Comparison of procalcitonin and c-reactive protein with blood culture in early diagnosis of neonatal sepsis

Swati Karad[1], Desma D'Souza[2*], Sujata Baveja[3]

[1]Resident Medical Officer, [2]Assistant Professor, [3]Professor and HOD, Department of Microbiology, 4th floor, College Building, LTMMC and GH, Sion, Mumbai, Maharashtra, INDIA.
Email: drdesma@gmail.com

Abstract

Background: Neonatal sepsis is an invasive infection which occurs in the first four weeks of life and is a leading cause of morbidity and mortality in neonates. Early diagnosis of neonatal sepsis is very important in controlling morbidity and mortality. The aim of present study was to evaluate C-reactive protein (CRP) and Procalcitonin (PCT) as diagnostic markers for early diagnosis of neonatal sepsis in comparison with conventional blood culture. **Method:** Total 72 clinically suspected cases of sepsis in neonatal intensive care unit (NICU) were analyzed for clinical profile and risk factors. Blood samples were obtained from each neonate prior to administration of antibiotics and processed for blood culture, CRP and PCT test. **Results:** Out of 72 cases, 36.11% showed growth in blood culture, 68.05% showed significantly high CRP levels and 56.95% showed significantly high PCT levels. Taking blood culture as gold standard the sensitivity, specificity, PPV and NPV of CRP was found to be 100%, 50%, 53.06% and 100% respectively and the sensitivity, specificity, PPV and NPV of PCT was found to be 100%, 67.39%, 63.41% and 100% respectively. There were 38 cases positive by both CRP and PCT and 20 cases negative by both CRP and PCT. 11 cases were positive by CRP and negative by PCT and 3 cases were PCT positive and CRP negative. **Conclusion:** Both CRP and PCT help in early diagnosis of neonatal sepsis. But PCT test has higher specificity as compared to CRP test, thus should be incorporated routinely for early diagnosis of neonatal sepsis.
Key words: Neonatal Sepsis, C-reactive protein, Procalcitonin, Blood culture, Antibiotics, Sensitivity, Specificity.

Access this article online	
Quick Response Code:	**Website:** www.medpulse.in
	Accessed Date: 27 December 2019

INTRODUCTION

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life. It encompasses various systemic infections such as meningitis, pneumonia, arthritis, osteomyelitis, and urinary tract infections [1].The incidence of neonatal sepsis varies from 1 to 4 cases per 1000 live births in developed countries. According to the data from National Neonatal Perinatal Database (NNPD 2002-03) it is 30 per 1000 live births in India. Nearly one-fifth of neonates with sepsis die in the hospital; the figure rises to 50% for those with culture proven sepsis. They stay longer in the hospital, consume more resources and are also at a high risk of major neurodevelopmental disabilities at a later age [2]. Therefore timely diagnosis of neonatal sepsis is very important in controlling morbidity and mortality. The diagnosis of neonatal sepsis is based on clinical presentation and the laboratory investigations. Blood culture is the most valuable diagnostic method for neonatal sepsis and it is found to be positive in 25-54% cases.[3] Although blood culture is gold standard for diagnosis of neonatal sepsis and allows targeted antimicrobial therapy, its result may be delayed for up to

48 hours and it may yield negative results in many cases of septic shock. Haematological parameters useful in evaluation of neonatal sepsis are complete blood count, white blood cell count, absolute neutrophil count and immature/total neutrophil ratio, however these tests have low sensitivity and are nonspecific [4]. During the last decades efforts have been made to improve the laboratory diagnosis of neonatal sepsis by studying a large variety of inflammatory markers with diverse success. Some like PCT and CRP have demonstrated their benefit in clinical practice and have been implemented in neonatal intensive care units. Some studies reported that PCT is more reliable than CRP for the diagnosis of neonatal sepsis [5, 6] others did not find any advantage of PCT over CRP [7, 8]. Thus the present study was undertaken to find out the correlation between blood culture, serum PCT and CRP positivity in clinically suspected cases of sepsis in neonates admitted in the hospital and to compare the efficacy of CRP and PCT tests.

