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Original Research Article

A STUDY OF SERUM PROCALCITONIN LEVEL AS AN EARLY DIAGNOSTIC TOOL FOR NEONATAL SEPSIS

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ABSTRACT

Background: Infants with early onset sepsis (EOS) usually present with respiratory distress and pneumonia. Early recognition is very important but is notoriously difficult as the clinical signs of sepsis mimic almost every other neonatal problem. PCT has been shown to be useful not only in the diagnosis but also monitoring the prognosis and response to treatment of patients with neonatal sepsis. This study aims to evaluating procalcitonin as an early or first line marker in the diagnosis of neonatal septicemic infection.

Materials & Methods: A hospital based observational study done on neonates suspected to have neonatal sepsis based on their clinical symptoms and risk factors admitted NICU in SPMCHI and attached group of hospital SMS Medical College, Jaipur during one year period after approval of institutional ethical committee. The procalcitonin level of 0.5 ng/ml was considered as abnormal. The cut off point of the diagnostic test was determined by ROC curve analysis. Apart from Serum procalcitonin level, complete blood count with Absolute neutrophil count, CRP, Blood culture, serum calcium, serum phosphorus serum urea, serum creatinine, serum bilirubin, SGOT, SGPT blood sugar of neonate was investigated. Data was collected and then subjected to statistical evaluation.

Results: Our study showed that overall mean age of patients was 2.21±2.236 days, in proven sepsis cases was 2.02 ± 2.34 days, in suspected sepsis cases was 2.46± 2.38 days and serum procalcitonin positive cases was 2.01 ± 2.26 days. The S PCT level (> 0.5 ng/ml) positive 58 cases out of 61 shows sensitivity 96.66%, S PCT (< 0.5 ng/ml) Negative seen in 91 cases out of 93 shows specificity 96.80% and PPV 95.08% and NPV was 97.80%. A plot ROC curve (AUC= 0.827), the prevalence of disease 39.60% at admission and cut off value was >0.5 ng/ml with a statistically significant (p<0.001**). Out of 154 study population maximum cases were sterile (60.93%) in blood culture, in proven sepsis (61 cases) most commonly isolated organism was staphylococcus aureus (32.79%) followed by klebsiella (19.67%).

Conclusion: We concluded that a competent diagnostic marker also needs to have a reasonably high specificity and a good positive predictive value, preferably better than 85%, in order to minimize unnecessary use of antibiotics in false positive cases. On comparing single, combination of two or more than two sepsis markers PCT alone had highest sensitivity (96.66%) and negative predictive value (97.80%).

Keywords: Neonatal Sepsis, Serum Procalcitonin, EOS, LOS, Culture.

INTRODUCTION

Neonatal sepsis is characterized by signs and symptoms of infection with or without accompanying bacteraemia in the first 28 days of life. Bacterial infection in the newborn account for considerable morbidity and mortality, as the newborn especially the premature are prone to serious infections by organisms and partly because

the signs of these infections may be absent or minimal and are hard to detect.[1] Hence the timely diagnosis of sepsis in neonates is important as the illness can be rapidly progressive and in some instances fatal.[2]

Worldwide neonatal sepsis is responsible for 4 million deaths annually, most of them occur in developing countries3 where mortality rate is between 11-68 per 1000 live birth. Neonatal sepsis is responsible for about 30-50% of the total neonatal deaths in developing countries.[4,5]

As per National Neonatal Perinatal Database (NNPD) 2002-2003 suggest that Klebsiella pneumoniae is the most frequent cause of sepsis followed by Staphylococcus aureus in India.6 Neonatal diagnosis may be difficult as the early signs of sepsis may be subtle and different at different gestational ages.[6]

Infants with early onset sepsis (EOS) usually present with respiratory distress and pneumonia. The source of infection is generally the maternal genital tract. Some maternal/perinatal conditions have been associated with an increased risk of EOS. Knowledge about these potential risk factors would help in early diagnosis of sepsis. 85% of newborns with early onset infection present within 24 hours, five percent present at 24-48 hours and smaller percentage of patients between 48 hours and 6 days of life.[6]

