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Relationship Between Serum Procalcitonin (PCT) Levels and Acute Kidney Injury (AKI) in Critical Patients Taking Attention in the Intensive Care Unit (ICU) of Adam Malik Hospital, Medan

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Abstract:-

Background: AKI that occurs in critically ill patients in the ICU is associated with high mortality and significant morbidity.

Methods: This study was an observational analytic study with a case-control survey study design without machining to assess the relationship between serum PCT levels and the incidence of AKI in critically ill patients admitted to the intensive care unit (ICU). This research was conducted at Haji Adam Malik General Hospital Medan from January-December 2020. The parameters measured were Procalcitonin (PCT) and Acute Kidney Injury (AKI).

Results: From 80 patients with 52 patients without AKI and 28 patients with AKI, patients with high PCT values (more than 1.575 ng/ml) were 14.93 times more likely to have AKI than those with low PCT values (less than 1.575 ng/ml)). There is a relationship between serum PCT levels and the incidence of AKI in critically ill patients admitted to the intensive care unit (ICU) with a strong positive correlation.

Conclusion: High procalcitonin is more common in critically ill patients with AKI compared to those without AKI who are admitted to the ICU.

***Keywords**:- AKI, Procalcitonin, Critical Patient in ICU.*

I. INTRODUCTION

Acute kidney injury (AKI) occurs in about 5-7% of patients hospitalized, and occurs in about 36-57% in critically ill patients treated in the intensive care unit (ICU). [1–3]. The incidence of AKI has also increased over the same time period in hospitalized patients from 4.9% in 1983, to 7.2% in 2002, and increased by 20% in 2012.[4]. In developing countries, the incidence of AKI is rarely reported, this is because not all patients are referred to the hospital. Several world reports show that the incidence varies between 0.7-18% in hospitalized patients, up to 20% in patients admitted to the intensive care unit (ICU), while the worldwide mortality rate ranges from 25% to 80%.[5].

The incidence of AKI in the ICU is 22% with variations in the incidence ranging from 9% to 30%. Variations in incidence are obtained regardless of the cause or risk factor for AKI[6]. AKI occurs in 67% of ICU patients based on RIFLE criteria (risk injury failure loss end stage), class R (risk) 12%, class I (injury) 27% and class F (failure) 28%[7]. In Indonesia, in a retrospective study of patients treated in the ICU, 987 patients were admitted to the ICU and 60 of them (6.1%) had AKI.[8].

AKI that occurs in critically ill patients in the ICU can occur as a result of the underlying disease etiology, such as sepsis, trauma, and major surgery, but AKI conditions that occur are associated with high mortality and significant morbidity AKI is an independent risk factor for mortality up to 70% in patients. critically, with the higher the degree of AKI, the higher the mortality rate [1].

Early prediction and avoidance of aggravation of AKI will be useful in identifying patients who are at risk of developing a higher degree of AKI. Many studies have been carried out to prevent AKI and find biomarkers to predict AKI[9,10]. Experimental studies of AKI using models of ischemic reperfusion, septic endotoxicemia and nephrotoxins have shown that a strong inflammatory component is associated with AKI that is responsible for initiating the development of more severe AKI.[11]. Many studies have identified biomarkers of AKI such as neutrophil associated lipocalin (NGAL), cystatin C, interleukin-18, and tissue inhibitor of metalloproteinase-2 (TIMP-2), but few have investigated the role of PCT as a predictor of AKI.[12] Recent studies have shown that there is an increase in PCT levels in AKI patients, which is a biomarker of inflammation and is widely used in the ICU as a biomarker of bacterial sepsis and response to antibiotic therapy. [13].

According to research conducted by Chun et. al. (2019) that elevated procalcitonin levels increase the risk of AKI by 1.7 to 2.4 times, with higher PCT levels found in AKI patients compared to non-AKI.[14]Another study also

showed that in univariate and multivariate analyzes of the predictors of AKI, it was reported that increased PCT was an independent predictor of AKI about 4.4 times the probability of AKI. However, according to Rodriguez et. al. (2016) reported different results that PCT cannot be used as a biomarker of AKI. This study concluded that AKI and non-AKI patients reported the same median PCT values in postoperative cardiac surgery patients.[15]

There are differences in research results and the mechanism of PCT as a biomarker of AKI which is still not fully understood, so this needs to be re-examined. In addition, PCT is also a routine examination carried out in the ICU of the Haji Adam Malik General Hospital (RSUP HAM) so it is hoped that this examination can be an early prediction to identify AKI, so as to reduce the mortality rate of critical patients in the ICU of RSUP HAM. Based on the above background, the researchers were interested in seeing the relationship between PCT levels and the incidence of AKI in critically ill patients who were treated in the ICU room at HAM Hospital Medan.

