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Role of Procalcitonin as diagnostic marker in neonatal sepsis and its correlation with clinical, biochemical and haematological profile

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Abstract

Neonatal sepsis is the most common cause of morbidity and mortality in neonatal period particularly in the developing countries. Early diagnosis and treatment of sepsis is essential since a delay in treatment can lead to neonatal death. Different investigative techniques are assessed for usefulness, either singly or in combination, for the early detection of neonatal sepsis. The results of blood culture may be negative despite presence of bacterial infection. Therefore, early diagnosis is difficult, despite advanced bacteriological techniques. Inflammatory markers can also be used for early diagnosis such as C-reactive protein but it does not reliably differentiate between systemic inflammatory response and sepsis. Therefore, there is a need to identify a biomarker by which an infected neonate can be identified rapidly before the onset of life threatening symptoms and for the promt institution of anti-microbial therapy, which improves outcomes. Assessment of Procalcitonin (PCT) in the serum may help in the rapid and accurate diagnosis of sepsis as it is a reliable and specific biomarker.

Keywords: Neonatal sepsis, SIRS, CRP, PCT

Introduction

Neonatal septicaemia is defined as bacterial infection documented by a positive blood culture in a first four week of life. The incidence of neonatal sepsis varies from 11-24.5/1000 live births in India.[1] Neonatal sepsis is classified into early or late according to the age at onset of infection during the neonatal period. The most widely used definition of early onset neonatal sepsis is sepsis that occurs within the first 72 hours after birth. Onset of sepsis between 72 hours and 28 days of life is defined as late onset neonatal sepsis.

Early onset sepsis (EOS): It presents within 72 hrs of life. The main source of infection is maternal genital tract. In the west, early onset infections are mostly caused by group B streptococci and Escherichia coli, while in our setup most cases are due to gram negative organisms especially *E.coli, Klebsiella* and *Enterobacter* species. Majority of the neonates with early onset sepsis manifest as respiratory distress due to intrauterine pneumonia.[2]

LOS (Late- onset sepsis): It is acquired by horizontal transmission of infection at home, hospital or in the community after day 4 of postnatal period. It is acquired as nosocomial infection from the nursery or ward. In most cases, symptoms appear by the end of first week or during second week of life. About two third cases of late onset septicaemia are caused by Gram negative organisms like *Klebsiella pneumoniae*, *E. coli, Pseudomonas aeruginosa* while the rest are Gram positive organisms including *Staphylococcus aureus* and Coagulase Negative Staphylococci (CONS).[3]

The diagnosis of neonatal sepsis by clinical features is difficult due non specific signs and symptoms and it is often mimicked by lot of other disorders affecting the newborn.

Investigations:

Blood culture

Although blood culture remains the gold standard in the diagnosis of neonatal sepsis but it is time consuming and often yield false-negative results. The result is ready only 24-72 hours after sampling and during this period, it is necessary to treat the suspicious neonates for sepsis with antibiotics the basis of clinical features and risk factors. Thus, leading to unnecessary antibiotic consumption, a higher incidence of side effects due to their use, increased resistance to antibiotics, long hospitalization and increased health costs[4.]

The readily achievable complete blood count and the leucocyte differential assays have a relatively poor specificity for diagnosing sepsis. The associated band count and a leftward shift of the myeloid immaturity measurements may improve the diagnostic yield but their subjective measurement is problematic. Therefore, there is a need of using fast diagnostic methods including laboratory parameters for the early and accurate diagnosis of neonatal sepsis. Subsequently studies have suggested that additional markers such as C-reactive protein (CRP) and more recently, Procalcitonin (PCT) can be useful.

PCT is a 116-amino acid protein, a precursor of calcitonin which is produced by thyroid. In sepsis, macrophages and monocytic cells of the liver are involved in the synthesis of PCT.PCT is detected in the blood of healthy people but may increase to about 1000 folds or more when there is an active infection. PCT levels are believed to rise within 2 hours of infection, detectable within 4 hours, peaking at 6 hours and remaining there for 8 to 24 hours. This favourable kinetics of PCT makes it ideal to be used as a biomarker.[5,6]

The use of PCT in the diagnosis of sepsis may be advantageous because unlike many other biomarkers which suffer from elevations in conditions other than bacterial infection, PCT offers an improved specificity in bacterial infections. It is known to be able to distinguish between patients with confirmed bacterial versus viral infections and infectious versus non-infectious inflammatory conditions. The advantage of PCT as compared to CRP is that, it has an early increase in concentration in bacterial infection and even its restoration to normal is more rapid.[7]

PCT has also been studied in critical care patients both as a diagnostic and prognostic test and for its ability to aid antibiotic stewardship by safely shortening antibiotic course length.[8]

Therefore, the present study is aimed to evaluate the role of PCT levels in early and accurate diagnosis of neonatal sepsis and its correlation with clinical, biochemical and haematological profile in these patients.