Late onset sepsis (LOS): It is usually presents after 72 hours of age. The source of infection in LOS is either nosocomial (hospital-acquired) or community-acquired and neonates usually present with septicaemia, pneumonia or meningitis.[3,4]

This life-threatening condition is treatable if diagnosed early but unfortunately, the early signs and symptoms are often non-reliable and confusing which makes it difficult to establish an early clinical diagnosis.[7]

As a result of this uncertainty, antibiotics are often started on the slightest clinical suspicions of sepsis. This approach is effective in fighting against acute infections but increases the risks of antibiotics induced side effects and the emergence of drug resistant organisms in neonatal units.[7,8]

Early recognition is very important but is notoriously difficult as the clinical signs of sepsis mimic almost every other neonatal problem. Blood culture which is the gold standard for the confirmation of neonatal sepsis is associated with high false negative rate, it being positive in only up to 50–60% of cases.[9] The inability of any single laboratory test to provide rapid, reliable, and early identification of infected (and, as importantly, non-infected) neonates has led to a search for other diagnostic markers.[9]

Concentrations of PCT exceeding 0.5ng/ml are interpreted as abnormal values suggestive of a sepsis syndrome. Concentrations above 10 ng/ml are found in patients with severe sepsis. PCT serum concentration will increase within 2-3 hours of beginning of infection peaking by 6-12 hours and return to normal concentration in 2 days. Half-life of PCT is 20-24 hours and this enables not only rapid detection but also response to treatment. PCT has been shown to be useful not only in the diagnosis but also monitoring the prognosis and response to treatment of patients with neonatal sepsis.[10]

The return to baseline is usually rapid and the second peak of PCT is interpreted as development of a new episode. Estimation of PCT levels has been reported to be useful for critically ill patients with severe systemic inflammatory response.[10] This study aims to evaluating procalcitonin as an early or first line marker in the diagnosis of neonatal septicaemic infection.

MATERIALS AND METHODS

A hospital based observational study done on neonates suspected to have neonatal sepsis based on their clinical symptoms and risk factors admitted NICU in SPMCHI and attached group of hospital SMS Medical College, Jaipur during one year period after approval of institutional ethical committee. Written informed consent was obtained from all subjects at the time of enrolment.

Inclusion Criteria

- All neonates suspected of neonatal sepsis based on their symptoms and risk factors
- Prior informed consent

Exclusion Criteria

- Refusal for consent
- Major congenital anomaly
- Anaemia or icterus within 48 hrs of administration

Suspected neonates for neonatal sepsis

1. Prematurity
2. Febrile illness in the mother within 2 weeks of delivery
3. Foul smelling or meconium-stained liquor
4. Prolonged rupture of membrane >18 hours.
5. Single unclean or more than 3 sterile vaginal examination
6. Prolonged labor >24 hours
7. Difficult delivery with instrumentation or birth asphyxia.

Newborns with any of the following features were kept under clinical sepsis category

1. Neurological (convulsions, irritability, drowsiness, abnormal Moro's reflexes, decreased activity, bulging fontanels),
2. Respiratory (RR>60/min, grunting, apnea, chest in drawing, central cyanosis),
3. Cardiovascular (capillary refill time more than 3 seconds, rapid and weak pulse, pallor, mottling, bradycardia or tachycardia),
4. Abdomen (abdominal distension, increased Residual of feeding, significant vomiting or loose stools),
5. Skin (pustules, petechiae, periumbilical erythema or purulent discharge, deep jaundice),

6. Musculoskeletal (bone or joint tenderness, joint swelling /effusion),
7. Temperature instability (temperature>99.9 F or <95.9 F),
8. Poor feeding.
9. Renal impairment. (decreased urine output, edema).