II. RESEARCH METHODOLOGY

Research design

This study is an observational analytic study with a case-control survey design without machining to assess the relationship between serum PCT levels and the incidence of AKI in critically ill patients admitted to the intensive care unit (ICU). The study was conducted at the Intensive Care Unit (ICU) General Hospital Haji Adam Malik Medan. Samples of research data were collected from January-December 2020.

Population and Research Sample

The population in this study were all patients who had been treated in the ICU of RSUP H Adam Malik Medan from January-December 2020. The research sample was secondary data obtained from medical records. The sampling technique in this study used simple random sampling. In simple random sampling, first the number of subjects in the population is calculated. Each subject is numbered, and partially selected with the help of random software (www.randomizer.org).

Research Criteria

Inclusion criteria in this study were 18–60 years of age, patients who had been admitted to the ICU, patients who had been tested for procalcitonin during treatment in the ICU. Meanwhile, the exclusion criteria were patients with chronic kidney disease, pancreatitis, thyroid carcinoma, severe trauma, lung carcinoma.

Procedure

After being approved by the health research ethics committee, Faculty of Medicine, University of North Sumatra and the health research ethics committee at Haji Adam Malik Hospital. As well as obtaining approval to obtain data from medical records. Research data that fall into the inclusion and exclusion criteria, then used as research samples. All patients suffering from AKI in the population were treated as cases, while controls were taken randomly from the rest of the population who did not suffer from AKI. Then tabulation was made to excel, starting from the data on the characteristics of the research data and the PCT value when entering the ICU. Patients with AKI were determined according to the RIFLE criteria. Furthermore, the data were analyzed using the SPSS 25.0 computer application. Data is presented in the form of tables and graphs.

Analysis Design

The data is tabulated into a master table using SPSS software. Numerical data is shown in mean + SD (standard deviation) and median (minimum-maximum) values, while categorical data is shown in sum (percentage). The normality test used the Shapiro-Wilk normality test. Bivariate test was carried out using the Chi-Square test if the data was normally distributed, and using the Mann-Whitney test if the data was not normally distributed with a significance degree of $p<0.05$. The analysis of the results of the case-control study was carried out by determining the odds ratio

III. RESEARCH RESULT

The Process of Selection, Randomization, and Monitoring of Research Subjects

Data collection was carried out on septic patients who were treated in the ICU of HAM Hospital sinceJanuary-December 2020, after obtaining approval from the ethics committee of the USU Medical Faculty / RSHAM. The number of subjects who met the inclusion criteria were 80 patients with 52 control patients (no AKI) and 28 case patients (AKI). Furthermore, the control and case groups were randomized (www.randomizer.org) to obtain a balanced group of 19 patients in each group.

Normality test

Normality test was conducted to assess whether the variables of the sample tested in this study were normally distributed or not. The normality test in each group in this study used the Shapirow-Wilk test. The data is declared normally distributed if the p value > 0.05 and declared not normally distributed if the p value < 0.05.

Table 1 Normality test on 38 patients

Sample characteristics	p value
Age	0.200*
Gender	0.001
FOLDER	0.200*
SOFA Score	0.010
Procalcitonin	0.001
Creatinine	0.031

Description: Shapirow-Wilk test; Normal distribution ifα>0.05

Based on Table 1, the age and MAP data in this study were normally distributed, so the statistical test used t-test. Meanwhile, for data on sex, SOFA, procalcitonin, and creatinine scores, the normality test was obtained which was

not normally distributed so that the statistical test used the Mann-Whitney test.

Sample Characteristics

The characteristics of the research subjects were recorded on the attached research form at the beginning of the study. The data contained age, gender, mean arterial pressure (MAP), SOFA score, procalcitonin levels, and creatinine levels. Characteristic data from 38 research subjects who met the inclusion and exclusion criteria can be seen in Table 2.

Table 2. Sample characteristics

Sample characteristics	Case(n=19)	Control(n=19)	p value
Age, years (mean ± SD)	48.2 ± 15.6	42.9 ± 17.8	0.340
Gender Male, n (%) Female, n (%)	 6 (31.6) 13 (68.4)	 8 (42.1) 11 (57.9)	0.583
MAP, mmHg (mean ± SD)	91.8 ± 18.7	87.4±15.6	0.196
SOFA score, median (min-max)	3 (1-18)	3 (1-11)	0.863
Use of vasopressors. n(%)	19 (100)	19 (100)	1.00
Serum creatinine (mg/dl), median (min-max)	2.79 (1.19-9.81)	0.82 (0.57-1.16)	<0.001*
Urea (mg/dl), median (min-max)	116 (21-276)	26 (11-58)	<0.001*

Description: Mann-Whitney test (gender comparison, SOFA score, PCT, creatinine, and urea in case and control groups); t-test (comparison of age and MAP in case and control groups); significantly different whenα<0.05.

