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Original Article

Comparison of Procalcitonin Levels with Different Micro-Organisms Recovered from Neonates with Suspected Septicemia

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ABSTRACT

Background: Septicaemia is a leading cause of mortality and morbidity in neonates. The aim of our study was to evaluate usefulness of serum PCT as a diagnostic marker of neonatal sepsis by taking blood culture as gold standard.

Material and Method: This study was conducted at tertiary care hospital in Lahore over a period of 6 months. 365 neonates with suspected septicaemia from NICU (Neonatal Intensive Care Unit) were enrolled in our study. Blood cultures and levels of serum procalcitonin were performed in all the neonates with clinically suspected septicaemia. Different levels of Procalcitonin were measured and compared with the positive blood cultures by using three different cut-off values for PCT ≥0.5 ng/ml, ≥ 2 ng/ml and ≥10 ng/ml respectively. Different levels of procalcitonin were compared with different micro organisms recovered from blood culture.

Results: Among neonates with suspected septicemia(n=356), 2.07% positive blood cultures had procalcitonin levels upto 0.5 ng/ml. 26.4% positive blood cultures had procalcitonin levels > 0.5-2.0 ng/ml. while 45.3 % and 100% blood cultures had procalcitonin levels >2-10 ng/ml and > 10 ng/ml respectively.

Among gram positive organisms (n=30) ,4(13.3%) blood cultures were negative for Procalcitonin levels and 12(40.0%) blood cultures were week positive.

No gram positive organism was strong positive for procalcitonin levels. Among gram negative organisms (n=38), 8(21.7%) organisms were mild positive for serum procalcitonin. 25(65.8%) gram negative organisms were moderate positive for serum procalcitonin while 5(13.1%) organisms were strong positive for serum procalcitonin levels.

2(100%) fugi were week positive for procalcitonin levels. Strong procalcitonin levels (>10 ng/ml) were 68.75% in ESBL producing strains of gram negative organisms and 31.25 % in Non ESBLs organisms

Conclusion: These findings support that serum procalcitonin levels can be useful in early detection and prompt treatment in neonatal sepsis.

Keywords: Procalcitonin, Neonatal sepsis and diagnosis

Introduction

Neonatal sepsis is defined as a medical condition of bacteremia with specific clinical findings in the first month of life [1]. Currently an exaggerated hyper inflammatory response is regarded as sepsis [2]. In Asia, the occurrence of neonatal sepsis differs from 25. 3/1000 live births out of which early onset neonatal sepsis is 22.2 /1000 live birth and late neonatal sepsis is 2.9/1000 [1]. A study was conducted in Quetta who reported 31 % incidence of neonatal sepsis.

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In the continent of Africa 17 % of deaths in newborn are due to neonatal sepsis including incidence rate as high as 10% per 1000 live birth [3]. After survival from sepsis about 20 to 30% of neonates may show neuorological disorders [2].

Organisms responsible for neonatal sepsis variate along with time period and there is marked alteration globally. Gram-negative bacteria is the most common cause of neonatal sepsis in developing countries while in developed countries the most common cause is Gram-positive bacteria [2].

Procalcitonin is considered as the most reliable and favorable laboratory marker in the early diagnosis, prompt treatment and follow-up of neonatal sepsis . Procalcitonin is a peptide which contains 116 amino acid having about 14.5 kDa of molecular weight.It is

related to calcitonin superfamily of peptides. Chromosome 11 contains the *CALC-1* gene which encodes Procalcitonin [4].

In bacterial infections PCT is produced ubiquitously by liver cells and macrophages in response to endotoxin mediators including tumor necrosis factor [TNF]-α ,interleukin [IL]-1β, and IL [5]. Both the presence and the severity of bacterial infection in sepsis is intensely correlated with procalcitonin [6].

In response to viral infections Interferon (INF), a cytokine is secreted which reduces upregulation of PCT hence for bacterial infections procalcitonin is more specific and may help to differentiate between bacterial and viral illnesses. The Procalcitonin have capability to distinguish infections caused by Gram positive or Gram-negative organism [7].

In Serum PCT is one of the most important biomarker of sepsis which helps to differentiate infectious from noninfectious conditions in critically ill newborns [8].

Blood culture is gold standard lab test to identify causative agents in diagnosis of neonatal sepsis but it takes number of days along with false negative results [9].

Materials & Methods

Study design and population: The diagnostic value of serum procalcitonin was examined and compared with blood culture in the diagnosis of neonatal sepsis. 256 neonates with suspected septicaemia were enrolled in the study by taking blood culture as gold standard.

