DOI: https://doi.org/10.53350/pjmhs221621238

ORIGINAL ARTICLE

Baseline Procalcitonin as a Predictor of Bacterial Infection and Clinical Outcomes in Covid-19

SHEIKH ALI AHMAD AJMAL[1], SYED FARAZ AHMAD[2], SYEDA SUMMIAYA SHAH[3], SAUD JAVED CHOUDHRY[4], SARA KHAN[5], IMTIAZ NAZAM[6]
[1]Medical Officer (MO), THQ Hospital Khairpur Tamewali
[2]Medical officer (MO), Institute: Rural health center, Basira, Muzaffargarh
[3]Women Medical Officer (WMO), Blood Bank Bahawal Victoria Hospital
[4]Medical Officer (covid ICU), Sadiq Abbasi Hospital, Bwp.
[5]Assistant Professor Chemical Pathology, CMH Institute of Medical Sciences Bahawalpur.
[6]Medical Officer (MO), Nawal Medicare And Maternity Home Bahawalpur
Corresponding author: Sheikh Ali Ahmad Ajmal, Email: shaliahmadajmal@ymail.com, Cell: 03356829387

ABSTRACT
Objective: The purpose of our study is to determine either bacterial infection or poor outcomes among patients with Covid-19 caused by increased level of procalcitonin.
Study Design: Retrospective/ observational study
Place and Duration: THQ Hospital Khairpur Tamewali. Jan 2021-Jun 2021
Methods: In this research, there were a total of 190 patients of both sexes. Patients ranged in age from 20 to 85. Detailed demographics, including age, sex, BMI, residence, and literacy, were obtained from all patients. Association of comorbidities among cases was determined. All the patients diagnosed Covid-19 by nasopharyngeal PCR. Baseline level of procalcitonin was measured among all cases before hospitalization and patients were separated either had bacterial infection or not. Outcomes among all the patients were measured in terms of mortality and survivors. Complete data was examined using the SPSS 23.0 version for statistical purposes alone.
Results: Among 190 cases, most of the patients were males 110 (57.9%) and 80 (42.1%) patients were females. Mean age of the patients were 52.13±13.44 years with mean BMI 26.14±11.54 kg/m^2. 85 (44.7%) patients were from rural areas and 115 (55.3%) had urban residency. 100 (52.6%) patients were educated. Hypertension was the most common comorbidity found in 120 (63.2%), followed by diabetes 95 (50%), kidney disease found in 40 (21.1%) patients and asthma in 25 (13.2%) patients. Mean PCT among all cases was 1.4±6.13 ng/mL. Bacterial infection (positive blood culture) was found among 130 (68.4%) cases with procalcitonin. Severity of pneumonia was found among 123 cases of bacterial infection. Mortality among all cases were 102 (53.4%) with positive blood culture for bacterial infection. Mean PCT of died patients was 1.1±4.6 ng/mL significantly higher than that of survived patients 2.13±4.45. Blood urea nitrogen and aspartate aminotransferase (AST) were also found a predictive value among died patients.
Conclusion: According to our findings, procalcitonin was the only biomarker strongly associated with patient mortality and satisfaction in the intensive care unit. With increasing procalcitonin concentrations, death rates increased as quartiles of procalcitonin levels rose. This study shows that intensivists may use procalcitonin to guide the management of COVID-19 and the utilization of ICU resources.

INTRODUCTION
COVID-19 was declared a global pandemic by the World Health Organization in 2020. Single-stranded RNA virus, SARS-CoV-2, was revealed to be the culprit in Wuhan, China [1–4]. 1.8 percent of those infected with SARS-CoV-2 have died, according to the 28 million cases documented in the US thus far [5]. The United States has the greatest death toll in the world, with 514,000 deaths.

The most frequent symptoms of COVID-19 infection are fever, dry cough, fatigue, and myalgia. However, bacterial superinfection may develop in certain persons. Acute respiratory distress syndrome (ARDS) and respiratory failure, necessitating intensive care unit (ICU) treatment, can occur in more severe instances [1–4]. A significant immunological dysfunction leading to multiorgan dysfunction is a characteristic of advanced illness [6]. It has been found that obesity, past lung, heart and diabetes conditions and senior age are all risk factors for severe COVID-19. A patient's chances of developing bacterial superinfection and experiencing bad outcomes are still difficult to predict. To treat COVID-19 patients, antimicrobials have been widely used [7,8], which may have contributed to an increase in Clostridioides difficile colitis, antimicrobial resistance, and pharmaceutical adverse effects.

