

Research Article



INTERNATIONAL RESEARCH JOURNAL OF PHARMACY

www.irjponline.com

ISSN 2230-8407 [LINKING]

INVESTIGATING PROCALCITONIN'S EFFECTIVENESS AS A STRONG BIOMARKER FOR NONSEPTIC BACTERIAL INFECTIONS

Dr. Chaitanya Nigam,¹ Dr. Pallavi Kumari,² Dr Maikal Kujur,³ Dr. Prem Chand Dhruw^{4*}

¹Assistant Professor, Department of Microbiology, Shri Shankaracharya Institute of Medical Sciences, Junwani, Bhilai, District Durg, Chhattisgarh

²Assistant Professor, Department of Pathology, Shri Rawatpura Sarkar Institute of Medical Sciences and Research, Raipur

³Associate professor, Department of Pathology, Shri Rawatpura Sarkar Institute of Medical Sciences and Research, Raipur

^{4*}Assistant Professor, Department of Pathology, Shri Rawatpura Sarkar Institute of Medical Sciences and Research, Raipur

Corresponding Author

Dr. Prem Chand Dhruw

Email Id- drpremchand25@gmail.com

How to cite: Nigam C, Kumari P, Kujur M, Dhruw PC. Investigating procalcitonin's effectiveness as a strong biomarker for nonseptic bacterial infections. International Research Journal of Pharmacy. 2025; 16: 5: 34-38.

Doi:10.7897/2230-8407.110525

ABSTRACT

Background: The hormone calcitonin plays a critical role in maintaining calcium and phosphorus balance.

Aim: Using a large sample of Indian participants, the current study assessed the procalcitonin test's capacity to distinguish between different bacterial (non-sepsis) aetiologies.

Methods: During the designated research period, standard laboratory and clinical data collected from the Institute's Central Lab were used to evaluate the current study. The importance of serum biomarker C reactive protein was evaluated using the collected data. Total leucocyte count and procalcitonin test for early bacterial infection identification.

Results: Compared to the population with gram-positive bacterial infections, the study found that a greater frequency of elevated procalcitonin levels was observed in instances of gram-negative bacterial infections, namely those caused by *Klebsiella pneumoniae* and *Escherichia coli*.

Conclusions: The current study finds that, similar to a rise in TLC and CRP, which are considered the gold standard for blood biomarkers in any bacterial infection, there is an increase in PCT levels even in people with non-septic bacterial infections. It is also observed that, regardless of gender, the rise in these biomarkers is comparable in gram-positive and gram-negative infected people. Additionally, compared to gram-positive infections, gram-negative infections have greater elevated PCT.

Keywords: Biomarkers in bacterial infection, Biomarkers in Gram-negative bacteria infection, Serum PCT in non-sepsis infection, PCT

INTRODUCTION

In healthy individuals, the CALC-1 gene on chromosomal number 11 is responsible for the synthesis of PCT (procalcitonin) in the thyroid's C cells. The resulting mRNA product is called preprocacitonin, which is processed further to produce three molecules: N-terminal procalcitonin, ketacalcitonin, and active calcitonin. The hormone calcitonin is essential for maintaining calcium and phosphorus balance.¹

Under normal circumstances, the CALC-1 gene found in thyroid C cells is induced by elevated levels of β -adrenergic stimuli, gastrin, glucagon, CGRP (calcitonin gene-related peptide), and glucocorticoids. Additionally, all of the

procalcitonin produced during these calls is converted to calcitonin, reducing the amount of procalcitonin released into the bloodstream and keeping levels in healthy persons at extremely low levels of 0.05 ng/mL.

Adipose tissue, kidney, liver, and lungs are among the tissues that produce procalcitonin during systemic inflammation, particularly when bacterial infections are present. This occurs primarily through the two mechanisms that have been highlighted. 2 The indirect pathway is initiated by inflammatory mediators including TNF- α , IL-6, and others, while the direct pathway is triggered by harmful microbial metabolites such as lipopolysaccharide (LPS).

Procalcitonin synthesis during infection is thought to be influenced by bacterial LPS and sepsis-induced cytokines, which in turn affect the liver and peripheral blood mononuclear cells. However, the precise mechanism behind this process is yet unknown. Increased CALC-1 gene expression from microbial infection raises procalcitonin levels, sometimes by a factor of 1000 depending on illness severity and mortality.³

Procalcitonin levels rise as early as two to four hours after stimulation and peak between six and twenty-four hours later. This may explain why procalcitonin, as opposed to CRP (C-reactive protein), is regarded as a stable and early marker, and its levels are unaffected by immunodeficiency, neutropenia, steroidal anti-inflammatory medicines, and non-steroidal anti-inflammatory drugs. Additionally, a number of studies in the literature have generally regarded systemic indicators like C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) as having low sensitivity and specificity for the detection of bacterial infections.⁴

Therefore, a biomarker that can quickly and correctly determine the underlying bacterial infection is required for application in clinical settings to avoid mortality, especially from sepsis caused by bacterial infections.

