https://doi.org/10.15218/zjms.2025.011

# Association of procalcitonin, C-reaction protein and other risk factors with mortality among COVID-19 patients in Erbil city

Received: 14/03/2023 Accepted: 10/05/2023

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## Abstract

**Background and objective:** The coronavirus disease pandemic, was a serious threat to global health, which attacked the community in December 2019 without warning and had disastrous effects. Inflammatory factors are important for COVID-19 mortality. We aimed to identify potential demographic risk factors as well as the potential role of procalcitonin and other inflammatory biomarkers as indicators of severity and outcome in patients with COVID-19.

**Methods:** A cross-sectional prospective study that was conducted in Lalav Hospital, West Emergency Hospital and a Private clinical center in Erbil city, Iraq. The cases (106) were collected from August 2021 to November 2021. All included patients were diagnosed with COVID-19 through laboratory confirmation using real-time reverse transcriptase–polymerase chain reaction (RT-PCR).

**Results:** Our results showed that serum procalcitonin levels were significantly higher and positively correlated with mortality in COVID-19 patients ($P$ = 0.005). The severity of COVID-19 and abnormal serial measurements of plasma D-dimer and serum C- reactive protein levels were found to be significantly correlated ($P$ = 0.028 and $P$ = 0.041, respectively). Diabetes, hypertension, and advanced age were noted as risk factors.

**Conclusion:** Procalcitonin may be an indicator of disease severity. Serial procalcitonin measurements and the recognition of potential risk factors are crucial for predicting the prognosis among COVID-19 patients.

**Keywords:** COVID-19; Procalcitonin; CRP; D-Dimer; Risk factor.

## Introduction

The community was hit by the mysterious outbreak of atypical pneumonia in December 2019, resulting in devastating health, economic, and social outcomes.[1] Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was identified as the etiological agent in January 2020, and the World Health Organization (WHO) declared a pandemic in March 2020.[2] SARS-CoV-2 is a member of the Nidovirales order and the Coronaviridae family.[3] Moreover, the Coronaviridae family had caused two other viral pandemics, SARS-CoV-1 in 2002 and Middle East respiratory syndrome (MERS-CoV) in 2012.[4]

The clinical features ranged from asymptomatic to mild and moderate symptoms as well as fatal cases; the infection was treated similarly to any other respiratory infection, with the exception of the possibility of pneumonia complications.[5] However, it was soon discovered that the infection caused a number of deadly complications, including disseminated intravascular coagulation, acute respiratory distress syndrome, and multiple organ dysfunction syndrome.[6]

Transmission routes of Coronavirus are thought to be mainly through direct contact with an infected person and indirect contact through infectious droplets

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https://doi.org/10.15218/zjms.2025.011

suspended in air, the virus is proven to be transmissive within 2-3 meters, studies have also identified fecal transmission and linked higher rates of transmission from infected person with diarrhea.[7]

It took around one–two months for the infection to spread globally, and there were no specific criteria as to why the disease was mild in some patients and severe in others, or why some patients would be doing fine then unexpectedly admitted to ICUs and placed on respiratory support. The fear of each infected person's unknown prognosis was likely the most challenging aspect of the pandemic; it had rattled both public and healthcare societies.[8,9]

Throughout the crisis, in addition to Real-time Polymerase Chain Reaction (PCR) detection of viral RNA for initial diagnosis, many other clinical parameters were recognized as enabling characteristic to monitor COVID-19 patients, including inflammatory biomarkers such as C-Reactive Protein (CRP), D-Dimer, Ferritin, Alanine Transaminase (ALT), and Aspartate Aminotransferase (AST).[10]

Co-morbidities and age considered risk factors, and several studies were conducted to investigate the inclusion of Procalcitonin (PCT) as another inflammatory biomarker as an indicator of severity and outcome.[11] Procalcitonin is a protein composed of 116 amino acids and is the precursor of the hormone calcitonin, which is usually synthesized by thyroid cells and is clinically used to distinguish bacterial from viral infections.[12]

PCT can be regarded as a good biomarker with a high diagnostic accuracy in order to make an early and accurate diagnosis, the main difference between PCT and other biomarkers may be the demonstration of superior diagnostic accuracy for a variety of infections, including sepsis.[13] COVID-19 patients are at risk of sepsis, hospital-acquired bacterial infections, and superbug infections. PCT has been recognized as a stewardship factor in antibiotic treatment.[14]