MATERIALS AND METHODS

After obtaining approval from the Institutional Ethics Committee, an observational study was conducted in Department of Microbiology at a Tertiary Care Hospital during the period of one year. A total of 72 patients admitted with suspected neonatal sepsis and antibiotic naive neonates were included in this study. Neonates with hematological disorders, any congenital abnormalities, neonates on corticosteroid / antimetabolite therapy and on antibiotics were excluded from the study. Written informed consent was taken from the guardian of child for participation in the study. A detailed history including the presenting complaints, past history and risk factor was elicited for each patient and duly recorded in the case record forms. Blood samples (2-3 ml) were collected from each neonate prior to administration of the antibiotics for the laboratory investigations of blood culture, serum CRP and serum PCT. The first 1 ml of blood was immediately inoculated into blood culture bottle containing tryptic soy broth after disinfecting the top of the bottle with an alcohol swab. Culture bottle was gently rotated to mix the blood and culture medium. Remaining 1-2 ml blood sample was collected in sterile vaccutainer tube. The blood culture bottle and sterile vaccutainer tube were transported immediately to the microbiology laboratory for further processing.

A) Blood Culture Processing

After receiving the blood culture bottle in microbiology laboratory it was incubated at 37°C overnight. After overnight incubation, first subculture was done on blood agar and MacConkey agar and plates were further incubated for 24 hrs at 37°C. The blood culture bottles were also re-incubated. Any growth on these plates was identified by standard biochemical tests [9]. Antibiotic susceptibility test was put for each growth as per CLSI 2015 guidelines. If there was no growth in first subculture, second subculture was done on fourth day and third subculture on seventh day and the same procedure as above was repeated. The bottle was discarded after seventh day, if there was no growth at all. For serum separation 1-2 ml of blood collected in sterile vaccutainer tube was allowed to clot. After centrifugation for 3000 RPM for 15 minutes, serum was separated and divided into 2 aliquots. First aliquot of serum was used for CRP detection immediately. It was performed by Omega Diagnostics rapid latex agglutination kit. [Kit used: DZE201120978; Lot no: 201502; Exp. date: 2015-08]. A positive result was indicated by the obvious agglutination pattern of the latex in a clear solution and a negative result was indicated by no change on the test slide. The other aliquot was was used for procalcitonin analysis using Sunred human Procalcitonin ELISA kit. [Kit used:7049947; Lot No:2015-02; Expiry date:2017-10]. The positive and negative controls were included for each test. The absorbance values were plotted and calculated on standard linear regression equation.

Statistical analysis

Statistical analysis was performed with the software package: PASW statistic 18 for Windows. The significance of difference of proportion of categorical variables among groups was examined by the chi-square test and difference in mean by student's t test. A value of P of ≤0.05 was considered significant for all statistical analysed.

OBSERVATIONS AND RESULTS

Out of 72 patients, 58.3% were male and 41.7% were female, (p>0.05). Male: Female ratio was 1.4:1. Maximum cases of neonatal sepsis belonged to age group less than 3 days (65.3%)followed by age group between 3-28 days (34.72%), (p<0.05).Mean age of the study cases was 4.6d ± 3.4days. Early onset neonatal sepsis (< 3days) was significantly higher than late onset sepsis (3-28 days). Most common presenting symptoms were poor feeding (68.1%),fever (25%) and birth asphyxia (22.2%) while jaundice (5.6%) and seizures (1.4%) were uncommon. This variation in percentage in presenting symptoms was found to be statistically significant (p<0.001). Out of 72 cases, 42 (58.3%) were term babies and 30 (41.7%) were preterm babies. The mean birth weight of the study cases was 1815g ± 342g, ranging from 820g- 2570g. Out of 72 cases, 26 (36.11%) were blood culture positive, 49 (68.05%) were CRP positive and 41(56.95%) were PCT positive as shown in figure 1. Taking blood culture as gold standard sensitivity, specificity, PPV and NPV of C-reactive protein and procalcitonin were analysed. (Table 1). All blood culture