Procalcitonin's potential as a biomarker in patients with bacterial infections that do not progress to sepsis is not well understood. It is also unclear how certain bacterial illnesses that are often encountered might alter PCT levels.⁵

Therefore, the current study sought to determine the incidence of different bacterial infections as well as the effectiveness of other biomarkers, such as procalcitonin, in identifying bacterial infections that are not sepsis.

MATERIALS AND METHODS

The purpose of the current longitudinal observational study was to determine the incidence of different bacterial infections and investigate the effectiveness of different biomarkers, such as procalcitonin, in identifying bacterial infections that are not sepsis. The research participants came from the Institute's Central Lab. Prior to participation; all individuals gave their written and verbal informed permission.

The importance of many biomarkers, including PCT (procalcitonin) count, TLC (total leucocyte count), and CRP (cytoplasmic reactive protein), in the early diagnosis of bacterial infection was evaluated using normal laboratory and clinical data collected from participants over the research period. The study evaluated data from 970 participants, all over the age of 18, who were brought to the institute with a main diagnosis of infection-related symptoms, including fever, chills, and hypothermia. There were 426 female individuals and 544 male ones.

Participants in the study had to be between the ages of 18 and 45, of both sexes, present with fever, chills, and hypothermia, have a diagnosis of acute bacterial infection without septicemia, have PCT, CRP, and TLC values greater than 0.25 ng/mL, 10 mg/l of blood, and 11000 cells/cu mm, and have a neutrophil count differential leucocyte count of greater than 80%.

Any organic problems, including hormone disorders, renal disease, heart disease, diabetes mellitus, hypertension, and any kind of persistent bacterial infection, including tuberculosis, were excluded from the research. any cancerous or autoimmune condition, including rheumatoid arthritis.

Participants in the research who had been diagnosed with an acute bacterial infection but did not have septicemia were selected for sample collection. The kinds of bacterial infections were evaluated using a variety of samples, including blood, urine, respiratory suction, and wound swabs. Gram staining was used to identify the kind of bacterial infection—gram-positive or gram-negative—in isolated colonies from incubated culture medium. Serum biomarker data were collected for both kinds in order to compare the roles of different biomarkers in different bacterial infection types.

The lower detection limit for PCT serum marker assessment was 0.25 ng/mL, whereas the laboratory standard cut-off for aberrant readings in TLVC and CRP cases was 10 ng/l for CRP and less than 11,000 cells/cumm of blood, respectively. Using a standard autoanalyzer, all parameters, including TLC, CRP, and PCT, were evaluated.

The collected data was statistically evaluated using the Student t-test, ANOVA (analysis of variance), Chi-square test, and SPSS (Statistical Package for the Social Sciences) software version 24.0 (IBM Corp., Armonk, NY, USA) for evaluating descriptive measures. The findings were presented as frequency, percentages, mean, and standard deviation. A p-value of less than 0.05 was taken into account.

RESULTS

The purpose of the current longitudinal observational study was to determine the incidence of different bacterial infections and investigate the effectiveness of different biomarkers, such as procalcitonin, in identifying bacterial infections that are not sepsis. The study evaluated data from 970 participants who were above the age of 18 and admitted to the Institute with a main diagnosis of infection-related symptoms, including fever, chills, and hypothermia. There were 426 female individuals and 544 male ones. Of these individuals, 302 had a gram-positive bacterial infection and 668 had a gram-negative bacterial infection. Gram-negative and Staphylococcus species were dominated by *E. coli* and *Klebsiella pneumoniae*. in gram-positive infections seen in samples of all kinds. Urine samples primarily included Enterobacteria in addition to Staphylococcus.

According to the study's findings, when cultures were produced from blood samples and swabs, a comparatively small number of infected people had higher PCT levels; nevertheless, when cultures were grown on urine samples or pulmonary suction, a considerable number of participants had elevated PCT levels. Raised TLC and CRP levels, however, are most noticeable in respiratory suction and urine samples. Additionally, this demonstrated that 104 gram-negative infected participants had elevated PCT levels, and approximately 480 gram-negative bacterially infected people had elevated CRP. Regardless of sample variance, the prevalence of elevated blood PCT, CRP, and TLC levels indicated that fewer people with gram-positive bacterial infections had elevated serum PCT.

In both gram-positive and gram-negative bacterial infection-affected participants, the percentage rise in TLC, PCT, and CRP was shown to be considerably greater than reference normal levels. According to the study's ANOVA results, all participants with gram-positive and gram-negative bacterial infections had a percentage rise in PCT, TLC, and CRP that was substantially different from all other kinds with $p < 0.05$ from their typical cut-offs (Table 1). The percentage rise in CRP in males and females with gram-negative infections did not differ significantly, according to the study's findings. Additionally, the percentage increase in PCT and TLC did not differ according on gender. Subjects with gram-positive bacterial infections showed similar outcomes, with no gender-based variation in the percentage rise of PCT, TLC, and CRP.