Unfortunately, in some countries, due to the need for quick responses, most patients are blindly given a set of antibiotic treatments with no clinical data to support a bacterial infection, which increases the risk of antibiotic resistance and, in turn, can worsen the patient's health status.[15]

There is limited data regarding inflammatory factors associating with severity and outcome of COVID-19 patients on international level and there no such study in our population in Erbil city. Our primary goal in this study was to assess each study participant's PCT levels at various points during the infection period. To demonstrate the relationship between serial PCT measurements and COVID-19 severity and to assess PCT as a predictor of COVID-19 prognosis and outcome. We assessed the morbidity and mortality of COVID-19 comorbid patients, as well as the association of inflammatory factors and different demographic characteristics of the participants with the severity of the infection, as COVID-19 has been linked to several comorbidities, such as hypertension, diabetes, and cardiovascular disease.

## Methods

This cross-sectional prospective study was conducted in Lalav hospital, West Emergency hospital and a private clinical center in Erbil city, Kurdistan region, Iraq. The cases (106) were collected during three months interval, from August 2021 to November 2021. All included subjects were diagnosed with COVID-19 infection through laboratory confirmation using real-time reverse transcriptase–polymerase chain reaction (RT-PCR).

Based on a set of guidelines for diagnosis and management of COVID-19, National Institute of Health (NIH) has classified COVID-19 patients according to severity into three groups: mild, moderate, and severe. Mild COVID-19patients had no fever or signs of pneumonia, moderate cases were identified based on symptoms of respiratory infection and fever, and

https://doi.org/10.15218/zjms.2025.011

severe cases were identified as patients admitted to the intensive care unit / respiratory care unit (ICU/RCU) with Oxygen saturation of 93% or less at rest.[16]

Patients were subjected to several blood tests upon admission for assessing patients' status and serial laboratory tests were conducted for following patient's condition such as serum procalcitonin, C-reactive protein and plasma D-dimer. The samples were divided into three groups based on the time and date of collection. Group I consisted of samples collected within the first three days after hospitalization, Group II included samples collected during the hospital stay, and Group III comprised samples collected during the final seven days of the hospitalization period. The number of samples collected in each batch fluctuated depending on the length of the patients' hospital stay, as some died, were transferred to another hospital, or were discharged by the second or third sample collection period.

Five ml of blood was collected in two tubes (gel separation tube and sodium citrate tube) and centrifuged where the serum and plasma collected for subsequent laboratory tests. The procalcitonin test was performed on the ROCHE Cobas 6000 instrument using the electrochemiluminescence immunoassay (ECI) method with the kit (Elecsys BRAHMS PCT, Lot No.: 552945-01) and a normal range of (0.0-0.1 ng/mL) based on the kit insert. On the Cobas C311 instrument, the immunoturbidimetric assay principle was used to perform the C-reactive protein and D-dimer tests using the (D-DI; Cat no. 08105618190) kits with a normal range of (Up to 400 ng/mL) and (CRP4; Cat no. 07876033190) kits with a normal range of (0.0-10.0 ug/mL), respectively.

Based on a previous study on SARS-CoV -2 incubation duration across different age groups,[(17)] participants were divided into three age groups: young people (ages 18-35 years; n = 13), middle-aged adults (ages 36-55 years, n = 39), and elderly individuals (ages older than 55 years, n = 54).

For ethical purposes, consent was collected from patients to include them in the study, and the clinical and demographic data of each participant were collected either through a prepared questionnaire or from their hospital medical records. Patients who did not have all the required clinical and demographic information, as well as a confirmatory COVID-19 test result (PCR test), were excluded from the study.

**Statistical analysis:**

SPSS version 26 was used for data entry and analysis. Three approaches were used, in first approach descriptive statistics used to determine frequencies, percentages and mean ± Sd. For means, while in second approach Chi square association test and Fisher Exact test were used for categorical variable. ANOVA test was used to differentiate between more than two means. *P* value ≤0.05 regarded as a statistically significant.

## Results

This study included a total of 106 COVID-19 patients (54 male and 52 female). Participants' ages ranged from (18-83 years) with a mean age of 56 years. For statistical purposes, we categorized the patients into three age groups: young adults (ages 18-35 years; n= 13), middle – aged adults (ages 36-55 years; n=39), and older adults (> 55 years; n=54) as shown in Table 1.The statistical relationship between age groups and severity was not significant. However, nearly half of the patients in the older age group (40.7%) and middle age group (41.1%) were classified as severe. Moreover, in comparison with the other two age groups the older age group has the highest death rate (n= 24, 44.5%).

