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**Original Research Article**

# Role of procalcitonin levels on COVID-19 patients at Siti Fatimah hospital south Sumatera

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## ABSTRACT

**Background:** COVID-19 is a systemic disease that affects a broad spectrum of tissues and cells. Infected patients experience a wide variety of clinical signs, ranging from mild clinical signs to bilateral interstitial pneumonia. COVID-19 patients who also experience acute respiratory distress syndrome can result in multi-organ failure without comorbidities. Procalcitonin (PCT) also indicates severity and prognosis to reduce mortality.
**Method:** The research method is descriptive with a cross-sectional approach. The research was conducted at the Siti Fatimah hospital in South Sumatra province in February to May 2022. The sample for this research was the results of a PCT examination in 2021 totaling 66 people. The method for examining PCT levels uses the enzyme-linked method with serum or plasma samples.
**Results:** Obtained PCT levels showed that there was a low risk of PCT levels (≥0.05-<0.5) in 26 patients (39.4%), severe risk of PCT levels (≥0.5-<2) in 15 patients (22 .7%) and high risk of PCT levels (≥2) in 25 patients (37.9%). Based on mortality status, high levels were obtained in 43 patients with a low-risk living category in 21 patients. Based on the history of the disease, high levels were obtained in 41 patients with a history of high-risk disease in 18 patients. Based on the category of treatment in the inpatient room, high levels were obtained in 37 patients treated in the non-ICU room, resulting in low-risk PCT levels in 17 patients.
**Conclusions:** There is a 39.4% PCT level (≥0.05-<0.5) which indicates low risk is more common in COVID-19 patients than severe risk and high risk.

**Keywords:** COVID-19, PCT, Procalcitonin

## INTRODUCTION

Since the emergence of the disease in China's Wuhan province in November 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread to all corners of the world and was declared a pandemic by the world health organization (WHO). Coronavirus disease 2019 (COVID-19) is a systemic disease that affects a broad spectrum of tissues and cells. Infected patients experience a wide variety of clinical signs, ranging from mild clinical signs to bilateral interstitial pneumonia, if not properly identified and treated individually.[1] COVID-19 infection in humans can result in clinical manifestations that usually appear within 2 days to 14 days after exposure. WHO classifies the spectrum of clinical manifestations of contagion infection into asymptomatic and symptomatic. Nimbus contagion infection with symptoms classified into acute respiratory disorders such as fever, cough to shortness of breath. In severe cases it can cause pneumonia, acute respiratory syndrome, kidney failure, and even death.[1] COVID-19 patients who also experience acute respiratory distress syndrome can result in multi-organ failure without comorbidities. Septic shock and secondary bacterial infection are common complications in patients in the intensive care unit (ICU).[2,3] Handling COVID-19

certainly requires laboratory tests which play an important role in the handling process, starting from opinions, monitoring therapy, and prognostic determination, to surveillance. Laboratory tests that can be done for Covid tests include PCR, immunology, and hematology tests. For this examination, early identification is needed to predict the condition of patients who are at risk of worsening symptoms becoming more severe. Simple laboratory tests such as the measurement of known PCT ratio values can be used as a prognostic factor for determining the prognostic of patients in various clinical situations.[3] PCT also indicates severity and prognosis to reduce mortality. High serum levels of PCT, D-dimer, and ferritin predict an increased risk of worsening in patients with COVID-19.[2] PCT is a part of the calcitonin glycoprotein without hormonal activity, produced and released by thyroid follicular cells. Serum PCT levels are generally low or impossible to detect. During bacterial infection and sepsis, PCT is significantly increased because it is produced by sources outside the parathyroid glands in response to bacterial endotoxins and inflammatory cytokines. However, PCT synthesis is inhibited by interferon (INF) increasing concentrations in viral infections, so PCT levels tend to be low in viral infections. Therefore, PCT can be used to differentiate between bacterial and viral infections.[4] The purpose of this study was to find out the role of PCT in COVID-19 patients at Siti Fatimah hospital, South Sumatra province in 2021.

