The correlation between creatinine serum with total iron binding capacity (TIBC) on patients with sufferers chronic renal disease in Gambiran regional public hospital Kediri city

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ABSTRACT

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Chronic kidney disease (CKD) is kidney damage that occurs for more than 3 months with a glomerular filtration rate of less than 60 ml/sec/ 1.73 m\textsuperscript{2}. WHO estimates that in Indonesia, there will be an increase in PGK in 1995-2025 by 41.4%. Over the past 40 years, Creatinine serum has become the most common and cheap serum marker for kidney function. One of the most common complications in patients with PGK is anemia. Anemia in PGK can be caused by several factors such as EPO deficiency, iron deficiency, etc. One of the usual parameters checking is the iron status of TIBC. This study aims to determine the relationship of serum Creatinine level with TIBC in chronic kidney patients in Gambiran regional public hospital Kediri and sampling taken by quota sampling. The study used cross-sectional using Rank Spearman statistic test. This test is used for abnormally distributed data types. The measured variable was serum Creatinine level with TIBC. The results of this study indicate that the value of p = (0.000)> α = (0.05), so H1 rejected and H0 accepted, then there is no relationship between serum Creatinine levels with TIBC in patients with chronic kidney disease in Gambiran Hospital Kediri.

INTRODUCTION

Chronic kidney disease (CKD) is a pathophysiological process with a variety of etiologies, resulting in a progressive decrease in kidney function, and generally ends with kidney failure. Chronic kidney disease has become a major health problem in the world community.\textsuperscript{1}

Chronic kidney disease (CKD) is one of the common causes of renal failure. It involves a progressive loss over the course of months in the structure and function of the kidneys, with or without a decreased glomerular filtration rate (GFR). CKD can be diagnosed by its pathological abnormalities, changes in the levels of kidney function markers in the blood or urine, or by imaging investigations.\textsuperscript{2}

Chronic kidney disease is a significant cause of morbidity and mortality world wide. In India, there is a rising incidence and prevalence of kidney failure, with poor outcomes and high cost. The hallmark of CKD is structural and functional damage of the glomeruli of the kidney. The most important outcomes of this kidney damage are loss of kidney function and cardiovascular disease leading to premature death.\textsuperscript{3}

The prevalence of chronic kidney failure in America is around 5% -37% between 1980-2001.\textsuperscript{4} The prevalence of chronic kidney failure in Indonesia is around 0.2%.\textsuperscript{5} The prevalence of the ≥ 75 year age group is 0.6% higher than other age groups.\textsuperscript{5} Based on
data from RSUD Gambiran Kediri, the results of preliminary observations of chronic kidney disease patients were approximately 135 per month in 2017.

Chronic kidney disease is kidney damage with a glomerular filtration rate / LFG of less than 60 ml / min / 1.73m2 characterized by a structural abnormality or impaired renal function irreversible and has lasted for three months or more, with or without a gradual and sustained reduction in glomerular filtration rates.⁷

Rate Glomerular filtration (LFG) is a plasma volume that can be completely cleaned of certain compounds by the kidneys in one unit of time. Serum creatinine is the most well-known endogenous marker used to estimate LFG. Although its use has been recognized since the beginning of the 20th century, serum creatinine has limitations both physiologically and analytically. Physiologically, the two main limitations of using serum creatinine to estimate LFG are variations in creatinine tubular secretion and the dependence of serum creatinine excretion on muscle mass.⁸

According to Astrid's research, with the title "Overview of Serum Creatinine Levels in Kidney Disease patients in Stage 5 non-dialysis Chronic" using a cross-sectional descriptive design, a sample of 35 people was used. Test results obtained for all patients diagnosed with non-dialysis stage 5 chronic kidney disease have increased serum creatinine levels (100%) due to renal dysfunction. Creatinine filtration ability will decrease and serum creatinine will increase.¹

Chronic kidney disease is usually associated with anemia and the level of anemia correlates with the severity of the renal failure. The anemia of renal failure has been attributed to a relative deficiency of erythropoietin, but absolute deficiencies of iron or folate may also play a role. Other contributing factors include heavy metal toxicity, blood loss, and a reduction in red cell survival induced by toxic radicals. The treatment of the anemia of renal disease has advanced with the development of recombinant human erythropoietin.⁹

