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Correlation Of Triglyceride Serum Levels To Estimated Glomerular Filtration Rate (Egfr) In Patients With Chronic Renal Failure At Jemursari Islamic Hospital Surabaya

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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 chronic renal failure is dyslipidemia. Dyslipidemia occurs due to abnormalities of lipid metabolisms in patient with CRF. Dyslipidemia is characterized by increased levels of total cholesterol, LDL cholesterol, triglycerides, and decreased HDL cholesterol levels. eGFR is a parameter for assessing excretion function, by calculating the amount of filtrate produced by the renal glomerulus. The degree of decrease in eGFR indicates the severity of renal damage. This study aims to determine the relationship of serum triglyceride levels with eGFR in patient with CRF at Jemursari Islamic Hospital in Surabaya. This type of research is descriptive experimental with cross-sectional design. The study population was patients with chronic renal failure, outpatient and hospitalization at Jemursari Islamic Hospital in Surabaya as many as 25 serum samples. As much as 12% of patients are in the 40 – 50 year age category, 36% are 51 – 60 years old, 44% are 61 – 70 years old, and 8% are 71 – 80 years old. Seventy-two percent of patients are male. The mean triglyceride level was 146,68 mg/dL and the average eGFR was 19,86 mL/min/1,73m2. The relationships between triglyceride levels and eGFR was carried out by the Spearman-rho test obtained by the value r = -0,442 and ρ = 0,027. It was concluded that there is a significant negative correlation between serum triglyceride levels and eGFR in patients with chronic renal failure at Jemursari Islamic Hospital Surabaya.
Keywords: Chronic renal failure, Triglycerides, eGFR, GPO-PAP (Glycerol Phospat Oxidase-Para Amino Phenazone)

1. Introduction

Renal failure is a condition of decreased kidney 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. While chronic renal failure is a condition in which there is progressive damage to the function of many nephrons that have an effect on reducing 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 said to be chronic if it is chronic, permanent, and progressive so that the glomerular filtration rate (LFG) will progressively decrease and will eventually reach terminal renal failure. Patients with chronic renal failure (CRF) are often asymptomatic until kidney damage increases (2).

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

Triglycerides (also called trisilgliserol) 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 is circulated in the blood to the liver in the form of chylomicrons (exogenous). The people who consume foods high in lipids will cause the

appearance of cloudy serum such as milk or cream (lipem). 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 and has a role as a reserve of energy that can produce a lot of ATP. Triglycerides are a major cause of arterial disease and are often compared with cholesterol through lipoprotein electrophoresis tests. When the triglyceride concentration increases, VLDL also increases, causing hyperlipoproteinemia (4).

According to a study conducted by Bhagaskara, Et. Al (2015) the mean triglyceride levels in patients with chronic renal failure amounted to 163.26 mg / dL and included in the fairly high category. The results of this study are in accordance with Raju's research, Et. Al. (2013), which stated that patients with chronic renal failure with dyslipidemia showed 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 / 1.73 m2 showed an increase in lipid profile. According to Sengsuk, (2017) in the Diabetes and Obesity International Journal, the determination of GFR estimation based on the Cockroft –Gault formula which uses 3 variables, that is age, weight and sex with the normal value of eGFR is 90 ml / min / 1.73 m2. Circulating lipoproteins play a direct role in the pathogenesis of glomerulosclerosis and tubulointersisial changes (6).

Based on the above explanation, 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.

2. Research Methodology

2.1. Research methods

The research method used was descriptive experimental research with a cross-sectional study design. The study population was patients with chronic renal failure at the Jemursari Islamic Hospital in 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 centrifuged at 3,000 rpm for ± 15 minutes at room temperature (7). The size of the sample used calculated using the Slovin formula (8) obtained as many as 25 serum samples.

2.2. Time and Place

The research was conducted at the UNUSA Laboratory, B Tower campus, on Jl. Raya Jemursari no. 57, Jemur Wonosari, Wonocolo, Surabaya city, East Java. February 2019.

2.3. Tools and Materials

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, patients with chronic renal failure who have or have not done hemodialysis, patients with chronic renal failure who perform creatinine examination and measurement of body weight in the time the same, and patients with chronic kidney failure who are undergoing hospitalization or outpatient care. The exclusion criteria for the study sample included: patients aged <40 years, patients with a diagnosis of CRF+hypertension, GGK+diabetes mellitus, CRF+renal cysts, and CRF+urosepsis.

2.4. Procedure

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, patients with chronic renal failure who have or have not done hemodialysis, patients with chronic renal failure who perform creatinine examination and measurement of body weight in the time the same, and patients with chronic kidney failure who are undergoing hospitalization or outpatient care. The

exclusion criteria for the study sample included: patients aged <40 years, patients with a diagnosis of CRF+hypertension, GGK+diabetes mellitus, CRF+renal cysts, and CRF+urosepsis.

