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ORIGINAL ARTICLE

Evaluation of Procalcitonin Diagnostic Accuracy with Comparison to Blood Culture

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ABSTRACT

Background: Procalcitonin has been used globally as indicator marker of sepsis to define bacteremia or blood stream infection for early patient management or antibiotic therapy. Blood culture refers to a microbiological culture of a peripheral blood sample. The blood cultures help to determine the presence of systemic infections, such as septicaemia. If the culture is positive, the causative micro-organism can usually be identified, and antibiotic sensitivity testing performed. On the other hand, the sensitivity of procalcitonin in comparison to its specificity to certain bacterial infections is still in question.
Methodology: In this study, we selected 309 patients without restriction of age gender with pre-diagnosed sepsis or septic shock syndrome. Blood culture samples were collected in bactAlert media plus culture bottles and were incubated in BactAlert 3D semi-automated blood culture system; blood sample was collected for serum procalcitonin on immunoassay principle.
Results: Out of 309, a total 87 blood cultures were positive and PCT was positive in 134 whereas 179 were PCT negative. In positive PCT, 63 were having bacterial growth in their blood culture while 71 were with negative blood culture. Although in total, 179 PCT were negative, only 16 were having bacterial growth in blood culture samples whereas all others revealed no growth that showed maximum number of positive blood cultures were having PCT positive but not all PCT positive demonstrated bacterial growth in blood culture suggesting that the bacteremia or sepsis can only be suspected with positive PCT. In addition, blood culture positive or negative results cannot be predicted by PCT value to make diagnostic confirmation of sepsis.
Keywords: Procalcitonin (PCT), Blood culture, Sepsis, 95%CI; confidence interval, IQR; Interquartile range

INTRODUCTION

PCT or Procalcitonin is a protein consisted of 116 amino acid long chain, which is actually a precursor of calcitonin used in calcium regulation inside the body. This hormone is produced under specific physiological condition by endocrine cells and thyroid gland but it is considered that procalcitonin serum level remains very low in normal conditions[1]. Serum range of procalcitonin increases rapidly upon any inflammatory response in the body especially during sepsis. It is considered as an important marker to differentiate infectious inflammation specially as a consequence to bacterial infection from non-infections inflammation or syndrome. There is a strong evidence found in previously published literature including systemic reviews which supports the diagnostic accuracy in addition to reliability of procalcitonin as a sepsis marker for bacterial infection, and results of reliability have been equally greater in both adults and pediatrics population group. It has also been observed that the serum procalcitonin level demonstrates the antibiotic therapy from mutual aspects of imitation as well as duration of doze in many acute infections. This leads to a significant decrease of mortality or failure of treatment by directing good intervention.

Some other markers like C Reactive protein, WBC count and Interleukins are also used for sepsis, but these all are non-specific because they cannot distinguish the inflammation root either viral or bacterial so unable to give appropriate direction for initial therapy[2]. In comparison to all these, the procalcitonin possesses far more significance in the prognosis and diagnosis of sepsis. Additionally, patients with severe sepsis or septic shock who report to the emergency department have a high PCT specificity for inflammation of bacterial origin. Prompt detection of sepsis is always a challenging situation for infectious disease consultant that can escalate the mortality and morbidity. In a survey conducted in EU, 45% physicians claim that they may have missed a diagnosis of sepsis[3].

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PCT is an excellent biomarker for bacterial infection because of its rapid rise in concentration and connection with sickness severity. It also rises more rapidly than CRP in the blood and if treatment goes rightly the PCT gets back to baseline in short period of time which helps to improve any healthcare facility.

Blood culture is considered as a gold standard for diagnosis of sepsis till date, but blood culture has some limitations and most big one is its time, a positive blood culture may take hours to days to be finalized. Early PCT detection can be used as a marker for early sepsis detection to avoid septic shock and organ failure, but this marker is still not fully endorsed around the globe.

In this research we will correlate the PCT early detection with blood culture results in patients with suspected sepsis.

MATERIALS & METHODOLOGY

After permission from Ethical Review Board, it was a cross-sectional study in which we have recruited 309 patients who were visited a private clinic and diagnosed as suspected sepsis during the time period of September 2021 to December 2021. Inclusion criteria of selected patients was based on both Blood culture and PCT tests which were ordered and the samples were collected at the same time. Exclusion criteria was defined as patients with single test or samples taken at different time. No age or gender filter was applied.