## METHOD

The research method is descriptive with a cross-sectional approach. The research was conducted at Siti Fatimah hospital in South Sumatra province in February-May 2022. The population of this study was COVID-19 patients. The research sample was COVID-19 patients who underwent a PCT examination at the Siti Fatimah hospital in South Sumatra province for the January-December 2021 period with a total of 66 patients. The patient selection criteria were COVID-19 patients who underwent a PCT examination. The method for examining PCT levels uses the enzyme-linked method with serum or plasma samples which have stability of 48 hours at 2-8°C or 6 months at -25±6°C. In this study, secondary data was used, namely data on the results of examining PCT levels in COVID-19 patients. Procedure: Turn on the tool. The system control center (SCC) i.e., the CPU and the device's computer monitor (Snapshot screen) must remain on, to maintain the Abbott mail connection. Turn on the processing module and robotic sample handler (RSH) by pressing the power button on the back near the power cable to ON. The 11000SRTM is a single module so turning on the Processing Module turns on the RSH as well. Wait until the OFFLINE status becomes STOPPED, and press the RSH and Processing modules (modules 0 and 1). Press START UP. Wait until the STOPPED status becomes READY. Manage consumable inventory: Via the supplies icon on the snapshot screen, click supply status. Or via supply status in the processing module image (Module 1), click RV's/ liquid/ waste. Emptying solid or liquid waste: Open the Supply and Waste Centre door. Remove the tubing from the liquid waste container. Pull sate drawer. Remove the solid waste container. Dispose of solid waste along with the biohazard bag. Replace with a new bag. Dispose of liquid waste at a waste disposal site. Replace the tubing from the liquid waste container. Select F2-update supplies. choose solid and/or liquid waste emptied solid/liquid waste, depending on which waste is disposed of. Select done.

### *Added reaction vessel-RV*

Open the RV Hopper lid. Add RVs. maximum RV storage is 360 RV. Close the RV Hopper lid again. Select F2-update supplies. Select RV's-added filled hopper. Select done.

### *Add wash buffers*

Wash buffer must be diluted before adding it to the system. Make sure the wash buffer conc has not passed its expiration date. Invert the bottle slowly so that the solution is homogenized. Pour wash buffer conc inside. Pour slowly water type II (Aquadest) to avoid excessive foam up to the 10 L mark. Open the Supply and Waste door. Attach the transfer tubing to the wash buffer preparation vessel. Attach the transfer tubing to the insertion of the wash buffer above the waste area. Select F2-update supplies. Select wash buffer-add buffer. Select done. Select OK on the confirmation screen to start charging. Wash buffers. On the supply status screen, it will say Fill in progress on the Wash Buffer status. Wait until charging is complete. Remove the transfer tubing by pressing the gray button. Remove the transfer tubing from the preparation container and clean it with distilled water. Clean the wash buffer preparation container with Aquadest. Replace pre-trigger or trigger solution. Make sure the pre-trigger and/or trigger solution has not passed its expiration date. Open the supply and waste centre door. Pull out the pre-trigger/ trigger rack. Move the bottle to be replaced to the centre position. Place the new bottle in the appropriate position. Unscrew a new bottle and place it in the cap in front of the bottle. Unscrew the bottle to be replaced. The level sense sensor is attached to the bottle cap. Transfer the cap to the new bottle with the arrow facing forward and screw it on. Close the old bottle and dispose of it according to waste disposal regulations. Push it into the pre-trigger/ trigger rack. Close the supply and waste centre doors. select f2-update supplies. Select pre-trigger/ trigger- replaced bottle. Select done.

Ethical approval was carried out by the health research ethics committee, health polytechnic of the ministry of health Palembang, number: 0449/KEPK/Adm2/VI/2022, date: 02 June 2022. Data processing and analysis was carried out using statistical analysis and the results of examining PCT levels in COVID-19 patients were

presented as a percentage based on mortality status, medical history, and hospitalization.

## RESULTS

From research results, the demographic characteristics of patients based on gender are presented in Table 1.

**Table 1: Demographic characteristics by gender.**

| Gender | N (%) | Mean | SD |
|---|---|---|---|
| **Male** | 44 (66.7) | | |
| **Female** | 22 (33.3) | 1.6667 | 16.2368 |
| **Total** | 66 (100) | | |

Based on the table above, it can be seen from a total sample of 66 patients, there were 44 males (66.7%) and 22 females (33.3%), mean 1.67, and the standard deviation was 0.47.

Research results based on demographic characteristics based on gender are presented in Figure 1.