Anemia is one of the complications that occur in CKD patients with an incidence rate of 80-90%. If severe kidney damage occurs, the production of erythropoietin in the kidneys is disrupted so that red blood cell production is reduced. Along with kidney damage, bleeding, iron deficiency accompanied by a decrease in glomerular filtration rate, the degree of anemia will increase.¹⁰

Anemia of renal failure begins relatively early in the development of kidney disease. As the destruction of the kidney progresses, the degree of anemia increases. Although there is a large degree of the patient to patient variability, the Hct generally begins to fall when the plasma creatinine concentration is above 2 mg/dl and gets lower as glomerular filtration rate (GFR) declines.¹¹

Anemia prevalence worldwide was estimated at 33% in 2010 with iron deficiency being the leading cause in half of the cases. In chronic kidney disease (CKD) patients, anemia is a clinically significant burden and it becomes more prevalent with declining glomerular filtration rate (GFR). Anemia is associated with reduced quality of life and increased cardiovascular morbidity and mortality. Erythropoietin (EPO) deficiency remains the major cause of anemia in CKD patients due to the decrease in renal EPO production.¹²

Anemia in CKD can also be caused by iron deficiency. Iron deficiency anemia can be diagnosed using conventional iron status laboratory examinations such as serum iron (SI), Total Iron Binding Capacity (TIBC), transferrin saturation, and serum ferritin.¹³

Iron is essential for oxygen binding in red blood cells and is crucial for many other cellular functions. Iron deficiency, even without anemia, has been demonstrated to be an independent risk factor for increased mortality.² Iron deficiency anaemias also common in patients with chronic kidney disease. Iron deficiency may be absolute, often due to poor dietary intake or sometimes occult bleeding, or functional, when there is an imbalance between the iron requirements of the erythroid marrow and the actual iron supply.¹⁴
According to previous research, uses descriptive research design, the sample used 92 people and processed using Pearson correlation statistical test and Kolmogorov-Smirnov categorical test. Evaluating TIBC values, where 80% of CKD patients experience decreased TIBC levels.\textsuperscript{15}

The high prevalence of anemia in patients with Chronic Kidney Disease (GGK) and the number of iron status parameters that can be used to see changes in iron metabolism in these patients requires a specific and sensitive parameter to determine iron status, namely Fe and TIBC parameters (Total Iron Binding Capacity). Both parameters are better than if only checking hemoglobin levels, which are less sensitive to determine iron status, especially in mild anemia in patients with chronic renal failure.\textsuperscript{13}

\section*{MATERIALS AND METHODS}

This research was conducted at the Laboratory of Gambiran Hospital in Kediri City in July-August 2017. The population of this study was all patients with Chronic Kidney Disease at Gambiran Hospital, Kediri City. The sample used in this study was 32 patients with CKD in Gambiran Hospital, Kediri City. The sampling technique in this study was to use a Non-Random (Non Probability) Quota Sampling. Quota sampling is quotient sampling or quota, done by determining how many samples are needed. Any population member to be taken is not a problem, the important number of quotas that have been determined can be fulfilled.\textsuperscript{16} With a sample size of 32 chronic kidney disease in Gambiran Hospital, Kediri City. The number of samples where the appropriate sample size in the study is between 30 and 500.\textsuperscript{17}

In this study using data analysis using a correlation study test. Correlation test is a statistical tool that can be used to compare the measurement results of 2 different variables in order to determine the level of relations between variables. Correlation test used is Pearson test for a parametric test (normal data distribution) which is used to find the relationship of two or more variables, but if the distribution of data is not normal it can be used non-parametric statistical test namely spearman test SPSS 16.0 program.\textsuperscript{18}