In this study, a difference test using t-test was carried out for data that were normally distributed and obtained homogeneous results for the variables of age (p=0.340) and MAP (P=0.196). Meanwhile, for data that are not normally distributed using the Mann-Whitney test and obtained homogeneous results for the variables gender (p=0.583), MAP (p=0.196), SOFA score (p=0.863), and use of vasopressors (p=1, 00), while for the PCT variable, serum creatinine and urea had significant differences between case and control groups with p<0.05.

Table 2 shows the average age of the sample in this study was higher in the case group of around 48.2±15.6 years compared to the control group 42.9 ±17.8 years. The male sample was the most in the control group and the highest number of women in the case group. In this study, the highest MAP was found in the case group, although both groups all used vasopressors during intensive care. The SOFA score in this study had the same median value in the control and case groups, which was 3, but the case group had a larger range of SOFA scores from 1 to 18.

Procalcitonin levels in AKI and non-AKI patients

Procalcitonin levels in patients with AKI and without AKI are shown in Table 3

Table 3 Frequency Distribution Characteristics of PCT . levels

PCT (ng/ml)	Case (n=19)	Control (n=19)	p value
Mean ± SD	24.4±33.3	2.3±6.2	0.001*
Median (Min-Max)	7.9 (0.15-100)	0.32 (0.02-25.98)	

Description: Mann-Whitney test, significant <0.05

Based on Table 3, it was found that PCT levels were higher in the case group (24.4±33.3 ng/ml) compared to the control group (2.3±6.2 ng/ml). The results of the study proved that there was a significant difference between PCT levels in the case (AKI) and control (no AKI) group and was statistically significant (p=0.001).

Frequency distribution of AKI and non-AKI patients based on PCT

The frequency distribution of AKI and non-AKI patients based on PCT is shown in Table 4

Table 4 Frequency Distribution Characteristics of PCT . levels

PCT	Case (n=19; %)	Control (n=19; %)	OR (95% CI)	p value
Tall	14 (82.3)	3 (17.6)	14.93 (3.0-74.0)	0.001*
Low	5 (23.8)	16 (76.1)		

Note: OR is calculated using the Mantel-Haenszel common odds ratio estimate; p-values were calculated using the two-sided Wald test.

Based on Table 4, it was found that patients with high PCT values (more than 1.575 ng/ml) were 14.93 times more likely to experience AKI than those with low PCT values (less than 1.575 ng/ml). Asymp Value. Sig (2-Sided) shows the p value or the significance of the OR value which is meaningful with p value = 0.001

Correlation of PCT levels with the incidence of acute kidney injury (AKI) in critically ill patients treated in the intensive care unit (ICU).

The correlation between PCT levels and the incidence of acute kidney injury (AKI) in critically ill patients admitted to the intensive care unit (ICU) is shown in Figure 1 below.

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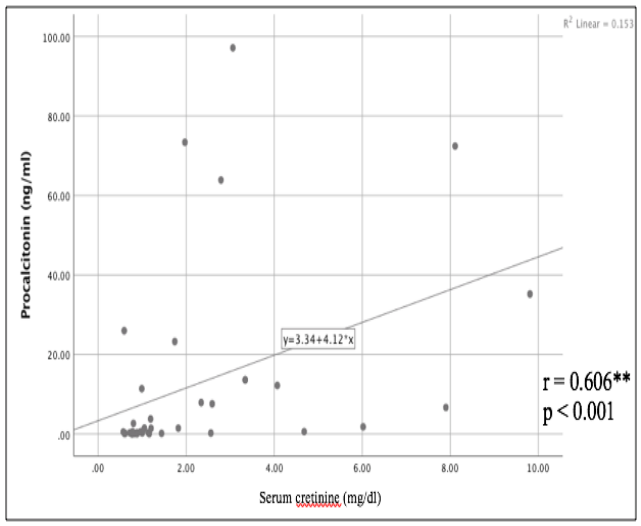

Figure 1. Trend plot of PCT levels against serum creatinine levels in critically ill patients admitted to the ICU

Figure 1 shows a strong positive correlation between PCT levels and serum creatinine, meaning that the higher the PCT level, the greater and more significant the increase in serum creatinine ($p < 0.001$; $r = 0.606$).