Aims and Objectives

1. To evaluate the role of procalcitonin as diagnostic inflammatory marker in neonatal sepsis.
2. To study its correlation with clinical, biochemical and haematological profile in neonates.

Materials and Methods

This study was conducted in the Pathology Department, GMC Amritsar in collaboration with the departments of Paediatrics and Microbiology after seeking permission from the Institutional Ethical Committee Government Medical College, Amritsar.

The present study included blood samples taken from Neonates more than 4 days old and less than 28 day old with suspected bacterial infection who were hospitalized in neonatal intensive care units, nursery and paediatric wards of Guru Nanak Dev Hospital Amritsar. A prospective study from January 2017 to June 2018 was done.

Inclusion criteria:

Any neonate with signs and symptoms suggestive for sepsis or who developed signs of sepsis while in the ward in 4-28 days of life.

Exclusion criteria:

The exclusion criteria for this study was administration of antibiotic therapy prior to admission, neonates with birth asphyxia, aspiration syndromes, laboratory findings suggestive of inborn errors of metabolism and in neonates with any congenital anomalies.

Detailed history was obtained from the parents and a complete physical examination was done.

Sample collection and transportation:

Under complete aseptic conditions, blood samples were obtained from each neonate prior to commencement of antibiotics: each sample was divided into 3 parts: first part in sterile vaccutainer tube for CRP and PCT, second part in EDTA tube, and the third part in blood culture bottle. Then samples were transported immediately to Microbiology and Haematology laboratory. Lumbar puncture and other investigations were done as when indicated.

Written informed consent was obtained from parents for participation of their neonates in the study.

All neonates admitted in Guru Nanak Dev Hospital were investigated as follows:

1. Sepsis screen:

Blood smears were studied after leishmann stain for morphological features which were looked under 400x and oil immersion lens.

Total leucocyte count was done.

WBCs=differential count for 100 cells

Absolute neutrophil count was calculated, degenerative changes in the neutrophils such as toxic granulation, and vacuolization were also noted.

Calculation of I/T Ratio:

We calculated I/T ratio by dividing the total immature neutrophil count (including bands, myelocytes and metamyelocytes) by total neutrophil count (both immature and mature). I/T ratio ≥0.2 was considered positive for sepsis.

Platelet count was done. Thrombocytopenia (< $100X10^9$ /lt) was considered positive for sepsis. Other investigations were done as when required.

2. Blood culture:

Blood sample was collected under aseptic precautions and sent to bacteriology lab for further processing. Sample with positive blood culture was considered as confirmed sepsis.

3. Measurements of biomarkers:

CRP & PCT Assays:

Patients' blood samples in sterile vaccutainer tube was allowed to clot for 30 minutes then centrifuged at 3000 RPM for 15 minutes. Serum was separated and divided into 2 parts, one was tested immediately for CRP and the other stored at -20° C till PCT analysis.

Serum CRP:

Serum CRP level measurements were tested by the semi-quantitative latex agglutination test.

Calculation: CRP concentration (mg/l) = Sensitivity X Titre (highest dilution serum showing agglutination) where,CRP sensitivity=6 mg/l

Value > 6 mg/lt was taken as cut off.

Serum Procalcitonin:

Serum PCT was measured quantitatively by ELISA technique (Enzyme-Linked Immunosorbent Assay) using RD191006200R Biovendor Human PCT ELISA kit as per manufacturer instructions. This assay employs an antibody specific for human PCT coated on a 96-well plate. It is a sandwich enzyme immunoassay for the quantitative measurement of human PCT.

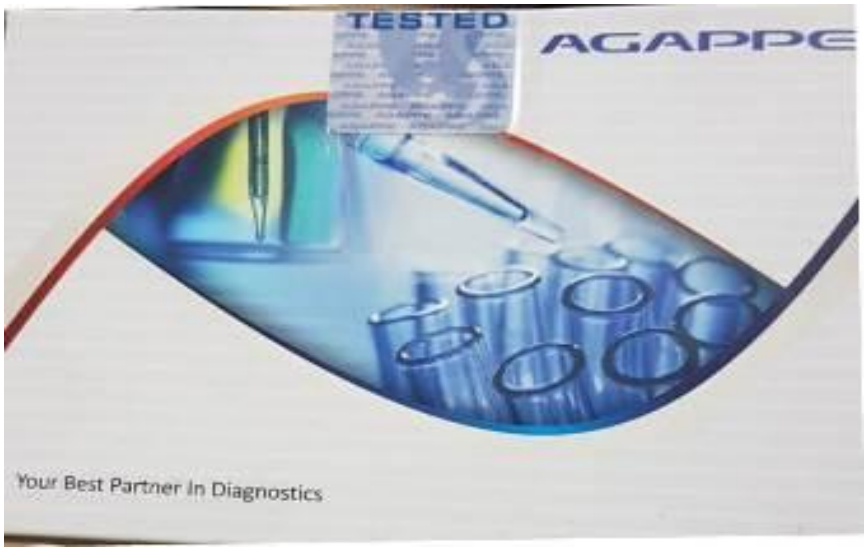
Interpretation:

The standard curve is constructed by plotting the mean absorbance (Y) of Standards against the known concentration(X) of Standards in logarithmic scale, using the four- parameter algorithm. Results are reported as concentration of PCT in samples.