Methods

Blood sample for procalcitonin level was taken before antibiotics administration. Blood smear was obtained from the venous blood in tubes without anticoagulant and blood cultures were performed to confirm diagnoses of septicemia. Two ml of venous blood were taken using a 2 ml syringe, put into transport medium for the bactec culture method and two ml of venous blood also was taken for serum procalcitonin level centrifuged for 15 minutes, and the serum examined by Cobas 6000. The procalcitonin level of 0.5 ng/ml was considered as abnormal.

Sensitivity, specificity, positive predictive value, and negative predictive value of procalcitonin were determined using a 2x2 table with 95% confidence intervals. The cut off point of the diagnostic test was determined by ROC curve analysis.

Apart from Serum procalcitonin level, complete blood count with Absolute neutrophil count, CRP, Blood culture, serum calcium, serum phosphorus serum urea, serum creatinine, serum bilirubin, SGOT, SGPT blood sugar of neonate was investigated. Data was collected and then subjected to statistical evaluation.

Statistical Analysis

Correlation between two variables was analyzed using Pearson correlation coefficient. A p value < 0.05 was taken as statistically significant. All statistical analyses were done using Epi info version 7.2.1.0.

RESULTS

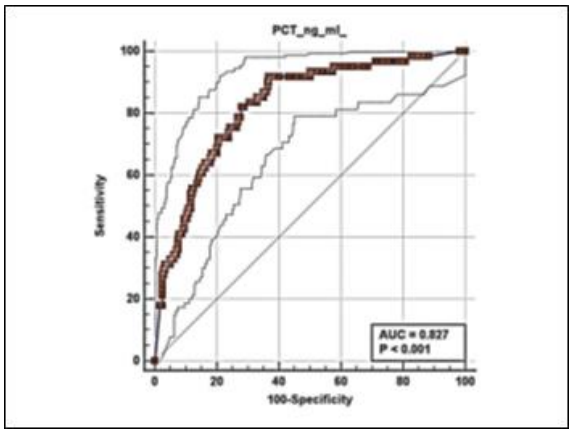

Figure 1: ROC curve depicting PCT as a diagnostic tool for identification of neonatal sepsis

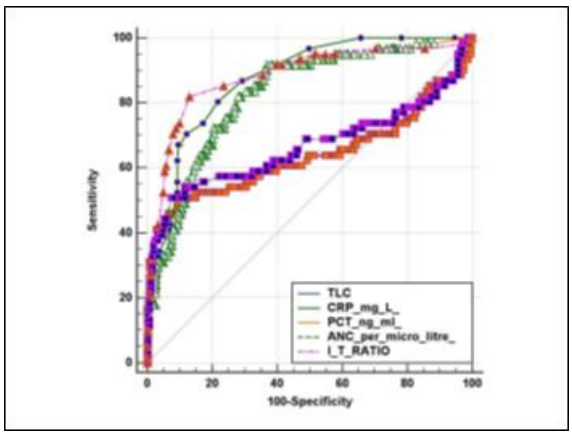

Figure 2: Comparison of ROC curves

Our study showed that overall mean age of patients was 2.21±2.236 days, in proven sepsis cases was 2.02 ± 2.34 days, in suspected sepsis cases was 2.46± 2.38 days and serum procalcitonin positive cases was 2.01 ± 2.26 days. Among the total 154 children, 93(60.39%) were males and 61(39.61%) were females and ratio was1.52:1. Out of 61 proven sepsis cases were females and ratio was1.65 1, 1.4 1 in suspected sepsis cases and 1.73:1 in serum procalcitonin positive cases.

Mean gestational age was 34.82±2.78 weeks and birth weight were 2.13±0.71kg in study population (table 1).

Respiratory symptoms were present in most no. of cases i.e. 92(59.74%) cases out of which culture was positive in 23(14.93%) cases, second most common observation was poor feeding (19.48%) out of which blood culture was positive in 23(14.93%) cases. P-value was statistically significant in respiratory symptoms and poor feeding (table 2).

