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Study of Procalcitonin as a Biomarker and Its Correlation with Total Leucocyte Count in Patients with Sepsis

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Abstract: ***Introduction: Bacterial sepsis is a common cause of morbidity and mortality in admitted patients and should receive prompt antibiotic treatment for better outcome. Fever can also be caused by noninfectious causes such as autoimmune diseases, malignancy, drugs, venous thromboembolism. Markers of systemic inflammation, such as CRP, erythrocyte sedimentation rate (ESR) have proven to be of limited utility due to their poor sensitivity and specificity for bacterial infection. Blood culture which is considered as the gold standard for diagnosing bacterial infection has a drawback in the form of a long turnaround time. Aim of the study: This study is aimed to evaluate the levels of procalcitonin (PCT) and its correlation with total leucocyte count (TLC) in adults presenting with features suggestive of sepsis. Methods: It is an observational study conducted in a zonal hospital in eastern part of India. 50 patients admitted with clinical diagnosis of sepsis were included. Patients already on treatment with antibiotics were excluded from the study. Correlation between procalcitonin level and total leucocyte count were studied using appropriate statistical tools. Results: Moderate positive correlation was found between TLC and procalcitonin (R: 0.458) and was statistically significant with a P value of 0.0008. Procalcitonin was found to be positive in all patients while TLC remained within normal range in 15 patients. Conclusion: Procalcitonin can be used as an early biomarker for sepsis. PCT also gave an idea regarding the severity of infection. Moderate positive correlation was found between TLC and procalcitonin and was statistically significant.***

Keywords: Sepsis, Procalcitonin, Total leucocyte count

1. Introduction

Sepsis is one of the leading causes of death. There have been more than 200000 deaths in the USA due to sepsis each year and mortality in admitted patients approaches 30% despite advances in critical care. [1] The 2016 guidelines redefined sepsis as 'a life-threatening organ dysfunction caused by a dysregulated host response to infection'. [2]

The microorganisms invade to the blood stream and proliferate releasing various virulent factors into the bloodstream. [3] This leads to sepsis. Blood culture which is considered as the gold standard for diagnosing bacterial infection has a drawback in the form of a long turnaround time. [4] Procalcitonin is a biomarker which can aid in early and rapid diagnosis of sepsis. It can also be used to monitor the prognosis following antibiotic treatment.

In the year 1975, Moya F et al. suggested the existence of a precursor of calcitonin in chicken. [5]

PCT is produced in thyroid C cells in an individual, from a CALC-1 gene which is located on chromosome 11 [6].

PCT that is formed in thyroid C cells are converted to calcitonin so that no PCT is released into the circulation normally resulting in very low level (0.05ng/mL) of PCT in healthy subjects but the inflammatory release of PCT is independent of the normal regulations. The exact mechanism of production of PCT during infection is not known, but it is thought that the bacterial lipopolysaccharides and cytokines released in the process of inflammation modulate the liver and peripheral blood mononuclear cells to produce PCT. Microbial infection induces increased expression of CALC 1 gene followed by the release of PCT.

Asscot et al. demonstrated increase in PCT levels during bacterial infection and its association with sepsis [7]

There have been many studies that have demonstrated that serum PCT levels increases in sepsis, and the high levels of PCT has a correlation with the outcome of the disease.[8]

This study was done to see for the correlation between total leucocyte count and serum procalcitonin levels in cases with sepsis.

2. Method

The study was conducted in a zonal hospital in eastern India. It was an observational study. 50 patients who were admitted to ICU with features suggestive of sepsis were included in the study and were subjected to the following tests.

a. Hemoglobin
b. Total leucocyte count
c. Platelets
d. Biochemistry
e. Blood culture
f. Peripheral blood smear for toxic granules, toxic vacuoles and left shift
g. Serum procalcitonin

h. X ray chest
i. Urine culture
j. Sputum culture

The blood samples were withdrawn before the initiation of antibiotics. Serum procalcitonin was done using VIDAS immunofluorescence method and the normal value was taken as <0.5 ng/ml.

Patients already on antibiotics were excluded from the study.

Statistical analysis was carried out using ANOVA and regression statistics.

3. Results

Demography

Total of 22 females and 28 males were included in the study.