The measured concentration of samples calculated from the standard curve are multiplied by their respective dilution factor:-concentration obtained (from standard curve) x 3(dilution factor) =PCT concentration

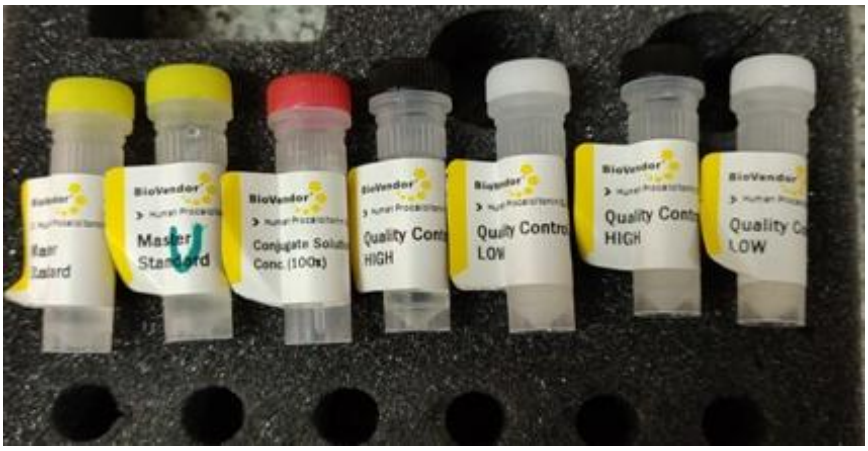
PCT concentration and interpretation for diagnosis of sepsis is as follows:[9] 0.05 - <0.5 ng/ml-no bacterial infection

≥0.5 - < 2 ng/ml- local infection/moderate SIRS
≥2.0 - <10 ng/ml-severe SIRS
≥10ng/ml- severe bacterial sepsis/septic shock.



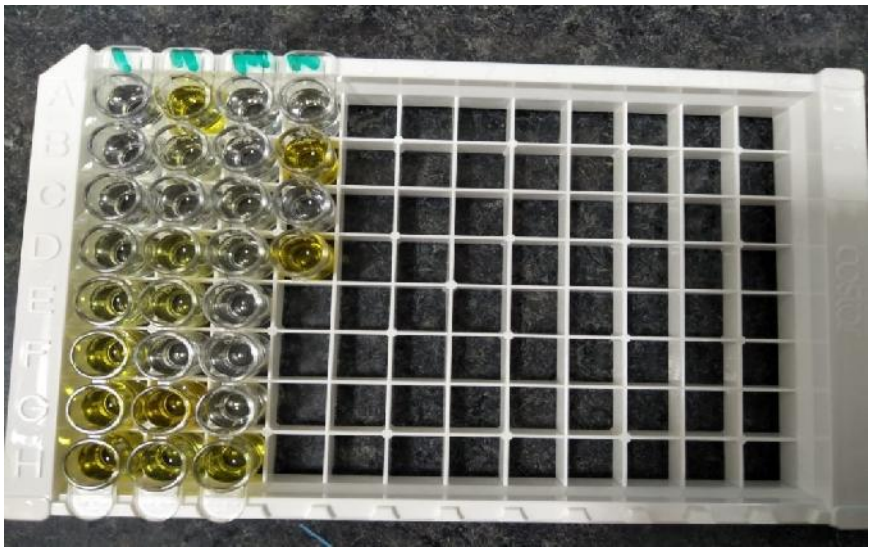
CRP Latex agglutination kit

Photograph showing various kit components of RD191006200R biovendor human procalcitonin ELISA



Photograph showing various kit components of RD191006200R biovendor human procalcitonin ELISA