Our study shows that S PCT level (> 0.5 ng/ml) positive 58 cases out of 61 shows sensitivity 96.66%, S PCT (< 0.5 ng/ml) Negative seen in 91 cases out of 93 shows specificity 96.80% and PPV 95.08% and NPV was 97.80% (table 1). A plot ROC curve (AUC= 0.827), the prevalence of disease 39.60% at admission and cut off value was >0.5 ng/ml with a statistically significant (p<0.001**) (Figure 1).

We have taken various parameters with different cut-off values (i.e. platelets<1.5 lacs per ml, TLC ≤5440, CRP>9 etc.). All these parameters were found statistically significant which explained the reliability of any single test as a biomarker in diagnosing neonatal septicemia (Figure 2).

The present study shows that sepsis proven group has more deranged hepatic and renal parameters as compared to suspected sepsis. This is statistically significant (p-value<0.05) and also denotes that hepatic and renal derangement may be a part of generalized host infection (Table 4).

Out of 154 study population maximum cases were sterile (60.93%) in blood culture, in proven sepsis (61 cases) most commonly isolated organism was staphylococcus aureus (32.79%) followed by klebsiella (19.67%) (table 5).

In the present study most, common organism isolated in blood culture was Staphylococcus aureus which was most sensitive to vancomycin (70%) followed by ofloxacin (65%). Coagulase –ve Staphylococcus was most sensitive to amikacin (46.15%), Klebsiella was maximum sensitive to amikacin (100%) followed by imipenem (91.67%), E.coli was maximum sensitive to amikacin (100%) followed by levofloxacin (66.67%), Pseudomonas was maximum sensitive to ceftazidime (80%) and Piperacillin+ tazobactam (80%), Enterococcus to linezolid (100%) and nalidixic acid (100%) (table 6)

Table 1: Clinical characteristics of patients

		No of Cases (n) (N=154)	Proven sepsis cases (N=61)	Suspected sepsis cases (N=93)	Serum procalcitonin positive cases (N=60)
Mean Age (in days)		2.21±2.36	2.02 ± 2.34	2.46± 2.38	2.01 ± 2.26
Gender	Male	93 (60.39%)	38 (62.30%)	55 (59.14%)	38 (62.30%)
	Female	61 (39.61%)	23 (37.70%)	38 (40.86%)	22 (36.67%)
Mean gestational age (weeks)		34.82±2.78	34.61 ± 2.34	35.65± 2.85	34.26 ± 2.24
Mean Birth Weight (Kg)		2.13±0.71	2.03 ± 0.60	2.11 ± 0.74	2.01 ± .36

Table 2: Associated comorbidity in proven and suspected sepsis cases

INDICATION	Proven sepsis (n=61)	Suspected sepsis (n=93)	Total (n=154)	Percentage	P value
Respiratory distress	23	69	92	59.74	0.0001
Grunting	03	00	03	1.95	0.208
Fever	06	01	07	4.54	0.09
Meconium-stained liquor	00	03	03	1.95	0.605
Abdomen distension	03	00	03	1.95	0.100
Poor feeding	23	07	30	19.48	0.0001
Convulsion	02	00	02	1.30	0.184
Birth Asphyxia	15	08	23	14.93	0.001
Pustules	01	00	01	0.65	0.203
Not passing urine	00	02	02	1.30	0.587

Table 3: Co-relation of serum procalcitonin level with proven and suspected sepsis cases

S. procalcitonin level (ng/ ml)	Blood Culture results positive	Blood Culture results Negative
Positive (> 0.5ng/ml)	58	2
Negative (<0.5ng/ml)	3	91
Total	61	93

