Original Research Article

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Study of procalcitonin in neonatal sepsis with blood culture in suspected sepsis in North India

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ABSTRACT

Background: Sepsis can occasionally be difficult to demonstrate, and its difference from non-infectious conditions in critically ill patients is often a challenge. Serum procalcitonin (PCT) assay is one of the biomarkers of sepsis. The aim of the study was to investigate the value of procalcitonin, in the early diagnosis of neonatal sepsis.

Methods: A cross-sectional study was conducted at tertiary care hospital in New Delhi. It included all neonates with clinical signs of sepsis. The neonates were divided into two groups as sepsis, and healthy neonates. The PCT level was measured by using ELISA technique and compared between the two groups. Statistical analysis was performed using SPSS windows version 20.0 software.

Results: In this study total number of patients included 350, out of which 175 were clinically suspected sepsis cases and 175 were healthy controls. 68 (39%) neonates were show positive blood culture and 107 (61%) neonates were representing negative blood culture report in study group. The mean serum value of PCT was significantly (p<0.001) higher in sepsis neonates. The serum PCT value was significantly increased in neonate's sepsis with positive blood culture (p<0.001) and negative blood culture (p<0.001) as compared to healthy neonates.

Conclusions: It is concluded from this study that the PCT assay was established to be a valuable biomarker of sepsis in this study. The assay might be performed and reported quickly and gave precious information before availability of culture results. This might assist in avoiding unnecessary antibiotic therapy.

Keywords: Blood culture, Neonatal sepsis, Procalcitonin, Suspected sepsis

INTRODUCTION

The child care is the most susceptible part of the culture not only for himself but as a future adult. The worldwide burden of neonatal death is estimated to be 4.8 million, of which 3.2 million deaths occur during the first week of life. Out of them as many as 1.24 million neonates die every year in India. Sepsis is the most common cause of neonatal mortality. Sepsis is defined as a systemic inflammatory response syndrome (SIRS) caused by infection. The connection between infection and sepsis has been documented for many years. In India it contributes to 19% of all neo-natal deaths. Sepsis can lead to multi organ failure and is worldwide a major cause of death by

infection.² In contrast to numerous pro-inflammatory cytokines e.g. TNF-alpha, IL-IB that increase and declined in the premature course of sepsis, serum Procalcitonin (PCT) increase in patients with sepsis, and those with systematic inflammation. It is correlated with mortality and severity of illness and leftovers elevated over a relatively extensive period of time.³ PCT offers constructive kinetics for biomarker, increasing prior to 2 hours, consistently measurable between 2 to 4 hours, reaching a peak of 6 hours and preserving a plateau through 8-24 hours. PCT is detected in very low levels in the serum of well individuals at physiological homeostasis and can increase 1000-fold during active infection.⁴ In addition, studies have suggested that PCT is a useful

marker for diagnosis of acute bacterial infection, especially for bacterial sepsis but not for viral or fungal infection.⁵ PCT direction could limit antibiotic more use in most viral acute respiratory tract infection. Procalcitonin released as an acute phase reactant does not result in increased serum calcitonoin level. PCT has been projected as a marker of bacterial sepsis in critically ill patients. PCT is a precursor of calcitonin and a 116 amino acids protein. In contrast to calcitonin that has a short half-life of 10 min; PCT has a much longer half-life as 25-30 hours. 6 In healthy persons, PCT levels are hardly measurable. Although, the exact sites of production of PCT in sepsis have not been recognized, monocytes and hepatic cells are believed to be potential sources. Since early identification of infections and sepsis is crucial for patient management, an effective marker specific for bacterial infection is very useful in the critical care settings.^{7,8} There are a number of markers of sepsis, like C-reactive protein, serum PCT, IL- 6, IL-8, lactate, etc., of which PCT has been found to be the most effective.⁵ PCT has been proposed as an indicator of the presence of infection and as a useful marker of the severity of sepsis. The aim of the study was to investigate the value of procalcitonin in establishing the early diagnosis of neonatal sepsis in North India.

