Journal of Namibian Studies, 33 S2(2023): 5120–5129 ISSN: 2197-5523 (online)

Procalcitonin impact in bacterial co-infection among Iraqi patients with SARS-CoV-2 virus

Aymen Mohammed Ahmed[1], Jinan M.J. Alsaffar[2]

[1]Department of Biotechnology, College of Science, University of Baghdad, phd.aymen88@gmail.com

[2]Department of Biotechnology, College of Science, University of Baghdad

Abstract

The thyroid gland produces a protein known as procalcitonin (PCT) in reaction to inflammation. The identification of PCT as a biomarker has been established for the purpose of distinguishing between bacterial and viral infections. The contentious nature of the role of procalcitonin (PCT) in the medical management of COVID-19, which is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been noted. The SARS-CoV2 virus is known for its high level of infectivity and pathogenicity, with a primary impact on the respiratory system. The present investigation involved the enrollment of 300 patients who had received laboratory confirmation of COVID-19 in Iraq during the period that extended from February to May of the year 2022. The objective of this investigation is to demonstrate the potential utility of measuring PCT levels as a diagnostic indicator for bacterial co-infections in individuals with COVID-19. The study involved the examination of 75 patients with varying degrees of SARS-CoV2 infection (mild, acute, and severe) and 75 healthy controls, with consideration given to gender and the presence of the patient. The results of this study could aid in the promotion of antimicrobial stewardship and the enhancement of patient outcomes. The findings of this study indicate that barely 21.3% of the overall patient population exhibits PCT levels within the normal range, which is defined as less than 0.05 ng/mL. Conversely, the majority of patients, comprising 78.8% of the sample, display PCT levels that fall outside of the normal range, exceeding 0.05 ng/mL. To sum up, procalcitonin (PCT) has the potential to serve as a biomarker for the detection of bacterial coinfections in patients with COVID-19. This could aid in the implementation of antimicrobial stewardship and lead to better clinical results.

Keywords: COVID-19, SARS-CoV2, Serum PCT, Bacterial co-infection and status.

Introduction

The SARS-CoV2 virus was involved in the catastrophic COVID-19 event, posing a constant threat to worldwide sanitation and health care precautions. The impact on human immunity is a significant aspect of this issue. Research has indicated that the impact of the virus on the immune system can result in subsequent infections with bacteria that are significantly more detrimental than the virus in isolation. Research has indicated that individuals who are infected tend to display a compromised immune reaction in terms of combating bacterial-induced illnesses [1]. The term "procalcitonin" refers to the precursor of the hormone calcitonin (PCT), which is composed of 116 amino acids. Neutropenia or other immunosuppressive states do not appear to have a detrimental effect on PCT production[2]. The levels of procalcitonin (PCT) exhibit a positive correlation with the intensity of the inflammatory response or infections, indicating that individuals with more severe pathological conditions tend to exhibit elevated PCT levels. Moreover, procalcitonin exhibits certain usefulness as a prognostic marker, whereby elevated levels in the bloodstream are associated with an increased likelihood of mortality. Procalcitonin (PCT) has been acknowledged as a sepsis indicator since 1993[3]. In its early stages, procalcitonin (PCT) was primarily employed for the purpose of diagnosing bacterial sepsis and distinguishing between bacterial and non-bacterial causes of systemic inflammation. Currently, indications have been expanded to encompass a more dynamic application, such as monitoring and directing therapy for sepsis, which includes administering antibiotics and controlling the focus of infection. This is applicable to both outpatients and patients in the intensive care unit[4]. The utilizations of procalcitonin (PCT) presents certain benefits over other commonly employed biomarkers in clinical settings, such as C-reactive protein (CRP) and white blood cell count. PCT exhibits several advantages over its predecessors, including its specificity for bacterial infection as opposed to general inflammation, its swift elevation within 6 hours of a disparage, its rapid decrease with immune control on infection with a half-life of 24 hours, its strong correlation with the severity of illness, with higher levels observed in more severely ill patients, and its independence from anti-inflammatory and immunosuppressive states with respect to production[5]. According to[6], recent research indicates a positive correlation between elevated PCT levels and increased COVID-19 intensities. The measurement of serum procalcitonin (PCT) quantities has the potential to aid in the identification of comorbidities in individuals with COVID-19. In instances where COVID-19 is isolated, it has been observed that the patient's procalcitonin (PCT) levels tend to remain within the normal range, which is consistent with the behavior of other viral illnesses. The absence of a PCT-triggered escalation in viral infections could potentially be attributed to the virus-induced generation of interferon by macrophages, which impedes the production of TNF in the course of the immune response[7]. The utilization of procalcitonin (PCT) has exhibited potential as a means to facilitate the decision-making process concerning antibiotic treatment for lower respiratory tract infections, as per the findings of[8].Although the role of procalcitonin (PCT) in COVID-19 management is a topic of debate, it is crucial to acknowledge the potential advantages of PCT testing in COVID-19 patients who are suspected to have bacterial confections. The excessive use of antibiotics can result in heightened antimicrobial resistance, a significant issue in the realm of public health. Research has demonstrated that administering antibiotics based on procalcitonin (PCT) guidance is efficacious in decreasing antibiotic utilization while maintaining favorable clinical outcomes among individuals with presumed bacterial infections. According to[9], the implementation of PCT testing can enable a more precise and suitable administration of antibiotics in individuals with COVID-19.