Table 4: Hepatic and Renal derangements of study population

Investigations	Proven sepsis (n=61)	Suspected sepsis (n=93)	P value
Blood sugar (mg/dl)	99.13±41.0	97.39±30.74	0.715
Urea (mg/dl)	63.03±29.73	41.36±16.03	<0.0001
Creatinine (mg/dl)	1.25±0.66	0.70±0.38	<0.0001
Bilirubin Total	8.60±4.93	5.78±3.15	<0.0001
Bilirubin Direct	1.13±0.63	0.72±0.38	<0.0001
SGPT	43.18±15.70	40.61±18.01	0.308

Table 5: Microbiological spectrum of culture proven sepsis

Organism	Culture proven sepsis	
	Frequency	Percentage (%)
Sterile	93	60.39
Staph aureus	20	32.79
Klebsiella	12	19.67
E. coli	9	14.75
Coagulase Negative Staphylococci	9	14.75
Pseudomonas	5	8.2
Enterococci	2	3.28
Non-Hemolytic Streptococci	1	1.64
Acinetobacter	1	1.64
Candida	1	1.64
Citrobacter	1	1.64

Table 6: Blood culture sensitivity pattern

Antibiotics	Staph aureus [n=20]	Coagulase –ve Staph [n=13]	Klebsiella [n=12]	E.coli [n=9]	Pseudomonas [n=5]	Enterococcus [n=2]
Ampicillin	00	00	00	00	00	00
Cefotaxime	00	00	01 (08.33%)	00	00	00
Amikacin	08 (40.0%)	06 (46.15%)	12 (100%)	09 (100%)	02 (40%)	00
Gentamicin	00	03 (23.80%)	00	00	00	00
Colistin	00	01 (7.69%)	06 (50%)	00	00	00

Piperacillin+ tazobactam	09 (45.0%)	05 (38.46%)	04 (33.33%)	05 (55.56%)	04 (80%)	02 (100%)
Levofloxacin	06 (30.0%)	00	01 (08.33%)	6 (66.67 %)	01 (20%)	00
Ofloxacin	13 (65%)	00	00	05 (55.56%)	00	00
Vancomycin	14 (70.0%)	00	00	00	00	00
Imipenem	01 (5.0%)	01 (7.69%)	11 (91.67%)	04 (44.44%)	02 (40%)	00
Linezolid	12 (60.0%)	03 (23.80%)	00	00	00	02 (100%)
Ceftriaxone	04 (20.0%)	02 (15.38%)	00	03 (33.33%)	00	00
Cefoperazone	00	00	00	00	01 (20%)	00
Ceftazidime	00	00	00	00	04 (80%)	00
Ticarcillin	00	00	00	00	02 (40%)	00
nalidixic acid	00	00	00	00	00	02 (100%)
Amoxiclav	00	02 (15.38%)	00	00	00	00

DISCUSSION

Neonatal sepsis with its high mortality and morbidity despite the use of higher antibiotics and advanced supportive care still remains a diagnostic and treatment challenge to the health care providers. An early and prompt diagnosis helps in the institution of therapy at the earliest and also prevents the unnecessary use of antibiotics thereby keeping the emergence of drug resistance in check.

Bacterial sepsis is the main cause of morbidity and mortality in neonates. Early diagnosis and appropriate treatment can reduce the mortality rate. Blood culture is the gold standard for diagnosis of bacterial sepsis, but it requires 3-5 days for results since the disease may progress rapidly in neonates, a faster diagnostic test is needed. Measurement of procalcitonin levels may be a quick method to diagnose bacterial sepsis in neonates.

In our study, a total of 154 neonates were enrolled on the basis of inclusion and exclusion criteria as described in methodology. A total of 61 newborns (39.61%) out of 154 had positive blood culture. That was the proven sepsis group in which blood culture was positive. In the remaining 93 (60.39%) newborns blood culture was negative. Our sample size was similar to the study done by Rajarshi Basu et al,[11] on 164 neonates found that 39 had positive blood culture and López Sastre et al,[12] On 152 neonates, 63 had serum procalcitonin. A similar study conducted by Arkder R et al,[13] found that out of 173 patients 99 (57%) had a final diagnosis of systemic infection. PCT level was significantly higher in neonates in all sepsis groups in comparison with those in control group.