Our findings revealed no significant relationship between sex and infection rate; in fact, almost equal numbers of male and female participants were included in this study. Females had

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a higher percentage of severe cases (46.1%) than males (33.3%) while moderate cases were mostly recorded among the males (40.7%) these differences were shown to be not significant. In terms of gender and outcome, although not significant but males had a slightly higher mortality rate (46.3%) than females (40.3%), as shown in Table 2.

COVID-19 patients were mainly presented with respiratory symptoms as shown in Table 3, which compares the clinical symptoms of patients on admission. Dyspnea(83%) was the most common presentation at illness onset, followed by cough (72.6%), fatigue (71.7%), and fever (67.9%).

**Table 1** Association of age with severity and outcome of COVID-19 patients

| Variables | | Age Groups | | | Total | |
|---|---|---|---|---|---|---|
| | | 18-35 | 36-55 | >55 | | *P*- value |
| **Severity** | Mild | 7 (53.8%) | 11 (28.2%) | 14 (25.9%) | 32 (30.2%) | 0.109 |
| | Moderate | 2 (15.3%) | 12 (30.7%) | 18 (33.3%) | 32 (30.2%) | |
| | Severe | 4 (30.7%) | 16 (41.1%) | 22 (40.7%) | 42 (39.6%) | |
| **Outcome** | Discharged | 10 (76.9%) | 20 (51.3%) | 30 (55.5%) | 60 (56.6%) | 0.316 |
| | Passed | 3 (23.1%) | 19 (48.7%) | 24 (44.5%) | 46 (43.4%) | |
| **Total** | | 13 (12.2%) | 39 (36.7%) | 54 (50.9%) | 106 (100%) | |

**Table 2** Association of gender with severity and outcome of COVID-19 patients

| Variables | | Male | Female | Total | *P*- value |
|---|---|---|---|---|---|
| **Severity** | Mild | 14 (25.9%) | 18 (34.6%) | 32 | 0.054 |
| | Moderate | 22 (40.7%) | 10 (19.2%) | 32 | |
| | Severe | 18 (33.3%) | 24 (46.1%) | 42 | |
| **Outcome** | Discharged | 29 (53.7%) | 31 (59.6%) | 60 | 0.539 |
| | Passed | 25 (46.3%) | 21 (40.3%) | 49 | |
| **Total** | | 54 (100.0%) | 52 (100.0%) | 106 | |

**Table 3** Clinical presentations of COVID-19 patients (106)

| Presentations | Number | Percent |
|---|---|---|
| Fatigue | 76 | 71.7 |
| Dyspnea | 88 | 83.0 |
| Cough | 77 | 72.6 |
| Fever | 72 | 67.9 |
| Sore throat | 19 | 17.9 |
| Headache | 29 | 24.7 |
| Dizziness | 6 | 5.7 |
| Vomiting | 14 | 13.2 |
| Nausea | 6 | 5.7 |
| Runny nose | 3 | 2.8 |
| Loss of taste and smell | 7 | 6.6 |
| Chills | 18 | 17.6 |

https://doi.org/10.15218/zjms.2025.011

Comorbidity were common among COVID-19 patients such as hypertension, diabetes, and ischemic heart disease being the most common. Among (106) patients, (51.8%) were hypertensive, (41.5%) were diabetic, and (17.9%) had ischemic heart disease, as shown in Table 4.

A significant correlation with disease severity was found among hypertensive patients, as (18.1%) mild cases had hypertension, while (32.7%) of moderate and (49.2%) of severe cases had hypertension, as shown in Table 5.