Materials and Methods

2.1. Patient Clinical Data

Between February 2 and May 10, 2022, a total of 300 samples were gathered from various local healthcare facilities, including Al-Numan Hospital, AL-Kindy Hospital, and AL-Shiffaa Centre, as well as multiple private laboratory centres. These samples initially tested positive for SARS-CoV-2 via real-time RT-PCR. The specimens were obtained instantly from each COVID-19 patient upon enrollment. The medical records were the source of the laboratory and clinical diagnostic outcome results. A variety of factors were taken into account on admission: gender, medical status, the presence of bacterial growth, and the location of the patient. The Control Ethics Committee granted approval for all procedures involving human materials in this study.

2.2. Criteria for Specimen

Serum samples obtained from patients with varying statuses were matched to those of healthy controls with regard to both condition and gender. Furthermore, a volume of 3 millilitres of peripheral blood was collected from each participant through venipuncture. The blood was transferred to plain gel tubes and left to coagulate for 30 minutes at ambient temperature. The serum was acquired via centrifugation at a speed of 3000 xg for a period of 10 minutes prior to utilisation. The serum samples were preserved at a temperature of -20 ºC.

2.3. Experimental methods

The serum concentrations of PCT were measured using the enzyme-linked immunosorbent assay (ELISA) in accordance with the procedures supplied by elabscience USA and Monobind Inc. USA.

2.4. Statistical analysis

The data was subjected to statistical evaluation using the SPSS-25 software package, which stands for Statistical Packages for Social Sciences, version 25. The statistical information was conveyed using basic metrics such as percentage, the mean, and deviations from the mean. The one-way ANOVA test and post hoc test were employed as the statistical methodology to assess the statistical significance of differences among means in distinct groups with quantitative data.

Results

3.1. Patient Characteristics

Table 1 presents the baseline characteristics of all cases and various groups. A study group of 300 individuals has been identified with SARS-CoV-2 infection and subsequently categorized into three distinct clinically significant groups: severe, acute, and mild. The study reveals that the highest proportion of cases (61.3%) involved participants who were hospitalized. The observation revealed that a higher proportion of men (54.3%) were present compared to women (45.7%). A study has been conducted and illustrated on the correlation between the gander (as shown in Figure 1a), the location of the patient (as shown in Figure 1b), and the medical status (as shown in Figure 1c) with regards to the existence of bacterial growth.

Table 1. Characteristics of patients infected with SARS-CoV-2.

