

Procalcitonin as a Biomarker for Bacterial Infections: Clinical Applications

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Abstract. Bacterial infections can induce substantial inflammatory responses that are often mirrored by alterations in hematological parameters and serum biomarkers, such as procalcitonin. The identification of reliable biomarkers plays a critical role in facilitating early diagnosis and assessing disease severity. This study was designed to assess the diagnostic significance of serum procalcitonin levels alongside hematological indicators in patients with confirmed bacterial infections, comparing these findings with values obtained from healthy individuals. Conducted as a case-control observational study in Southern Iraq between January and April 2024, the research included 150 participants—100 with laboratory-confirmed bacterial infections and 50 healthy controls. Blood samples were collected from all participants to perform complete blood count (CBC) analysis and to determine serum procalcitonin concentrations using enzyme-linked immunosorbent assay (ELISA). Sociodemographic variables including age, gender, body mass index (BMI), and smoking status were statistically comparable between both groups. However, patients with bacterial infections showed significantly elevated procalcitonin levels (mean 5.68 ± 2.74 ng/ml) compared to controls (mean 0.39 ± 0.21 ng/ml), with a p-value of less than 0.001. Moreover, there was a direct correlation between infection severity and procalcitonin concentration. Hematological alterations in the patient group included increased white blood cell (WBC) counts, neutrophilia, lymphopenia, decreased levels of hemoglobin and hematocrit, and a marked rise in platelet counts. Interestingly, procalcitonin levels did not differ significantly by gender, suggesting that sex-based variation may not influence its diagnostic utility. These findings reinforce the clinical value of procalcitonin as a biomarker for both diagnosing bacterial infections and monitoring their severity. Additionally, associated hematological changes provide complementary information reflecting the systemic inflammatory response, thereby enhancing the effectiveness of combined biomarker-based assessment in clinical settings.

Highlights:

1. **Diagnostic Value:** Procalcitonin levels significantly rise in bacterial infections, making it a reliable biomarker for diagnosis and severity assessment.
2. **Clinical Correlation:** A strong correlation exists between procalcitonin levels and white blood cell count, enhancing its diagnostic precision.
3. **No Gender Bias:** Procalcitonin levels are consistent across genders, indicating its universal applicability in both male and female patients.

Keywords: Procalcitonin, Bacterial Infection, Hematological Parameters, Inflammation, ELISA

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Introduction

Bacterial infection remains a leading threat to global health.⁵ It is a major cause of morbidity, mortality, and escalating health expenditure worldwide, particularly in cases of Sepsis, and Lower respiratory infections. Early, precise discrimination of inflammatory process whether bacterial or non-bacterial is an important component in order to provide appropriate therapy; limiting unjustifiable use of antibiotics and preventing development of antimicrobial resistance. [1]. In this regard, identification of dependable biomarkers that indicate bacterial infection status and guide therapeutic decisions has been a longstanding priority in infectious diseases and critical care medicine [2], [3]. Procalcitonin (PCT) is a 116 amino acid peptide and the precursor of calcitonin; it is constitutively produced in small amounts by the C-cells of the thyroid gland. PCT levels are very low or undetectable in the circulation under normal conditions [4]. However, it is markedly induced during systemic bacterial infections in different tissues such as a liver, lung and gut, mainly by a pro-inflammatory cytokine milieu including IL-6 and TNF- α . Crucially, viral infections as well as non-bacterial inflammatory conditions usually do not provoke a comparably significant rise in PCT levels, thus increasing its diagnostic specificity for bacterial infections [5], [6]. A number of clinical trials have shown that PCT is a useful biomarker for differentiating bacterial from viral infections, for estimating the severity of a condition and, for monitoring treatment outcomes. Unlike traditional markers (e.g., C-reactive protein, CRP and erythrocyte sedimentation rate, ESR) that exceed the level indicated by inflammatory changes, procalcitonin (PCT) levels give precise information on the bacterial infections.FALSE-PLUSUnlike other traditional markers (e.g., C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) responding to a range of inflammatory conditions, PCT levels are affected by inflammation, infection and bacterial infections [7]. Its concentrations increase within 2-6 hours following infection and peak at 12-24 hours, serving as early indices. In addition, procalcitonin levels fall swiftly when effective antibiotics are used, making it a dynamic test for guidance on therapy and antibiotic stewardship [8], [9]. Procalcitonin has been studied in clinical practice in a variety of health care settings, including emergency departments, ICUs, and out-patient departments. In patients with suspected sepsis or pneumonia PCT guided protocols result in decreased antibiotic use without reducing clinical efficacy [10]. Moreover, elevated PCT levels have been associated with poor prognosis in critically ill patients, offering potential prognostic value. Despite these

