (1). Renal failure is defined as chronic if it is chronic, permanent, and progressive, so that the glomerular filtration rate (GFR) will progressively decrease and will eventually reach terminal renal failure. Patients with chronic renal failure (CRF) are often asymptomatic until there is an increase in kidney damage (2).

Based on data in various centers of nephrology in Indonesia, the prevalence of chronic renal failure increases with age. It sharply increases in the age group of 35–44 years old (0.3%), followed by 45–54 years of age (0.4%) and 55–74 years of age (0.5%). The highest prevalence of chronic renal failure are ≥75 years of age (0.6%). In addition, the prevalence of CRF in men is 0.3% which is higher than that of women (0.2%) (3).

Triglycerides (also called triacylglycerol) are one of the fats in the blood formed by esterification of glycerol and three fatty acids carried by lipoproteins in plasma (4). The digestive process of triglycerides begins with absorption in the intestine and it is circulated in the blood to the liver in the form of chylomicrons (exogenous). The people who consume foods which high in lipids will cause the appearance of cloudy serum such as milk or cream (lipemic). The liver has a role in the treatment of triglycerides. Most triglycerides are stored as fat in adipose tissue. The function of triglycerides is to provide energy to the heart muscle and skeletal muscle as well as to reserve of energy that can produce a lot of ATP. Triglycerides are a major cause of arterial disease and are often compared to cholesterol through lipoprotein electrophoresis test. The increase in triglyceride concentration will cause hyperlipoproteinemia (4).

According to a study conducted by Bhagaskara, et.al (5), the mean triglyceride levels in patients with chronic renal failure was 163.26 mg/dL (it belongs to fairly high category). The results of this study are in accordance with Raju’s research, et.al (5), which stated that chronic renal failure patients with dyslipidemia showed the characteristics such as elevated triglyceride levels and LDL cholesterol levels (5). Hyperlipidemia or an increase in lipid profile contributes not only to heart disease, but also contributes to the progression of renal failure.

Glomerular Filtration Rate (GFR) is one of the physiological examinations of the kidneys in assessing excretory function by calculating the filtrate released by the glomerular kidney. Patients with GFR 60–89 mL/min/1.73m^2 showed an increase in lipid profile. According to Sengsuk[(6)] in the Diabetes and Obesity International Journal, the determination of GFR estimation was based on the Cockroft–Gault formula which uses 3 variables (age, weight, and sex) with the normal value of eGFR is 90 mL/min/1.73m^2. Circulating lipoproteins play a direct role in the pathogenesis of glomerulosclerosis and tubulointerstitial changes (6).

Based on the explanation above, the authors are interested in examining the Correlation of Triglyceride Serum Levels to Estimated Glomerular Filtration Rate (eGFR) in Patients with Chronic Renal Failure at Jemursari Islamic Hospital Surabaya.

MATERIALS AND METHODS

The research method used was descriptive experimental research with a cross–sectional study design. The equipment's that used in this research were TMS 24i Premium automatic device (Tokyo Boeki Medisys, Japan), 10–1000 µl micropipette, blue micropipette tip, and Eppendorf tube. The primary data in this study was the result of examination of serum triglyceride levels in patients with chronic renal failure. Secondary data (serum creatinine levels, body weight, age, and sex) was obtained from medical records of patients with CRF at Jemursari Hospital Surabaya in February 2019.

The study population was patients with chronic renal failure at the Jemursari Islamic Hospital Surabaya in the period of February 2019 who had fulfilled the retention criteria to be taken as research subjects. The sample used was fresh serum (fasting 12 hours), which was obtained from whole blood without anticoagulants that was centrifuged at 3.000 rpm for ±15 minutes at room temperature–(12). The sample size was calculated using Slovin formula and was resulted as many as 25 serum (8).

The research sample was taken using purposive sampling technique which was based on certain considerations that had met the inclusion criteria set by the researcher. The sample inclusion criteria used in this study were: patients with chronic renal failure, men and women aged ≥40 years old, patients with chronic renal failure who were either have or have not undertaken hemodialysis, patients with chronic renal failure who perform creatinine examination and measurement of body weight in the same time, and patients with chronic renal failure who were undergoing hospitalization or outpatient care. The exclusion criteria for the study sample included: patients aged <40 years, patients with a diagnosis of CRF+hypertension, CRF+diabetes mellitus, CRF+renal cysts, and CRF+urosepsis.