\section*{RESULTS AND DISCUSSION}

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|}
\hline
Sample & age & Creatinine (mg/dl) & TIBC (µl/dl) \\
Code & & & \\
\hline
A1 & 60 & 5,1 & 200,2 \\
A2 & 57 & 11,95 & 251,5 \\
A3 & 47 & 7,8 & 217,9 \\
A4 & 47 & 5,6 & 318 \\
A5 & 55 & 13,4 & 213,6 \\
A6 & 73 & 16,3 & 233,5 \\
A7 & 71 & 10,1 & 262,6 \\
A8 & 69 & 12,3 & 233,9 \\
A9 & 53 & 9,19 & 258 \\
A10 & 67 & 10,84 & 268 \\
A11 & 60 & 6,5 & 321 \\
A12 & 75 & 25,3 & 238,3 \\
A13 & 56 & 7,4 & 304 \\
A14 & 71 & 13 & 226 \\
\hline
\end{tabular}
\caption{Data on Creatinine and TIBC results in patients with chronic kidney disease in Gambiran Hospital Kediri city}
\end{table}
In chronic renal failure, there is a steady and continued decrease in renal clearance or glomerular filtration rate (GFR), which leads to the gathering of urea, creatinine and other chemicals in the blood. GFR of less than 60 mL/minute/1.73 m² is the indication of CKD. KDIGO additional classified the CKD in different stages which are: GFR 30 to 60 mL/minute as stage three; GFR 15 to 30 mL/minute as stage four; and GFR less than 15 mL/minute as stage five of CKD. In stage five level of serum creatinine is greater than 5.0 mg/dl in men, and greater than 4.0 mg/dl in women.

It can be seen that 32 CKD patients experienced an increase in serum creatinine (100%). This result is not much different from the research conducted at the RSUD dr. Moewardi Surakarta, which shows that there were 31 patients (93.9%) who had high creatinine levels. Over the past 40 years, serum creatinine has become the most common and inexpensive serum marker to determine kidney function. Serum creatinine examination is also very helpful in carrying out therapy in patients with kidney function disorders. High and low creatinine levels in the blood are used as important indicators in determining whether a person with impaired renal function needs hemodialysis or not. If renal dysfunction occurs, creatinine filtration ability will decrease and serum creatinine will increase. A doubling of serum creatinine levels indicates a decrease in kidney function by 50%, as well as a threefold increase in serum creatinine reflecting a decline in kidney function by 75%. One of the most important kidney functions is the excretion of metabolic waste products such as creatinine. The function is very disturbed in patients with non-dialysis kidney failure as a result of increased serum creatinine levels. Therefore, serum creatinine levels are used as an important indicator to determine kidney function.

The amount of creatinine released by a person every day depends more on muscle mass than muscle mass or protein metabolism, this causes creatinine values in men to be higher because the amount of male muscle mass is greater than the amount of muscle mass of women. Muscle mass and protein metabolism generally cause a constant effect of creatinine formation, except if there is a severe physical injury or degenerative disease that causes damage to muscles.

In this study, it was found that many samples had decreased TIBC values. This is consistent with previous research, that the sample with a TIBC value decreased more than the normal TIBC value. TIBC which decreases in CKD can be caused by increased...
ferritin or can occur in anemia of chronic diseases that occur inflammation. However, in regular hemodialysis patients can experience iron deficiency anemia due to blood loss.\textsuperscript{15}

In CKD group, iron metabolism is altered compared to controls. Here, serum iron levels are low due to inadequate secretion of erythropoietin, erythropoiesis is halted leading to decreased Hb and serum iron. Serum ferritin stores are not utilized due to associated inflammation giving rise to near normal ferritin levels.\textsuperscript{23}

From the results of the study entitled the relationship of serum creatinine with TIBC in patients with chronic kidney disease in Gambiran Hospital, Kediri City showed that there was no statistical relationship between serum creatinine and TIBC with $p > 0.05$. The results of this study support the theory in the study entitled "Iron chronic disease kidney disease patients" that there was no significant relationship between serum creatinine and TIBC in chronic kidney patients.\textsuperscript{5} This is probably because not all people with chronic kidney disease are caused by iron deficiency anemia. Iron deficiency anemia in patients with CKD is mainly caused by poor nutritional intake, impaired absorption, chronic bleeding, inflammation or infection, and increased iron requirements during correction of anemia with Erythropoietin Stimulating Agent (ESA) therapy.\textsuperscript{24} The other causes than iron deficiency, such as erythropoietin deficiency, uremia related inhibition of erythropoiesis, and short life span of the red blood cell may be responsible for anemia in those subjects.\textsuperscript{25}

**CONCLUSIONS**

Based on the results of the study, the relationship between serum creatinine levels and TIBC in patients with chronic kidney disease in Gambiran Hospital, Kediri City can be concluded that Statistically, there is no correlation between serum creatinine and TIBC in patients with chronic kidney disease with $p > 0.05$. This is because anemia in CKD is mainly caused by reduced production of erythropoietin (EPO) and not all sufferers of chronic kidney disease have iron deficiency anemia.

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