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Original Research Article

Comparison between sepsis markers and blood culture in diagnosis of neonatal sepsis: a prospective study

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ABSTRACT

Background: Neonatal septicaemia is one of the commonest causes of neonatal mortality and morbidity. Accurate and timely diagnosis of neonatal sepsis remains a major challenge to the pediatricians and neonatologists. In the present study, correlation between sepsis screening and blood culture in neonate presenting with features of sepsis is done to accelerate the diagnostic process and blood culture (considered gold standard) was evaluated as marker for sepsis detection and its effectiveness was compared with other septic markers.
Methods: In present study, we emphasize to study early indicators of sepsis screen and their statistical correlation with blood culture (considered as gold standard).
Results: As any sepsis screen parameters showed little correlation with blood culture, yet on combination it was found that specificity and positive predictive accuracy increased while sensitivity decreased them individual tests. Also combination of tests yield better results than single tests.
Conclusions: The combination of sepsis makers yielded diagnostic results than single tests and proved to be an invaluable aid for early diagnosis of neonatal sepsis.

Keywords: Blood culture, Neonatal sepsis, Sepsis screen

INTRODUCTION

Neonatal Septicemia is one of the commonest causes of neonatal mortality and morbidity. Accurate and timely diagnosis of neonatal sepsis remains a major challenge to the pediatricians and neonatologists. According to national neonatal perinatal database (NNPD) 2000 neonatal sepsis is the most common cause of deaths in the country followed by prematurity and birth asphyxia.[1,2]

Early treatment is possible with the support of certain indirect markers such as neutropenia (<1800 cells/mm^3), leucopenia (<5000 cells/mm^3), band cells, micro ESR and C-reactive protein (CRP) which are collectively known as sepsis screen and aids in early diagnosis of neonatal sepsis in absence of negative blood cultures.[3-5]

Thus, in presence of high risk factors; early clinical suspicion, combined with sepsis screen will detect neonatal septicemia earlier which will enable the paediatricians to treat the infection timely and thus reduce neonatal morbidity and mortality.[6,7] In the present study, correlation between sepsis screening and blood culture in neonate presenting with features of sepsis is done to accelerate the diagnostic process and blood culture (considered gold standard) was evaluated for sepsis detection and its effectiveness was compared with other septic markers.

Aim of the study was to study of comparison between sepsis screening and blood culture (considered Gold standard) in diagnosis of neonatal Sepsis also to evaluate effectiveness of various sepsis markers.

METHODS

A Prospective Study design was used to evaluate the efficacy and to study on comparison between sepsis screening and blood culture in early diagnosis of neonatal sepsis. This is a hospital based study conducted in M.G.M Medical College and Hospital, Navi Mumbai, Maharashtra, India from July-2009 to August-2011(2 years).

Eighty neonates (40 study group and 40 control group), delivered in the hospital, having risk factors for neonatal sepsis, along with those coming to hospital with signs and symptoms of sepsis up to 28 days of life (study group) also normal newborns admitted to the postnatal ward without high risk factors (control group) were enrolled for this study.

Inclusion criteria

- As study group

1. Newborns with high-risk factors for sepsis
2. Suspected newborns based on sepsic score system

- As control group

1. Normal newborns admitted to the postnatal ward without high risk factors

Exclusion criteria

- Babies who were referred to our hospital and who had received antibiotics (oral or I.V) prior to their admission
- Severe hepatic and renal dysfunction
- Major cardiac, respiratory, CNS or gastrointestinal or congenital malformations
- Refusal of parental consent

This study was approved by Ethical Committee of this hospital. Informed Written Consent was obtained from parents before entry into this study.

Information of selected neonates including detailed history and clinical examination was recorded on a predesigned proforma. In this study, following laboratory tests were done as soon as presumptive diagnosis of sepsis was made based on septic score system and on clinical grounds also on normal healthy newborns. All investigations were done within 24 hours of birth or at presentation before starting antibiotics.

Data analysis

Data was collected, classified, tabulated and analyzed. Tests of significance were applied at appropriate places and interpretation was done accordingly. To evaluate the difference between the categories, McNemar Chi Square test was used as a test of significance. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Of total of 80 cases, with risk factor and clinical signs and symptoms of sepsis (40 cases as study group) and normal healthy newborns without risk factors (40 cases as control group).

The study group consists of 28 males (70%) and 12 females (30%) while control group consists of 21 males (52.50%) and 19 females (47.50%). Among 40 babies of study group, 24(60%) are blood culture (BacTalert) positive and16 (40%) are blood culture (BacTalert) negative while in control group, 1 (2.50%) is blood culture (BacTalert) positive and 39 (97.50%) are blood culture (BacTalert) negative (Figure 1).