IV. DISCUSSION

This study was conducted to explain the relationship between serum PCT levels and the incidence of AKI in critically ill patients admitted to the intensive care unit (ICU). The information found in this study can serve as a scientific review to complement previous research and clarify evidence that there is an increased risk of AKI in patients with high PCT levels. This study was conducted on 198 medical records of critically ill patientswho were treated in the ICU of Haji Adam Malik Hospital in Medan, in the period January-December 2020. All medical records were examined and found only 52 patients without AKI and 28 AKI patients, who met the inclusion and exclusion criteria, and the completeness of the medical record data was good. Furthermore, the sample was randomized using a computer (www.randomizer.org) in order to obtain the same number of samples and in accordance with the calculation of the estimated study sample as many as 18 samples for each control and case group.

The characteristics of the research sample showed that the 2 study groups with a total of 38 patients had more women than men. This finding is not in accordance with several previous studies, critical patients in the ICU are more common in men than women[16]. A multicenter study in Italy showed the prevalence ratio between men and women who were admitted to the ICU was about 3 to 2.[17]. This study shows the opposite result. This may be due to the large number of samples in the study that were excluded due to incomplete information data. In addition, studies in America show that the incidence of critical sepsis in the ICU is more influential on age, underlying disease and source of infection.[18]. DalaIn this study, the authors found a SOFA score with a range of 1-18 and a median value of 3 with a mortality prediction of 6.4%.. In this study, the variables of age, MAP, gender, SOFA score, use of vasopressors were evenly distributed in both groups, controls and cases. So it is hoped that these variables do not affect the outcome of the variables studied in this study.

In this study, it was shown that PCT levels were higher in the case group (AKI) compared to the control group (no AKI). This is in accordance with the meta-analysis research conducted by Feng et al. (2021), who reported that PCT had good predictive value in predicting AKI with a sensitivity of 76% and a specificity of 75%.[19]. Given the possibility of using PCT in estimating the increased risk of renal damage, so that the incidence of AKI becomes very important, early detection and prevention to avoid further damage are key management of AKI repair. Increased PCT in AKI as an inflammatory biomarker is a potential early biomarker of AKI and several studies have shown an association with activation of proinflammatory cytokines and chemokines in patients with acute renal dysfunction.[20,21] increased cytokines including interleukin (IL)-2, IL-6, tumor necrosis factor (TNF-α) has also been reported to be elevated in acute renal failure. In addition, previous studies have also reported that PCT has a direct cytotoxicity effect in humans and animals with acute renal failure[22,23].

This study succeeded in proving that an increase in PCT showed a 14.93-fold increased risk of experiencing AKI than those with a low PCT value (less than 1.575 ng/ml). In the literature, the relationship between PCT levels and residual renal function has been found to be almost consistent in several studies. PCT was demonstrated to be excreted in the urine by the kidneys and renal clearance of PCT decreased significantly in parallel with the decrease in eGFR.[24–26] Some studies have even reported an increase in PCT found in patients with CKD [27] The potential explanation that can explain the relationship between PCT and AKI according to several studies is thought to be due to the direct cytotoxic effect of PCT on mesangial cells that causes damage to the kidneys, the role of PCT is still unknown in the pathogenesis of AKI, pro-inflammatory in AKI and the situation that causes AKI to induce PCT secretion occurs, and the decrease in early PCT clearance in AKI is associated with an increase in serum creatinine levels [28]

In addition, other studies have previously reported that the presence of infection or AKI was associated with increased serum PCT levels compared with patients who did not have infection or AKI. In addition, we found that the influence of infection and AKI on PCT levels could be due to infection and the association of AKI with inflammatory/pro-inflammatory status leading to more release of PCT into the circulation, in addition AKI was associated with impaired renal PCT clearance from the circulation. , which indirectly keeps serum PCT levels high.

Serum PCT levels found in this study can provide an illustration of an increased risk of up to 14 times the occurrence of AKI as an independent factor for AKI in critically ill patients admitted to the ICU. This finding is supported by Heredia-Rodríguez et al. who revealed that

AKI patients had significantly higher PCT rates than non-AKI patients regardless of the presence of sepsis in these patients. The effect of PCT levels in AKI patients with infection when compared with AKI patients without infection can be found in other examinations[29,30]. However, there have been conflicting results, with several studies reporting that serum PCT levels fail to predict the incidence of AKI in patients with sepsis or influenza infection.[30].

V. CONCLUSIONS AND SUGGESTIONS

Conclusion

Patients with high PCT values (more than 1.575 ng/ml) were 14.93 times more likely to develop AKI than those with low PCT values (less than 1.575 ng/ml). There is a strong positive correlation between PCT levels and serum creatinine in critically ill patients admitted to the intensive care unit (ICU).

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