positive samples were analyzed for type of organism and antimicrobial susceptibility of the isolated pathogen. The distribution of organisms isolated in blood culture is shown in figure 2. The most common organisms isolated were *Acinetobacter* species(27%), *Klebsiella pneumoniae* (19%), *E.coli* (19%) and *Enterobacter spp.*(15%). Out of 7 *Acinetobacter* species 71.4% were sensitive to ciprofloxacin and imipenem, 57.1% were sensitive to piperacillin-tazobactam and netilmycin, 42.9% were sensitive to amikacin and ampicillin-sulbactam, 14.35% were sensitive to cefotaxime and piperacillin. 28.6% *Acinetobacter* species were resistant to carbapenem but all were sensitive to tigecycline and colistin. Out of 5 *Klebsiella* species, 60% were sensitive to amikacin, ciprofloxacin, cefotaxime and imipenem. 20% were sensitive to netilmycin. 40% *Klebsiella* species were resistant to carbapenem. Out of 5 *Escherichia coli*, 60% were sensitive to netilmycin and 40% were sensitive to amikacin, ciprofloxacin, imipenem, piperacillin-tazobactam and 60% Escherichia coli were resistant to carbapenem. Out of 4 *Enterobacter* species 50% were sensitive to ciprofloxacin and imipenem; 25% were sensitive to amikacin, piperacillin; 50% were sensitive to carbapenem and 50% were multi drug resistant. Out of 4 Gram positive cocci, 2 were *Enterococcus species* sensitive to vancomycin and linezolid. There was single isolate of Methicillin sensitive *Staphylococcus aureus* (3.8%) (MSSA) and Methicillin sensitive coagulase negative *Staphylococcus* (3.8%), (MSCONS) and both were sensitive to all drugs except penicillin. Blood culture positivity indicated definitive sepsis and this was analyzed with presence and absence of risk factors, also with platelet count and total leucocyte count (Table 2). The variation in percentage of risk factors was found to be statistically significant (p<0.001). Total of 69 cases were analyzed for outcome and 3 cases were excluded from the analysis as their actual outcome is unknown. Out of 25 blood culture positive cases 12(48%) expired and 13(2%) were discharged whereas out of 45 blood culture negative cases 5(11.4%) expired and 39(88.6%) were discharged. This difference was found to be statistically significant, (p=0.001).

Table 1: Comparison of CRP and PCT positivity with Blood Culture as well as comparison of CRP positivity with PCT positivity (n=72)

CRP	Blood Culture		Total	p value
	Positive	Negative		
Positive	26 (100%)	23 (50%)	49 (68.1%)	<0.001
Negative	00 (0.0%)	23 (50%)	23 (31.9%)	
Total	26 (100%)	46 (100%)	72 (100%)	
PCT	Blood Culture		Total	
	Positive	Negative		
Positive	26 (100%)	15 (32.6%)	41 (56.9%)	<0.001
Negative	00 (0.0%)	31 (67.4%)	31 (43.1%)	
Total	26 (100%)	46 (100%)	72 (100%)	
CRP	PCT		Total	
	Positive	Negative		
Positive	38 (92.7%)	11 (35.5%)	49 (68.1%)	<0.001
Negative	3 (7.3%)	20 (64.5%)	23 (31.9%)	
Total	41 (100%)	31 (100%)	72 (100%)	

*p value ≤ 0.05 is significant

Table 2: Correlation of Risk Factors, platelet and total leucocyte count (TLC) with Blood Culture Positivity