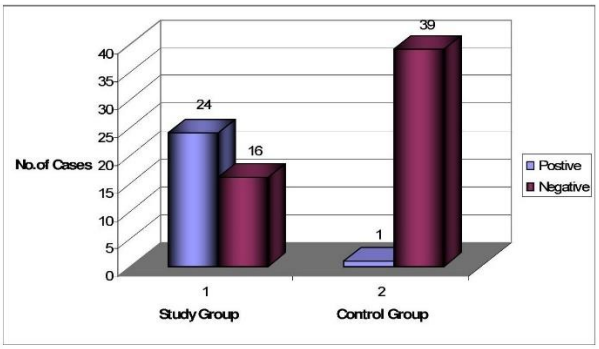

Figure 1: Distribution of cases according to blood culture (BacTalert).

In study group, *E-coli* comprised the maximum number of cases accounting for sepsis i.e. 7 (17.5%) followed by 5 cases (12.5%) of *Acinetobacter baumanii*, 5 cases (12.5%) of *Klebsiella Pneumoniae*, 2 cases (5%) each for *Citrobacter* and *Staphylococcus aureus* and 1 case (2.5%) has shown *Pseudomonous Sp*., *Burkholderia cepacia* and Fungus while no growth in 16 (40%) cases. In control group, only 1 case (2.5%) shows growth of *Acinetobacter baumanii and* 39 cases (97.5%) are sterile (Table 1).

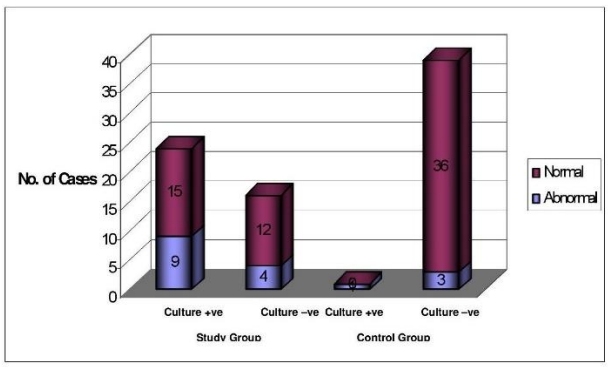

Figure 2: Distribution of cases according to CBC.

Out of 40 cases in study group, CBC is abnormal in 13 cases (32.5%), Blood Culture (BacTalert) was positive in 24 cases (60%) and 4 cases (10%) has CBC abnormal with sterile blood culture (Figure 2).

Table 1: Distribution of cases according to microbiological growth on blood culture (BacTalert).

Study Group			Control group		
Organism	**No. of cases**	**%**	**Organism**	**No. of cases**	**%**
E. Coli	7	17.5	*Acinetobacter baumanii*	1	2.5
Acinetobacter baumanii	5	12.5	-	-	-
Klebsiella Pneumoniae	5	12.5	-	-	-
Citrobacter	2	5	-	-	-
Staphylococcus aureus	2	5	-	-	-
Pseudomonous Sp.	1	2.5	-	-	-
Burkholderia cepacia	1	2.5	-	-	-
Fungus	1	2.5	-	-	-
Sterile	16	40	Sterile	39	97.5
Total	40	100	Total	40	100

Out of 40 cases in study group, Micro-ESR is abnormal in 18 cases (45%), Blood Culture is positive in 24 cases (60%) and 6 cases (15%) has Micro ESR abnormal with sterile blood culture (Figure 3). Same group of patients are tested with both Blood Culture (BacTalert) as well as sepsis markers.

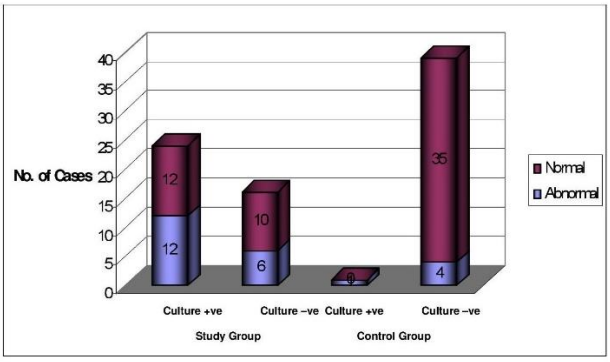

Figure 3: Distribution of cases according to microESR.