Antimicrobial usage decisions are influenced by the likelihood/diagnosis of infection, informed by microbiological sample and culture, as well as the severity of sickness and danger of mortality. The WHO's recommendation for COVID-19 care recommends the use of broad-spectrum antibiotic coverage in cases of severe illness [9]. Antimicrobial de-escalation tactics would be supported if patients at low risk of bacterial infection and clinical deterioration and mortality could be identified.

Neuroendocrine thyroid parafollicular C cells generate procalcitonin (PCT), a 116-amino acid glycoprotein, which is typically found in the bloodstream at a concentration of 0.1 ng/mL in healthy persons. Inflammatory cytokines, such as TNF-, interleukin (IL)-1, and IL-6, frequently produced by bacterial infection, increase the expression of PCT in practically all tissues.[10,11] Prognostication in sepsis and antibiotic de-escalation in lower respiratory tract infections have been authorised by the FDA [12]. Thus, PCT has been shown to be beneficial in determining whether lower respiratory tract infections are caused by bacteria or not, with the exception of severe COVID-19, and is especially helpful in pneumonia for reducing antibiotic doses [13].

Biomarkers such as C-reactive protein (CRP), procalcitonin (PCT), and D-dimer have all been shown to be high in the seriously sick COVID-19 patients studied [14]. COVID-19 illness severity and mortality have been linked to higher levels of inflammatory markers [15]. Resource allocation for respiratory assistance has been greatly aided by the use of biomarkers in predicting illness severity [14]. There was a strong correlation between ICU acceptance and death in COVID-19 in this research.

SARS-CoV-2 infection is the primary focus of this study, which will examine if PCT concentrations may be used to predict subsequent bacterial infections and patient outcomes.

MATERIAL AND METHODS
This retrospective/ observational study was conducted at THQ Hospital Khairpur Tamewali and comprised of 190 patients had corona virus disease. Detailed demographics, including age, sex, body mass index, residence, and literacy, were obtained from all patients with signed permission. In this investigation, patients

under the age of 20 without a PCT value or written permission were ruled out.

Patients ranged in age from 20 to 85. Depending on the clinical suspicion of bacterial co-infection, a baseline PCT was sent and repeated as necessary at intervals of 24–48 hours. All positive blood and/or respiratory bacterial cultures were checked against the electronic medical record system, and the resulting data was gathered. The adjudication committee analysed positive cultures for species generally regarded as a contamination, such as coagulase-negative Staphylococcus. Every day, the patient's clinical condition was assessed using the ordinal scale, an eight-category measure [16]. Those who aren't hospitalised and aren't requiring supplemental oxygen are ranked as 1 (no limitation of activities), 2 (no limitation of activities), 3 (no limitation of activities) and 4 (no limitation of activities but ongoing medical care). 5 (no limitation of activities but ongoing medical care), 6 (no limitation of activities but ongoing medical care), 7 (no limitation of activities but ongoing medical care) 8(death).

Complete data was examined using the SPSS 23.0 version for statistical purposes alone. Categorical variables were assessed by using frequency and percentages. Mean standard deviation was used to present data.

RESULTS

Among 190 cases, most of the patients were males 110 (57.9%) wee males and 80 (42.1%) patients were females.(fig 1)