The samples obtained were centrifuged at 3.000 rpm for ±15 minutes. The serum was separated into eppendorf tubes. A total of 25 fresh serum samples were analyzed for triglyceride levels using the GPO–PAP enzymatic colorimetric method using the automatic TMS 24i Premium (Tokyo Boeki Medisys, Japan). Determination of eGFR value was calculated manually using the Cockcroft–Gault (C–G) formula:

$$GFR = \frac{(140 - age) \times weight(kg) \times 0{,}85(female)}{72 \times S_{cr}\left(\frac{mg}{dL}\right)}$$

S_{cr} : Serum creatinine

The results of the analysis of triglyceride levels were carried out to invistigate the correlation analysis of the eGFR value.

The variables in this study were age, gender, triglyceride level, and eGFR of CRF patients. The data were analyzed by univariate and bivariate. Bivariate analysis (eGFR and triglycerides) used the Spearman correlation test with the data normality test. Data is presented in textular, graphical and tabular forms. The statistical program used is IBM SPSS Statistics 23.0.

Ethical Clearance

This research was approved by the Research Ethics Committee of Jemursari Islamic Hospital Surabaya (005/KEPK–RSI JS/I/2019). Involvement of respondents was based on a written agreement by filling a consent form. Respondents may withdraw at any time if they do not agree or are not satisfied with any study procedures.

RESULTS

Table 1 shows the distribution of samples by age and gender. The age of the men and women respondents was ≥40 years. About 75% of respondents were outpatient care and 25% of respondents were undergoing hospitalization. Most of CRF patients were 61–70 years old (44%), followed by 12% of patients belongs to 40–50–years age group, 36% of patients falls in 51–60 years age group and 8% of patients were categorized in 71–80 years age group. Table 2 shows the distribution of samples according to laboratory examination results. The eGFR results was calculated manually using the Cockcroft–Gault formula. The variable serum creatinine levels, body weight, age, and sex data were obtained from medical records of patients in February 2019. Based on the Table 2, there were 0% of CRF patients with eGFR values between 60–89 and ≥90 mL/min/1.73m^2. A total of 5 stage III patients (20%) have eGFR values 30–59 mL/min/1.73m^2. Ten stage IV patients (40%) have eGFR values 15–29 mL/min/1.73m^2 and 10 stage V patients (40%) have eGFR values <15 mL/min/1.73m^2. The mean eGFR value was 19.87 with standard deviation 11.41.

All of respondents suffered from dyslipidemia. There were 64% of respondents have triglyceride level <150 mg/dL. Four patients (16%) have triglyceride level of 150–199 mg/dL and 5 patients (20%) have TG level 200–499 mg/dL. The mean triglyceride level was 146.68 with standard deviation 86.95.

Table 1. Sample Distribution by Gender and Age

Gender	Aged	Additional Inspection		Hemodialysis (HD)	%
		Weight (kg)	S_{cr} (mg/dL)		
Male	40–50	53	5.54	Non–HD	4%
	51–60	61–78	1.49–18.28	Non–HD	28%
	61–70	61–78	1.76–9.93	Non–HD	32%
	71–80	68–74	1.79–2.48	Non–HD	8%
Female	40–50	48–51	1.79–6.01	Non–HD	8%
	51–60	49–51	1.45–7.12	Non–HD	8%
	61–70	50–53	3.70–9.74	Non–HD	12%
	71–80	0	0	Non–HD	0%

Table 2. Sample Distribution According to Laboratory Examination Results

Laboratory Test	Range	Mean	Std. Dev.	%
eGFR (mL/min/1.73m^2)	≥90	19.87	11.41	0%
	60–89			0%
	30–59			20%
	15–29			40%
	≤15			40%
Triglyceride (mg/dL)	<150	146.68	86.95	64%
	150–199			16%
	200–499			20%
	≥500			0%

Figure 1 shows the data distributions of triglyceride levels in patient with CRF. Kolmogrov–Smirnov Normality Test shows that the distribution was normal (ρ<0.05). Figure 2 shows the data distributions of eGFR, which were normal (ρ<0.05).