According to gender, the study population had 93 (60.39%) males and 61 females (39.61%) with male: female ratio was 1.52:1. The male to female ratio was 1.65:1 in proven sepsis, 1.45:1 in suspected sepsis. In a study conducted by Champa Panwar et al,[14] they also observed that male has more prone to sepsis rather than female. Similarly, study conducted by Yadolla Zahedpasea et al,[15] and Minoo Adib et al,[16] showed male preponderance with 52.7% male 47.5% female, 60% male 40% females respectively. Hence in this study sepsis was found to be more common in males which could be because of the attitude of parents who seek medical services more for their male babies than female babies in this region. The reason for male preponderance is unknown but this could be due to sex dependant factors. The synthesis of gamma globulins is probably regulated by X linked immunoregulatory genes and as males are having one X chromosome, they are more prone for neonatal septicaemia than females.[17]

Out of 154 newborns admitted, maximum 67 (43.50%) were of gestational age 37 weeks or more. While minimum 4 (2.60%) newborns had gestation of ≤ 28 weeks, 43 (27.92%) had gestational age of 28 to 32 weeks and 40 (25.97%) newborns had gestational age between 32 to 37 weeks. The mean gestational age of study population was 34.82 ± 2.78 weeks. The mean gestational age of newborns with proven sepsis was 34.65±2.34 weeks, 35.65±2.85 weeks of newborns with suspected sepsis. There was no statistically significant difference in mean gestational age of the two groups ($p<0.05$). This was similar from the study done by Vinod Kumar et al,[18] in their study they stated that preterm babies were significantly more susceptible to infection than term babies (61.9% vs 16 40.4%; $P<0.001$).

Birth weight of maximum 60 (38.96%) newborns out of 154 was between 1.5 to 2.49 kg. 56 (36.36%) had birth weight 2.5 kg to 3.49 kg, 31 (20.13%) had birth weight 1 to 1.49 kg, 6 (3.89%) had weight more than 3.5 kg and 1 (0.64%) newborn had weight less than 1 kg. The mean birth weight of the study population was 2.13 ± 0.71 kg. The mean birth weight of newborns with proven sepsis was 2.03±0.60 kg which was low than the mean birth weight of newborns with suspected sepsis that was 2.11±0.74 kg. There was no statistically significant difference in mean weight of the two groups ($p=0.230$). This was in accordance with the studies done by Hakeem et al,[19] and Adib et al.[20] This could be because of prematurity being a risk factor for sepsis and infections being more common in low-birth-weight babies.

Out of 154 newborns, maximum 92 (59.74%) had respiratory symptoms followed by 30(19.48%) with poor feeding as the main symptoms requiring admission in NICU. There was a statistically significant difference found for these two presenting symptoms with proven sepsis. Others were having fever (5%) etc. This was very similar to the study done by Rajarshi Basu et al,[11] who also found that the common clinical manifestations of neonatal sepsis were respiratory distress and poor feeding.

In our study creatinine was deranged in 52(33.77%) cases out of which Serum PCT level was positive in 36(69.23%) cases and creatinine was normal in 102 (66.23%) cases out of which Serum PCT level was positive in 25(24.03%) cases. By applying chi square test we found P value <0.0001 which was highly significant. Similarly, we also found that thrombocytopenia was significant in newborns with Serum PCT positive cases (66.66%) implying that inflammation leads to platelet destruction. It was statistically significant with p-value<0.001. A similar study by Champa et al,[14] found that neonatal thrombocytopenia had high sensitivity of 90.3%, NPV of 93.8%, specificity of 71.8% and PPV of 60.8% in terms of sepsis.