Risk Factors		Blood Culture Positive (n=26)	Blood Culture Negative (n=46)	Total	P Value
PROM		21 (80.8%)	20 (43.5%)	41 (56.9%)	0.002*
Intrapartum Fever		4 (15.4%)	8 (17.4%)	12 (16.7%)	0.826
UTI during pregnancy		7 (26.9%)	14 (30.4%)	21 (29.2%)	0.753
Chorio-Amnionitis		9(34.6%)	9 (19.6%)	18 (25.0%)	0.157
Low birth weight		24 (92.3%)	31 (67.4%)	55 (76.4%)	0.017*
Meconium stained Liquor		9 (34.6%)	3 (6.5%)	12 (16.7%)	0.002*
Gestational Age	<37 week	20 (76.9%)	10 (21.7%)	30 (41.7%)	<0.001*
	>37 week	06 (23.1%)	36 (78.3%)	42 (58.3%)	
Platelets count	<1.5 lakhs	12 (46.15%)	11 (23.91%)	23 (31.94%)	0.773
	1.5 lakhs	14 (53.85%)	35 (76.08%)	49 (68.06%)	
TLC	<5000	5 (19.23%)	6 (13.04%)	11 (15.28%)	0.214
	5000-20000	14 (53.85%)	39 (84.78%)	53 (73.61%)	
	>20000	7 (26.92%)	1 (2.17%)	8 (11.11%)	

*p value ≤ 0.05 is significant
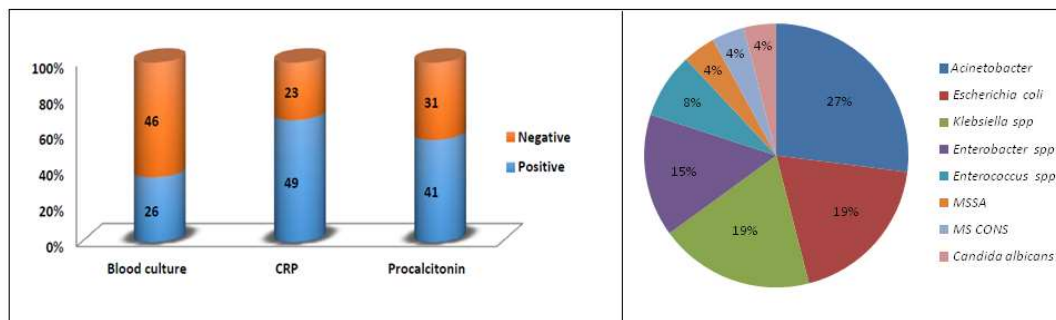
Figure 1   **Figure 2**

Figure 1: Percentage Positivity of Blood Culture, C - reactive protein, Procalcitonin in Study Cases (n= 72); **Figure 2:** Distribution of organisms isolated in blood culture (n=26)

Methicillin sensitive Staphylococcus aureus (MSSA), Methicillin sensitive coagulase negative Staphylococcus (MS CONS)

DISCUSSION

Male predominance was observed in the present study. Male: female ratio was 1.4:1. These findings are in concordance with the study done by M Mutlu et al [24] but discordant with the study done by Naglaa et al [29]. Early onset neonatal sepsis (65.3%) was higher than late onset neonatal sepsis (34.72%) in this study as seen in the study done by Basu et al [30] and Zahedpasha et al [31]. In current study the most common presenting symptom was poor feeding, fever, birth asphyxia and vomiting. Katua et al [32] and by NK Anand et al [11] also observed that refusal to feeds, lethargy, diarrhea, temperature abnormality, abdominal distension, jaundice and vomiting were among the most common presenting features. These studies show that clinical features of neonatal septicaemia are nonspecific and may be clinically indistinguishable from those occurring in non-infectious conditions during neonatal period. In the present study the most common maternal risk factors observed were PROM, UTI, chorioamnionitis and intrapartum fever. Similar findings were observed by Bhat et al [34] and Naher et al [5]. Present study did not observe an association between prematurity and risk of neonatal sepsis and this finding correlates with the study done by Gebremedhin et al [12]. However, in the study done by Vinay B S et al [36], Basu et al [30] and M Mutlu et al [24] prematurity was found to be a risk factor. In present study maximum cases had birth weight less than 2000 g. Mean birth weight was 1815 ± 342gm. These findings correlated well with study done by M Mutlu et al [24] and Basu et al [30]. It was thus seen that infection was more common in low birth weight baby as compared to normal birth weight babies. Out of 72 cases 36.11% were blood culture positive and 63.89% were blood culture negative. Sepsis cannot always be excluded even when blood cultures are found to be negative. Inoculation of only 0.5-1 ml of blood decreases blood culture sensitivity, as approximately 60-70% of infants have a low level of