Procalcitonin Assay



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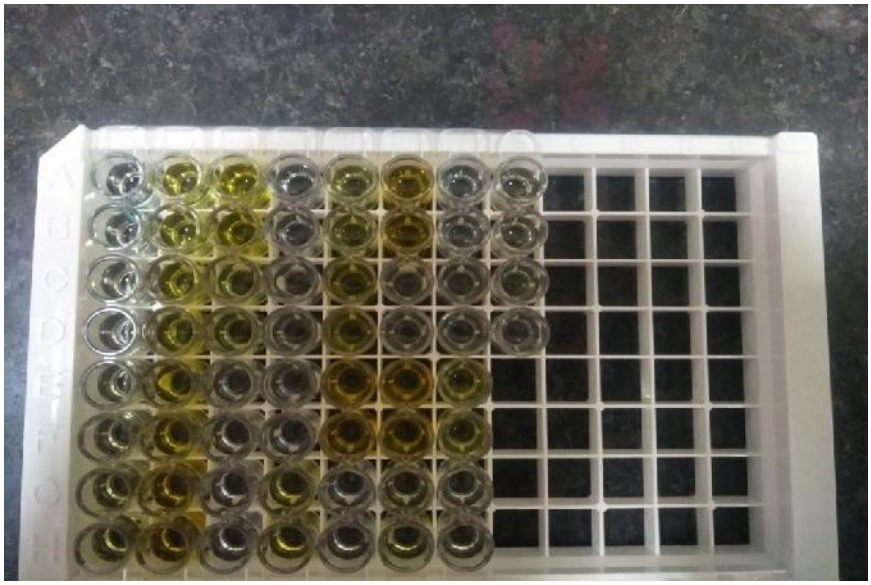

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Results

Based on our clinical findings and laboratory data, 50 neonates were eligible for the study. The age range of clinical presentation was 4-28 days. Majority of the cases, i.e. 17 (34%) in our study belonged to 4-7 days of age range while the least patients were in the age range of 22-28 days (16%).Males (68%) outnumbered the females (32%) in the study. Fever (34%) was the most common presenting feature followed by refusal to feed (20%) and respiratory distress (18%). Bacteria could only be isolated in 9 (18%) cases while no growth was detected in 41 (82%) cases. The most common organism isolated was *E. coli* followed by *Klebsiella pneumoniae.*

Out of total 9 cases, 7 cases (77.7%) of sepsis were caused by gram negative bacteria while 2 cases (22.2%) were caused by gram positive bacteria.

Septic screen:

Leucopenia with count <5000/cmm was considered positive for septicemia. Out of total 3 cases with leukopenia, positive culture was present in 2 cases while 1 case showed no growth on culture. Similarly, out of total 47 cases with>5000/cmm, positive culture was present in 5 cases while 42 cases showed no growth on culture. Thus Leukopenia had 28.5% sensitivity, 97.6% specificity and 66.6% positive predictive accuracy.

Out of total 24 cases with Toxic granulation, positive culture was present in 9 cases while 25 cases showed no growth on culture. Similarly Out of total 26 cases without Toxic granulation, all cases showed no growth on culture. Thus toxic granulation had 100% sensitivity, 63% specificity and 37.5% positive predictive accuracy.

Out of total 14 cases with I//T≥0.2 ratio, positive culture was present in 7 (50%) cases while 7 (50%) cases showed no growth on culture. Similarly, out of total 36 cases with I/T<0.2 ratio, positive culture was present in 2 (5.5%) cases while 34 (94.4%) cases showed no growth on culture. Thus I/T ratio had 77.7% sensitivity, 83% specificity and 50% positive predictive accuracy.

Out of total 6 cases (12%) with platelet count ≤ 1 lakh/cmm, positive culture was present in 4 (66.6%) cases while 2 (33.3%) cases showed no growth on culture. Similarly, out of total 44 cases (88.8%) with > 1 lakh/cmm, positive culture was present in 5 (11.36%) cases while 39 (88.6%) cases showed no growth on culture. Thus platelet count had 44.4% sensitivity, 95% specificity and 66.6% positive predictive accuracy.

Correlation of serum CRP and PCT with culture was done and sensitivity, specificity and PPV were calculated (table1, 3).

Table 1 :CRP Profile in study population

CRP	Culture		Total
	Positive culture	Negative culture	
Positive (>6mg/dl)	6	11	17
Negative (≤6mg/dl)	3	30	33
Total	9	41	50

Table 1: Out of total 17 cases (34%) with Positive CRP, positive culture was present in 6 (35.2%) cases while 11 (64.7%) cases showed no growth on culture. Similarly, out of total 33 cases (66%) with negative CRP, positive culture was present in 3 (9.09%) cases while 30 (90.9%) cases showed no growth on culture. In the present study, CRP had 66.6% sensitivity, 73.1% specificity and 35.2% positive predictive accuracy.

