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Original research Articles

Correlation Between Procalcitonin and Creatinine Levels in Sepsis Patients

Muhammad Faisal Kusumaputra[1], Ronald Irwanto Natadidjaja[2, 3*]

1. Undergraduate Medical Study Program, Faculty of Medicine, Universitas Trisakti

2. Department of Internal Medicine, Faculty of Medicine, Universitas Trisakti

3. Trisakti-RASPRO Indonesia Antimicrobial Stewardship (TRIASE) Learning Centre

Abstract:-

BACKGROUND: Procalcitonin is a very important biochemical marker that is closely correlated with the severity of the host's inflammatory response to microbial infection. Creatinine is a breakdown product of creatine that provides energy for muscles, which is then released into the blood, after which it passes through the kidneys and is excreted. These two parameters are related in several circumstances, especially in patients with severe bacterial infections that can affect kidney function. The purpose of this study was to determine the correlation between procalcitonin and creatinine levels in sepsis patients.

METHODS: This study used an observational analytical design with a cross-sectional approach. The population of this study was sepsis patients who were in the emergency unit of the Karawang Regional General Hospital. The sample selection technique used was consecutive sampling. Data were obtained through patient medical records. Data were processed and analyzed using the Spearman Correlation Test.

RESULTS: Based on the results of the study on 30 respondents, there was a significant correlation between procalcitonin levels and creatinine in sepsis patients at the Karawang General Hospital ($r = 0.755$; $p = <0.001$).

CONCLUSION: There was a significant correlation between procalcitonin levels and creatinine in sepsis patients at the Karawang General Hospital.

Keywords: Procalcitonin, Creatinine, Sepsis

Supplementary information The online version of this article (https://doi.org/xx.xxx/xxx.xx) contains supplementary material, which is available to authorized users.

Corresponding Author: Ronald Irwanto Natadidjaja[2, 3*], Department of Internal Medicine, Faculty of Medicine, Universitas Trisakti
Trisakti-RASPRO Indonesia Antimicrobial Stewardship (TRIASE) Learning Centre.

Introduction:

Death due to sepsis is caused by organ failure and dysregulation of the body's immune response. [1] Procalcitonin (PCT) is one of the most important biochemical markers that closely correlates with the severity of the host's inflammatory response to microbial infection. PCT levels increase selectively in bacterial infections, whereas in viral infections, their concentration is always normal. [2] On the other hand, creatinine is a breakdown product of creatine that provides energy for muscles. Creatine is a substance produced from normal muscle contractions and then released into the blood, after which it passes through the kidneys and is excreted. [3]

These two parameters are often used to assess the severity of infection and the patient's physiological condition, especially in cases of sepsis. Increased procalcitonin levels in severe bacterial infections not only reflect the intensity of inflammation but can also worsen organ damage, including the kidneys. Increased creatinine levels, which reflect decreased kidney function, often occur together with inflammation caused by infection. This indicates a complex relationship between the immune system response and organ function in dealing with severe bacterial infections. [4,5]

Based on the results of research conducted by Zhang et al in 2017, it was shown that there was a relationship between procalcitonin levels and creatinine levels. [6] Meanwhile, research conducted by Liu et al in 2012, the results showed no relationship between procalcitonin levels and creatinine levels; this was due to differences in the diseases that were the focus of the research. [7] The results of previous studies regarding the relationship between procalcitonin levels and creatinine in sepsis patients are still being debated. So, based on this, researchers want to evaluate the relationship between procalcitonin and creatinine in sepsis patients. This research is expected to provide new insights and education to the public and fellow doctors regarding procalcitonin and creatinine levels in sepsis patients.

Materials and Methods:

This study was conducted using an observational analytical design through a cross-sectional approach to assess the correlation between procalcitonin and creatinine levels in sepsis patients through the collection and monitoring of medical record data. This study was attended by 30 respondents and was conducted in September 2024. The location of the study was at the Karawang Regional General Hospital. The population in this study was people aged 30-60 years in the Karawang area. The target population in this study was Sepsis patients at the Karawang Regional General Hospital. The research sample had inclusion criteria: Sepsis sufferers. Sample exclusion criteria included: patients with a history of chronic kidney disease and patients diagnosed with malignancy. The procalcitonin and creatinine results taken were the first procalcitonin and creatinine levels examined when the patient was declared sepsis.