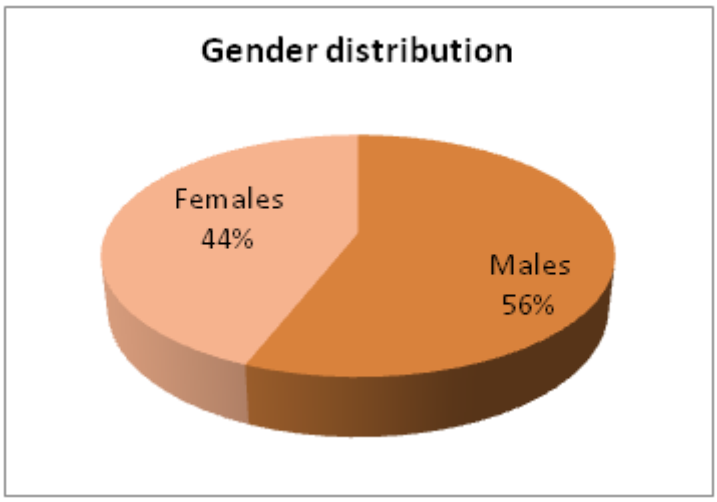

Figure 1: Gender distribution of patients

Table 1: Age group of study population

Age group	No.	Males	Females
1 - 30	3	1	2
31 - 60	25	12	13
Above 60	22	15	7

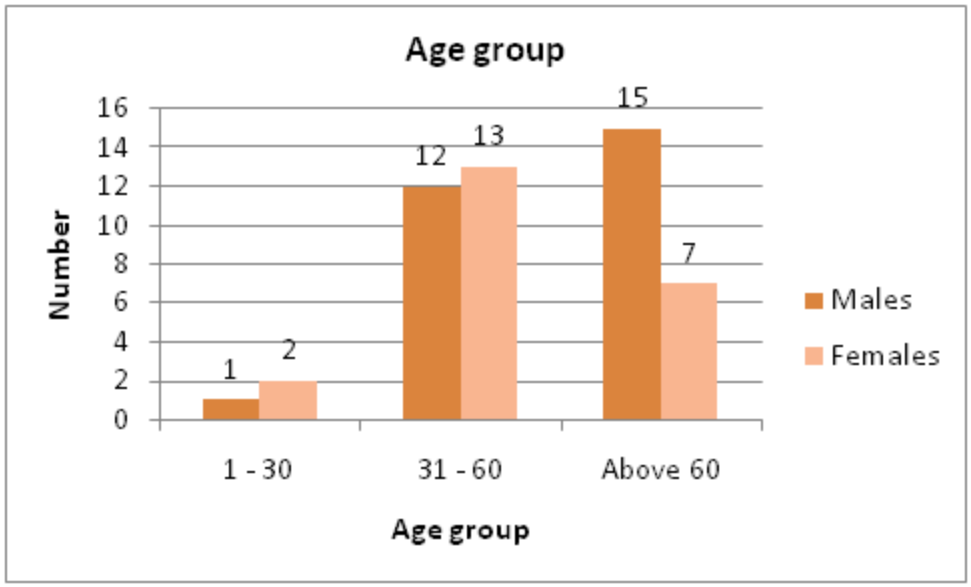

Figure 2: Age group of study population

Primary sources of infection:

The primary sources of infection were as follows.

Table 2: Primary source of infection

Diagnosis	No. of patients
Respiratory tract	15
Urinary tract infection	12
Abdominal infection	10
Cellulitis and skin	04
Central nervous system	01
Source not found	08

16 (32%) patients had respiratory tract infection as the primary cause. 12 (24%) patients had urinary tract infection. Most of these patients were elderly having Type 2 Diabetes Mellitus. Primary source of infection was not found in 8 patients.

Blood culture was positive in 28 patients. The organisms which were grown include E.Coli, Staphylococcus aureus, Staphylococcus epidermidis, Klebsiella, Acinetobacter baumannii, Pseudomonas aeruginosa, Salmonella typhi.

The peripheral blood smear was positive for toxic granules and shift to left in all of them.

PCT was positive in all 50 patients ranging from 1 to 71.32 ng/ml. The mean value of PCT was 7.991 ng/ml and the mean TLC was 13860/cumm.

Graph showing TLC and procalcitonin

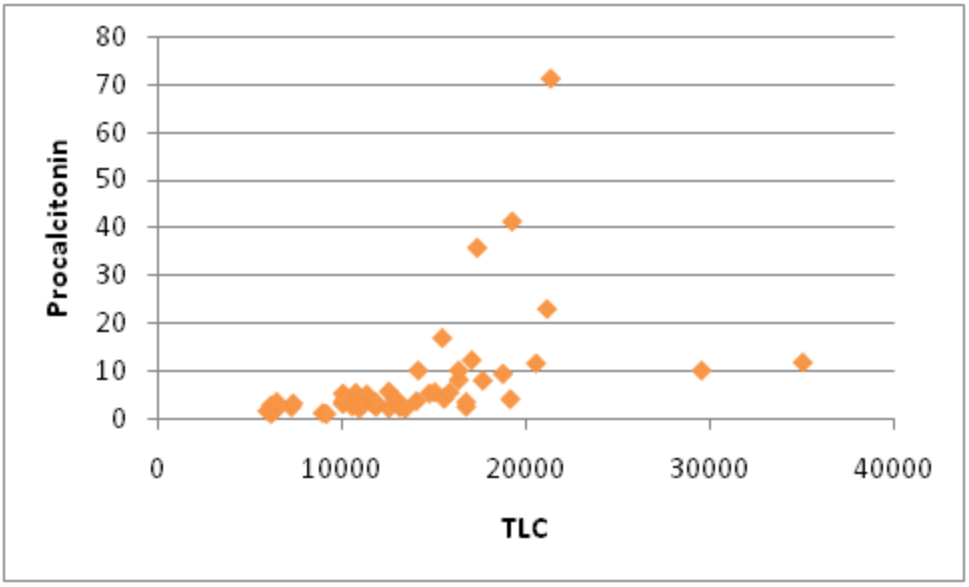

Figure 3: Graph showing TLC and PCT

Table 3: Regression statistics

Regression Statistics	
Multiple R	0.458096
R Square	0.209852
Adjusted R Square	0.193391
Standard Error	10.82082
Observations	50

Moderate positive correlation between TLC and procalcitonin was found on analyzing the data and was statistically significant with a P value of 0.0008.

4. Conclusion

Total of 50 patients were included in this study. 44% were females and 56% males. It was found that all of them had raised procalcitonin. The TLC remained within normal range in 15 patients. However, their peripheral blood smear showed toxic granules. Out of these 15 patients who had TLC within normal range, 06 showed growth of organism in blood culture. PCT was positive in all 50 patients.

A moderate positive correlation was seen between TLC and procalcitonin and was found to be statistically significant.

Procalcitonin can be used as a early biomarker for sepsis. Though assessment of PCT levels alone may not be enough but when combined with other markers, PCT can be used for diagnosis of sepsis.

An ideal biomarker of bacterial infection should be sensitive enough to detect the presence of infection in patients with minimal host response also. TLC may not increase markedly in few patients; however PCT was positive in all these patients.
This study had few limitations as we did not follow up with procalcitonin values after initiation of treatment.

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