Table 2: Distribution of cases according to serum PCT levels

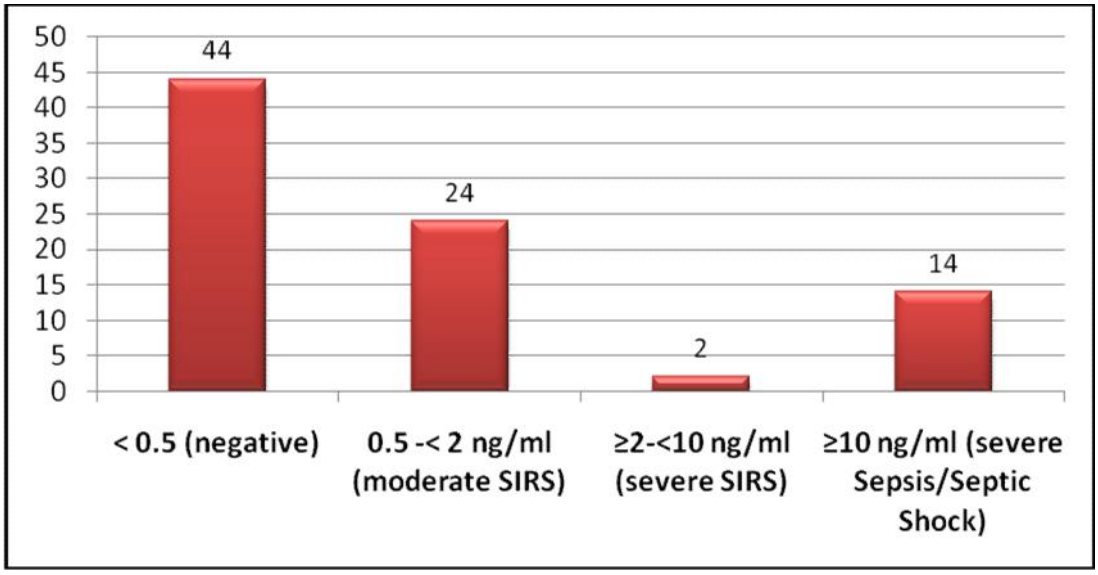

Table 3: Correlation of serum PCT levels with culture (n=50)

PCT	Culture		Total
	Positive culture	Negative culture	
Positive (≥0.5 ng/dl)	8	20	28
Negative (<0.5 ng/dl)	1	21	22
Total	9	41	50

Table 3: Out of total 28 cases (56%) showing positive serum PCT, positive culture was present in 8 (28.6%) cases while 20 (71.4%) cases showed no growth on culture.

Table 4: Comparison of CRP and serum PCT levels

Biomarkers		Positive cases	
		Number	%age
PCT		28	56%
CRP		17	34%
CHI Square Test	*p*-value<0.05	Significant	

The chi-square statistic is 4.8889. This result is significant (p <0.05).

Table 5: Mean PCT values according to the organism isolated on culture:

Organism		Frequency	Pct value
Gram negative bacteria (n=7)	*Kleibsiella pneumoniae*	3	14.1
	E. coli	4	21.6
Gram positive bacteria (n=2)	*Staphylococcus aureus*	2	9.33

Table 5: Mean PCT value was found to be highest in *E. coli* positive samples (21.6ng/ml), followed by *K. pneumoniae* (14.1ng/ml) and then *Staphylococcus aureus* (9.33ng/ml).

Table 6: Diagnostic accuracy in combination of any two tests:

Test	Result	Culture positive	Culture negative	Total	Statistics
Toxic granulation + platelet count	Positive	5	16	21	Sensitivity: 55.5% Specificity:60.9% Positive Predictive Value: 23.8%
	Negative	4	25	29	
	Total	9	41	50	
Toxic granulation +I/T ratio	Positive	6	7	13	Senstivity:66.6% Specificity:82.9% Positive Predictive Value 46.1%
	Negative	3	34	37	
	Total	9	41	50	
Toxic granulation + CRP	Positive	7	10	17	Senstivity:77.7% Specificity:75.06% Positive Predictive Value 41.1%
	Negative	2	31	33	
	Total	9	41	50	
Toxic granulation +PCT	Positive	8	9	17	Senstivity:88.8% Specificity:78% Positive Predictive Value 47.1%

	Negative	1	32	33	
	Total	9	41	50	
Platelet count + I/T ratio	Positive	4	6	10	Senstivity:44.4% Specificity: 85.3% Positive Predictive :40% Value
	Negative	5	35	40	
	Total	9	41	50	
Platelet count+ CRP	Positive	4	9	13	Senstivity:44.5% Specificity:78% Positive Predictive :30.7% Value
	Negative	5	32	37	
	Total	9	41	50	
Plateletcount+PCT	Positive	5	18	23	Senstivity:55.5% Specificity:56.1% Positive Predictive :21.7% Value
	Negative	4	23	27	
	Total	9	41	50	
CRP + I/T	Positive	4	5	9	Sensitivity: 44.4% Specificity:87.8% Positive Predictive :44.4% Value
	Negative	5	36	41	
	Total	9	41	50	
PCT+i/t	Positive	5	4	9	Senstivity:55.5% Specificity:90.2% Positive Predictive :55.5% Value
	Negative	4	37	41	
	Total	9	41	50	
CRP+PCT	Positive	6	8	14	Senstivity:66.6% Specificity:80.48% Positive predictive :42.8% Value
	Negative	3	33	36	
	Total	9	41	50	