Characteristics		Frequency	Percent %
Gender	Female	137	45.7
	Male	163	54.3
Location of patient	Non-Hospitalizes	116	38.7
	Hospitalizes	184	61.3
Medical status	Sever	75	25.0
	Acute	75	25.0
	Mild	75	25.0
	Healthy Control	75	25.0
Bacterial Growth	Growth	190	63.3
	No Growth	110	36.7

Figure 1-a. Clarify the relationship between gender of SARS-CoV-2 patients and bacterial growth

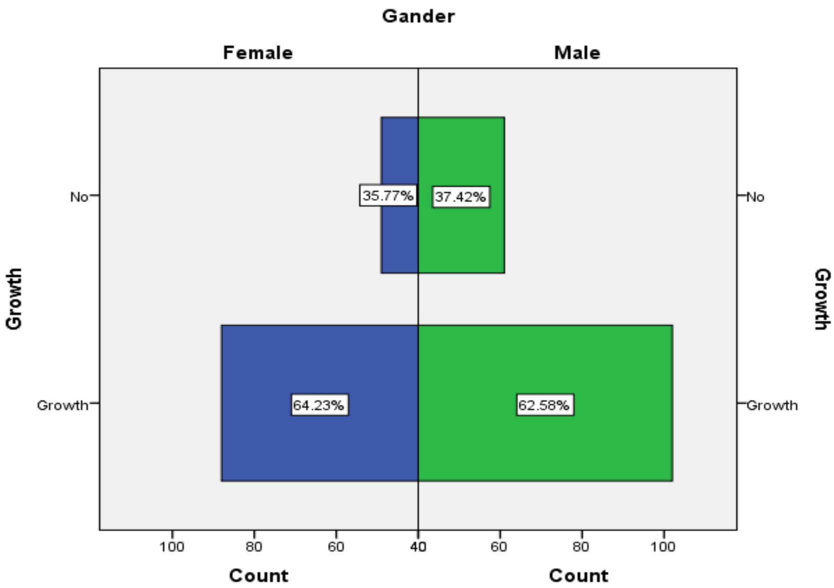


Figure 1-b. Illustrate the relationship location of SARS-CoV-2 patients and bacterial growth

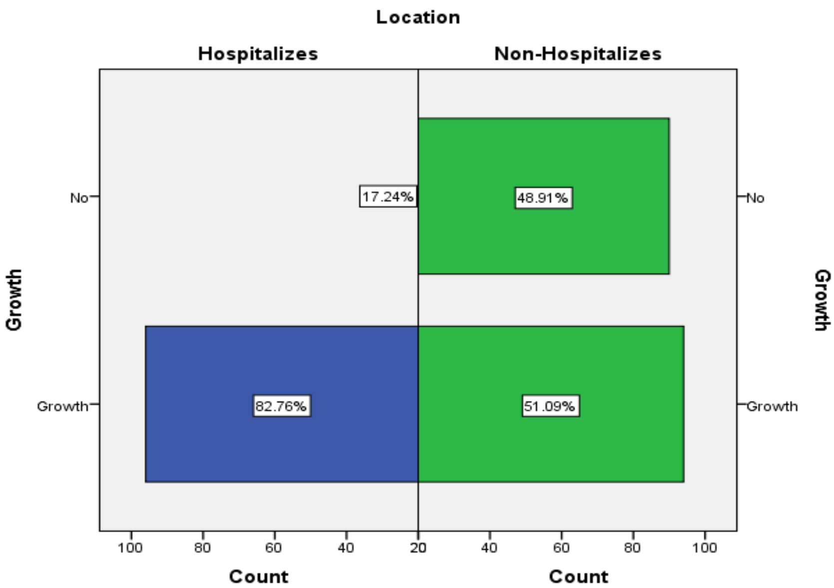
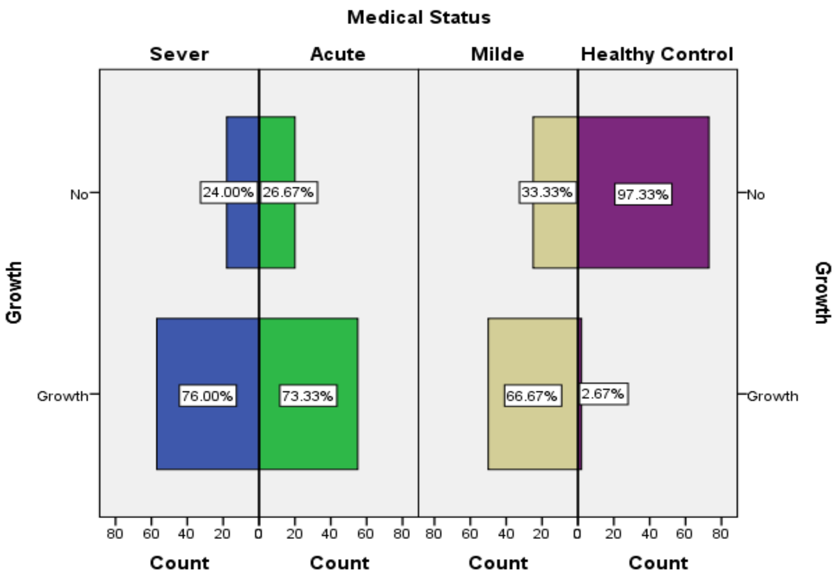