Methods: To collect blood samples for culture tryptic soya broth blood culture bottles were provided to the medical house staff in pediatric emergency of hospital. Thorough instructions about aseptic blood collection technique for blood collection were given to the house staff. One blood sample 1.5ml was drawn. Out of 1.5ml blood sample 0.5ml blood was inoculated into paediatric blood culture bottle containing 9ml of tryptic soya broth and 1ml of blood was transferred to a sterilized vacutainer vial for ELISA.

The information about name, age, sex, clinical signs and symptoms, duration of stay in hospital, any type of invasive procedure or surgery done at hospital and other relevent findings were recorded in the proforma. The blood culture bottles were labelled with the name of patient, serial number, date and time of collection of sample.

Laboratory measurements: For all newborns with suspected septicaemia enrolled in our study blood culture and serum procalcitonin levels were performed. Blood samples were taken before antibiotic therapy. Blood cultures were performed after 24 hr incubation of the blood sample. To measure PCT levels via ELISA each blood sample was centrifuged for 30 min. Serum was separated and stored at the temperature -20 °C. Procalcitonin levels were measured by ELISA method.

Ethical consideration: Ethical Committee of post graduate medical institute Lahore approved the study to be continued.

Inclusion and exclusion criteria: Inclusion criteria was 2-28 day term newborns suspected of neonatal infection before starting antibiotics. Exclusion criteria was neonates with no symptoms of septicemia or having suspected septicemia with the initialization of the treatment.

Results

Figure 1 shows comparison of PCT levels with results of positive blood culture from neonates with suspected septicemia(n=356), 2.07% positive blood cultures had PCT levels upto 0.5 ng/ml, while 26.4% organisms were > 0.5-2.0 ng/ml, 45.3 % having >2-10 ng/ml and 100% had > 10 ng/ml PCT levels respectively.

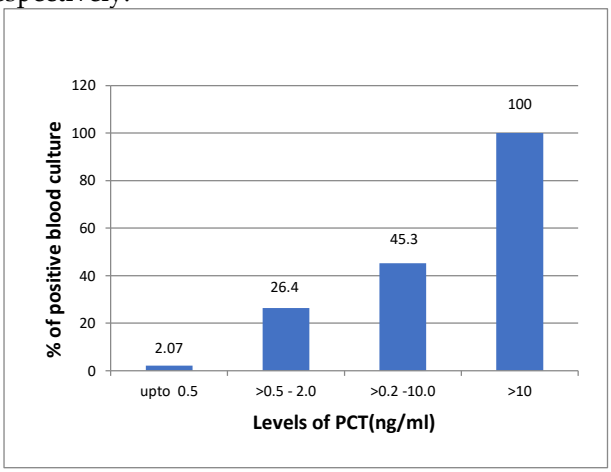

Figure 1: **Comparison of PCT levels with results of positive blood culture from neonates with suspected septicemia(n=356)**

Table-1 shows the Comparison of different Procalcitonin levels with different micro-organisms recovered from neonates with suspected septicaemia. Among gram positive organisms (n=30) ,4(13.3%) gram positive organisms were negative for Procalcitonin levels, (40.0%) week positive and 14(46.6%) were moderate positive.

No gram positive organism was strong positive for PCT levels. Among gram negative organisms (n=38), 8(21.7%) organisms were mild positive for serum procalcitonin. 25(65.8%) gram negative organisms were moderate positive for serum procalcitonin while 5(13.1%) organisms were strong positive for serum procalcitonin levels. 2(100%) fugi were week positive for PCT levels.

Table 1:Comparison of different PCT levels with different micro organisms recovered from neonates with suspected septicemia

PCT levels (ng/ml)	Gram positive organisms (n=30)		Gram negative organisms (n=38)		Fungi (n=02)	
	No.	%	No	%	No.	%
Negative	4	13.3	0	0%	0%	0.00
Mild positive	12	40.0	8	21.0	02	100.0
moderate positive	14	46.6	25	65.8	%	0.0
Strong positive	0.0	0.0	5	13.1	%	0.0

*Number of neonates in each category

Negative: Upto 0.5, Mild positive: >0.5 – 2.0, Moderate positive >2 – 10, Strong positive >10, Strong PCT levels (>10 ng/ml) were 68.75% in ESBL producing strains of gram negative organisms and 31.25 % in Non ESBLs organisms. Figure 2 shows comparison of PCT levels in ESBLS and Non ESBLS microbes isolated from neonates with suspected septicemia.