However, there was no discernible difference in the percentage rise of TLC and CRP between the two variables when comparing the percentage increase of PCT, TLC, and CRP in research participants who were not infected to those who had gram-positive bacterial infections. However, in gram-negative infected participants, the PCT percentage rise was more pronounced. Additionally, PCT level changes in patients with gram-positive bacterial infections are not always favorable. Additionally, 14% of participants with gram-positive bacterial infections, a considerable proportion, showed no change in PCT levels from the cut-off value of 0.25 ng/mL.

DISCUSSION

The current study assessed data from 970 adults over the age of 18 who were brought to the institution with a primary diagnosis of infection-related symptoms, including fever, chills, and hypothermia. There were 426 female individuals and 544 male ones. Of these individuals, 302 had a gram-positive bacterial infection and 668 had a gram-negative bacterial infection. Gram-negative and Staphylococcus species were dominated by *E. coli* and *Klebsiella pneumoniae*. in gram-positive infections seen in samples of all kinds. Urine samples primarily included Enterobacteria in addition to Staphylococcus. These findings were similar to those of studies by Shuhua L et al.⁶ and Martini A et al.⁷, in which the authors evaluated participants who did not have sepsis bacterial infections and had similar demographics to the current research.

When culture was grown on blood samples and swabs, it was shown that PCT rose in a comparatively small number of infected people; however, when culture was grown on urine samples or respiratory suction, PCT levels were elevated in a high number of participants. Raised TLC and CRP levels, however, are most noticeable in respiratory suction and urine samples. Additionally, this demonstrated that 104 gram-negative infected participants had elevated PCT levels, and approximately 480 gram-negative bacterially infected people had elevated CRP. Serum PCT was found in fewer individuals with gram-positive bacterial infections, regardless of sample variance, according to the prevalence of elevated serum levels of PCT, CRP, and TLC.

These findings were in line with those of Tavares E. et al. (2005) and Elsen G. et al. (2007), who also noted greater PCT in small participants in blood and swab cultures, as well as a larger number in respiratory suction and urine swabs, as demonstrated by the current study's findings.

In both gram-positive and gram-negative bacterial infection-affected participants, the percentage rise in TLC, PCT, and CRP was considerably greater than reference normal values, according to the study's findings. An ANOVA of the study's findings showed that a percentage rise in PCT, TLC, and CRP in all participants from both gram-positive and gram-

negative bacterial infections is substantially different from all other kinds ($p < 0.05$) in comparison to their typical cut-offs (Table 1). The results of the study showed no significant difference in the percentage increase in CRP between males and females with gram-negative infections. Furthermore, there was no gender difference in the percentage rise in PCT and TLC. There was no gender-based difference in the percentage increase of PCT, TLC, and CRP among subjects with gram-positive bacterial infections. These outcomes were in line with those of Hatzistilianou M et al. (2010) and Su L et al. (2012), who found that increases in PCT, TLC, and CRP were substantially different from their cut-off thresholds in all participants with gram-positive and gram-negative bacterial infections.

The study's findings also revealed that, when comparing the percentage increases in PCT, TLC, and CRP among study participants who were not infected to those who had gram-positive bacterial infections, no significant difference was seen in the percentage increase of TLC and CRP between the two variables. However, a percentage increase of PCT was more profound in gram-negative infected subjects. Also, change in PCT levels in gram-positive bacterial infection subjects is not always in a positive direction. Additionally, PCT levels may not necessarily alter in a good way in patients with gram-positive bacterial infections. The PCT level did not vary from its cut-off value of 0.25 ng/mL in 14% of participants with gram-positive bacterial infections, which was a substantial percentage. Our findings were consistent with those of Wu SC et al. (12) and Waterfield T et al. (13), who similarly showed a more significant rise in PCT in gram-negative infected participants in 2020.

CONCLUSION

Relative to the standard of blood biomarkers in any bacterial infection, which are CRP and TLC, the current study, within its limits, finds that there is a rise in PCT levels even in people with non-septic bacterial infections. Also, raised PCT is higher in gram-negative infections compared to gram-positive infections.

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S. No	Parameter	CRP	TLC	PCT	Total
1.	Number (n)	394	326	328	1080
2.	Mean $\pm$ S> D	351.3297 $\pm$ 31.19	87.0831 $\pm$ 18.53	216.4779 $\pm$ 52.52	259.229 $\pm$ 0.00

Table 1: Comparison of significance level change of various serum biomarkers in bacterial-infected subjects