advantages, some limitations remain. Procalcitonin levels may be influenced by major trauma, surgery, or chronic kidney disease, and the cost and availability of testing can vary across institutions [11], [12]. The goal of the current study was to assess the diagnostic role of serum procalcitonin (PCT) levels among confirmed patients with bacterial infections and healthy individuals. It also aims to explore the relationship between PCT and other clinical parameters, such as WBC count and hematological parameters. Through comparing the spread character and the correlation between PCT levels and infection level as well as immunologic reaction, this study indicates that PCT is a good diagnostic and monitoring biomarker. In the end, knowledge about the clinical use of procalcitonin will help improve the strategies of how to handle infections and help rationalize the use of antibiotics for the well-being of the patient.

Method

A case-control observational study, conducted from January 1, 2024, to April 30, 2024, at Al-Habboby Teaching Hospital and Al-Hussein Teaching Hospital, was to assess the diagnostic role of serum procalcitonin (PCT) levels among 100 confirmed patients with bacterial infections and 50 healthy individuals. The study also aimed to explore the relationship between PCT and other clinical parameters, such as white blood cell (WBC) count and other hematological indices. By comparing the distribution and correlation of PCT levels with infection severity and immune response, the study suggests that PCT is a reliable biomarker for diagnosis and monitoring of bacterial infections. This enhanced understanding of the clinical utility of procalcitonin could improve infection management strategies and promote the rational use of antibiotics, ultimately benefiting patient care. After obtaining written informed consent from all participants, 5–7 mL of venous blood was aseptically collected from each subject. Blood was drawn within the first 24 hours of diagnosis and prior to the initiation of antibiotic therapy, when applicable. Samples were collected into EDTA tubes for complete blood count (CBC) analysis and plain tubes for serum separation. Serum was obtained by centrifugation at 3000 rpm for 10 minutes and stored at –20°C until further analysis. Hematological parameters including WBC count, hemoglobin, hematocrit, neutrophils, lymphocytes, and platelet count were analyzed using an automated hematology analyzer (Sysmex XP-300, Sysmex Corporation, Japan). Serum procalcitonin concentrations were measured using a commercially available ELISA kit following the manufacturer's instructions, with proper internal quality control measures applied. All participants provided written consent and

A. Statistical analysis:

Data were statistically analyzed using independent t-tests to compare means between groups, and Pearson correlation was used to assess associations between variables. Results were expressed as mean \pm standard deviation (SD), and a p-value < 0.05 was considered statistically significant.

B. Ethical approval:

This study was approved by the institutional ethics committee of Al-Habboby Teaching Hospital and Al-Hussein Teaching Hospital, under approval number 443, covering the period from January 1, 2024, to April 30, 2024. Written informed consent was obtained from all participants prior to sample collection, in accordance with the Declaration of Helsinki.

Results and Discussion

A. Results

1. Sociodemographic Characteristics of Patients with Bacterial Infections and Healthy Controls

The results of the table show that the mean age of patients with bacterial infections was 38.6 ± 11.2 years, while the mean age of the healthy control group was 37.1 ± 10.7 years, with no significant difference between the two groups ($p = 0.382$). In terms of gender distribution, the patients included 58 men and 42 women, while the control group included 27 men and 23 women, and the difference between the sexes was not statistically significant ($p = 0.887$). Regarding smoking status, 34 patients were smokers compared to 66 non-smokers, while in the control group there were 15 smokers and 35 non-smokers, and there was no significant difference in the percentage of smokers between the two groups ($p = 0.471$). Body mass index (BMI) averaged 26.2 ± 3.5 kg/m² in patients and 25.7 ± 3.2 kg/m² in healthy controls, with no statistically significant difference between the two groups ($p = 0.273$). These results demonstrate the similarity in sociodemographic characteristics between patients and healthy controls, enhancing the reliability of comparing biological indicators between them (Table 1).