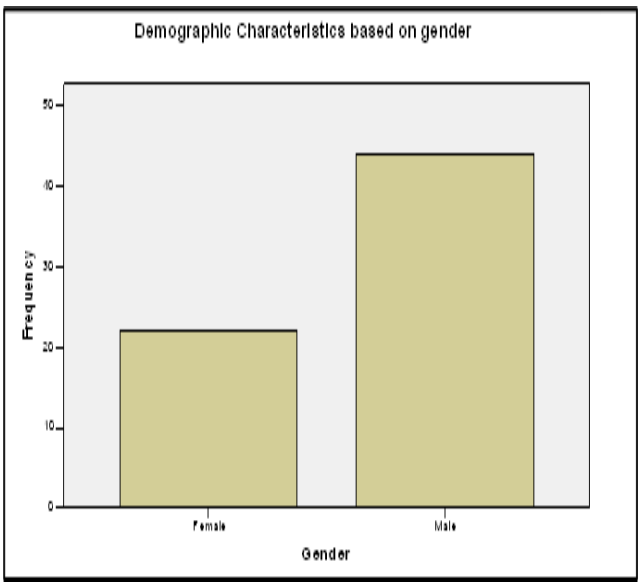


**Figure 1: Demographic characteristics based on gender.**

From the research results, the demographic characteristics of patients based on age are presented in the Table 2.

**Table 2: Demographic characteristics by age.**

| Age (years), N | Mean | SD |
|---|---|---|
| **66** | 54.1515 | 15.2368 |

Based on the table above, it can be seen from a total sample of 66 patients, mean 54.15, and the standard deviation was 15.23.

The results of the research based on demographic characteristics based on age are presented in Figure 2.

Based on an analysis conducted on the description of PCT levels in COVID-19 patients at the Siti Fatimah hospital in South Sumatra province in 2021, the results are presented in Table 3.

**Table 3: Frequency distribution of PCT levels in COVID-19 patients at Siti Fatimah Hospital, South Sumatra province in 2021.**

| Procalcitonin levels | Frequency | Percentage (%) |
|---|---|---|
| **PCT (≥0,05-<0,5)** | 26 | 39.4 |
| **PCT (≥0,5-<2)** | 15 | 22.7 |
| **PCT (≥2)** | 25 | 37.9 |
| **Total** | 66 | 100 |

Based on the table above, it is known that the results of the study of 66 COVID-19 patients obtained PCT levels (≥0.05-<0.5) in 26 patients (39.4%), PCT levels (≥0.5-<2) in 15 patients (22.7%) and PCT levels (≥2) in 25 patients (37.9%).

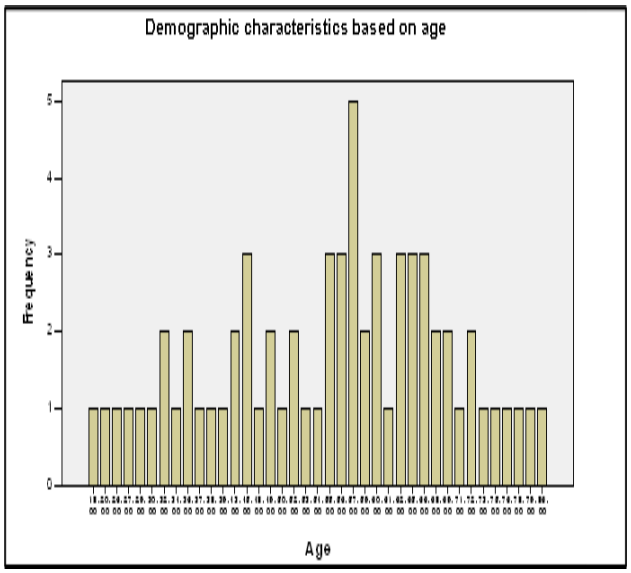


**Figure 2: Demographic characteristics based on age.**

The research results were analyzed bivariate and the results are presented in the form of a frequency distribution in Table 4.