**Table 4** Frequency of past medical and surgical histories among COVID-19 patients (106)

| Variable | Number | Percent |
|---|---|---|
| HTN | 55 | 51.8 |
| RH | 6 | 5.7 |
| IHD | 19 | 17.9 |
| Stroke | 3 | 3.0 |
| Asthma | 2 | 2.0 |
| Diabetes | 44 | 41.5 |
| Cancer | 2 | 2.0 |

**Table 5** Relation between past medical history and severity of the disease

| Variable | Status | Mild | Moderate | Severe | Total | *P*-value |
|---|---|---|---|---|---|---|
| **HTN** | No | 22 (43.1%) | 14 (27.4%) | 15 (29.4%) | 51 (48.1%) | 0.010 |
| | Yes | 10 (18.1%) | 18 (32.7%) | 27 (49.2%) | 55 (51.8%) | |
| **Total** | | 32 (30.1%) | 32 (30.1%) | 42 (39.6%) | 106 (100%) | |
| **IHD** | No | 26 (29.8%) | 27 (31.0%) | 34 (39.0%) | 87 (82.0%) | 0.92 |
| | Yes | 6 (31.5%) | 5 (26.3%) | 8 (42.1%) | 19 (17.9%) | |
| **Total** | | 32 (30.1%) | 32 (30.1%) | 42 (39.6%) | 106 (100%) | |
| **Diabetic** | No | 22 (35.4%) | 22 (35.4%) | 18 (29.0%) | 62 (58.4%) | 0.030 |
| | Yes | 10 (22.7%) | 10 (22.7%) | 24 (54.5%) | 44 (41.5%) | |
| **Total** | | 32 (30.1%) | 32 (30.1%) | 42 (39.6%) | 106 (100%) | |

https://doi.org/10.15218/zjms.2025.011

Several laboratory tests including (CRP, and D-dimer) were chosen and monitored at different time intervals (Within 3-4 days after admission, during hospital stay, and 7 days before discharge or death). Statistical analysis was performed to compare the values of the chosen laboratory tests with the severity of the patient's condition at the time of hospitalization. Table 6 shows a significant correlation between CRP levels and severity, as well as D-dimer levels and severity. Many patients with moderate and severe infections had an elevated CRP and D-dimer levels. High CRP levels were observed in (25/31 (80.6%)) of moderate cases and (37/42 (88.1%)) of severe cases, whereas high D-dimer levels were observed in (27/32 (84.4%)) among moderate cases and (36/42 (85.7%)) among severe cases.

A correlation of severity with CRP and D dimer results was also found in the last 7 days, as shown in Table 6, significant relations was found between severity of the studied cases with CRP and D dimer. For CRP, (21/23; 91.3%) of moderate cases and (34/36; 94.4%) of severe cases had high CRP levels while (25/26; 96.2%) of moderate and (32/35; 91.4%) of severe cases had high D dimer levels.

**Table 6** Clinical data collected the first 3 days and last 7 days of hospital stay

| **Variables (First 3 days)** | | **Status** | | | ***P*-value** |
|---|---|---|---|---|---|
| | | **Mild** | **Moderate** | **Severe** | |
| CRP | Normal (0.0-10.0) | 6 (22.2%) | 6 (19.4%) | 5 (11.9%) | 0.050 |
| | High >10.0 | 21(77.8%) | 25(80.6%) | 37 (88.1%) | |
| **Total** | | 27 (100%) | 31 (100%) | 42 (100%) | |
| D dimer | Normal ( Up to 500) | 11 (40.75) | 5 (15.6%) | 6 (14.3%) | 0.020 |
| | High >500 | 16(59.3%) | 27(84.4%) | 36 (85.7%) | |
| **Total** | | 27 (100%) | 32 (100%) | 42 (100%) | |
| **Variables (last 7 days)** | | **Status** | | | |
| | | **Mild** | **Moderate** | **Severe** | |
| CRP | Normal (0.0-10.0) | 3 (15.8%) | 2(8.7%) | 2 (5.6%) | 0.041 |
| | High >10.0 | 16(84.2%) | 21(91.3%) | 34 (94.4%) | |
| **Total** | | 19 (100%) | 23 (100%) | 36 (100%) | |
| D dimer | Normal ( Up to 500) | 1 (5.6%) | 1 (3.8%) | 3 (8.6%) | 0.028 |
| | High >500 | 17(94.4%) | 25(96.2%) | 32 (91.4%) | |
| **Total** | | 18 (100%) | 26 (100%) | 35 (100%) | |

https://doi.org/10.15218/zjms.2025.011

Three serial PCT measurements were done (PCT 1; within 3 days of admission, PCT 2; during the hospital stay, and PCT 3; within 7 days before hospital discharge). During the first 3-4 days of admission, the mean PCT level in the mild group (n = 32) was 0.2 ng/mL, while 2.2 ng/mL in the moderate group (n = 32), and 0.33 ng/mL in the severe group (n = 42) as shown in Table 7.