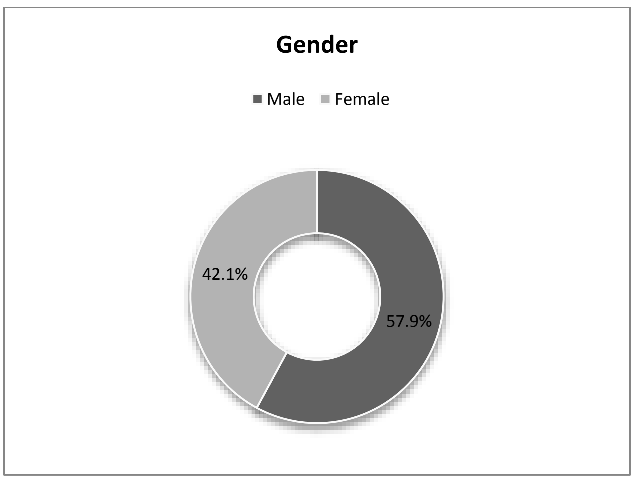

Figure 1: Gender distribution among all the cases

Mean age of the patients were 52.13±13.44 years with mean BMI 26.14±11.54 kg/m^2. 85 (44.7%) patients were from rural areas and 115 (55.3%) had urban residency. 100 (52.6%) patients were educated. Hypertension was the most common comorbidity found in 120 (63.2%), followed by diabetes 95 (50%), kidney disease found in 40 (21.1%) patients and asthma in 25 (13.2%) patients.(table 1)

Table 1: Patients detailed demographics of enrolled cases

Variables	Frequency	Percentage
Mean age (years)	52.13±13.44	
Mean BMI (kg/m^2)	26.14±11.54	
Residency		
Urban	75	44.7
Rural	115	55.3
Literacy		
Educated	100	52.6
Non-educated	90	47.4
Comorbidities		
HTN	120	63.2
Diabetes	95	50
Kidney failure	40	21.1
Asthma	25	13.2

Mean PCT among all cases was 1.4±6.13 ng/mL. Bacterial infection (positive blood culture) was found among 130 (68.4%) cases with procalcitonin. Severity of pneumonia was found among 123 cases of bacterial infection.(table 2)

Table 2:

Variables	Frequency	Percentage
Mean PCT ng/ml	1.4±6.13	
Bacterial Infection		
Yes	130	68.4
No	60	31.6
Severity of Pneumonia		
Yes	123	64.7
No	67	35.3

Mortality among all cases were 102 (53.4%) with positive blood culture for bacterial infection. Mean PCT of died patients was 1.1±4.6 ng/mL significantly higher than that of survived patients <0.23±3.25.(table 3)

Table 3: Frequency of mortality and PCT among cases

Variables	Positive Blood Culture	Negative Blood Culture
Mortality		
Yes	102 (53.4%)	0
No	28 (14.7%)	60 (31.6%)
PCT (ng/mL)	1.1±4.6	<0.23±3.25
Blood Urea Nitrogen	2.3±6.2	<0.2±3.5
aspartate aminotransferase (AST)	1.88±4.3	<0.2±5.6

Frequency of hospitalization (ICU stay) among all the cases were 41 (21.6%) cases.(table 4)

Table 4: Frequency of ICU stay among all the cases

Variables	Frequency	Percentage
ICU stay		
Yes	41	21.6
No	149	78.4

DISCUSSION

One of the biggest threats to world health is the SARS-CoV-2 virus. There are a number of factors to consider while developing biomarkers that might assist in determining a patient's prognosis and severity. Predictors of subsequent bacterial infection and mortality in patients with SARS-CoV-2 infection are examined in this study.

Antimicrobials may be reduced if the appropriate source control is confirmed using computerised tomography, which may help identify bacterial from viral illnesses. When PCT is negative (NPV >95 percent), biomarkers like PCT seem to be effective in predicting death, ICU admissions, and future bacterial infections. Treatment teams should take note of these results, as they might help them build better methods for predicting patient prognosis and treatment, although PCT's elevation in response to COVID-19 must also be taken into account [17]. A link between baseline PCT levels and the daily ordinal scale and PSI in our study validated the predicted severity of COVID-19 in hospitalised patients. Because of the extensive use of antimicrobials, it is possible that the natural flora may become overrun, resulting in incorrect identification of microorganisms [18].