A total of 55 (18.33%) of newborns had abnormal TLC in our study. As TLC level≤ 5440/microlitre was considered as abnormal according to the value derived with the help of ROC curve. Taking ≤ 5440/microlitre as the cut off for to be positive screen, the sensitivity was found to be 50.82%, specificity was 89.96%, positive predictive value was 56.40%, negative predictive value was 87.80% and accuracy was 82%. The odds ratio for TLC was 9.25 and median was 10800/microlitre. In the study done by Vinod Kumar CS et al,[18] in their study they found that TLC had sensitivity of 58%, NPV of 28% with a PPV of 87% However, they took the cut off of <10000/microlitre. In their study NPV was very low and PPV was more than our study.

CRP level more than 9mg/l was considered as positive according to the derived value with the help of ROC curve. the sensitivity was found to be 80.83%, specificity was 78.24%, positive predictive value was 48.50%, negative predictive value was 94% and accuracy was 78.70%. The odds ratio for CRP was 14.68 and median was 8.0. In Ho Park et al,[21] found that the sensitivity and specificity of CRP were 100% and 78.09%, respectively, with a diagnostic threshold of 6 mg/L, and 100% and 85.66% with a threshold of 10 mg/L and considered CRP as a highly accurate marker of sepsis. Similarly, Dhanlakshmi et al,[22] also found sensitivity, specificity and positive predictive value of 90.2%, 100% and 100% respectively which was higher than our study. Adib et al,[20] found that at a cutoff value of 12 mg/l CRP was found to have a sensitivity of 45%, specificity of 95%, positive predictive value (PPV) of 30%, negative predictive value (NPV) of 30% for the diagnosis of neonatal sepsis.

PCT was said to be positive when value was>2.4ng/ml which was derived with the help of ROC curve. Out of them blood culture was positive in 58 newborns (96.66%) and only 3 newborns (4.91%) with positive blood culture had normal PCT levels. The P value was <0.0001 and this relation was highly statistically significant. This infers that most of the babies who had proven sepsis had elevated PCT levels.

After considering the value of PCT>0.5ng/ml to be positive, we found sensitivity 96.66%, specificity 96.80%, Positive Predictive Value 95.08%, Negative Predictive Value 97.80%. Hakeem et al,[19] detected significantly higher levels of PCT in newborns with sepsis compared to the control group (p=0.001). Usharani et al,[23] found that of all the diagnostic markers, PCT level had the highest correlation with culture positive cases.

In our study PCT has maximum sensitivity (91.80%) and negative predictive value(96.80%), micro- ESR has maximum specificity(92.82%) and positive predictive value (75.41%) while I/T ratio has maximum accuracy(86%) as tested separately and when tested as a combination we found maximum sensitivity(91.80%) was seen when PCT and I/T ratio were combined, maximum specificity(86.80%) was seen when TLC and ANC were combined, similarly maximum positive predictive value(55%) was seen when ANC and micro-ESR were combined, combination of PCT and I/T ratio shows maximum negative predictive value(96.80%), while maximum accuracy (82%) was seen when ANC and micro-ESR were combined. A study by Sowmya Thayi et al,[24] found the sensitivity of procalcitonin is 88.88%, specificity is 75%, Positive predictive value is 61.5%, and negative predictive value is 93.75%, which was similar to our study. Ghaliyah Aziz Kutty et al,[25] found specificity of micro-ESR76.50% and positive predictive value of 57.90%.

Rajarshi Basu et al,[11] found maximum sensitivity (54.62%) and NPV (71.86%) when CRP and TLC were combined, maximum specificity (96.15% for each) when CRP+I/T Ratio and micro-ESR+I/T Ratio were combined and maximum PPV (87.76%) seen when CRP and I/T Ratio were combined, and they also found that combination of more than two parameters had less diagnostic value. In their study all these combinations of two parameters were statistically significant (p-value<0.001).