Table 6: In our study, the best combination was toxic granulation with PCT which had sensitivity of 88.8%, specificity of 78% and PPV of 47.1%. Combination of PCT and I/T ratio had highest specificity (90.2%)

Discussion

Sepsis includes a cascade of inflammatory process whose diagnosis is complicated due to the nonspecific signs and symptoms. Neonatal sepsis, sepsis neonatorum and neonatal septicemia are terms that have been used to describe the systemic response to infection in newborn infants.[10]It is a challenging task to establish an ideal diagnostic marker of sepsis as most of these makers rise in any kind of non-infective inflammatory process. Neonatal sepsis with its high mortality rate still remains a diagnostic and treatment challenge for the neonatal health care providers.[11]

An early diagnosis of neonatal sepsis helps the clinician in instituting antibiotic therapy at the earliest, thereby reducing the mortality rates in the neonates. The blood culture not only takes time but it is also complicated with a low yield. The readily achievable complete blood count and the leucocyte differential assays have a relatively poor specificity for diagnosing sepsis. The associated band count and a leftward shift of the myeloid immaturity measurements may improve

the diagnostic yield but their subjective measurement is problematic. Therefore, new and efficacious laboratory tests are needed in the diagnosis of neonatal sepsis.[10]

Clinical manifestations of sepsis in the study population:

In the present study, most commonly observed clinical manifestations were fever (34%) followed by refusal to feed (20%) and respiratory distress (18%).This was in accordance with study conducted by Das et al. and Shashikala et al., which also reported refusal of feed (61%), respiratory distress (40%), convulsions (29%) and abdominal distension (23%) as common signs and symptoms.

Blood Culture:

Definitive diagnosis of neonatal sepsis is based on blood or CSF culture, both of which take at least 24 to 48 hrs. In the present study, among 50 cases of neonatal sepsis positive culture could only be isolated in 9 (18%) cases while negative culture was detected in 41 (82%) cases. Gram negative bacilli constituted the predominant isolate (77.7%) followed by the gram positive cocci (22.2%). Among gram negative organisms, most common was *E.coli* (44.4%) followed by *K.pneumoniae* (33.3%) and among gram positive organisms *Staphylococcus aureus* (22.2%) was the only bacteria to be isolated. Naher BS et al reported that blood culture was found positive only in 3 cases (6%) and negative in 47 cases (94%). It has been observed that usually Gram negative organisms are more common in late onset neonatal sepsis.

The mean PCT levels in our study were found to be highest in *E. coli* positive samples (21.6ng/ml), followed by *K. pneumoniae* (14.1ng/ml) and *Staphylococcus aureus* (9.33ng/ml). Thus, mean PCT values were higher in gram negative organisms as compared to gram positive organisms. The ability of PCT to discriminate infections by Gram positive or Gram –negative organisms have recently described in various studies. In accordance with our results, Charles et al in a retrospective study on 97 bacteremia episodes, found that serum PCT levels were markedly higher for Gram-negatives than Gram-positives.[12]

Sepsis screen:

Sepsis Screen is an extremely reliable index of early neonatal septicaemia, with less expenditure and serves as a good guide for initiating antibiotic therapy. As seen in most of the studies, conflicting results have been obtained in different studies on diagnostic accuracy of individual markers of sepsis screen. TLC, ANC, I/T ratio, morphological or degenerative changes in neutrophils such as vacuolisation, toxic granulation, and platelet count have been studied. In this study, sepsis screen was studied in culture positive and culture negative cases. Bacterial culture positivity gave definitive diagnosis of septicemia.

In our study, leukopenia had 28.5% sensitivity, 97.6% specificity and 66.6% positive predictive accuracy. Vandana G et al reported sensitivity 40.9%, specificity 79% & positive predictive accuracy 48% for the same.[13]

Our results showed that both sensitivity and positive predictive value of an abnormal WBC count is poor while other studies had shown only positive predictive value being poor. This can be explained on the basis that many non-infections conditions can be associated with an abnormal neonatal WBC count. Thus, the initial WBC with differential cell count may not be helpful in the decision to initiate antibiotic therapy for an asymptomatic new born infant with identified risk factor for sepsis. Nevertheless, it is common practice to perform these tests as a part of the immediate post natal assessment of the “at risk” infant.[14] Sucilathangam G. et al., also reported that the total WBC count was normal in 12 out of 13 cultures with proven sepsis. [15] Recently, Xanthou studied these changes more precisely in healthy and diseased neonates and established its usefulness as a supportive test for the diagnosis of neonatal sepsis.[16]

In the present study, toxic granulation had 100% sensitivity, 63% specificity and 37.5% positive predictive accuracy. Thus, it proves to be a sensitive marker in neonatal sepsis. Vandana S et al showed that toxic granulation had 68% sensitivity, 54% specificity and 31.25% positive predictive accuracy. Namedo et al observed toxic granulation had 80% sensitivity, 70% specificity and 69% positive predictive accuracy.[14,17]