In our study 190 patients had coronavirus disease were included. Majority of the patients 57.9% were males and 42.1% were females. Mean age of the patients were 52.13±13.44 years with mean BMI 26.14±11.54 kg/m^2. 85 (44.7%) patients were from rural areas and 115 (55.3%) had urban residency. 100 (52.6%) patients were educated. These results showed resemblance to the previous researches.[19,20] Hypertension was the most common comorbidity found in 120 (63.2%), followed by diabetes 95 (50%), kidney disease found in 40 (21.1%) patients and asthma in 25 (13.2%) patients. The elevated death rate in this patient cohort may be due to the existence of certain cofactors. Our results were comparable to the previous studies.[21]

Mean PCT among all cases was 1.4±6.13 ng/mL. Bacterial infection (positive blood culture) was found among 130 (68.4%) cases with procalcitonin. Severity of pneumonia was found among 123 cases of bacterial infection. Elevated procalcitonin levels were shown to be significantly related with both mortality and ICU admission, adding to the increasing body of evidence suggesting procalcitonin may be helpful in patients infected with COVID-19 [21,22]. Calcitonin is generally expressed in neuroendocrine cells but its procalcitonin (PCT) precursor, which is particular to bacterial sepsis, has been found. [23] Within four hours following an infection, procalcitonin levels in the blood rise as part of the innate immune system's reaction.[24] A research by Self et al. found a clear association between greater procalcitonin levels and an increased risk of bacterial infection; however, there was no threshold that could separate bacterial from viral infections.[25]

To add to the expanding body of research demonstrating the value of procalcitonin in COVID-19 infection, our findings showed that it was highly linked with mortality and ICU acceptability. Mortality among all cases were 102 (53.4%) with positive blood culture for bacterial infection. Mean PCT of died patients was 1.1±4.6 ng/mL significantly higher than that of survived patients <0.23±3.25. Increased PCT levels >0.5 ng/mL have been linked to a greater risk of SARS-CoV-2 infection in earlier investigations. SARS-CoV-2 infection clinical course and/or bacterial superinfection might be suspected by any significant rise in PCT.[26,27] Procalcitonin was found to be a predictor of disease severity and death in COVID-positive patients in an early Chinese investigation, which supports our findings [28]. The researchers discovered that procalcitonin levels rose significantly as the condition progressed (PCT levels: 0.05 ng/mL in the moderate group, 0.23 ng/mL in the severe group, and 0.44 ng/mL in the critical group, p 0.05). This is similar to our findings in a Caribbean community. Procalcitonin's use in the treatment of COVID-19 infection is supported by these studies, which were undertaken in a range of ethnic groups.[29]

CONCLUSION

According to our findings, procalcitonin was the only biomarker strongly associated with patient mortality and satisfaction in the intensive care unit. With increasing procalcitonin concentrations, death rates increased as quartiles of procalcitonin levels rose. This study shows that intensivists may use procalcitonin to guide the management of COVID-19 and the utilization of ICU resources.

REFERENCES

1 Guan W, Ni Z, Hu Y, et al.. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020;382(18):1708–1720.

2 Wang D, Hu B, Hu C, et al.. Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA—J Am Med Assoc. 2020;323(11):1061–1069.

3 Hui DS I Azhar E, Madani TA, et al.. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health—The latest 2019 novel coronavirus outbreak in Wuhan, China. Int J Infect Dis. 2020;91:264–266.

4 Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. Int J Antimicrob Agents. 2020;55(3).

5 Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. Lancet Infect Dis. 2020;20(5):533–534.

6 Tay MZ, Poh CM, Rénia L, MacAry PA, Ng LFP. The trinity of COVID-19: immunity, inflammation and intervention. Nat Rev Immunol. 2020;20(6):363–374.

7 Rawson TM, Moore LSP, Zhu N, et al.. Bacterial and Fungal Coinfection in Individuals with Coronavirus: A Rapid Review to Support COVID-19 Antimicrobial Prescribing. Clin Infect Dis. 2020;71(9):2459–2468.

8 Rothe K, Feihl S, Schneider J, et al.. Rates of bacterial co-infections and antimicrobial use in COVID-19 patients: a retrospective cohort study in light of antibiotic stewardship. Eur J Clin Microbiol Infect Dis. 2021;40(4):859–869.

9 World Health Organisation. Clinical management of COVID-19 - interim guidance. 2020.

10 Morgenthaler NG, Struck J, Fischer-Schulz C, Seidel-Mueller E, Beier W, Bergmann A. Detection of procalcitonin (PCT) in healthy controls and patients with local infection by a sensitive ILMA. Clin Lab. 2002;48(5–6):263–270.