Interestingly, (25/32; 78.1%) of the mild cases had normal PCT levels upon admission, while among the cases categorized as severe cases a total of (28/42, 66.6%) patients had high PCT levels as shown in Table 8.

**Table 7** Mean difference of PCT levels of patients during hospital stay

| Variables | | N | Mean | SD | *P*-value |
|---|---|---|---|---|---|
| **PCT 1** | Mild | 32 | 0.2 | 0.4 | 0.36 |
| | Moderate | 32 | 2.2 | 9.6 | |
| | Severe | 42 | 0.3 | 0.4 | |
| | Total | 106 | 0.8 | 5.1 | |
| **PCT 2** | Mild | 46 | 0.6 | 2.4 | 0.32 |
| | Moderate | 29 | 0.2 | 0.3 | |
| | Severe | 30 | 3.1 | 14.9 | |
| | Total | 105 | 1.2 | 8.1 | |
| **PCT 3** | Mild | 21 | 0.3 | 0.8 | 0.42 |
| | Moderate | 17 | 1.0 | 2.8 | |
| | Severe | 17 | 1.2 | 2.8 | |
| | Total | 55 | 0.8 | 2.2 | |

**Table 8** PCT levels of COVID-19 patients during the first three days after admission in correlation with severity

| PCT | Results | Status | | | *P*-value |
|---|---|---|---|---|---|
| | | Mild | Moderate | Severe | |
| | Normal 0.0-0.1 | 25 (78.1%) | 18 (56.3%) | 14 (33.3%) | 0.06 |
| | Local Systemic Inflammation 0.2-0.5 | 7 (21.8%) | 10 (31.5%) | 18 (42.8%) | |
| | Moderate Systemic Inflammation 0.6-2.0 | 0 (0.0%) | 2 (6.3%) | 6 (14.3%) | |
| | Severe Systemic Inflammation 2.0-10.0 | 0 (0.0%) | 2 (6.3%) | 2 (4.8%) | |
| | Severe Bacterial Sepsis/Septic Shock 11.0-100. | 0 (0.0%) | 0 (0.0%) | 2 (4.8%) | |
| **Total** | | 32 (100%) | 32 (100%) | 42 (100%) | |

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Because of the short hospital stay among the 106 included patients, only 55 patients had three serial PCT measurements (within 3 days of admission, during the hospital stay, and within 7 days before hospital discharge). Serial PCT values measurements for the 30 patients who were discharged revealed that serum PCT levels fell as they recovered, with a significant difference between levels measured within three days of admission and within seven days of hospital discharge. As shown in Table 9, Most of the discharged patients had normal PCT levels(22/30), and only 8 discharged patients had abnormal PCT levels (8/22), PCT values measured for the death cases gradually increased significantly from the admission date ($P$ = 0.005).

## Discussion

The COVID-19 pandemic which started in December 2019 n Wuhon, China caused by SARS-CoV-2 virus from the Coronaviridae family.[3] Devastating effects were experienced worldwide as a result of the pandemic, this study was conducted in Erbil, Iraq's Kurdistan region, during the peak wave of the pandemic, when public hospitals and health communities were under emissive stress due to the large number of patients arriving at the hospitals.

Our hospital data collection revealed that more than half of the patients admitted to hospitals were aged 55 and above; among the severely categorized cases (40.7%) were aged 55 and above, and the case fatality rate for this group was (44.5%), while the middle age group had the highest mortality rate (48.7%). However, these results were statistically insignificant, but there is a distinct difference in the rate of infection, severity, and outcome among different age groups, which agrees with multiple other studies that have demonstrated the link of age with severity.[18-21]

Approximately equal numbers of male (N=54) and female (N=52) patients were recorded in this study, which correlates with another study done in Wuhan, China that showed no relation between rate of infection and gender.[22] Our study showed a higher rate of severe cases in females than males but a higher death rate recorded in males in comparison with females which correlates with other studies that have shown more adverse outcomes by SARS-CoV-2 infection in males than females, although many of those studies were not able to pinpoint the reason for such a discrepancy in their data, some studies related it to the advantage of a more robust immune response of