METHODS

This cross-sectional study was done in the department of paediatrics and microbiology at Swami Dayanand tertiary care hospital in New Delhi, North India for the period of one year from April 2019 to March 2020. This study enrolled patients from the paediatric intensive care unit (NICU) with suspected sepsis from department of paediatrics. Sepsis was confirmed clinically and by positive blood culture system. Total number of patients included in this study was 350, out of which 175 were clinically suspected sepsis cases and 175 were healthy controls. Age and sex matched 175 normal healthy neonates were included in this study as a control group. Age and sex wise distribution of subjects in both groups were 100 males and 75 females. The clinical condition, signs and symptoms of sepsis, antibiotics used, blood culture and final outcome of patients were recorded for all patients. The written informed consent was obtained from all patients' relative from prior to start of study. The study protocol was approved by institution Ethics Committee human (IHC-H). Clinically suspected cases of neonatal sepsis with sign and symptoms of disease were included in study group and normal healthy neonates were included in control group as inclusion criteria. Patients with history of any disease, malignancy and cardiovascular, hepatic disease were excluded from present study.

The blood samples were collected from all neonates with diagnosed clinical signs of sepsis before the administration of antibiotics. About 4.0 ml of the blood was collected from the ante-cubital peripheral vein under aseptic precautions by neonatologist using an appropriate technique with 23-gauge syringe. 2 ml of blood was transfer in to plain vial for serological test and another 2

ml blood was pure into anticoagulant vial for blood culture. The culture vials were placed in Bect-alert automated blood culture system. The culture vials were removed on positive indication from the system. The positive blood culture samples were sub-cultured in to blood agar, Mac-Conkey agar, and chocolate agar.

All blood samples were collected into plain vial centrifuged at 5000 rpm for 5 min and sera were separated. It used for estimation of serum PCT. It was estimation using commercially available diagnostic kit (ERBA-PCT ELISA Chem. Germany) by ELISA method.

The result was independently read by two technologists to reduce reading bias and interpreted as per the manufacturer's recommendations: PCT >10 ng/ml: severe bacterial sepsis or septic shock; PCT 2 to 10 ng/ml: severe systemic inflammatory response, most likely due to sepsis unless other causes are known; PCT 0.5 to 2 ng/ml: a systemic infection cannot be excluded; and PCT <0.5 ng/ml: local bacterial infection possible.

Statistical analysis

The data were statistically analyzed and expressed descriptive analysis as percentage and mean±SD. Statistical analysis of the variance between control and study groups was done using Student's-t test. Values of p<0.05 were considered significant. The statistical analysis was done using SPSS for Windows, version SPSS 16.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

The demographic characteristics of neonates in study group and control group were expressed in Table 1. Total 175 neonates in study groups out of 57.1% and 42.9% were male and female neonates respectively, in both groups.

Table 1: Demographic characteristics of study group and control group.

Demographic characteristics	Study group (%)	Control group (%)
Male	57.1	57.1
Female	42.9	42.9
Total	100	100

Table 2 shows distribution of neonates of study and control group based on age. Highest numbers of neonates (90) were present in between aged group 1-6 years and lowest neonates (10) were present in aged group 15-21 and 22-28 years in study group and similar trend also found in neonates of control group. Distributions of neonates in study and control group based on birth weight were expressed in Table 3. It represents that 65 neonates had very low birth weight, 85 had low birth weight and 25 were normal birth weight in study group and similar trend also found in neonates of control group.

Table 2: Distribution of neonates of study and control group based on age.

Age in days	Study group N=175	Control group N=175
1-6	90	125
7-14	65	35
15-21	10	05
22-28	10	10
Total	175	175

Table 3: Distribution of neonates in study and control group based on birth weight.

Birth weight (g)	Study group N=175	Control group N=175
VLBW <1500	65	63
LBW 1500-2500	85	75
Normal >2500	25	37
Total	175	175

Distribution of neonates in study and control group based on gestational age (maturity) were present in Table 4, it shows that 165 neonates were premature and 10 were mature in study group out of 175 while only 70 neonates were premature and 105 were mature in the control group. On the basis of blood culture report 68 (39%) neonates were show positive blood culture and 107 (61%) neonates were representing negative blood culture report in study group (Table 5). Table 6 demonstrate the mean±SD serum value of PCT in neonates of study group and control group. The mean serum value of PCT was significantly (p<0.001)

higher in neonates of study group as compared to neonates in control group. The serum PCT value was significantly increased in neonate's sepsis with positive blood culture (p<0.001) and negative blood culture (p<0.001) as compared to neonates in control group.

Table 4: Distribution of neonates in study and control group based on gestational age.

Gestational age maturity (weeks)	Study group N=175	Control group N=175
Pre-mature <37-27	165	70
Mature above 37	10	105
Total	175	175

Table 5: Blood culture reports of study group.