bacteremia. Theoretically for optimal results, 6 ml of blood required which is not feasible [16] hence there is need for an alternative solution. CRP is an acute phase reactant and highly sensitive indicator of infection. It is synthesized by the liver and is increased up to 1000 fold within 4-6 hours of an inflammatory process.[39] Its level rapidly declines with elimination half-life of 19 hours.[38] Use of CRP for the diagnosis of neonatal sepsis has been widely studied. CRP is easy, rapid, cost effective and readily available test. In the present study 49 cases were C-reactive protein positive. 23 cases were positive by C-reactive protein and negative by blood culture. Taking blood culture as a gold standard sensitivity of C-reactive protein was 100%, specificity was 50%, positive predictive value was 53.06% and negative predictive value was 100%. The CRP sensitivity, specificity, PPV and NPV were found to be 100%, 75%, 77% and 100% respectively in a study by Gandhi T et al [40] and 100%, 87.3%, 88.3% and 100% respectively in a another study by Anuradha et al[41]. These findings correlate well with present study. In a study by Boo et al [42] CRP sensitivity, specificity, PPV and NPV were found to be 55.6%, 89.9%, 58.8% and 88.6% respectively. This finding is discordant with present study. PCT a precursor of calcitonin is a 116 amino acid protein secreted by the C cells of thyroid gland in normal situation but its levels increase in septicaemia, meningitis, pneumonia and urinary tract infection.[44,45] It is also produced by macrophage and monocyte cells in severe bacterial infection and sepsis.[46] In the present study 41 cases were procalcitonin positive. 15 cases were positive by procalcitonin and negative by blood culture. Taking blood culture as gold standard sensitivity of procalcitonin was 100%, specificity was 67.39%, positive predictive value was 63.41% and negative predictive value was 100%. The PCT sensitivity, specificity, PPV and NPV were found to be 92.8%, 75.0%, 59.0% and 96.0% respectively

in a study by In Sucilathangam *et al*(37) and in another study by Vazzalwar *et al* [47], sensitivity of PCT was found to be 97% and the specificity was 80%. In a another study by Bonac *et al*[43] sensitivity of procalcitonin was 59%, specificity was 82%,positive predictive value was 36% and negative predictive value was 96%. These findings are discordant with present study. In the present study all blood culture positive cases were positive by C-reactive protein and Procalcitonin test. Sensitivity of CRP and PCT was 100% in detecting neonatal sepsis. Specificity of PCT was 67.4% and specificity of CRP was 50%. Thus PCT has better specificity than CRP in detecting neonatal sepsis. Both PCT and CRP were found to have the same sensitivity and negative predictive value. Koksal *et al* [48] study also concluded that procalcitonin level was superior to CRP in terms of an early diagnosis of neonatal sepsis. PCT is highly specific for bacterial infection and it helps differentiating it from viral infection. PCT helps in an early diagnosis of the sepsis on the day of the admission itself, before the blood culture report is ready (usually after 3-5 days). PCT helps in avoiding antibiotic therapy where it is not [49] required and thereby reducing the cost and the occurrence of bacterial resistance. PCT can also be employed for the prognosis of sepsis. Nelly *et al* [50] concluded that PCT is more reliable than CRP for the diagnosis of neonatal sepsis. In contrast in Blommendahl *et al* [51], Janota *et al* [52], Koskenvuo*et al* [33] *and* Perez solis *et al* [35] study the specificity of PCT was found to be lower than that of CRP.