**Table 9** PCT levels in COVID-19 patients measured in the last seven days before discharge or death

| PCT | Results | Status | | Total | *P*-value |
|---|---|---|---|---|---|
| | | Discharged | Passed | | |
| | Normal 0.0-0.1 | 22 (73.3%) | 8 (32.0%) | 30 (54.5%) | |
| | Local Systemic Inflammation 0.2-0.5 | 7 (23.3%) | 6 (24.0%) | 13 (23.6%) | |
| | Moderate Systemic Inflammation 0.6-2.0 | 1 (3.3%) | 7 (28.0%) | 8 (14.5%) | 0.005 |
| | Severe Systemic Inflammation 2.0-10.0 | 0 (0.0%) | 2 (8.0%) | 2 (3.6%) | |
| | Severe Bacterial Sepsis/Septic Shock 11.0-100. | 0 (0.0%) | 2 (8.0%) | 2 (3.6%) | |
| **Total** | | 30 (100%) | 25 (100%) | 55 (100%) | |

https://doi.org/10.15218/zjms.2025.011

females.[23] While studies done in China related the high rate of male infections to their occupation specially those working in the wet markets.[24]

The SARS-CoV-2 clinical presentations are similar to those of SARS-CoV and MERS-CoV, which caused pandemics in 2002 and 2012, respectively. The most common presentations recorded in the study were dyspnea, fever, and dry cough, while only a few patients had upper respiratory symptoms, such as sneezing and runny nose, which is consistent with several other studies.[22,24,27,28] The most frequent presentations were dyspnea followed by cough, fatigue, and fever. Other studies have also shown dyspnea as the most common clinical feature in fact the result of a meta-analysis conducted on the basis of 11 studies, which included a total of 2091 cases concluded that dyspnea was the most frequently recorded symptom among COVID-19 patients.[29] Other studies have shown coughing to be the most common feature,[30] whereas others have reported fever as the most frequently reported symptom.[31,32]

Nearly half of patients had comorbid conditions, the most prevalent of which was hypertension, followed by diabetes and ischemic heart disease. Several studies have also demonstrated the relation between CVD, HTN, and Diabetes with COVID-19 mortality.[33,34] Our results showed significant correlations between Hypertension with severity and Diabetes with severity, Nearly half of the severe cases had hypertension and/or diabetes, this correlates with other study results as well.[21,35] For which Angiotensin-converting enzyme 2 (ACE2) were claimed.

According to one study, diabetes can increase ACE2 expression and treatment with Angiotensin-converting enzyme 2 (ACE2) inhibitors and angiotensin receptor blockers (ARBs) can also increase ACE2 expression. This increased expression of ACE2 may make it easier for the COVID-19 virus to infect the body, but this is a hypothesis that needs to be investigated further.[36] For diabetic patients, elevated levels of ACE2 were reported in diabetic patients through Mendelian randomization analysis and because phagocytic cell abilities are compromised in people with diabetes, they are more likely to contract infections.[37]

Among the studied serial measurements of participant's laboratory data, significant correlation was found between inflammatory biomarkers such as D-dimer and CRP with severity upon admission and during the last 7 days of hospital stay, similar to our study other studies have shown these inflammatory biomarkers as tool for prediction of severity and outcome among COVID-19 patients.[10,38] Our study showed that serial measurement of PCT levels is significant for prognosis and outcome of COVID-19 patients. However, (68%) of the passed patients had abnormal PCT levels during the last few days of their hospital stay, while (73.3%) of the discharged group had normal PCT levels. High serum procalcitonin levels typically indicate bacterial infections or super infections, while viral infections typically have no effect on procalcitonin levels, which could explain why most patients have normal procalcitonin levels upon admission to hospitals or care centers, but later due to secondary bacterial infections, PCT gradually increases during the hospital stay, which is consistent with the results of our study and several other studies,[39-41] which also showed that PCT could be used as an independent factor for the prognosis of COVID-19 patients. Another study showed that PCT was sensitive and reliable for classifying critically ill and severe/moderate cases, but could not distinguish between severe and moderate types.[42] A study conducted in China showed no significant correlation between PCT levels and severity of COVID-19.[43] Some limitations were faced in this study, including sample size limitation, serial samples were not available for all patients, and the fate for discharged patients were not clear.

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## Conclusion

Overcrowding and poor ventilation increase infection risk, patients with underlying diseases are more likely to develop the severe form of COVID-19. Our study found that procalcitonin can be used as a biomarker to predict the outcome of COVID-19 patients, and that CRP and D-dimer have a strong correlation with severity. We missed patients who were asymptomatic or had mild cases, so our findings may represent COVID-19's more severe end.

## Competing interests

The authors declare that they have no competing interests.

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