Blood culture test: Blood culture samples were taken in FN and FA media plus culture bottles of Bectalert blood culture system bioMérieux All positive blood cultures were further subculture on Blood, Chocolate and MacConkey agar for isolation of bacterial colonies[4].

Identification of bacteria and sensitivity testing: Bacterial growth was identified by API system of bioMerieux, and bacterial antimicrobial sensitivity was tested on minimum inhibitory concentration base Vitek 2 compact unit[5].

PCT testing: PCT was measured from serum sample and a fresh clotted sample was tested based on immunoassay principle in automated instrument named Alinity of Abbot following protocol as per supplie[6].

Sepsis interpretation: Before PCT value and positive blood culture interpretation, the blood culture contamination was ruled out on the criteria defined by Lee et al[7]. True infectious bacteria were considered as pathogens in blood culture growth isolation.
Statistical analysis: Regression model was applied on the two groups; low and high PCT groups with age and gender to measure the possible outcome such as septic shock, death or recurrent admission.

RESULTS

Selected 309 patients were having following age gender distribution in table 1

Table 1: Age gender distribution

Sex	<10	11-50 years	>50 years	Total
Male	31	87	49	167
Female	17	64	61	142
Total	48	151	110	309

Positive blood culture results: Out of 309 patients, a total 87 patients including males and females were positive of blood culture as shown in the figure. 87 blood cultures were positive with maximum 10 to 50 years of range. Male number was higher.

Figure 1: Blood Culture positive

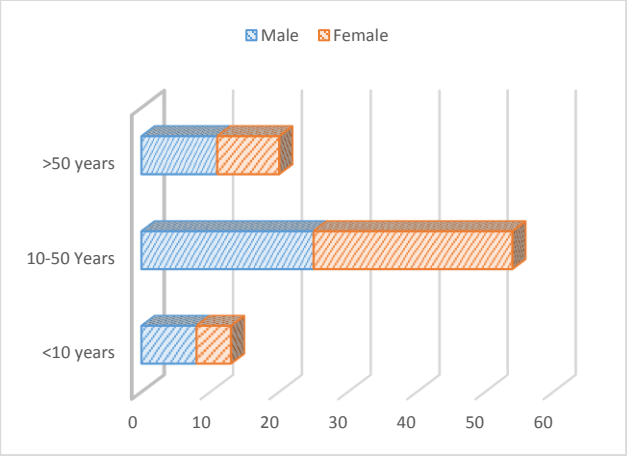

Table 2: Frequency of bacteria

Bacterial Isolates	Frequency	% of total
Gram-Positive bacteria 21(24%)		
Staphylococcus aureus	17	19
Enterococcus faecalis	4	4
Gram-Negative bacteria 66(76%)		
Escherichia coli	33	38
Klebsiella pneumoniae	19	21
Pseudomonas aeruginosa	9	10
Acinetobacter baumannii	5	6

Table 3: PCT value with organism isolated

Organism	n	%age	95% CI	PCT value range	
				Median	IQR
Staphylococcus aureus	17	17	16.7-17.2	1.39	0.47-7.1
Enterococcus faecalis	4	4	3.9-4.2	1.2	0.5-4.7
Escherichia coli	33	38	33.2-41.7	2.9	1.0-15.7
Klebsiella pneumonia	19	21	18.7-24.4	2.7	0.9-11.8
Pseudomonas aeruginosa	9	10	9.2-10.8	1.5	0.7-10.6
Acinetobacter baumannii	5	6	4.8-7.6	1.6	0.5-1.8

Bacterial isolation and identification: Positive blood cultures were further subcultured in order to isolate the bacterial growth. Growth was identified by using API system of bioMérieux. Following organisms were isolated as given in table 2.
PCT value: PCT value was measured in all 309 samples. PCT value was divided in two groups with PCT value >2.0ng/mL and PCT value <2.0ng/mL. and possible outcome was measured as sepsis, morbidity and blood culture positive. Out of 309 suspected sepsis patients, only 87 were positive for blood culture which is 28%.

With comparison of PCT value it was observed that in most of the cases where blood cultures were also negative, PCT value was less than 0.5ng/Ml, which is considered as normal range. Generally, if we see the ranges for blood culture, the gram negative bacteria reveal the PCT value significantly higher than in gram positives especially for E.coli where the PCT value was maximum. Same case was not for all gram negative cultures as Acinetobacter baumannii has PCT value on lower side. With 95% confidence interval, the value of P was less than 0.05, which shows rising growth of bacteria in blood culture has significant correlation with increasing serum PCT level.