Blood culture report	Study group N=175 (%)
Positive blood culture (N=68)	39
Negative blood culture (N=107)	61
Total	100

Table 6: value of mean serum PCT in study and control group.

Group	Parameter PCT (Mean±SD)
Study group N=175	132±167.09
Control group N=175	63±47.32
t value	3.324
P value	0.001*
*p<0.001	

Table 7: Concentration of serum PCT in neonatal sepsis with positive blood culture and negative blood culture.

Parameter	Neonatal sepsis with positive blood culture	Neonatal sepsis with negative blood culture	Control	P value
PCT	130±65*	75±41*	43±21*	p<0.001

^{*}p<0.001

DISCUSSION

In this study total number of patients included 350, out of which 175 were clinically suspected sepsis cases and 175 were healthy controls. Age and sex matched 175 normal healthy neonates were included in this study as a control group. Out comes from present report, total 175 neonates in study groups out of 57.1% and 42.9% were male and female neonates respectively, in both groups. Highest numbers of neonates (90) were present in between aged group 1-6 years and lowest neonates (10) were present in aged group 15-21 and 22-28 years in study group and similar trend also found in neonates of control group. In our study 65 neonates had very low birth weight, 85 had low birth weight and 25 were normal birth weight in study group. In our study 165 neonates were premature and 10 were mature in study group out of 175 while only 70

neonates were premature and 105 were mature in the control group. On the basis of blood culture report 68 (39%) neonates were show positive blood culture and 107 (61%) neonates were representing negative blood culture report in study group. Result from present study the mean serum value of PCT was significantly (p<0.001) higher in neonates of study group as compared to neonates in control group. The serum PCT value was significantly increased in neonate's sepsis with positive blood culture (p<0.001) and negative blood culture (p<0.001) as compared to neonates in control group.

To the best of our acquaintance, there are very little studies on serum PCT and sepsis from India. These include studies on its use in determining bacterial sepsis in children with febrile neutropenia, its use as a marker of renal parenchymal infection and its use as a marker of the severity of acute pancreatitis. Most studies using PCT for interpretation of bacterial infection and sepsis have used the quantitative PCT assay which is agreement with our outcomes. 9-10 Several studies have accomplished high sensitivity and modest specificity with cut-off values 1 to 1.2 ng/ml. Others have used 2 ng/ml as the diagnostic threshold value for infection and sepsis in neonates. Various studies have found the PCT values in sepsis ranging from 0.5 to 3.5 ng/ml; in severe sepsis, 6.2-9.1 ng/ml; and in septic shock, 12.8 to 38.5 ng/ml. the results of these above studies are comparable with present study. 4,6,11,12

PCT has been intensively investigated for its diagnostic role in neonatal sepsis. It has been reported that high concentration of plasma PCT was found in infants with severe infection, while PCT levels were very low in those with no infections which is similar to our study. 13 Many authors found that procalcitonin is a promising marker for the diagnosis of neonatal sepsis. In these studies, PCT sensitivity in the early diagnosis of neonatal sepsis was found to be 83-100% while the specificity was 70-100% PCT secretion begins within 4 hours after stimulation and peaks at 8 hours. 14,15 Serum PCT increases early after trauma and peaks within 48 to 72 hours post-trauma and declines thereafter in the absence of infection or sepsis. 16-¹⁸ In contrast, initial falsely low PCT levels, typically seen during the early course or localized state of infection; often show a gradual increase during follow-up measurements after 6-24 hours. Reduction in concentration of PCT has been described in response to antibiotic administration and may be used to detect antibiotic responsiveness.²⁰

Limitations

Limitation of the current study was that sequential measurements of PCT were not performed for most of patients. In addition, the number of patients assessed in this study was short. An additional limitation of the study was that C-reactive protein (CRP) levels were not measured. Though, most of studies have observed advantage of PCT in comparison to CRP as a marker of infection and sepsis.

CONCLUSION

From the outcomes of our study, we conclude that PCT analyze was set up to be a talented biomarker of sepsis in this tiny investigative study and offered precious and early information before the culture consequences were available. The assay is easy to carry out, and outcome is available quickly. PCT assay might help in avoiding unnecessary antibiotic treatment in seriously ill patients who show with symptoms comparable to those in infective conditions. However, the assay consequence must be interpreted in association with the clinical findings and other diagnostic investigations.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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