CONCLUSION

Neonatal sepsis is an important cause of morbidity and mortality in developing countries. Therefore an early diagnosis of neonatal sepsis will help to reduce morbidity and mortality. Blood culture is routinely used diagnostic method for neonatal sepsis but it lacks timeliness to influence initiation of antibiotic therapy. Thus newer rapid diagnostic markers like CRP and PCT help in early diagnosis of neonatal sepsis. In this study both CRP and PCT tests showed 100% sensitivity but Procalcitonin ELISA test showed higher specificity (67.39%) as compared to C-reactive protein test which has specificity (50%) and should thus be incorporated routinely for early diagnosis of neonatal sepsis.

REFERENCES

1. Sankar MJ, Agarwal R, Deorari AK, Paul VK. Sepsis in the newborn. The Indian Journal of Pediatrics. 2008; 75(3):261-6.
2. Bang AT, Bang RA, Baitule S *et al*. Burden of morbidities and the unmet need for health care in rural neonates-a prospective observational study in Gadchiroli, India. Indian Pediatr. 2001; 38:952-65.
3. Kayange N, Kamugisha E, Mwizamholya DL, Jeremiah S, Mshana SE. Predictors of positive blood culture and deaths among neonates with suspected neonatal sepsis in a tertiary hospital, Mwanza-Tanzania. BMC pediatrics. 2010; 10(1):1.
4. Resch B, Hofer N, Müller W. Challenges in the Diagnosis of Sepsis of the Neonate. INTECH Open Access Publisher; 2012.
5. Naher BS, Mannan MA, Noor K, Shahidullah M. Role of serum procalcitonin and C-reactive protein in the diagnosis of neonatal sepsis. Bangladesh Medical Research Council Bulletin. 2011; 37(2):40-6.
6. Joram, N., C. Boscher, S. Denizot, V. Loubersac. Umbilical cord blood procalcitonin and C reactive protein concentrations as markers for early diagnosis of very early onset neonatal infection. Arch Dis Child Fetal Neonatal, 2006; Ed 91: F65-F66.
7. Koskenvuo MM, Irjala K, Kinnala A, *et al*. Value of monitoring serum procalcitonin in neonates at risk infection. Eur J Clin Microb Infect Dis 2003; 22(6): 377–8.
8. Perez Solis D *et al*. Procalcitonin for the diagnosis of bacterial neonatal infections of vertical transmission. An Pediatr (Barc) 2006; 64(4):341–8.
9. Standard biochemical test Culture of bacteria and Tests for the identification of bacteria. In Mackie and McCartney's Practical Medical Microbiology. 14th Ed. Eds. Collee JG, Fraser AG, Marmion BP, Simmons A. Churchil Livingstone, Elsevier imprint. 2006;122(3):131-49.
10. Khatua S, Das A, Chaterjee B.Neonatal septicaemia. J Pediatr.1986;53(4):509-14.
11. Anand NK, Gupta AK, Mohan M, Lamba IM, Gupta R, Srivastava L. Coagulase negative staphylococcal septicemia in newborns. Indian pediatrics. 1991; 28(11):1241-8.
12. Gebremedhin D, Berhe H, Gebrekirstos K. Risk Factors for Neonatal Sepsis in Public Hospitals of Mekelle City, North Ethiopia, 2015: Unmatched Case Control Study. PloS one. 2016; 11(5): e0154798.
13. Agarwal A, Bhat S. Clinico-microbiological study of neonatal sepsis. Journal of International Medicine and Dentistry. 2015; 2(1):22-9.
14. Khan SN, Joseph S. Neonatal sepsis: antibiotic sensitivity and resistance pattern of commonly isolated pathogens in a neonatal intensive care unit of a tertiary care hospital, South India. Int J Pharm Bio Sci. 2012; 3(4):802-9.
15. Al-Zahrani AK, Ghonaim MM, Hussein YM, Eed EM, Khalifa AS, Dorgham LS. Evaluation of recent methods versus conventional methods for diagnosis of early-onset neonatal sepsis. The Journal of Infection in Developing Countries. 2015; 9(04):388-93.
16. Shah BA, Padbury JF. Neonatal sepsis: an old problem with new insights. Virulence. 2014; 5(1):170-8.
17. Nelly, Tjipta GD, Hakimi, Lubis BM. Procalcitonin as a diagnostic tool for bacterial neonatal sepsis. Paediatrica Indonesiana. 2015; 55(5):268-72.
18. Carol ED, Thomason AP, Hart CA. Procalcitonin as a marker of sepsis. Int J Antimicrob Agents 2002; 20:1-9.
19. Arora U, Jaitwani J. Acinetobacter spp. - an emerging pathogen in neonatal septicemia in Amritsar. Indian J Med Microbiol. 2006; 24:81.
20. Vinodkumar CS, Neelagund YF. Acinetobacter septicemia in neonates. Indian J Med Microbiol. 2004; 22: 71.