Statistical Analysis:

This study analyzed medical record data of outpatients at Karawang General Hospital, focusing on procalcitonin and creatinine levels. Data were analyzed using the SPSS program through univariate analysis to describe the characteristics of the procalcitonin (independent) and creatinine (dependent) variables displayed in the form of frequency and percentage. To determine the correlation of the two variables, bivariate analysis was performed using the Spearman or Pearson correlation method. The Spearman method is used if the data is not normally distributed, while Pearson is used if the data is normally distributed.

Results:

This study was conducted with 30 respondents, who had the following characteristics.

Table 1. Distribution of Subject Characteristics

Variable	Frequency (n)	Percentage (%)
Age		
30 - 40	9	30
41 - 50	11	36,7
51 - 60	10	33,3
Gender		
Male	16	53,3
Female	14	46,7
Procalcitonin Level		
Normal Procalcitonin	0	0
Procalcitonin increase	30	100
Creatinine Level		
Normal Creatinine	7	23,3
Creatinine increase	23	76,7

Table 1 shows that of the 30 subjects, 16 (53.3%) were male and 14 (46.7%) were female. Normal procalcitonin was not found, increased procalcitonin was found in 30 (100%), and normal creatinine was found in 7 (23.3%), while increased creatinine was found in 23 (76.7%). Age 30-40 years was found in 9 (30%), age 41-50 years was found in 11 (36.7%), and age 51-60 years was found in 10 (33.3%).

Table 2. Normality Test with Shapiro-Wilk

Normality Test with Shapiro-Wilk	
Variable	**P**
Procalcitonin	0,114
Creatinine	0,012

The results of the Shapiro-Wilk normality test in Table 2 show that the procalcitonin variable data show a normal data distribution ($p = 0.114$; $p < 0.05$), but the distribution of the creatinine variable data shows an abnormal data distribution ($p = 0.012$; $p < 0.05$). The correlation test between procalcitonin and creatinine was carried out using the Spearman correlation test in Table 3.

Table 3. Spearman Correlation Test

Spearman Correlation Test			
Measurement	**R**	**N**	**P**
Procalcitonin and Creatinine	0,755	30	<0,001

Based on the results of the Spearman correlation test in Table 3 between procalcitonin levels and creatinine, it was found that there was a strong significant correlation with a value of $r = 0.755$ and $p = <0.001$. The direction of the correlation is positive because a positive r value indicates that there is a correlation where the higher the procalcitonin level, the creatinine level tends to increase, and vice versa, the lower the procalcitonin level, the creatinine level tends to decrease.

Discussion

The study conducted at the Karawang Regional General Hospital, West Java, obtained 30 research samples, based on all sepsis patients being examined at the Karawang Regional General Hospital, West Java. This study was conducted to determine the correlation between procalcitonin levels and creatinine in sepsis patients.

A correlation test was carried out with the Spearman Test between procalcitonin levels and creatinine in sepsis patients at the Karawang Regional General Hospital, obtaining a p-value = <0.001. The findings in this study indicate a meaningful relationship between procalcitonin levels and creatinine in sepsis patients at the Karawang Regional General Hospital. The results of the study showed that procalcitonin levels and creatinine had a strong correlation ($r = 0.755$) and a positive pattern, meaning that the higher the procalcitonin levels, the higher the creatinine levels.

Sepsis can cause life-threatening organ dysfunction due to an abnormal and uncontrolled body response to infection. [8] Sepsis begins with an infection that is initially limited, but then triggers a systemic inflammatory response throughout the body. This response is characterized by the release of various pro-inflammatory mediators such as cytokines, interleukins, and tumor necrosis factor (TNF). When there is an imbalance between inflammatory and anti-inflammatory mechanisms, blood flow to the tissue is disrupted, causing damage to vital organs such as the kidneys, lungs, and liver. If this condition is not immediately recognized and treated, organ damage can develop progressively and lead to death. [9,10,11]