Table 3 shows the statistical distribution of triglyceride and eGFR. It shows the results of examination of triglyceride levels (a minimum value was 33 mg/dL and a maximum value was 357 mg/dL. While, the results of the eGFR value were a minimum value 4.75 mL/min/1.73m^2 and a maximum value of 47,76 mL/min/1.73m^2. The statistical correlations between serum triglyceride levels and eGFR can be seen in Table 4. The Spearman–rho correlation test results obtained significance value 0.027 < α (0.05).

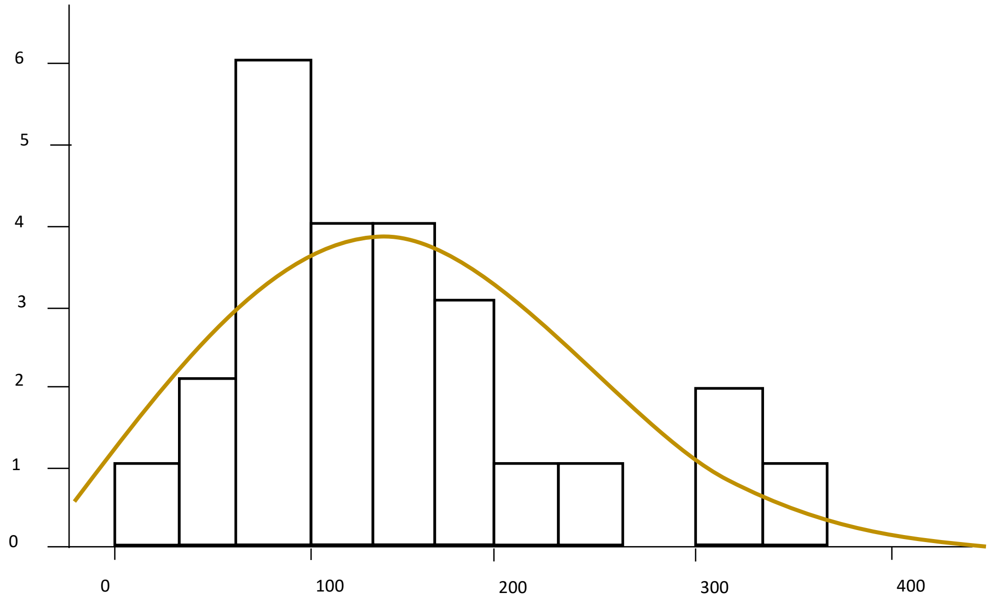

Fig 1. Distributions of Triglyceride Levels (mL/min/1.73m^2)

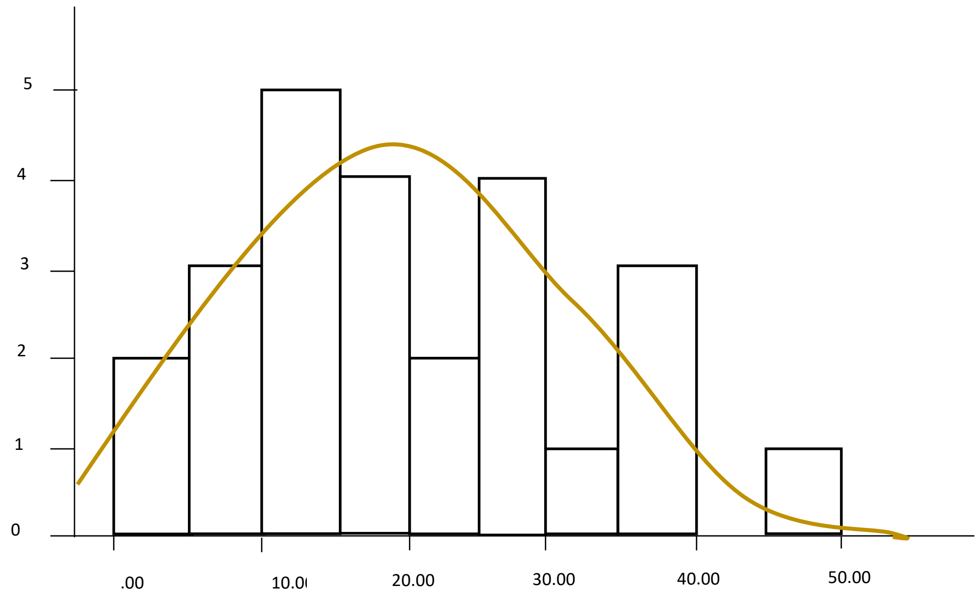

Fig 2. Distributions of eGFR (mg/dL)