The gold standard for diagnosis of septicaemia is the isolation of bacterial agents from blood culture. The total number of culture positive cases were found to be 61 (20.33%) out of 300 newborns. Out of these 61 cases, 40(65.57%) were presented with in 72hrs (EOS) and 21(34.43%) cases were presented after 72 hrs (LOS). This was similar to the study done by Jayanta Debnath et al,[26] there they found that number of cases were more in EOS (57.5%) than LOS (42.5%). In our study there was no statistically significant difference found between early onset sepsis and late onset sepsis when all haematological parameters for sepsis screen were compared.

In both early onset (30% out of 40 cases) and late onset sepsis (38.1% out of 21), most commonly isolated organism was staphylococcus aureus. The 2nd most common organism in early onset sepsis was E. coli (20% out of 40 cases) while in late onset sepsis it was klebsiella (33.33% out of 21 cases). V. L. Jayasimha et al,[27] found in their study that the most frequent isolate was Klebsiella pneumonia 22 (35.4%) in both EOS and LOS. In a study by Jayanta Debnath et al,[26] found that Staphylococcus

aureus was most commonly isolated in EOS (49.3%) followed by klebsiella (36.9%).

The most frequent organism isolated in our study was Staphylococcus aureus in 20 newborns (32.79%) followed by klebsiella in 12 newborns (19.67%). Among the isolates, a considerable percentage of CONS (14.75%) as pathogen could be due to immature immune system development of a large population of premature and debilitated newborns. E coli and Pseudomonas were gram negative pathogens found in 09(14.75%) and 05 (8.2%) newborns respectively. Enterococcus, non haemolytic streptococci, Citrobacter, Candida and Acinetobacter were also isolated although very few in numbers. Staphylococcus aureus which was most sensitive to vancomycin (70%) followed by ofloxacin (65%). Coagulase –ve Staphylococcus was most sensitive to amikacin (46.15%), Klebsiella was maximum sensitive to amikacin (100%) followed by imipenem (91.67%), E.coli was maximum sensitive to amikacin (100%) followed by levofloxacin (66.67%), Pseudomonas was maximum sensitive to ceftazidime (80%) and Piperacillin+ tazobactam (80%), Enterococcus to linezolid (100%) and nalidixic acid (100%).This was against the findings of Dhanlakshmi et al,[22] who found gram negative bacteria in 90% of their newborns with Klebsiella being the most common in 68.29% newborns. Gram positive coagulase negative staphylococcus was found in only 9.76% newborns. Similarly, Mustafa et al,[28] also found that gram negative organisms were more than gram positive organisms, constituting about 65% of total isolates. The most frequent isolate was Klebsiella pneumonia 22 (35.4%) in both EOS and LOS. Staphylococcus aureus was the commonest Gram-positive organism and was the second most common organism among all isolates in their study. All Gram-negative isolates were having considerable sensitivity to Amikacin and Ciprofloxacin but were highly susceptible to Meropenem (100%) and Colistin (100%). The Gram-positive isolates showed high susceptibility to Linezolid and Vancomycin which was similar to our study.

Usharani et al,[23] also found a contrary result with the commonest organism isolated being Klebsiella pneumoniae (31%), followed by E. coli (20.6%), Acinetobacter (13.8%) and Staphylococcus aureus (13.8%), CONS (10.4%), Citrobacter (6.9%) and Pseudomonas aeruginosa (3.5%).

CONCLUSION

We concluded that PCT has maximum sensitivity (96.66%) and negative predictive value (97.80%). A competent diagnostic marker also needs to have a reasonably high specificity and a good positive predictive value, preferably better than 85%, in order to minimize unnecessary use of antibiotics in false positive cases. On comparing single, combination of two or more than two sepsis markers PCT alone had highest sensitivity (96.66%) and negative predictive value (97.80%). These findings suggest that high PCT can be used to screen blood culture positive sepsis, if PCT is negative, the possibility of sepsis is very low.

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