Figure 1-c. Clarify the relationship between medical status of SARS-CoV-2 patients and bacterial growth



3.2 procalcitonin as a diagnostic tool.

The study reports on the mean serum procalcitonin (PCT) values in male and female individuals with severe, acute, and mild statuses, as well as healthy controls. The mean serum PCT values in males were found to be 18, 11.9, and 1.8 pg/mL for severe, acute, and mild status, respectively, compared to 0.5 pg/mL in healthy controls. Similarly, the mean serum PCT values in females were found to be 14.1, 11.1, and 2.3 pg/mL for severe, acute, and mild status, respectively, compared to 0.5 pg/mL in healthy controls. The findings presented in Table 2 indicate that the serum levels of procalcitonin (PCT) were significantly elevated in severe SARS-CoV2 patients compared to the control group, for both males and females.

Table 2. PCT levels against medical statues

Medical Status		**Sever**		**Acute**		**Milde**		**Healthy Control**	
Gander		Female	Male	Female	Male	Female	Male	Female	Male
N		34	41	31	44	32	48	40	35
Procalcitonine	Mean	14.1	18	11.1	11.9	2.3	1.8	0.5	0.5
	S.D.	4.8	4.8	5.8	6.3	2.1	1.3	0.3	0.3
	p-value	**0.001****		0.604NS		0.182 NS		0.892 NS	

S.D.: Std. Deviation, Data presented as One-way ANOVA test. NS Non-significant, * significant at P ≤ 0.05, ** significant at P ≤ 0.01.

The lab tests showed that the levels of serum procalcitonin (PCT) were significantly higher in people with severe SARS-CoV-2 infections, especially in those who also had a bacterial infection (63.3% of cases), as shown in Figure 2A. The study findings indicate a statistically significant increase ($P \leq 0.05$) in total serum levels of procalcitonin as the disease progressed, as illustrated in Figure 1B.

Figure 2-a. Illustrate the relationship between PCT levels of SARS-CoV-2 patients and bacterial growth

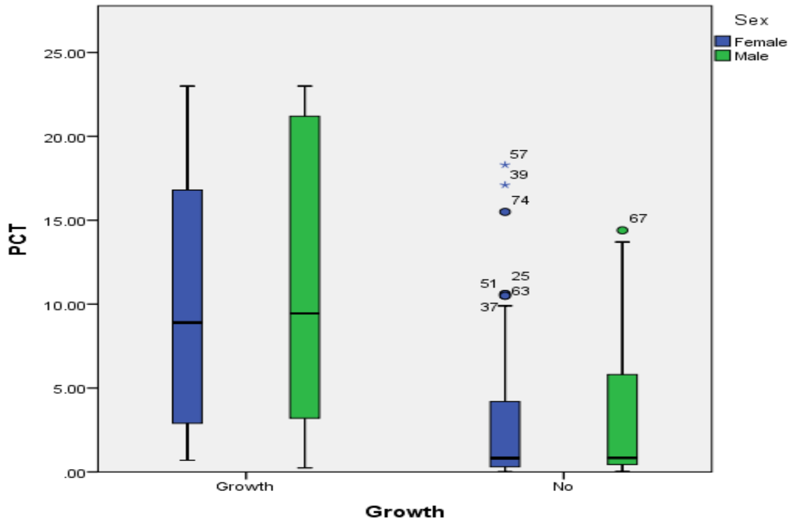
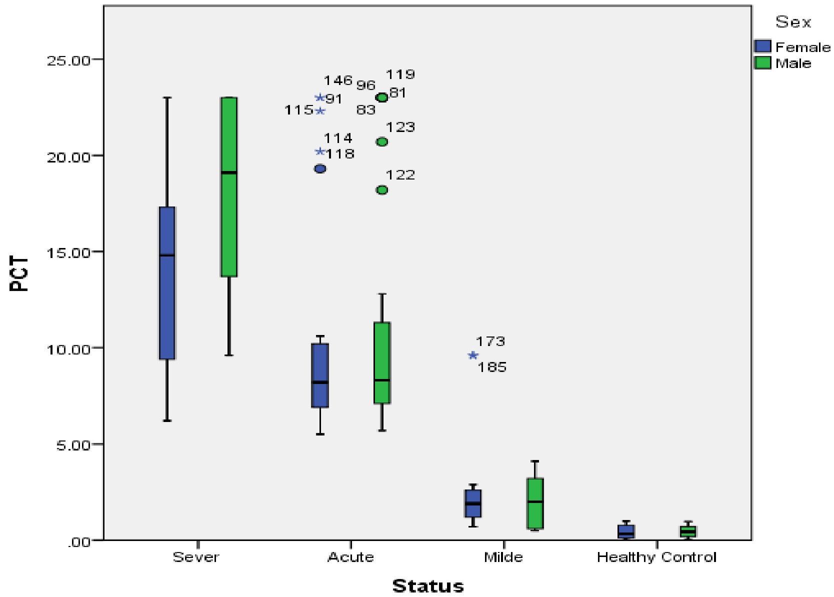