Based on the table above, it is known that the results of a study describing PCT levels in COVID-19 patients, based on mortality status, from 43 (100%) patients with the living category obtained PCT levels (≥0.05-<0.5) in 21 patients (48 .8%), PCT levels (≥0.5-<2) in 11 patients (25.6%) and PCT levels (≥2) in 11 patients (25.6%). While 23 (100%) patients who died obtained PCT levels (≥0.05-<0.5) in 5 patients (21.7%), PCT levels (≥0.5-<2) in 4 patients (17.4%) and PCT levels (≥2) in 14 patients (60.9%).

The results of the study were analyzed bivariate and the results are presented in the form of a frequency distribution in Table 5.

Based on the table above, it is known that the results of a study describing PCT levels in COVID-19 patients, based on medical history, out of 41 (100%) patients with a history of disease category obtained PCT levels (≥0.05-<0.5) in 17 patients (41.5%), PCT levels (≥0.5-<2) in 6 patients (14.6%) and PCT levels (≥2) in 18 patients (43.9%). Meanwhile, from 25 (100%) patients who did not have a history of the disease, PCT levels (≥0.05-<0.5) were found in 9 patients (36.0%), PCT levels (≥0.5-<2) in 9 patients (36.0%) and PCT levels (≥2) in 25 patients (37.9%).

The results of the study were analyzed bivariate and the results are presented in the form of a frequency distribution in Table 6.

Based on the table above, it is known that the results of a study describing PCT levels in COVID-19 patients, based on the category of inpatient care, of 29 (100%) patients treated in the ICU obtained PCT levels (≥0.05-<0.5) of 9 patients (31.0%), PCT levels (≥0.5-<2) in 5 patients (17.2%) and PCT levels (≥2).

**Table 4: Frequency distribution of PCT levels in COVID-19 patients at Siti Fatimah Hospital, South Sumatra province in 2021 based on mortality status.**

| Mortality status | PCT rate | | | | | | Total | |
|---|---|---|---|---|---|---|---|---|
| | PCT ≥0.05-<0.5 | | PCT ≥0.5-<2 | | PCT ≥2 | | | |
| | N | % | N | % | N | % | N | % |
| **Living** | 21 | 48.8 | 11 | 25.6 | 11 | 25.6 | 43 | 100 |
| **Died** | 5 | 21.7 | 4 | 17.4 | 14 | 60.9 | 23 | 100 |
| **Total** | 26 | 39.4 | 15 | 22.7 | 25 | 37.9 | 66 | 100 |

**Table 5: Frequency distribution of PCT levels in covid-19 patients at Siti Fatimah Hospital in South Sumatra province in 2021 based on disease history.**

| Disease history | PCT rate | | | | | | Total | |
|---|---|---|---|---|---|---|---|---|
| | PCT ≥0.05-<0.5 | | PCT ≥0.5-<2 | | PCT ≥2 | | | |
| | N | % | N | % | N | % | N | % |
| **Have disease** | 17 | 41.5 | 6 | 14.6 | 18 | 43.9 | 41 | 100 |
| **did not have disease** | 9 | 36.0 | 9 | 36.0 | 7 | 28.0 | 25 | 100 |
| **Total** | 26 | 39.4 | 15 | 22.7 | 25 | 37.9 | 66 | 100 |

**Table 6: Frequency distribution of PCT levels in COVID-19 patients at Siti Fatimah Hospital in South Sumatra province in 2021 based on inpatient room.**

| Inpatient room | PCT rate | | | | | | Total | |
|---|---|---|---|---|---|---|---|---|
| | PCT ≥0.05-<0.5 | | PCT ≥0.5-<2 | | PCT ≥2 | | | |
| | N | % | N | % | N | % | N | % |
| **ICU** | 9 | 31.0 | 5 | 17.2 | 15 | 51.7 | 29 | 100 |
| **Non-ICU** | 17 | 45.9 | 10 | 27.0 | 10 | 27.0 | 37 | 100 |
| **Total** | 26 | 39.4 | 15 | 22.7 | 25 | 37.9 | 66 | 100 |

## DISCUSSION

As a useful marker of systemic bacterial infection, PCT has higher specificity and sensitivity than acute-stage proteins such as creative protein (CRP) levels, even in the intensive care unit. The PCT values are within the normal range in uncomplicated COVID-19 patients. The mean serum PCT level was higher in patients with severe than moderate symptoms as well as eight times higher in the patients with severe symptoms than the moderate symptoms.[6]