In the present study, I/T ratio had 77.7% sensitivity, 83% specificity and 50% positive predictive accuracy. In accordance to our results, Basu S et al and Narasimha A et al reported that I/T PMN ratio and degenerative changes were the most reliable tests for diagnosing sepsis. An abnormal I/M PMN ratio was highly sensitive in identifying sepsis.[10,18]During the bacterial infections increased number of neutrophils are released from bone marrow into the blood stream providing neutrophils to migrate at the infected site. This appears to be essential for the host, resistant to bacterial infection. As more neutrophils are released, more and more immature cell reaches the circulation, a process called as “shift to left”. This finding have been found valuable in the early diagnosis of bacterial infection.[19]

Further in the present study, platelet count had 44.4% sensitivity, 95% specificity and 66.6% positive predictive accuracy. Thus, our result showed that it can be as reliable specific marker for neonatal sepsis.

In the present study, out of 50 neonates, 44% were PCT negative (serum PCT <0.5ng/ml) while Serum PCT levels was positive in 53% cases. Out of PCT positive cases (PCT ≥5 ng/ml), majority of the cases (28%) had PCT levels ≥ 10 ng/ml which indicates several bacterial sepsis/ septic shock; while least number of cases (4%) had PCT levels in range of ≥2- <10 ng/ml indicative of severe SIRS.

We observed that CRP had 66.6% sensitivity, 73.1% specificity and 35.2% positive predictive accuracy while serum PCT had 88.8% sensitivity, 51.2% specificity and 28.5% positive predictive accuracy. On comparison between serum PCT and CRP, the difference was statistically significant ($p < .05$).

In the present study, sensitivity and positive predictive value of serum PCT for detection of neonatal sepsis was higher than that of CRP. These findings support the usefulness of PCT over CRP in establishing an early diagnosis of neonatal sepsis.

Carol et al in their study showed that PCT is more sensitive than the CRP in the diagnosis of septicaemia, meningitis, urinary tract infections.[20]Chiesa et al reported that the sensitivity of diagnosing sepsis in neonates by PCT during the first 48 hours of life as 85.7%; the sensitivity of detecting late onset sepsis was 100%.[21]

Diagnostic accuracy of combination of markers of sepsis screen and biomarkers:

An ideal early diagnostic test for infection would have 100% sensitivity and specificity. Such an ideal test, however, is rather unlikely to be discovered, since most tests are measured on a continuous scale with an overlap between infected and non- infected infant.

As recent investigations have largely focused on advanced markers but many of these potential markers of sepsis besides being expensive and complex to perform, are still not routinely available to the laboratory especially in developing countries.

Furthermore, the greatest predictability usually not results from a single assay but with the combination of assays. So the focus of the researches was shifted to use markers of sepsis screen in combination for better diagnosis of neonatal sepsis. [22]

Accuracy in making early diagnosis of neonatal septicaemia by any test depends on sensitivity i.e., diagnosing infection when it is not present and positive predictive accuracy i.e., probability that a patient with a positive test result has, even when the disease in question.

In our study, the best combination was PCT with toxic granulation with a sensitivity of 88.8%, specificity of 78% and PPV of 47.1%. Combination of PCT with I/T ratio had highest specificity (90.2%). It was observed that when two on more tests were combined specificity and positive predictive accuracy were increased. Our observations are consistent with other studies which also observed that positive predictive accuracy and specificity of two test combination was higher than individual tests, at the cost of sensitivity. They also found that when two or more tests were combined the specificity was increased than the individual test.[22,23]

We hereby, suggest the use of combination of the two tests (including both septic screen and the latest diagnostic markers like PCT) for improved overall sensitivity, specificity and positive predictive value of these tests for a more reliable and definitive diagnosis.

Conclusion

Late-onset sepsis is one of the leading causes of morbidity and mortality in neonates. Its diagnosis is extremely challenging due to non specific clinical signs and symptoms which frequently mimic non infectious etiologies. Blood culture though diagnostic, is time consuming and often yields false-negative results. So, there is continuous research for the factors involved in the pathophysiology of neonatal sepsis that can uncover methods in recognizing and treating the disease. Recent use of markers like PCT and CRP has brought a new insight to the diagnosis of the neonatal sepsis. Based on our results, PCT proves to be a sufficiently reliable diagnostic marker in neonatal sepsis and in the evaluation of response of disease to the antibiotic therapy. As the current evidence shows no single factor can be used to diagnose sepsis but promising results have been seen when two of these factors are combined. Therefore, PCT alone and in combination with other tests can be used as diagnostic marker for the early diagnosis of neonatal sepsis.