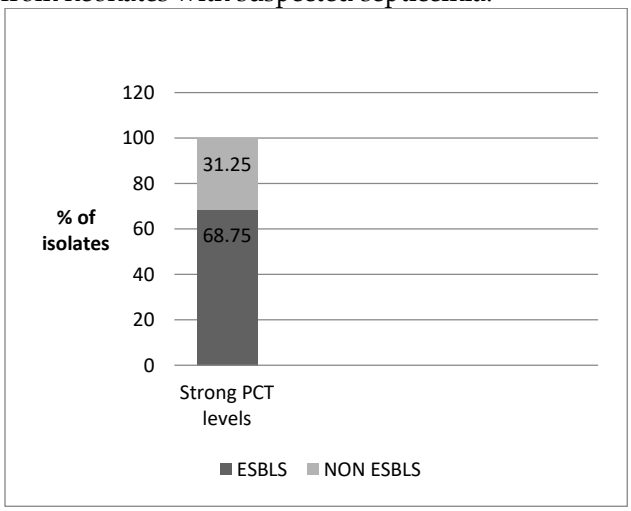

Figure 2: Comparison of PCT levels in ESBLS and Non ESBLS microbes isolated from neonates with suspected septicemia.

Discussion

In neonates of Pakistan major cause of mortality and morbidity is sepsis [10]**.** Among neonates sepsis is the third most important cause of casualities responsible for approximately 225,000 deaths per year [11]**.** Frequency and pattern of microorganisms responsible for neonatal sepsis variates globally.The most common cause of neonatal sepsis are Gram negative organisms [12].

Serum Procalcitonin levels can be physiological raised upto first 48 hours of life and decrease its level rapidly after administration of antibiotics in postnatal life. For diagnosis of neonatal sepsis Procalcitonin has been verified very useful marker of sepsis as compared to others [1]. In our study we recorded the levels of Procalcitonin before taking antibiotics. Neonates who were positive for Procalcitonin had more high ratio of positive blood cultures as compared to PCT negative Patients [3]. In this study we analyzed levels of procalcitonin to detect correlation with the presence of different types of micro organisms.

Among positive blood cultures 2.07% positive blood cultures were negative for PCT levels. 32.3% blood cultures were mild positive for PCT levels. 43.3% moderate positive and 100% blood cultures were strong positive for PCT levels. Similarly in another studies piloted by Watanabe et al,(2016) and Hassan et al,(2017) [1]significantly high ratio of blood culture-positive cases with positive Procalcitonin were recorded.

In this study table 1 shows the Comparison of different procalcitonin levels with different micro-organisms recovered from neonates with suspected septicemia. Among gram positive organisms 13.3% of positive blood culture were negative for Procalcitonin levels , 40.0% mild positive and 46.6% were moderate positive. No Gram positive organisms were strong positive for PCT levels. Among Gram negative organisms 21.0% were mild positive, 65.8% moderate positive and 13.1% were strong positive.While 2(100%) fugi were only mild positive for PCT level.

Nanda et al, (2016)[4] gave similar findings in their study showing moderate positivity (22%) in Gram positive organisms while week positive (14%), moderate positive (22%) and strong positive (50%) results to Procalcitonin levels among Gram negative organisms In Gram-negative rods propcalcitonin concentrations were higher than gram-positive cocci [13]. Similarly in other study there was only mild elevation of procalcitonin levels in fungi [12].

In comparison to blood culture findings there was relativly high sensitivity of PCT for detecting bacteremia although specificity was low. In bacteremia caused by Gram negative rods, including ESBL-producing types procalcitonin levels were significantly higher. In our study high procalcitonin levels were recorded in ESBL(68.75%) producing strains of gram negative organisms as compared to non ESBLs (31.25 %) organisms.These results are given in figure 2. Procalcitonin concentrations can distinguish between ESBL types and non-ESBL types.

Similar results were found in a study showing high concentration among ESBLs (70%) were found as compared to non ESBLs (30%) [13]. For detecting patients infected with such organisms PCT might be very useful..

Conclusion

Gold standard method to diagnose neonatal sepsis is blood culture. But it takes 48-72 hours to give positive results. So Procalcitonin can be used alternative to blood culture method.

As compared to the other markers procalcitonin has better sensitivity, positive predictive value and negative predictive value. In early diagnosis of neonatal sepsis it gives a reasonable degree of accuracy by rapid diagnosis. It will also help to decrease in the number of neonates treated unnecessarily and to start proper early antibiotic therapy.

In sepsis caused by Gram-negative rods including ESBL-producing types there were significantly higher levels of procalcitonin among neonates. Early detection of bacteremia and immediate antibiotic therapy can be done with the help of PCT levels.

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B. Active Participation in Active Methodology
C. Interpretation/ Analysis and Discussion