Table 2: Statistical correlation between septic markers.

Statistical analysis		
Sensitivity	95.83%	Chi-square (X^2) = 0.083
Specificity	87.50%	
Positive predictive value	92.00%	Degree of Freedom <1
Negative predictive value	93.33%	p-value <1.00
Accuracy	92.50%	

Therefore McNemar's (ChiSquare) test is used to evaluate whether results of these tests vary significantly from each other. It is observed that the results of both tests are statistically significant from each other with $x^2 = 0.083$, p-value <1.00 and degree of freedom <1 (Table 2). There is statistically significant difference between Blood Culture (BacTalert) and septic markers (p<1). Hence blood culture (BacTalert) is gold standard in diagnosis of neonatal sepsis whereas in combination of CBC can pinpoint accurate and specific diagnosis.

Table 3: Sensitivity, specificity, PPV, NPV and accuracy of various sepsis markers.

Tests	Sensitivity	Specificity	PPV	NPV	Accuracy
CBC	37.50%	75.00%	69.23%	44.44%	52.50%
Micro-ESR	50.00%	62.50%	66.67%	45.45%	55.00%
IT Ratio	62.50%	56.25%	68.18%	50.00%	60.00%
CRP	84.21%	28.57%	51.61%	66.67%	55.00%

IT Ratio has shown Sensitivity of 62.50%, Specificity of 56.25%, Positive Predictive Value of 68.18%, Negative Predictive Value of 50.00% and Accuracy of 60.00%. (Table 3) (Figure 4).

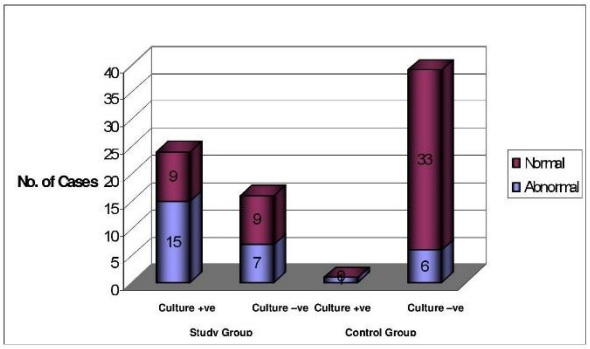

Figure 4: Distribution of cases according to IT ratio.

Micro-ESR has shown sensitivity of 50.00%, specificity of 62.50%, positive predictive value of 66.67%, negative predictive value of 45.45% and accuracy of 55.00% (Table 3). CRP has shown Sensitivity of 84.21%, Specificity of 28.57 %, Positive Predictive Value of 51.61 %, Negative Predictive Value of 66.67% and Accuracy of 55.00 % (Table 3) (Figure 5).

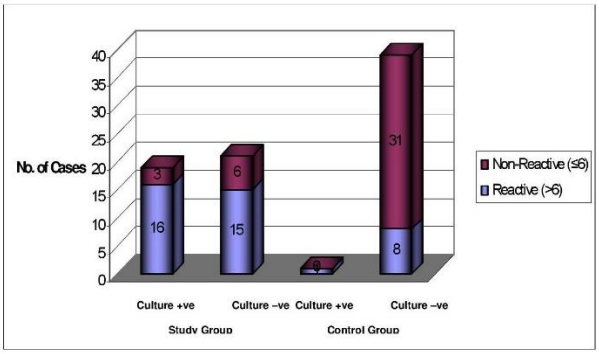

Figure 5: Distribution of cases according to CRP.

CBC has shown sensitivity of 37.50%, specificity of 75.00%, positive predictive value of 69.23%, negative predictive value of 44.44% and accuracy of 52.50% (Table 3). Thus, CRP has maximum sensitivity and CBC specificity in comparison with other septic markers in early detection of neonatal sepsis.

DISCUSSION

This study includes total of eighty cases (40 Study Group and 40 Control Group) with risk factor and clinical signs and symptoms of sepsis on basis of septic score system (as study group) also normal healthy newborns without risk factors (as control group).

The study group consists of 28 males (70%) and 12 females (30%) while control group consists of 21 males (52.50%) and 19 females (47.50%). Males have been reported to be more likely than females to develop septicemia as revealed in this study. Faridi et al also reported 66.67% males and 33.33% females out of 63 cases of neonatal septicemia. Male-Female ratio in their series was 2:1.[8] In this study of 80 cases, 22 (55%) were preterms and 18 (45%) were full terms in Study Group (n-40) while there are no preterms and all 40 (100%) are full term newborns in Control Group (n-40). This shows increased risk of neonatal sepsis in premature newborns.