Patients with a high PCT group have a disease risk 3.559 times higher than the normal PCT group.[3]

Serum PCT levels are generally low or impossible to detect. During bacterial infection and sepsis, PCT is significantly increased because it is produced by sources outside the parathyroid glands in response to bacterial endotoxins and inflammatory cytokines. However, PCT synthesis is inhibited by interferon (INF) increasing in viral infection concentrations, so PCT levels tend to be low in viral infections.[4]

These results are in line with a study conducted by Ticinesi et al with the results of a total of n=1074 patients, n=261 who were declared dead and n=813 alive. Of the 698 (96%) patients with PCT levels ≥0.05-<0.5 ng/ml, 552 (75%) were alive and 146 (10%) died.[7]

Based on the results of this study, researchers got an overview of the role of PCT levels in low-risk, severe-risk, and high-risk mortality status.

According to Abadi et al. PCT can be a marker of disease severity in COVID-19 and can contribute to determining the severity of patients infected with SARS-CoV-2. In addition, serial PCT measurements may be useful in predicting prognosis.[8]

This study is in line with the study of Antos et al that the risk of death associated with co-morbidities in the first degree increases with the risk of severe disease from COVID-19, with at least one comorbid disease. Of the several comorbidities, the top four comorbidities are: hypertension, diabetes, cardiovascular disease, and chronic kidney disease.[9]

According to Zhang et al more severe pneumonia with advancing age and a higher rate of lymphopenia may be associated with the development of inflammatory status. More severe disease is associated with older patients, given increased levels of CRP, SAA, PCT, and D-dimer.[10]

Based on research conducted, people who are exposed to COVID-19 and have co-morbidities can affect the patient's condition because previously there was illness in the patient's body that affected the patient's immunity as a result of which the healing process was difficult.[8]

This is in line with previous research conducted by Ticinesi et al which stated that out of n=1074 inpatient COVID-19 patients, it consisted of ICU inpatient rooms n (%)=45 (4.1%) and NON-ICU inpatient rooms n (%)=1029 (95.9%), stated that patients who had PCT levels ≥0.5-<2 ng/ml were more in the ICU inpatient room, while patients who had PCT levels <0.05 ng/ml were more in the intensive care unit. NON-ICU.[9]

According to Liu et al and Zhang et al PCT is a glycoprotein without hormonal activity and calcitonin precursor. S. PCT levels usually low/ undetectable.[11,12]

According to Rodríguez et al and Liu et al PCT levels are increased due to bacterial infections and relatively low with viral infections and, therefore, can be used to differentiate between bacterial and viral infections. The higher PCT levels in SG suggest that severe COVID-19 patients may have bacterial coexistence with the infection.[13,11] Serum PCT concentration can be increased in patients with renal dysfunction in the absence of bacterial infection.[13]

According to Liu et al it should be noted that the optimal cut-off value for PCT is 0.07 ng/ml and does not exceed the normal range (0-0.5 ng/ml), and this result may be due to the small sample size (eight patients). Therefore, the validity of PCT as an independent factor for predicting the severity of COVID-19 needs to be studied further using a larger sample size.[11]

According to Sayah et al several studies have reported that peripheral blood levels of immuno-inflammatory and CBC markers such as IL6, PCT, CRP, neutrophil count and NLR are significantly increased in severe forms of COVID-19.[14]

According to Tang et al traditionally, elevated PCT levels are more suggestive of bacterial infection and have long been used to guide the decision to initiate antibiotics.[15]

According to Kamat et al the ability of PCT to accurately differentiate between bacterial and viral infections is still controversial.[16]

The results of Twe et al study did not identify a clear significant association between elevated PCT levels and bacterial co-infection as evidenced by the lack of positive culture results in the majority of our patients.[17]

This study has limitations. First, the number of samples is small. Second, clinical data are limited.

## CONCLUSION

From the results obtained, it was concluded that there were 39.4% PCT levels (≥0.05-<0.5) which indicated a low risk that more occurred in COVID-19 patients compared to severe risk and high risk. For medical personnel, PCT can be used as a further examination to find out further risks and for future researchers, to conduct research on confirmed COVID-19 patients with different parameters such as hemostasis and complete blood count (Leukocytes, platelets, hemoglobin, platelets, lymphocytes, neutrophils, and NLR.

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