Figure 2-b. Illustrate the relationship between PCT levels and medical status of SARS-CoV-2 patients



Discussion

multiple findings have been documented in different investigations[10][11]. Prior studies have indicated that the level of procalcitonin (PCT) does not exhibit an elevation in cases of severe acute respiratory syndrome (SARS), in contrast to bacterial pneumonia, where it demonstrates an increase[12]. It has been postulated that due to the structural similarities between the coronaviruses responsible for SARS and COVID-19, the immune responses of humans to both viruses would be analogous. Consequently, it is believed that the level of procalcitonin (PCT) would not increase in individuals with COVID-19 in the absence of bacterial infections, as per the findings of[13]. The presence of a bacterial co-infection exacerbates both the prognosis and severity of the disease due to the heightened systemic inflammation it induces. The concentrations of PCT in individuals with COVID-19 were found to have a correlation with the severity of the disease[14]. It was postulated that a considerable number of patients, particularly those with advanced stages of the illness, may have a co-infection with bacteria [15].

The present investigation has undertaken a classification of fatal infections into two categories: severe individuals with bacterial infections and severe individuals without bacterial infections. The study findings indicate that the average serum procalcitonin (PCT) levels were comparable between patients with severe and acute conditions and were roughly six-fold higher in patients with both severe and acute conditions compared to those with mild conditions. The levels of procalcitonin (PCT) manifested an apparent dependence on the severity of the disease and could potentially be linked to a bacterial co-infection. This is supported by the observation that the incidence of co-infection was similar to the frequency of elevated PCT levels in patients with mild to moderate severity, which was approximately 10%. It is noteworthy that the co-infection rates were found to be 23% and 48% in patients with acute and severe conditions, respectively. In comparison to the control group, the rates of elevated procalcitonin (PCT) were observed to be 60% and 80%, respectively.

Conclusion

Procalcitonin (PCT) has the potential to serve as a biomarker for the detection of bacterial co-infections in individuals with COVID-19. This identification could aid in the promotion of antimicrobial stewardship and ultimately lead to improved patient outcomes. Nonetheless, the aetiology behind heightened levels of procalcitonin (PCT) in individuals with COVID-19 remains ambiguous, and additional investigation is imperative to ascertain the function of PCT in the diagnosis and treatment of COVID-19. Despite this, the use of PCT-guided antibiotic therapy has demonstrated efficacy in minimising antibiotic exposure among COVID-19 patients who are suspected of having bacterial co-infections. This is particularly significant in light of the issue of antimicrobial resistance.

Ethical clearance

the scientific research conducted in Iraq is subject to ethical approval by the Research Ethical Committee of the ministries directing environmental, health, higher education, and scientific research.

Conflict of Interest:

The authors state that they have no conflicts of interest with respect to the present inquiry.