This is similar to the observation made by Faridi et al where 53.97% preterms and 46.03% fullterms neonates.[8] In this study, prematuirty and LBW are leading high risk factors for sepsis in 55% of the newborns, followed by 35% of the newborns have meconium stained amniotic fluid, 25% of the newborns have premature rupture of membrane for >24 hours, 25% of the patients have birth asphyxia or and difficult resuscitation, 22.5% have prolonged or difficult labour, 20 % of the newborns have febrile illness in the mother, 20% of the newborns have >3 per-vaginal examination and 25% have other risk factors like multiple gestation, home delivery, unsterile cord handling and cutting technique, faulty feeding practices, nursing in unhygienic environment, etc.[9]

These are all considered as the possible high risk factors for development of sepsis in newborns. The most important risk factors for neonatal sepsis are prematurity and low birth weight as reported by Jain et al in their study.[10] Blood culture is the gold standard method to diagnose septicemia. In the present study, only 60% of cases with high risk factors as per septic score system also on clinical suspicion of sepsis are found to be culture showing 60% positivity.

Out of these total 80 selected cases, blood culture (BacTalert) has shown growth in 24 cases (60%) and out of these 24 cases, 23 have bacterial growth on culture and remaining 1 case showed fungal growth in the study group (n-40) while blood culture (BacTalert) is positive in 1 case (2.5%) and negative in 39 cases (97.5%) in the control group (n-40). The most common organism grown on blood culture is *E. Coli* (17.5%) followed by *Acinetobacter baumanii* (12.5%) and *Klebsiella Pneumoniae* (12.5%) both are the second most common pathogens. Other organisms are *Citrobacter* (5%), *Staphylococcus aureus* (5%), *pseudomonas* (2.5%), *Burkholderia cepacia* (2.5%) and fungus (2.5%).

Jain et al analyzed the signs and symptoms of neonatal sepsis in 106 neonates with suspected sepsis out of which 30 were culture positive.[10] The most common organism was *E. coli* which is like this study. Out of 40 cases in study group, CBC is abnormal in 13 cases (32.5%), Blood culture (BacTalert) is positive in 24 cases (60%) and 4 cases (10%) have CBC abnormal with sterile blood culture. Thus, in this study CBC has Sensitivity of 37.50%, Specificity of 75.00%, Positive Predictive Value of 69.23%, Negative Predictive Value of 44.44% and Accuracy of 52.50%.

Philip et al in their study found that 50% newborns with sepsis had Leucopenia.[11]

Out of 40 cases in study group, CRP is reactive in 31 cases (77.5%), Blood culture (BacTalert) is positive in 24 cases (60%) and 15 cases (37.5%) have CRP positive with sterile blood culture. Thus in this study CRP reported to have Sensitivity of 84.21%, Specificity of 28.57%, Positive Predictive Value of 51.61%, Negative Predictive Value of 66.67% and Accuracy of 55%.

Out of 40 cases in study group, MicroESR is significant in 18 cases (45%), Blood Culture (BacTalert) is positive in 24 cases (60%) and 6 cases (15%) have MicroESR significant with sterile blood culture. Thus, microESR has shown sensitivity of 50.0%, specificity of 62.5%, positive predictive value of 66.67%, negative predictive value of 45.45% and accuracy of 55%.

Out of 24 blood culture positive cases, 23 cases revealed bacterial pathogen and all these cases also have variable positive sepsis screen. Out of 40 cases of the study group, 16 cases have sterile blood culture while in the control group, 39 cases are having sterile blood culture and 1 case shows growth. In present study, neonatal mortality is seen in 4 cases (5%) of the total 80 cases. Of these 4 cases, all cases have shown positive sepsis screen and blood culture. Hence, strongly elevated sepsis markers in this study have found to be associated with bad prognosis as indicated by death.

Hence, it can be concluded that sepsis markers increase to significant level in the patient having bacterial septicemia. CRP has maximum sensitivity and CBC has maximum specificity in comparison with other septic markers.

Therefore, In the present study, correlation between sepsis screening and blood culture in neonate presenting with features of sepsis is done to accelerate the diagnostic process is justified and blood culture (considered gold standard) was proved for accurate sepsis detection and its effectiveness was compared with other septic markers.

CONCLUSION

It can be concluded blood culture (considered gold standard) was proved for accurate sepsis detection and its effectiveness was compared with other septic markers is justified as an early diagnostic marker of neonatal sepsis.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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