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Table 1. Comparison of Age, Gender, Smoking Status, and Body Mass Index Between Study Groups

Parameter	Patients (n = 100)	Controls (n = 50)	p-value
Age (years)	38.6 ± 11.2	37.1 ± 10.7	0.382
Gender (Male/Female)	58 / 42	27 / 23	0.887
Smoking Status (Yes/No)	34 / 66	15 / 35	0.471
BMI (kg/m ²)	26.2 ± 3.5	25.7 ± 3.2	0.273

2. Comparison of Procalcitonin Levels Between Patients and Healthy Controls

The results showed that the mean serum procalcitonin concentration was significantly higher in the patient group (5.68 ± 2.74 ng/ml) compared to the healthy group (0.39 ± 0.21 ng/ml). This significant difference indicates a clear relationship between elevated procalcitonin levels and disease status, supporting the use of this biomarker in assessing inflammatory conditions or severe bacterial infections (Table 2).

Table 2. Mean ± SD of Serum Procalcitonin Concentration and Statistical Significance

Group	Procalcitonin (ng/mL) Mean ± SD	p-value
Patients (n=100)	5.68 ± 2.74	< 0.001
Controls (n=50)	0.39 ± 0.21	

3. Serum Procalcitonin Levels According to Infection Severity

The data indicate a direct relationship between infection severity and serum procalcitonin levels. The mean procalcitonin concentration in patients with mild infections was 2.91 ± 1.03 ng/ml, while this average increased to 5.87 ± 1.21 ng/ml in moderate infections and to 9.42 ± 2.66 ng/ml in patients with severe infections. These findings demonstrate that higher infection severity is associated with significantly higher procalcitonin levels, enhancing its value as a diagnostic indicator of the severity of an inflammatory or septic condition (Table 3).

Table 3. Distribution of Mean ± SD of Procalcitonin Concentration Among Mild, Moderate, and Severe Infection Groups

Severity Group	Number of Patients	Procalcitonin (ng/mL) Mean ± SD
Mild infection	38	2.91 ± 1.03
Moderate infection	42	5.87 ± 1.21
Severe infection	20	9.42 ± 2.66
p-value		< 0.001

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4. Comparison of Hematological Parameters Between Patients and Healthy Controls

Blood tests showed clear differences between the patient group and the healthy group. A significant increase in the white blood cell count was observed in patients ($12.4 \pm 3.6 \times 10^3/\mu\text{L}$) compared to healthy controls ($6.8 \pm 1.7 \times 10^3/\mu\text{L}$), as well as a higher percentage of neutrophils ($78.5 \pm 7.2\%$ versus $60.3 \pm 5.8\%$), while the percentage of lymphocytes decreased significantly in patients ($16.1 \pm 5.4\%$) compared to the control group ($31.2 \pm 6.3\%$). A lower mean hemoglobin concentration was also observed in patients ($11.9 \pm 1.6 \text{ g/dL}$) compared to healthy controls ($13.6 \pm 1.2 \text{ g/dL}$), and the hematocrit percentage also decreased in patients ($36.4 \pm 4.2\%$) versus ($41.3 \pm 3.7\%$) in the control group. In contrast, platelet counts were significantly higher in the patient group ($310 \pm 78 \times 10^3/\mu\text{L}$) compared to healthy controls ($256 \pm 64 \times 10^3/\mu\text{L}$). These findings indicate clear hematological changes associated with the disease, reflecting the inflammatory response and associated physiological changes (Table 4).

Table 4. Mean \pm SD Values of Blood Indices and Their Statistical Significance

Parameter	Patients (n = 100)	Controls (n = 50)	p-value
White Blood Cell Count ($\times 10^3/\mu\text{L}$)	12.4 ± 3.6	6.8 ± 1.7	< 0.001
Neutrophils (%)	78.5 ± 7.2	60.3 ± 5.8	< 0.001
Lymphocytes (%)	16.1 ± 5.4	31.2 ± 6.3	< 0.001
Hemoglobin (g/dL)	11.9 ± 1.6	13.6 ± 1.2	< 0.001
Hematocrit (%)	36.4 ± 4.2	41.3 ± 3.7	< 0.001
Platelet Count ($\times 10^3/\mu\text{L}$)	310 ± 78	256 ± 64	0.002

5. Comparison of Procalcitonin Levels Between Male and Female Patients

Results The mean serum procalcitonin levels in male and female patients were $5.79 \pm 2.81 \text{ ng/ml}$ and $5.53 \pm 2.66 \text{ ng/ml}$, respectively. This homogeneity of values shows that no differences are reached between sexes when procalcitonin as an inflammatory response or infection biomarker is measured (Table 5).