Table4: PCT value with positive and negative blood culture

Patients	PCT positive	PCT negative	P value
Blood Culture positive	71	16	P<0.001
Blood culture negative	63	159	

Value of p is less than 0.001, whereas the defined significance is less than 0.01. Table shows that the positive blood culture revealing negative PCT value is found in 16 patients in comparison to negative blood culture PCT positive value in 63 out of 309 patients which is considerably high.

DISCUSSION

PCT is considered as an important diagnostic marker to rule out sepsis with bacterial infection specially. It was observed in previously conducted studies that sepsis due to bacterial infection, procalcitonin increases rapidly and on good intervention treatment also decline rapidly as compared to other markers like CRP and immunoglobulins.

We have analyzed 309 patients PCT and blood culture at the same time and all these patients were suspicious for sepsis. Most of the patients including male and females were lying between the age of 10-50 with positive blood culture and PCT positive value. Systemic inflammatory response syndrome and sepsis have been identified as similar terms having same criteria reported over a decade[8]. In recent studies by Singer, M et al, it was reported that not only sepsis but organ failure is also included in sepsis or septic shock. In our research we have not only considered a PCT to define sepsis but have also included positivity of blood culture with different underlying diseases according to SIRS criteria. On regular intervals, substantial elevation of procalcitonin expression in several organs, including the liver, lung and spleen has been demonstrated following infection with Escherichia coli on a consistent basis. Likewise, in our study, a maximum value of PCT was isolated in E.coli infected patients as shown in table 3. In a previously conducted study comparing to gram-positive bacteria, it has been demonstrated that gram-negative bacteria tend to increase larger amounts of blood procalcitonin level than Gram-positive bacteria[9-12]. Similarly, in this study except for Acinetobacter bauamnnii all gram negative bacteria have significantly high PCT value as compared to gram positive bacteria. There could be multiple reasons behind, one of the most important underlying reason is that klebsiella and E.coli produce toxins that increase the inflammation severity. An examination of 16,514 patients with probable illness found that 3420 had bacteremia, which was confirmed by laboratory testing. Researchers discovered that a PCT level of 0.5 ng/mL was 76 percent sensitive and 69 percent specific for diagnosing

bacteremia in patient. But the results of our study were different from the aspect of sensitivity and specificity; from total positive blood culture, the PCT positive samples were 71, which is about 81%. On the other hand, we can see a significant ratio of PCT positive in blood culture negative patients also, that makes weak relationship of blood culture positive with PCT. Same scenario was described in another study where the negative predictive value for Gram-negative and Gram-positive bacteria was 98.9 percent and 98.4 percent, respectively, for a PCT value of 0.4-0.75 ng/mL in 35,343 consecutive patients receiving PCT assays and blood cultures for suspected blood stream infection[13]. It was well explained that PCT can only be used within certain parameters. Biomarkers like PCT can be used to distinguish between bacteria and other pathogens. Despite this, PCT levels may be raised in clinical conditions other than infections such as malignancies, major surgeries, chronic kidney disease and severe burns. In that case, it was concluded that PCT should not be applied in all sepsis cases or it should be applied on very selective and suspected sepsis. Positive blood cultures with negative CPT were also reported in our study which was about 19% of total positive cases, this comprises multiple reasons like bacteremia without inflammation or most commonly reported contamination. Our results are supported by previously reported study, where it was shown that PCT concentrations were lower in patients with gram-positive coccemia than those with Gram-negative cocci infection. A common blood culture contamination is S. epidermidis, a Gram-positive coccobacillus. Patients with suspected sepsis, high fever, or severe inflammation, such as those with malignancies or collagen diseases, may not be at risk for such contamination because of their low PCT[14].

CONCLUSION

It was concluded that PCT can be used as an initial marker to treat early sepsis or blood stream infection but it cannot be used as a predictor of blood culture positivity. But the observation that the PCT positive can indicate the severity of septic shock with worse sepsis can be correlated. Sensitivity of PCT to define bacteremia was very high but specificity had limitations. PCT can only help to identify bacteremia for early antibiotic therapy.

Conflict of interest: Nil

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