Bibliography

[1] L. Wang et al., "An observational cohort study of bacterial co-infection and implications for empirical antibiotic therapy in patients presenting with COVID-19 to hospitals in North West London," J. Antimicrob. Chemother., vol. 76, no. 3, pp. 796–803, 2021, doi: 10.1093/jac/dkaa475.

[2] A. L. Vijayan, S. Ravindran, R. Saikant, S. Lakshmi, R. Kartik, and G. Manoj, "Procalcitonin: A promising diagnostic marker for sepsis and antibiotic therapy," J. Intensive Care, vol. 5, no. 1, pp. 1–7, 2017, doi: 10.1186/s40560-017-0246-8.

[3] C. Y. F. Yap and T. C. Aw, "The use of procalcitonin in clinical practice," Proc. Singapore Healthc., vol. 23, no. 1, pp. 33–37, 2014, doi: 10.1177/201010581402300106.

[4] R. Paudel, P. Dogra, A. A. Montgomery-Yates, and A. C. Yataco, "Procalcitonin: A promising tool or just another overhyped test?," Int. J. Med. Sci., vol. 17, no. 3, pp. 332–337, 2020, doi: 10.7150/ijms.39367.

[5] G. Y. Yitbarek et al., "The role of C-reactive protein in predicting the severity of COVID-19 disease: A systematic review," SAGE Open Med., vol. 9, p. 205031212110507, 2021, doi: 10.1177/20503121211050755.

[6] S. Ahn et al., "Role of procalcitonin and C-reactive protein in differentiation of mixed bacterial infection from 2009 H1N1 viral pneumonia," Influenza Other Respi. Viruses, vol. 5, no. 6, pp. 398–403, Nov. 2011, doi: 10.1111/j.1750-2659.2011.00244.x.

[7] I. Pink et al., "C-reactive protein and procalcitonin for antimicrobial stewardship in COVID-19," Infection, vol. 49, no. 5, pp. 935–943, 2021, doi: 10.1007/s15010-021-01615-8.

[8] L. Lai et al., "Diagnostic Accuracy of Procalcitonin Compared to C-Reactive Protein and Interleukin 6 in Recognizing Gram-Negative Bloodstream Infection: A Meta-Analytic Study," Dis. Markers, vol. 2020, 2020, doi: 10.1155/2020/4873074.

[9] A. Ticinesi et al., "The Clinical Significance of Procalcitonin Elevation in Patients over 75 Years Old Admitted for COVID-19 Pneumonia," Mediators Inflamm., vol. 2021, 2021, doi: 10.1155/2021/5593806.

[10] R. Hu, C. Han, S. Pei, M. Yin, and X. Chen, “Procalcitonin levels in COVID-19 patients,” Int. J. Antimicrob. Agents, vol. 56, no. 2, pp. 8–10, 2020, doi: 10.1016/j.ijantimicag.2020.106051.

[11] A. Roy, H. R. Powers, E. C. Craver, M. D. Nazareno, S. N. S. Yarrarapu, and D. K. Sanghavi, “Antibiotic stewardship: Early discontinuation of antibiotics based on procalcitonin level in COVID-19 pneumonia,” J. Clin. Pharm. Ther., vol. 47, no. 2, pp. 243–247, 2022, doi: 10.1111/jcpt.13554.

[12] B. Hamade and D. T. Huang, “Procalcitonin: Where Are We Now?,” Crit. Care Clin., vol. 36, no. 1, pp. 23–40, 2020, doi: 10.1016/j.ccc.2019.08.003.

[13] A. D’Abramo et al., “Acute respiratory distress syndrome due to SARS-CoV-2 and Influenza A co-infection in an Italian patient: Mini-review of the literature,” Int. J. Infect. Dis., vol. 97, pp. 236–239, 2020, doi: 10.1016/j.ijid.2020.06.056.

[14] Y. Z. Zhou et al., “The value of PCT, IL-6, and CRP in the early diagnosis and evaluation of COVID-19,” Eur. Rev. Med. Pharmacol. Sci., vol. 25, no. 3, pp. 1097–1100, 2021, doi: 10.26355/eurrev_202101_24680.

[15] N. R. Sproston and J. J. Ashworth, “Role of C-reactive protein at sites of inflammation and infection,” Front. Immunol., vol. 9, no. APR, pp. 1–11, 2018, doi: 10.3389/fimmu.2018.00754.