Table 2. Min–Max and Median Values of TG and eGFR

Laboratory Test	Value's Range Min–Max	Median
TG	33–357 mg/dL	123 mg/dL
eGFR	4.75–47.76 mL/min/1.73m^2	15.59 mL/min/1.73m^2

Table 3. Statistical Correlations

		eGFR
Triglyceride Levels	Correlation coefficient	–.442*
	Sig. (2–tailed)	.027
	N	25

DISCUSSION

This study aims to determine the correlation between serum triglyceride levels and eGFR values in subjects with chronic renal failure. The population of this study were all patients with chronic renal failure at Jemursari Islamic Hospital in Surabaya during February 2019. The number of patients with CRF was 93 patients, but only 25 patients met the inclusion criteria. A total of 8 excluded patients were under 40 years old. Moreover, 60 excluded patients had a diagnosis of CRF with complications. The results showed that 40% of respondents was stage IV CRF patients, 40% of respondents was stage V patients, followed by 20% of stage III patients, 0% of respondents was stage I and II patients. The degree of severity is obtained through the calculation of the eGFR value with Cockcroft–Gault (C–G) formula in mL/min/1.73m^2. GFR is parameter for assessing excretion function, by measuring the amount of filtrate produced by the kidney glomerulus (2). The lower value of GFR indicates the more severity of the kidney damage.

Table 1 shows that the most respondents (44%) with CRF occur at 61–70 years of age. 12% of respondents was in the 40–50–year age group, 36% of respondents was in the 51–60–year age group and 8% of them was in the *71–80–year* age group. A decline in kidney function is a normal process as the age increase. The increasing age shows a progressive decrease in GFR and Renal Blood Flow (RBF). The decrease occurs around 8 mL/min/1.73m^2 per decade since the 40 years of age (9).

Of 25 samples, 18 patients (72%) were male, while 7 patients (28%) were. This is in accordance with the Indonesian Renal Registry (9) data, which shown hemodialysis patients throughout Indonesia were dominated by men in 2007–2012 (10). These results might be related to the incidence of CRF, such as kidney stones, which also occur mostly in male. Other studies show that the prevalence of kidney stones in men was 10,6% and those in women was 7,1%.

Based on Table 2, that was 0% of CRF patients who has eGFR values between 60–89 and ≥90 mL/min/1.73m^2. A total of 5 stage III patients (20%) has eGFR values 30–59 mL/min/1.73m^2. Ten stage IV patients (40%) has eGFR values of 15–29 mL/min/1.73m^2 and 10 stage V patients (40%) has eGFR values <15 mL/min/1.73m^2. A decrease in GFR value can be affected by the increasing age and the cause of kidney damage itself.

Based on Table 2, the results of examination of triglyceride levels were a minimum value of 33 mg/dL, a maximum value of 357 mg/dL, and a mean of 146,68 mg/dL. While the results of the eGFR value obtained a minimum value 4,75 mL/min/1.73m^2, a maximum value of 47,76 mL/min/1.73m^2 with an average 19,86 mL/min/1.73m^2. The results of the study at the Laboratory Unit at Jemursari Islamic Hospital Surabaya stated that there was a relationship between triglyceride levels and eGFR values in CRF patients. The *Spearman–rho* correlation test results has a significance value (0.027) < α (0.05) then H_1 was accepted, which means that there was a statistically significant correlation between serum triglyceride levels and eGFR values. The number of correlation coefficients is negative, which is –0.444 *. A negative sign indicates that the correlation of the two variables is not in the same direction (the type of relationship is not unidirectional). While the asterisk (*) shows the level of strength (closeness) of the relationship between the two variables (Table 4). Thus, it can be concluded that there was a strong and unidirectional significant correlation between the variables of triglyceride levels and eGFR values. The higher the serum triglyceride level, the lower the eGFR value.