Bibliography

1. Jaswal RS, Kaushal RK Goel A, Pathania K. Role of C-reactive protein in deciding the duration of the antibiotic therapy in neonatal septicaemia. Indian Paediatrics 2003;40:800-83.
2. Da Silva O, Ohlsson A, Kenyon C. Accuracy of leukocyte indicesand C-reactive protein for diagnosis of neonatal sepsis: a criticalreview. Pediatr Infect Dis J 1995;14:362-6.
3. Aneja R.K., Varughese-Aneja R., Vetterly C.G. and Carcillo J.A. (2011) Antibiotic therapy in neonatal and pediatric septic shock. Current infectious disease reports 13(5), 433-441.
4. Blommendahl J, Janas M, Laine S, Miettinen A, Ashorn P. Comparison of procalcitonin with CRP and the differential white blood cell count for the diagnosis of culture-proven neonatal sepsis. *Scand J Infect Dis* 2002;34:620-22.
5. Dandona P., Nix D., Wilson M.F., Aljada A., Love J., Assicot M. and Bohuon C. (1994) Procalcitonin increase after endotoxin injection in normal subjects. The Journal of Clinical Endocrinology & Metabolism 79(6), 1605-1608.
6. Brunkhorst F., Heinz U. and Forycki Z. (1998) Kinetics of procalcitonin in iatrogenic sepsis. Intensive care medicine 24(8), 888-889.
7. Kafetzis DA, Tigani GS, Costalos C. Immunologic markers in the neonatal period: their diagnostic value and accuracy in infection. Expert Rev MolDign2005;5:231-39.
8. Kibe S, Adams K, Barlow G. Diagnostic and prognostic biomarkers of sepsis in critical care. J AntimicrobChemother. 2011 Apr 1;66(suppl 2):ii33-ii40.
9. Thermo fisher. Referance Values for PCT in Sepsis Patients http://www.procalcitonin.com/clinical-utilities/sepsis/reference-values-sepsis.html(Accessed Nov 18,2015).
10. Narasimha A, Harendra Kumar ML. Significance of Hematological Scoring System (HSS) in Early Diagnosis of Neonatal Sepsis. Indian J Hematol Blood Transfus. 2011;27(1):14-7.
11. Pravin Charles MV, Kalaivani R, Venkatesh S, Kali A, Seetha KS. Evaluation of procalcitonin as a diagnostic marker in

neonatal sepsis. Indian J Pathol Microbiol 2018;61:81-4.
12. Charles PE, Ladoire S, Aho S, Quenot JP, Doise JM, Prin S, et al. Serum procalcitonin elevation in critically ill patients at the onset of bacteremia caused by either Gram negative or Gram positive bacteria. BMC Infect Dis. 2008;8:38.
13. Fanaroff A A, Korones S B, Wright L L et al., Incidence , presenting features, risk factors and significance of late onset septicaemia in very low birth weight infants. Pediatr infect Dis 1998; 17: 594-598.
14. Dr.G.Vandana, Dr.S.Lokeshraomagar, Dr. Praveen, Dr.B .Kavita. devi Dr. sandhya rani, Dr.sandhyaanil. Haematological Profile In Neonatal Septiceamia. Volume 16, Issue 4 Ver. IX (April. 2017), PP 11-17.
15. Sucilathangam G., Amuthavalli K., Velvizhi G., Ashihabegum M.A., Jeyamurugan T., PalaniappanN.Early Diagnostic Markers for Neonatal Sepsis: Comparing Procalcitonin (PCT) and C-Reactive Protein (CRP),2012 ; 6 (4): 627 – 631.
16. Xanthou M, Leucocyte blood picture in healthy full-term and premature babies during neonatal period. Archives of diseases in childhood1970;45;242-249.
17. Namdeo UK, Singh HP, Rajput VJ, Shrivastava KK, Bacteriological profile of neonatal septicemia. Indian pedriatrics 1987;24;53-59.
18. Basu S, Guruprasad, Narang A, Garewal G. The diagnosis of sepsis in high risk neonates by using a hematologic scoring system. Indian J Hematolo Blood Transfusion 1999;17:32-34.
19. Gupta SK, Sharma V, Gupta ML, Sharma DK, Acridine orange stain a rapid diagnosis of neonatal septicemia. Indian peadriatrics 1989;26;153-155.
20. Carol ED, Thomason AP, Hart CA. Procalcitonin as a marker of sepsis, Int J Antimicrob Agents 2002;20:1-9.
21. Chiesa C, Panero A, Rossi N, Stegagno M, De Giusti M, Osborn JF, et al. Reliability of procalcitonin concentrations for the diagnosis of sepsis in critically ill neonates. Clin Infect Dis. 1998;26:664–672.
22. K Misra, P & Kumar, Rashmi& K Malik, G &Mehra, P &Awasthi, Shally. (1989). Simple hematological tests for diagnosis of neonatal sepsis.Indian pediatrics. 26. 156-60.
23. Singh M, Naran A, Bhakoo O. Evaluation of a sepsis screen in diagnosis of neonatal sepsis. Indian pedriatrics 1987;24;39-43.

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