The research instruments included the TMS 24i Premium automatic device (Tokyo Boeki Medisys, Japan), 10-1000 µl micropipette, blue micropipette tip, and eppendorf tube. The primary data collection technique 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) originated from medical records of patients with CRF at Jemursari Hospital in Surabaya in February 2019. The samples obtained were centrifuged at 3,000 rpm for ± 15 minutes. The serum is separated into eppendorf tubes. A total of 25 fresh serum samples were analysed for triglyceride levels using the GPO-PAP enzymatic colorimetric method using the automatic TMS 24i Premium tool (Tokyo Boeki Medisys, Japan). Determination of eGFR value is calculated manually using the Cockcroft-Gault (C-G) formula:

$$GFR = \frac{(140 - Age) \times Weight\,(kg) \times 0,85\,(female)}{72 \times s_{er}(mg/dl)}$$

Scr : Serum creatinine

The results of the analysis of triglyceride levels obtained were carried out correlation analysis of the eGFR value. The variables studied 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.

3. Result and Discussion

This study aims to determine the correlation of serum triglyceride levels to 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 for the period of February 2019. The number of patients with CRF was 93 patients, but only 25 patients met the inclusion criteria. A total of 8 patients were under 40 years old and 60 other patients had a diagnosis of CRF with complications. The results showed that the most of patients were stage IV CRF patients at 40%, and stage V at 40% followed by stage III at 20% while stage I and stage II at 0%. The degree of severity is obtained through the calculation of the eGFR value with the Cockcroft-Gault (C-G) formula in mL / min / 1.73 m2. GFR is a parameter for assessing excretion function, by measuring the amount of filtrate produced by the kidney glomerulus. The lower the value of GFR, indicates the more severe kidney damage.

Table 1 shows that the most people with CRF occur at 61-70 years of age at 44%. In the 40-50 year age group of 12%, the 51-60 year age group is 36% and in the 71-80 year age group is 8%. Decreasing kidney function is a normal process every increase in human age. Increasing age shows a progressive decrease in Glomerular Filtration Rate (GFR) and Renal Blood Flow (RBF). The decrease occurs around 8 mL / min / 1.73m2 per decade since the age of 40 years (9) .

As many as 25 samples, 18 patients (72%) were male, while female sex were 7 patients (28%). This is in accordance with the Indonesian Renal Registry (2012) data, that from 2007-2012 hemodialysis patients throughout Indonesia were dominated by men (10). These results may be related to the incidence of CRF, such as kidney stones, which also occur mostly in male sex. Other studies show that the prevalence of kidney stones in men is 10.6% and in women is 7.1% (11).

Based on Table 3, there are 0% of CRF's patients with eGFR values of 60-89 and 90 mL / min / 1.73 m^2. A total of 5 (20%) stage III patients with eGFR values of 30-59 mL / min / 1.73 m^2. Ten patients (40%) stage IV with eGFR values of 15-29 mL / min / 1.73 m^2 and 10 (40%) stage V patients with eGFR values <15 mL / min / 1.73 m^2. A decrease in GFR can be affected by increasing age and the cause of kidney damage itself.

Based on Table 5, the results of examination of triglyceride levels, obtained a minimum value of 33, a maximum value of 357, and a mean of 146.68. While the results of the eGFR value, obtained a minimum value of 4.75, a maximum value of 47.76 with an average of 19.86. The results of the study at the Laboratory Unit of 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 obtained a significance value (0.027) <α (0.05) then H1 was accepted, which means that

statistically there is a 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 6). Thus, it can be concluded that there is a strong and unidirectional significant.

11 subjects had high triglyceride levels. This is in accordance with the research of Anggun Desi Wulandari (2012) in Kariadi Hospital Semarang, where 73 patients with chronic renal disease were found accompanied by hypertriglyceride (52.9%). Whereas Senge, et al. (2017) 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 ($\rho = 0.030$), meaning that the higher triglyceride levels, the higher the eGFR value. This mismatch may be caused by several factors, such as a high creatinine diet, malnutrition, ketoacidosis and drugs (cimetidin, sulfa, trimethopin) which results in decreased creatinine secretion as one of the determinants of the glomerular filtration rate (12) correlation between the variables of triglyceride levels and eGFR values. The higher the serum triglyceride level, the lower the eGFR value.

Chronic renal failure (CRF) is a progressive and irreversible decrease in kidney function. Indonesian Renal Regulations (IRR) data states that in 2007 there were 6,862 people who suffered from chronic kidney failure and experienced an increase in 2012, amounting 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 / 1.73m2 (10). Decreasing the GFR value is related to the severity.

The National Kidney Foundation recommends that the estimated GFR (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 / 1.73 m2, stage II with a GFR value of 60-89 mL / min / 1.73 m2, stage III with a GFR value amounting to 30-59 mL / min /1.73 m2, stage IV with a GFR value of 15-29 mL / min / 1.73 m2, and stage V with a GFR of 15 mL / min / 1.73 m2 (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 (47%) patients with chronic kidney failure die of 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 (16).

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). When 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 apolipoprotein will form lipoprotein known as kilomicron. This Kilomycron will enter the lymph channels and eventually through the thoracic duct will enter the bloodstream. Triglycerides in kilomycrons 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 (16).

4. Conclusion

There is 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, the lower the eGFR value.

5. Thank You Note

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