21. Desai KJ, Malek SS. Neonatal Septicemia: Bacterial Isolates and Their Antibiotics Susceptibility Patterns. NJIRM 2010; 1(3):12-5.
22. Shah AJ, Mulla SA, and Revdiwala SB. Neonatal sepsis: high antibiotic resistance of the bacterial pathogens in a neonatal intensive care unit of a tertiary care hospital. Journal of Clinical Neonatology 2012;1(2):72–75.
23. Aurangzeb B, Hameed A. Neonatal sepsis in hospital-born babies: bacterial isolates and antibiotic susceptibility patterns. J Coll Physicians Surg Pak 2003: 13; 629-632.
24. Mutlu M, Aslan Y, Saygin B, Yilmaz G, Bayramo Lu G, Koksal I. Neonatal sepsis caused by Gram-negative bacteria in a neonatal intensive care unit: a six year analysis.HK J Paediatr 2011:16:253-7.
25. Gebrehiwot A, Lakew W, Moges F, Moges B, Anagaw B, Unakal C, Kassu A. Predictors of positive blood culture and death among neonates with suspected neonatal sepsis in Gondar University Hospital, Northwest Ethiopia. Euro. J. Exp. Bio. 2012;2(6):2212-8.
26. Swarnkar K, Swarnkar M. A Study of Early Onset Neonatal Sepsis with Special Reference to Sepsis Screening Parameters in a Tertiary Care Centre of Rural India. The Internet Journal of Infectious Diseases. 2012; 10(1):36-42.
27. Shrestha S, Singh SD, Shrestha NC, Shrestha RP, Madhup SK. Comparision of clinical and laboratory parameters in culture proven and unproven early onset sepsis in NICU. Kathmandu University Medical Journal. 2015; 11(4): 310-4.
28. Turkish Neonatal Society; Nosocomial Infections Study Group. Nosocomial infections in neonatal units in Turkey: epidemiology, problems, unit policies and opinions of healthcare workers. Turk J Pediatr 2010: 52; 50-7.
29. Naglaa FB, Abeer S, Mohammad A *et al*. Procalcitonin and C- Reactive Protein as Diagnostic Markers of Neonatal Sepsis. Australian Journal of Basic and Applied Sciences, 2012; 6(4): 108-14.
30. Basu R, Bandyopadhyay S. Study on Correlation between Sepsis Screening and Blood Culture in Neonatal Sepsis. IOSR Journal of Dental and Medical Sciences (IOSR JDMS). 2014 May; 13(5):52-6.
31. Zahedpasha, Y., M. Ahmadpour Kacho, M. Hajiahmadi, M. Haghshenas, 2009.Procalcitonin as a Marker of Neonatal Sepsis. Iran J Pediatr, 19(2): 117-122.
32. Khatua S,Das A,Chaterjee B.Neonatal septicaemia.J Pediatr.1986;53(4):509-14.
33. Koskenvuo MM, Irjala K, Kinnala A, *et al*. Value of monitoring serum procalcitonin in neonates at risk infection. Eur J Clin Microb Infect Dis. 2003; 22(6):377–8.
34. Bhat AA, Shamim A, Gul S, Akther R, Bhat I. Neonatal sepsis-Early detection comparing Procalcitonin and CRP as markers and newer tools. Ijmds 2016 v5i 1/83574
35. Perez Solis D, Lopez Sastre JB, Coto Cotallo GD, *et al*. Procalcitonin for the diagnosis of bacterial neonatal infections of vertical transmission. An Pediatr (Barc) 2006; 64(4):341–8
