Original Research Article

Evaluation of Procalcitonin (PCT) and C-reactive protein (CRP) as biomarkers in suspected cases of sepsis among patients attending Emergency Department and ICU of the tertiary care hospital in Western Uttar Pradesh

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Abstract

Background: Procalcitonin has characteristics of a biomarker, as there is a fast and specific increase in sepsis and it differentiates infections from non-infectious causes of sepsis. The present study was conducted to evaluate procalcitonin (PCT) and C-reactive protein (CRP) as biomarkers in suspected cases of sepsis. **Materials & Methods:** The study was conducted on 80 cases in the department of medicine at Uttar Pradesh University of Medical Sciences (UPUMS), Saifai, Etawah. Cases clinically suspected of sepsis on admission to emergency department were included. 5ml of venous blood sample was withdrawn simultaneously for detection of PCT and CRP. **Results:** There were 45 (56.2%) male and 35 (43.7%) female. Blood culture was positive in 26 (32.5%) and negative in 54 (67.5%). Among 26 positive blood culture cases, 5 (19.23%) were caused by Gram-positive bacteria and 21 (80.76%) by Gram-negative bacteria. In Gram-positive cultures all 5 isolates identified were of Staphylococcus aureus. In Gram-negative cultures most common isolates were E. coli 9 (34.61%), followed by Klebsiella pneumoniae 6 isolates (23.07%) and 6 isolates of non-fermenting gram-negative bacilli (NFGNB) were isolated. Clinical conditions present in study subjects were chronic lung disease in 31cases (38.7%) followed by acute kidney failure in 27 cases and anaemia in 24 cases. Three cases also had gastrointestinal disease. Source of infection in culture positive patients were pneumonia 9 cases (34.6%), UTI 8 cases (30.7%), skin wounds/cellulitis 4 cases (15.3%), meningitis and biliary tract infection 3 cases each (11.5%). Source of infection in culture negative cases was pneumonia 19 cases (35.1%) followedbyUTI11cases (20.3%). **Conclusion:** PCT proved to be a reliable marker for sepsis diagnosis and is more relevant than CRP in patients with a positive blood culture.

Keywords: Sepsis, Procalcitonin, Klebsiella pneumonia.

Introduction

Sepsis has been recently redefined and reconsidered as "a life-threatening organ dysfunction caused by dysregulated host-response to systemic infection" based on the Third International Consensus Definitions for sepsis and septic shock[1]. Sepsis is considered as one of the most important causes of morbidity and mortality worldwide. It is one of the common causes of multiorgan failure[2,3]. Recently, a global study estimated 48.9 million cases and 11 million deaths due to sepsis, accounting for 20% of all global deaths annually. Sepsis is a major health problem worldwide and is considered one of the most prevalent causes of hospital-related fatalities, accounting for more than $24 billion annually in the USA[4].

Various scoring systems used to assess the severity of organ dysfunction, that quantify abnormalities according to clinical observations, laboratory findings or therapeutic effects have been evaluated for the degree of organ malfunction[5]. There have been discrepancies in the reporting methods of these scoring systems as well.

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The growth in the population for e.g advanced age group, the prolongation of life cycles in chronic illness patients, the frequent use of immunosuppressive medication and the common use of invasive procedures for diagnosing or treatment, enhance sepsis frequency[6]. The most basic causes of mortality have been connected with significant chronic comorbidities and it has been unlikely that most sepsis-related fatalities are avoidable by better hospital treatment[7].

Procalcitonin has characteristics of a biomarker, as there is a fast and specific increase in sepsis and it differentiates infections from non-infectious causes of sepsis[8]. Another biomarker of inflammation, CRP is a non-specific acute-phase protein of sepsis, however, evidence on the diagnostic precision of CRP in order to differentiate infection from non-infection are ambiguous[9,10]. The present study was conducted to evaluate procalcitonin (PCT) and C-reactive protein (CRP) as biomarkers in suspected cases of sepsis among patients attending emergency Department and ICU.

