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EXAMINING PROCALCITONIN'S EFFECTIVENESS AS A POSSIBLE BIOMARKER IN BACTERIAL INFECTIONS THAT ARE NOT SEPSIS

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ABSTRACT

Background: The hormone calcitonin plays a critical role in maintaining calcium and phosphorus balance. Additionally, procalcitonin is generated in a variety of organs during systemic inflammation, including bacterial infections. After 2-4 hours of stimulation, the procalcitonin level increases and peaks in 6-2 hours. However, the majority of the evidence in the literature depends on bacterial infections brought on by sepsis.

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

Methods: During the designated research period, standard laboratory and clinical data collected from the Institute's Department of Microbiology were used to evaluate the current study. The importance of the procalcitonin test, total leucocyte count, and serum biomarker C reactive protein for early bacterial infection identification was evaluated using the collected data. Greater frequency of elevated procalcitonin levels in gram-negative bacterial infections, especially those caused by Escherichia coli and Klebsiella pneumoniae, compared to the group with gram-positive bacterial infections.

Results: Even in patients with non-septic bacterial illnesses, PCT levels rise in tandem with TLC and CRP, which are considered the gold standard for blood indicators of 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 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.[2]

Procalcitonin is produced in several tissues, including adipose tissue, kidney, liver, and lungs, mostly through the two mechanisms described above, during systemic inflammation, particularly in the presence of bacterial infections. The direct pathway is initiated by lipopolysaccharide (LPS) or other harmful bacteria metabolites, whereas the indirect pathway is initiated by inflammatory mediators including TNF-α, IL-6, and others. Although the precise process by which

procalcitonin is produced during infection is yet unknown, bacterial LPS and sepsis-induced cytokines both affect the liver's ability to create procalcitonin from peripheral blood mononuclear cells. Depending on mortality and illness severity, microbial infection causes a rise in CALC-1 gene expression, which raises procalcitonin levels by up to 1000 times.[3]

Procalcitonin levels rise as early as two to four hours after stimulation and peak between six and twenty-four hours later. Procalcitonin is regarded as a stable and early marker, and immunodeficiency, neutropenia, steroidal anti-inflammatory medicines, and non-steroidal anti-inflammatory drugs have no effect on its concentration. 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 outpatient department. Prior to participation, all individuals gave their written and verbal informed permission.

The study evaluated 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 using normal laboratory and clinical data collected from the participants during the study period.

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.

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 in DLC (differential leucocyte counts) 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.

Subjects having an acute bacterial infection but no septicemia were included in the research for the purpose of collecting samples. 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 this 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.

Among these subjects, Gram-positive and gram-negative bacterial infections were found in 302 and 668 of the individuals, respectively. 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 study data, when cultures were produced from blood samples and swabs, PCT levels rose in a comparatively small number of infected participants; but, when cultures were grown on urine samples or respiratory suction, PCT levels rose in a high number of subjects. 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 PCT, CRP, and TLC serum levels indicated that fewer people with gram-positive bacterial infections had 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. The percentage rise in PCT, TLC, and CRP in all participants from both gram-positive and gram-negative bacterial infection-affected patients is substantially different from all kinds with $p<0.05$ from their normal cut-offs, according to study results using ANOVA (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, gram-negative infected patients saw a more significant percentage rise in PCT. 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, exhibited no change in PCT levels from the cut-off value of 0.25 ng/mL.

DISCUSSION

The current 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. These findings were similar to those of studies conducted by Shuhua L et al. (2016) and Martini A et al. (2010), 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 was elevated in a comparatively small number of infected people; however, when culture was grown on urine samples or respiratory suction, elevated PCT levels were seen 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.

The present study's findings were in line with those of Tavares E et al. (2005) and Elsen G et al. (2007), who also observed greater PCT in tiny participants in swab and blood culture, as well as a larger number in respiratory suction and urine swabs. The study's findings demonstrated that in both gram-positive and gram-negative bacterial infection-affected participants, the percentage rise in TLC, PCT, and CRP was noticeably more 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. These results were consistent with the findings of Hatzistilianou M et al. (2010) and Su L et al. (2012), who reported that all subjects from both gram-positive and gram-negative bacterial infections had increases in PCT, TLC, and CRP that differed significantly from their cut-off points.

The research's findings also revealed that, when comparing the % increases in PCT, TLC, and CRP in study participants who were not infected to those who had gram-positive bacterial infections, there was no discernible difference in the percentage increases in TLC and CRP between the two variables. However, gram-negative infected patients saw a more significant percentage rise in PCT. 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, exhibited no change in PCT levels from the cut-off value of 0.25 ng/mL. According to the results of the current investigation, these findings were consistent with those of Wu SC et al. (2012) and Waterfield T et al. (2013), who similarly noted a more significant rise in PCT in gram-negative infected participants.

CONCLUSION

Given its limitations, the current study comes to the conclusion that, even in people with non-septic bacterial infections, PCT levels are higher than those of TLC and CRP, which are considered the gold standard for blood biomarkers in any bacterial illness. 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.

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

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