Furthermore, 11 subjects had high triglyceride levels. This is in accordance with the research conducted by Anggun (16) in Kariadi Hospital Semarang, where 73 patients with chronic renal disease were accompanied by hypertriglyceride (52.9%). Whereas, Senge, et al. (17) in the Kidney–Hypertension Polyclinic of RSUP Dr. R. D. Kandou Manado, found that there was a positive relationship between triglyceride levels and eGFR in CKD patients (ρ = 0.030), meaning that the higher triglyceride levels, the higher the eGFR value will be. This mismatch may be caused by several factors, such as a high creatinine diet, malnutrition, ketoacidosis and drugs (cimetidine, sulfa, trimethoprim) which results in decreased creatinine secretion which indicates as one of the determinants of the glomerular filtration rate (12).

Indonesian Renal Regulations (IRR) data stated that in 2007 there were 6,862 people who suffered from chronic kidney failure and experienced an increase in 2012, amount to 28,782 people. Chronic kidney failure is kidney damage that occurs for 3 months, based on pathological abnormalities or markers of kidney damage such as proteinuria. If there is no sign of kidney damage, the diagnosis of CRF can be made if the glomerular filtration rate is less than 60 mL/min/1.73m^2 (10). Decreasing the GFR value is related to the severity.

The National Kidney Foundation recommends that the eGFR can be calculated according to serum creatinine. Calculation of GFR based on serum creatinine, age, body size, gender, and race without the need for urinary creatinine levels using the Cockcroft and Gault equation (13). The classification of CRF stage based on GFR values is as follows: stage I with a GFR value of 90 mL/min/1.73m^2, stage II with a GFR value of 60–89 mL/min /1,73m^2, stage III with a GFR value amounting to 30–59 mL/min/1.73m^2, stage IV with a GFR value of 15–29 mL/min/1.73m^2, and stage V with a GFR of 15 mL/min/1,73 m^2 (14).

One risk factor that affects the progression of chronic renal failure is dyslipidemia. People with CRF are at an increased risk of cardiovascular disease and have a higher prevalence of hyperlipidemia (or dyslipidemia) than the general population. Dyslipidemia occurs due to abnormalities of lipid metabolism in patients with CRF. Most of patients (47%) with chronic kidney failure died from cardiovascular disease as the main cause (10). In fact, mild renal insufficiency has been shown to be associated with an increased rate of cardiovascular events (15).

Dyslipidemia characterized by increased triglyceride levels, total cholesterol and LDL cholesterol and decreased HDL cholesterol levels are often associated with CRF and contribute to an increased risk of cardiovascular disease. Various experimental studies have shown that lipid abnormalities can worsen the progression of kidney damage (17).

The process of forming triglycerides is derived from food. The fatty foods we eat consist of triglycerides and cholesterol. In addition to cholesterol derived from food, in the intestine, there is also cholesterol from the liver which is excreted with bile into the small intestine. Triglycerides and cholesterol in the small intestine will be absorbed into the intestinal mucosal enterocytes. Triglycerides will be absorbed as free fatty acids while cholesterol remains cholesterol (4).

Inside the small intestine, free fatty acids will be converted into triglycerides, while cholesterol will be esterified to cholesterol esters and both together with phospholipid and apolipoproteins will form lipoprotein, known as chylomicron. This chylomicron will enter the lymph channels and eventually through the thoracic duct will enter the bloodstream. Triglycerides in chylomicron will undergo hydrolysis by the *lipoprotein lipase* enzyme derived from endothelium into free fatty acids. Free fatty acids can be stored as triglycerides again in fat tissue, but if they are present in large amounts, some of them will be taken by the liver to become a material for the formation of triglycerides in the liver (17).

High triglyceride levels contribute to the process of atherosclerosis. Poor circulation to most organs causes hypoxia and tissue injury, and stimulates inflammatory reactions in the walls of blood vessels. If atherosclerosis occurs, the blood supply to the kidneys will decrease and can cause GFR abnormalities and decreased kidney function (17).

CONCLUSIONS

In conclusion, there was a significant negative correlation between serum triglyceride levels and the estimated value of the Glomerular Filtration Rate (eGFR) in patients with chronic renal failure at

Jemursari Islamic Hospital, Surabaya. The higher the triglyceride level, indicate the lower the eGFR value. Further research is needed to be done by considering the etiology and clinical picture of CRF patients which are confounding factors in this study.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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