Materials & Methods

The study was conducted on 80 cases in the Department of Medicine at Uttar Pradesh University of Medical Sciences (UPUMS), Saifai, Etawah. Cases clinically suspected of sepsis on admission to emergency department and ICU fulfilling the quick Sequential Organ Failure Assessment Score (qSOFA) criteria given by the Third International Consensus Definitions Task Force (Sepsis-3) were included. All cases of cardiogenic shock, cases of burns, trauma, post-

surgery patients, patients of pancreatitis and malignancy, immunotherapy and haemodialysis were excluded.

Aseptically bedside inoculated aerobic blood culture bottles for culture and antibiotic sensitivity and 5ml venous blood sample was withdrawn simultaneously for detection of PCT and CRP which were sent to the Bacteriology Laboratory of Microbiology Department of UPUMS, Saifai, and were processed. Blood culture and Gram's staining was performed. All the bacteria grown, isolated from the blood culture positive cases after initial characterization by colony morphology, Gram's stain, were subjected to species identification and AST determination by VITEK® 2 COMPACT automated identification method. The collected data were transformed into variables, coded and entered in Microsoft Excel. Data were analysed and statistically evaluated using SPSS-PC-25 version.

Results

Table 1:Gender wise distribution of cases

Gender	Number	Percentage
Male	45	56.2%
Female	35	43.7%

Table I shows that there were 45 (56.2%) male and 35 (43.7%) female.

Table 2: Blood culture profile of study subjects

Blood culture	Number	Percentage
Positive	26	32.5%
Negative	54	67.5%

Table II shows that blood culture was positive in 26 (32.5%) and negative in 54 (67.5%).

Table 3:Organism isolated in blood culture positive subjects with sepsis (n=26)

Bacteria	Type of bacteria	Number	Percentage
Gram positive	Staphylococcus aureus	5	19.2%
Gram Negative	E. Coli	9	34.6%
	Klebsiella Pneumoniae	6	23%
	Acinetobacter baumannii	2	7.6%
	Pseudomonas aeruginosa	4	15.3%

Table III shows that among 26 positive blood culture cases, 5 (19.23%) were caused by Gram-positive bacteria and 21 (80.76%) by Gram-negative bacteria. In Gram-positive cultures all 5 isolates identified were of Staphylococcus aureus. In Gram-negative cultures most common isolates were E. coli 9 (34.61%), followed by Klebsiella pneumoniae 6 isolates (23.07%) and 6 isolates of non-fermenting gram-negative bacilli (NFGNB) were isolated.

Table 4:Distribution of serum PCT and CRP concentrations corresponding to different causative pathogenic culture positive cases

Type of bacteria		PCT	CRP
Gram+ve(n=5)		4.06(0.06-6.06)	38.22(23.67-65.15)
Staphylococcus aureus		4.06(0.06-6.06)	38.22(23.67-65.15)
Gram-ve(n=21)		9.66(5.85-32.95)	35.91(26.20-54.97)
bacteriaceae(n=15)	E.Coli	18.22(4.56-36.35)	31.73(22.27-56.56)
	Klebsiella pneumonia	17.43(6.94-43.26)	33.18(26.38-45.09)
NFGNB(n=6)	Acinetobacter baumannii	11.75±4.01	55.34±9.72
	Pseudomonas aeruginosa	5.85(1.26-11.12)	32.56(19.70-60.17)

Table IV shows that the mean and median (interquartile range) concentrations of PCT and CRP values in organisms isolated. The median PCT concentrations in Gram-positive bacteria was 4.06 (0.06-6.06) ng/ml and the median PCT concentrations in Gram-negative bacteria was found to be 9.66 (5.85-32.95) ng/ml. The respective median levels among the Gram-negative bacteria were as follows: E. coli 18.22 (4.56-36.35) ng/ml followed by K. pneumoniae17.43 (6.94-43.26) ng/ml. Also, median CRP concentrations of Gram-positive bacteria was found to be 38.22 (23.67-65.15) mg/Land for Gram-negative bacteria 35.91(26.20-54.97) mg/L.

Table5: Clinical conditions in study subjects(n=80)

Clinical Diagnosis	No.	Percentage
Chronic Lung diseases	31	38.7%
Acute Kidney Failure	27	33.7%
Anaemia	24	30%
Diabetes Mellitus	22	27.5%
Hypertension	18	22.5%
Chronic Liver Diseases	9	11.2%
Chronic Kidney Diseases (without dialysis)	8	10%
Neurological diseases	7	8.7%
Pulmonary Koch's	6	7.5%
CAD	4	5%
CVA	4	5%
Gastrointestinal Diseases	3	3.7%

Table V shows that clinical conditions present in study subjects were chronic lung disease in 31cases (38.7%) followed by acute kidney failure in 27 cases and anaemia in 24 cases. Three cases also had gastrointestinal disease.