11 Gilbert DN. Role of Procalcitonin in the Management of Infected Patients in the Intensive Care Unit. Infect Dis Clin North Am. 2017;31(3):435–453.

12 Petrilli CM, Jones SA, Yang J, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: Prospective cohort study. BMJ. 2020;369:m1966.

13 Mewes JC, Pulia MS, Mansour MK, Broyles MR, Bryant Nguyen H, Steuten LM. The cost impact of PCT-guided antibiotic stewardship versus usual care for hospitalised patients with suspected sepsis or lower respiratory tract infections in the US: A health economic model analysis. PLoS One. 2019;14(4):e0214222.

14 Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020; 395:507.15.

15 Pink I, Raupach D, Fuge J, Vonberg RP, Hoeper MM, Welte T, Rademacher J. C-reactive protein and procalcitonin for antimicrobial stewardship in COVID-19. Infection. 2021 Oct;49(5):935-943.

16 Wickham H, Averick M, Bryan J, et al.. Welcome to the Tidyverse. J Open Source Softw. 2019;4(43):1686.

17 Fajgenbaum DC, June CH. Cytokine Storm. N Engl J Med. 2020;383(23):2255–2273.

18 Gilbert DN, Leggett JE, Wang L, et al. Enhanced Detection of Community-Acquired Pneumonia Pathogens With the BioFire® Pneumonia FilmArray® Panel. Diagn Microbiol Infect Dis. 2021;99(3):115246

19 Atallah NJ, Warren HM, Roberts MB, Elshaboury RH, Bidell MR, Gandhi RG, et al. (2022) Baseline procalcitonin as a predictor of bacterial infection and clinical outcomes in COVID-19: A case-control study. PLoS ONE 17(1): e0262342.

20 Shang W, Dong J, Ren Y, et al.. The value of clinical parameters in predicting the severity of COVID-19. J Med Virol. 2020;92(10):2188–2192.

21 Feng, T.; James, A.; Doumlele, K.; White, S.; Twardzik, W.; Zahid, K.; Sattar, Z.; Ukponmwan, O.; Nakeshbandi, M.; Chow, L.; et al. Procalcitonin Levels in COVID-19 Patients Are Strongly Associated with Mortality and ICU Acceptance in an Underserved, Inner City Population. Medicina 2021, 57, 1070

22 Tang, J.; Lin, J.; Zhang, E.; Zhong, M.; Luo, Y.; Fu, Y.; Yang, Y. Serum IL-6 and procalcitonin are two promising novel biomarkers for evaluating the severity of COVID-19 patients. Medicine 2021, 100, e26131.

23 Sarfaraz, S.; Shaikh, Q.; Saleem, S.G.; Rahim, A.; Herekar, F.F.; Junejo, S.; Hussain, A. Determinants of in-hospital mortality in COVID-19: A prospective cohort study from Pakistan. PLoS ONE 2021, 16, e0251754

24 Müller, B.; White, J.C.; Nylen, E.S.; Snider, R.H.; Becker, K.L.; Habener, J.F. Ubiquitous Expression of the Calcitonin-I Gene in Multiple Tissues in Response to Sepsis 1. J. Clin. Endocrinol. Metab. 2001, 86, 396–404

25 Gilbert, D.N. Procalcitonin as a Biomarker in Respiratory Tract Infection. Clin. Infect. Dis. 2011, 52, S346–S350.

26 Lippi G, Plebani M. Procalcitonin in patients with severe coronavirus disease 2019 (COVID-19): A meta-analysis. Clin Chim Acta. 2020;505(January):190–191.

27 Ponti G, Maccaferri M, Ruini C, Tomasi A, Ozben T. Biomarkers associated with COVID-19 disease progression. Crit Rev Clin Lab Sci. Published online 2020:389–399.

28 Hu, R.; Han, C.; Pei, S.; Yin, M.; Chen, X. Procalcitonin levels in COVID-19 patients. Int. J. Antimicrob. Agents 2020, 56, 106051

29 Ming, .K., Myall, A.C., Hernandez, B. et al. Informing antimicrobial management in the context of COVID-19: understanding the longitudinal dynamics of C-reactive protein and procalcitonin. BMC Infect Dis 21, 932 (2021).