36. Vinay BS, Girish GN, Adhikari S, Hugara S. Evaluation of Septic Screen as a Diagnostic Tool for Neonatal Sepsis in a Tertiary Hospital at Mysore. Sch.J.App.Med.Sci.2015;3 (2G):1005-10.
37. Sucilathangam G, Amuthavalli K, Velvizhi G, Ashihabegum GA, Jeyamurugan T, Palaniappan N. Early diagnostic markers for neonatal sepsis: comparing procalcitonin and C-reactive protein. J Clin Diag Res 2012; 6:627–631.
38. Weitcamp J, Aschner J. Diagnostic use of C-reactive protein in assessment of neonatal sepsis. Am Acad Pediatr 2005;6:508-15
39. Bataineh HA, Al-Rashid KM. C-reactive protein in neonates with suspected septicaemia. Rawal Med J 2007;32:24-26
40. Gandhi TN, Patel MG, Jain MR, Saxena RB, Bhuva PJ. Utility of C Reactive Protein as Inflammatory Marker in Early Diagnosis of Neonatal Septicaemia: A Cross Sectional Study. National Journal of Medical Research. 2012; 2(4):481-3.
41. De A, Saraswathi K, Gogate A, Raghavan K. C - reactive protein and Buffy coat smear in early diagnosis of childhood septicemia. Indian J Pathol Microbiol.1998; 41(1):23-26.
42. Boo NY, Nor Azlina AA, Rohana J. Usefulness of a semi-quantitative procalcitonin test kit for the early diagnosis of neonatal sepsis. Singapore Med J 2008; 49:204-08.
43. Bonac B, Derganc M,Wraber B, Hojker S. Interleukin-8 and procalcitonin in early diagnosis of early severe bacterial infection in critically ill neonates. Pflugers Arch-Eur J Physiol 2000; 440: 72-74.
44. Gendrel D, Bohoun C. Procalcitonin as a marker of bacterial infection. Pediatr Infect Dis J. 2000; 19(8):679-87.
45. Assicot M, Gendrel D, Carsin H *et al*. High serum procalcitonin concentrations in patients with sepsis and infection.Lancet.1993; 341(8844):515-518.
46. Dandona P, Nix D, Wilson MF *et al*. Procalcitonin increase after endotoxin injection in normal subjects. J Clin Endocrinol Metab.1994;79(6):1605-08
47. Vazzalwar R, Pina-Rodrigues E, Puppala BL, Angst DB, Schweig L. Procalcitonin as a screening test for late-onset sepsis in preterm, very low birth weight infants. J Perinatol 2005; 25:397-402.
48. Koksal N, Harmanci R, Getinkaya M. The roles of procalcitonin and CRP in the diagnosis and the follow up of neonatal sepsis cases. Turk J Paediatr 2007; 49:219.
49. Da Silva O, Ohlsson A, Kenyon C. Accuracy of leukocyte indices and C-reactive protein for diagnosis of neonatal sepsis:a critical review. Pediatr Infect DisJ.1995;14(5):362–366.
50. Nelly, Tjipta GD, Hakimi, Lubis BM. Procalcitonin as a diagnostic tool for bacterial neonatal sepsis. Paediatrica Indonesiana. 2015 Sep 1; 55(5):268-72.
51. 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.
52. Janota J, Stranak Z, Bělohlávková S, Mudra K, Šimák J. Postnatal increase of procalcitonin in premature newborns is enhanced by chorioamnionitis and neonatal sepsis. European journal of clinical investigation. 2001; 31(11): 978-83.

Source of Support: None Declared
Conflict of Interest: None Declared