Table 6:Source of infection in patients with blood culture positive and culture negative sepsis

Source of infection	Culture positive(n=26)	Culture negative(n=54)
Pneumonia	9(34.6%)	19(35.1%)
UTI	8(30.7%)	11(20.3%)
Skin wound/cellulitis	4(15.3%)	6(11.1%)
Meningitis	3(11.5%)	8(14.8%)
Biliary tract infection	3(11.5%)	1(1.8%)
Abdominal/Liver abscess	2(7.7%)	6(11.1%)
Gastrointestinal infection	1(3.8%)	7(13%)

Table VI shows that source of infection in culture positive patients were pneumonia 9 cases (34.6%), UTI 8 cases (30.7%), skin wounds/cellulitis 4 cases(15.3%), meningitis and biliary tract infection 3 cases each (11.5%). Source of infection in culture negative cases was pneumonia 19cases (35.1%)followed by UTI 11cases(20.3%).

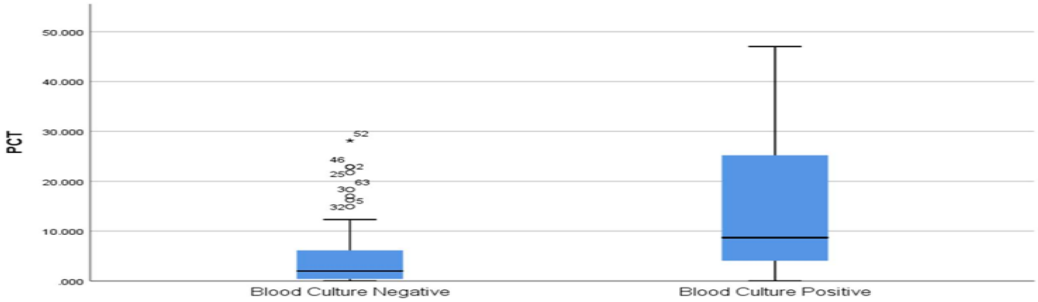

Fig 1:Distribution of PCT and CRP concentrations in patients with blood culture+ve and culture-ve group

Graph I shows that median PCT concentrations were 8.69 (4.27-23.46) ng/ml and 1.99 (0.40-5.81) ng/ml in the culture positive and culture negative groups respectively. Median CRP concentrations in culture positive and culture negative groups were 36.12 (26.69-51.07) mg/L and 34.14 (25.76-40.30) mg/L respectively.

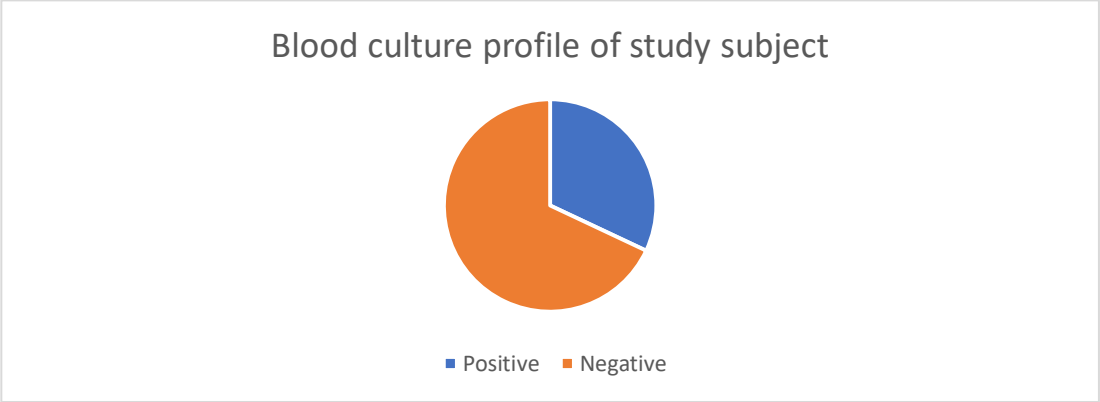

Fig 2:Blood culture profile of study subjects.