In the clinical context, for successful treatment and a positive outcome, early diagnosis and differentiation from non-infectious causes are essential, so that antimicrobial therapy and fluid resuscitation can be initiated promptly.[12] However, since the clinical manifestations of sepsis or suspected sepsis can be variable and often unclear, their diagnosis and treatment remain challenging. To date, there is no gold standard for detecting sepsis caused by bloodstream infection.[13] This study showed a positive relationship between procalcitonin and creatinine levels in septic patients. Increased procalcitonin caused by bacterial toxins, such as endotoxins and cytokines [14] in response to sepsis contributes to decreased renal function, as reflected by increased serum creatinine levels. This relationship may strengthen the role of PCT not only as an inflammatory marker but also as a predictor of the risk of

renal dysfunction in septic patients, allowing for early detection and better intervention. In this study, a correlation was found between procalcitonin levels and creatinine in subjects at the Karawang Regional General Hospital, this study is following the results of research from Kim, et al in 2022, this study discussed the relationship between procalcitonin levels and creatinine involving 649 patients undergoing intensive care at Yangsan Hospital, Pusan National University, based on the results of his research, an increase in procalcitonin levels was correlated with impaired kidney function, which was reflected in higher creatinine levels ($p < 0.0001$). [15] In this study, there could be the same results because there were similarities in the age range taken to be the subjects, and also, the research subjects were mostly male, just like the subjects successfully obtained by the researchers of this study. There were also similar results in another study conducted by Fu et al in 2021 involving 157 patients. Based on the results of their research, a positive relationship was found between increased procalcitonin levels and creatinine. [16] In a study conducted by Fu et al, they took research subjects who were the same age as the researcher, namely under 75 years. This is also confirmed by another study conducted by Zhang, et al in 2020, based on the results of their study, the correlation between PCT and creatinine was very strong ($r = 0.787$, $p < 0.001$), indicating that PCT can be a good predictive indicator for AKI in the context of sepsis. [6] In a study conducted by Zhang et al, they used 147 patients as subjects, and the average age studied was 62 years, with half of the research subjects being men.

However, another study conducted by Liu, et al involving 51 people based on the results of their study found that procalcitonin levels had no relationship with creatinine and uric acid [7] the difference was because this study did not focus on the variables of procalcitonin and creatinine and in the study conducted by Liu, et al even though they had a larger number of samples to analyze, there was a difference in the age of the subjects studied ranging from 20 - 35 years then in another study conducted by Rodríguez, et al based on the results of their study obtained a low correlation between procalcitonin and creatinine ($r = 0.18$). [17] The same thing was obtained because this study used secondary analysis in the form of a cohort study and this study was conducted in Spain which resulted in differences in the subjects taken, subjects from Asian countries may have different genetic factors or metabolic patterns compared to subjects from Spain, which has the potential to affect biomarker levels such as procalcitonin and creatinine.

The differences in the results of these studies indicate that the relationship between procalcitonin and creatinine levels in sepsis patients is greatly influenced by various factors, including study design, population characteristics, type of infection present, and the analysis method used. Variations in age, gender, race, and other health conditions can play a role in producing differences in inflammatory biomarker values and kidney function. In addition, genetic and environmental factors, such as geographic differences and diet, can affect the metabolism of these biomarkers, which can affect the interpretation of procalcitonin levels according to each clinical context.[18,19] It is also important to pay attention to the time of blood sampling because procalcitonin and creatinine levels can change as the disease progresses.[20]

Research Limitations:

This study applies an observational design with a cross-sectional design, conducted with a limited number of samples and a short time, so that it is not yet possible to determine the cause-effect relationship, and the reduction of confounding factors has not been carried out statistically, still applying exclusion and inclusion criteria.

Conclusion:

This study found that there was a significant correlation between procalcitonin levels and creatinine levels in sepsis patients, with a strong positive correlation ($r = 0.755$) and p value = <0.001. Although several previous studies have shown no significant correlation between the two variables, the results of this study do not support these findings. This may be influenced by variations in population characteristics or the methodology used. Therefore, further research is needed with a larger sample and more in-depth analysis methods to understand the correlation between procalcitonin and creatinine and its implications in diagnosing sepsis patients.

Ethical Declarations

Acknowledgments:

Thanks are expressed to the Karawang Regional General Hospital for granting permission to conduct this research.

Ethics Approval:

This research has received ethical approval from the Research Ethics Committee of the Faculty of Medicine, Universitas Trisakti. Number 038/KER/FK/08/2024.

Availability of Data and Material:

The data sets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Faculty of Medicine Universitas Trisakti, Jakarta, Indonesia.

Conflict of Interest:

The author states that there is no conflict of interest.

Research Contributions:

All of the authors listed have made substantial, direct, and intellectual contributions to this work and approved it for publication.

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