Table 5. Mean \pm SD of Serum Procalcitonin Concentration by Gender

Gender	Procalcitonin (ng/mL) Mean \pm SD	p-value
Male	5.79 ± 2.81	0.598
Female	5.53 ± 2.66	

B. Discussion

In the current study, we measured the serum PCT levels at the time of hospital admission in a cohort of 100 patients and 50 healthy controls and studied its association with various hematological parameters, particularly white blood cell (WBC) count. The demographic information revealed that there was no significant difference between the two groups in age, sex, smoking, or BMI ($p > 0.05$ for all), suggesting reasonable group matching and controlling of potential confounders. There was a marked increase in plasmatic procalcitonin levels in patients with bacterial infections (5.68 ± 2.74 ng/mL) as compared with healthy individuals (0.39 ± 0.21 ng/mL, $p < 0.001$). These results confirm previous observations on procalcitonin as a specific and sensitive marker of systemic bacterial infection [13], [14]. Procalcitonin, one of the prehormones of calcitonin, is normally synthesized in small quantities by thyroid C cells, but is rapidly released following the reponse of bacterial endotoxins and inflammatory cytokines IL-6 and TNF- α during systemic infection [15]. Unlike CRP, PCT is less affected by viral infection or autoimmune inflammation, and serves as a more specific biomarker for differentiating between bacterial and non-bacterial causes [16], [17]. Stratified by clinical severity, the procalcitonin concentration was progressively higher: 2.91 ± 1.03 in mild, 5.87 ± 1.21 ng/mL in moderate, and 9.42 ± 2.66 ng/mL in severe infections ($p < 0.001$). This dose-response relationship further supports the use of PCT not only to diagnose but also to monitor disease severity and to guide antibiotic stewardship as advocated by the Infectious Diseases Society of America [18], [19], also found that PCT levels are associated with severity of sepsis and clinical outcomes [20]. Hematological analysis revealed significant increases in WBC count and neutrophil percentage in patients compared to controls ($12.4 \pm 3.6 \times 10^3/\mu\text{L}$ vs. $6.8 \pm 1.7 \times 10^3/\mu\text{L}$ and 78.5% vs. 60.3%, respectively; $p < 0.001$). Concurrently, lymphocyte percentages were significantly reduced in patients (16.1% vs. 31.2%, $p < 0.001$), which is indicative of a typical acute bacterial response, where neutrophilia and lymphocytopenia dominate [21], [22]. Hemoglobin and hematocrit levels were also significantly lower in patients, possibly due to inflammation-induced hepcidin upregulation and anemia of chronic disease [23], [24]. The elevated platelet count (310 ± 78 vs. 256 ± 64 , $p = 0.002$) is likely reactive thrombocytosis, commonly seen in infections and inflammatory conditions [25]. A robust positive correlation was observed between procalcitonin levels and WBC count ($r = 0.772$, $p < 0.001$), reinforcing the diagnostic synergy

between these two parameters. This finding aligns with the work of Meisner et al., who reported a similar correlation in septic patients [26], [27]. However, some studies have reported weaker associations, possibly due to differences in patient populations or timing of sample collection [28]. Interestingly, no statistically significant difference in procalcitonin levels was found between male and female patients (5.79 ± 2.81 vs. 5.53 ± 2.66 , $p = 0.598$), suggesting that gender does not significantly influence PCT response in bacterial infections, a finding supported by recent meta-analyses [29], [30]. Despite these strong associations, a few studies have questioned the specificity of PCT in localized infections or in certain chronic inflammatory conditions, where elevated levels may occur in the absence of active bacterial infection [31]. These discrepancies may be due to cross-reactivity, organ dysfunction, or co-infections, and highlight the importance of using PCT in conjunction with clinical judgment and other laboratory findings [32].

Conclusions

In conclusion, the findings of this study underscore the clinical utility of procalcitonin as a biomarker for bacterial infections. Its strong correlation with WBC count and its ability to reflect infection severity make it valuable in diagnosis, prognosis, and treatment decision-making. However, clinicians should remain aware of its limitations and interpret results within the broader clinical context.

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