Graph II shows, out of 80 patients 26 of them (32.5%) were blood culture positive while the remaining 67.5% were blood culture negative respectively.

Table 7:Comparison of Diagnostic performance of PCT and CRP for diagnosis of sepsis

Parameters	PCT	CRP
AUC	0.717	0.544
95%CI	0.61-0.80	0.44-0.64
Cut off value	4	38
Sensitivity	76.9%	46.1%
Specificity	72.2%	72.2%
PPV	57.1%	44.4%
NPV	86.6%	73.6%
Accuracy	73.7%	63.7%

Table VII shows that the best cut off value for CRP was 38 mg/L, at which it showed a sensitivity, specificity, PPV, NPV and AUC of 46.1%, 72.2%,44.4%, 73.6% and 0.544 (95% CI 0.442-0.644)respectively. The area under the curve AUC of PCT was significantly larger than that for CRP (p=0.038).

Discussion

In the present study, we included 80 suspected cases of sepsis. Among these cases45(56.2%) were male and 35 (43.7%) were female. Gender distribution in our study demonstrated maximum male cases. The male dominancy may be explained due to the rural location of our hospital, which is further explained by gender-related bias in the provision of healthcare towards men in rural are as and on the other hand critically ill women have to depend on men for access to a tertiary care hospital. This finding has been consistently reported in all the large epidemiologic studies in ICU patients.In the present study, 19.23% were caused by gram-positive and 80.76% by gram-negative bacteria which is

concordant with various published studies. A study done by Prakash KP et al[11] have reported a higher (57.8%) prevalence of gram-positive and lower (42.2%) of gram-negative bacteria. The PCT levels in gram-negative bacteria were higher than those in the gram-positive bacteria. This was in accordance with the reports of Nargis et al., and Li S et al.The predominant source of infection in our study in both culture positive as well as culture negative patients were respiratory followed by urinary tract infection. This finding concurs with previous studies that reported lung infection as the highest source of development of infection in culture positive and culture negative patients[12].Serum levels of PCT in our study showed significant raised mean values 14.62±15.00ng/ml in culture positive group, this tells that it can be used as a nearly diagnostic marker in the emergency before culture results are available. Although CRP is known as a sensitive marker of infection and inflammation, in the present study there was no significant difference between mean concentrations of culture positive 40.22±18.54mg/L and negative groups 37.82±19.15mg/L. A previous study reported similar significant mean values in the bacteraemic group for PCT and non-significant for CRP. We also agree with the belief reported by Chanetal[13] that each biomarker performance is closely related to the characteristics of the study subjects and the clinical settings with a difference in the inflammatory effects produced by the biomarker.We found that serum PCT cut-off of 4 ng/ml was highly suggestive of culture positive sepsis with good sensitivity (76.9%), specificity (72.2%), PPV of57.1% and NPV of 86.6%. In our study, a CRP cut-off at 38 m g/L showed a sensitivity of 46.1% and specificity of 72.2% with a disappointingly low PPV 44.4% and NPV of 73.6%. Moreover, the AUC of PCT was significantly higher (p=0.038) than that of CRP(AUC 0.717 vs 0.544), suggesting that PCT is superior to CRP as a marker for identifying and diagnosing sepsis, which was consistent with the findings of Joen JS et al[14].Our study was conducted in a single institution, a tertiary care centre, considering a small sample size, results may not be generalisable to other populations. We, therefore suggest validating the predictive performance of PCT and CRP in future prospective studies. Another limitation of our study is serial measurements of PCT and CRP were not performed because of limited resources as such we could not report levels associated with mortality. We also could have used molecular methods for the identification of bacteria but it has its drawbacks whether this technique would help to detect viable bacterial pathogens. Also, due to the cost associated with molecular methods, their widespread use remains limited in a rural setting like ours.

Conclusion

PCT proved to be a reliable marker for sepsis diagnosis and is more relevant than CRP in patients with a positive blood culture.PCT levels can provide useful information for selecting the most appropriate antimicrobial therapy when blood culture results are not available or the infection site is unclear.The additive effect of PCT can help to improve the predictive power of routinely available sepsis parameters.

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