Doi: 10.32677/IJCH.2017.v04.i03.031

Original Article

Evaluation of efficacy of septic screen in diagnosis of early onset sepsis

Shital Kolhe[1], Puneet Mahajan[2], Sadaf Siddiqui[1], Ashok Sharma[1], Rajesh Rai[1]

From [1]Department of Pediatrics, Dr. D Y Patil Medical College, Navi Mumbai, Maharashtra, India, [2]Neonatal and Pediatric Intensivist, Mahajan Children Hospital, Gurdaspur, Punjab, India

Correspondence to: Dr. Shital Kolhe, Flat No 601, Mangal Prabha Society, Opposite D Y Patil Hospital, Sector 9, Nerul, Navi Mumbai - 400 706, Maharashtra, India. Phone: +91-7738033854. E-mail: kolhe.nelson@gmail.com

Received - 17 March 2017 Intial Review - 16 April 2017 Published Online - 16 June 2017

ABSTRACT

Background: Clinical features of sepsis are non-specific in all neonates and a high index of suspicion is required for the timely diagnosis of sepsis. Although blood culture is the gold standard for the diagnosis of sepsis, reports are available after 48-72 h. Therefore, a practical septic screen for the diagnosis of sepsis is needed. **Objectives:** To study the maternal and neonatal risk factors for early onset neonatal sepsis and to evaluate the efficacy of septic screen in diagnosis of same. **Methods:** Total 51 inborn were selected on basis of presence of maternal and neonatal risk factors, clinical features consistent with infection. The following investigations were done: Total leukocyte count, absolute neutrophil count, immature/total Neutrophil (I/T) ratio, haematocrit, platelet count, C-reactive protein (CRP) (after 6 h), gastric lavage, Micro erythrocyte sedimentation rate (ESR), chest X-ray (after 6 h). Blood culture was sent for any neonate with septic screen positive or those developing clinical sepsis within 72 h of birth and were correlated with the gold standard test (BACTEC). **Results:** Our study consisted of 51 inborn babies with 61% males and 39% females, 41% preterm <37 weeks of gestation and 59% term, 64.7% low birth weight <2500 g and 33% with history of premature rupture of membrane (PROM). Amongst 51 babies, 41.2% had leucocytosis, 15.7% with leucopenia, 21.6% had thrombocytopenia and 23.9% had anaemia. 86.3% had abnormal CRP, 33.3% had abnormal Micro ESR, and 54.9% had abnormal I/T ratio. Out of 51 babies, 17 (33.3%) were culture positive. Out of 17 culture proven sepsis, 64.7% were preterm, 88.8% were LBW <2500 g and 64.7% had history of PROM. Out of 17 culture proven cases, 75% had leucopenia, 70% had abnormal I/T ratio. 58.8% had abnormal Micro ESR, 86% were CRP positive which suggest that leucopenia, CRP and Micro ESR are good septic screen markers. Gastric aspirate is less significant. **Conclusion:** PROM, prematurity and low birth weight, especially, very low birth weight are the common high risk factors for early onset sepsis. Amongst septic profile, leucopenia, CRP and Micro ESR are associated with culture proven sepsis.

Key words: *Early onset sepsis, Maternal and neonatal risk factors, Septic screen*

Sepsis neonatarum is a symptomatic systemic illness of infants who are <1 month of age and are clinically ill and have a positive blood culture [1]. The incidence of neonatal sepsis has been described to range from 3.5 to 38 per 1000 live births worldwide and India reporting an incidence of approximately 3% [2]. Sepsis in neonates is associated with a high mortality ranging from 19 to 38% in the country. Neonatal sepsis can be classified into two types based on the age of onset: Early-onset sepsis (EOS) (<72 h) and late-onset sepsis (LOS) (≥72 h to 28 days). EOS is acquired before birth, during delivery, or after birth [3]. It is important to know the etiology, risk factors and antimicrobial sensitivity patterns of organisms that cause neonatal infections in developing countries in order to develop effective treatment strategies and to reduce neonatal mortality. The rate of neonatal infection increases if there is associated maternal or neonatal risk factors [4].

Incidence of neonatal sepsis increases significantly in low birth weight infants and in the presence of maternal (obstetric) risk factors or signs of chorioamnionitis such as prolonged rupture of membrane (premature rupture of membrane [PROM] >18 h), maternal intrapartum fever (>38°C), maternal leukocytosis (>18,000/mm^3), uterine tenderness, and fetal tachycardia (>180 beats/min) [5]. The factor associated most significantly with bacterial sepsis and meningitis is low birth weight [6]. Prematurity is another significant risk factor associated with neonatal sepsis due to deficiency in the most arms of immune system including immunoglobulin production, complement function, and phagocytic capability [7]. In neonates, the disease can progress more rapidly than in adults; therefore, early diagnosis is of utmost importance. Though blood culture is gold standard, it is time consuming (48-72) h and demands a well-equipped laboratory. Investigations of various inflammatory markers such as procalcitonin are been used for diagnosis of sepsis but these are expensive and impractical for use in developing countries [8]. Screening tests such as total and differential leukocyte counts, band cells, absolute neutrophil counts (ANCs), Micro erythrocyte

sedimentation rate (ESR) and rapid immunological techniques like C-reactive proteins (CRPs) assays may help in the diagnosis of early septicaemia [9]. Presence of two or more parameters is considered as a positive septic screen. The results of these tests are obtained much earlier than blood culture and hence, antibiotic therapy can be initiated early which reduces the neonatal morbidity and mortality.

MATERIALS AND METHODS

A prospective descriptive study was carried out in a tertiary level neonatal intensive care unit (NICU) over a period of 1 year after obtaining ethical approval. A total of 51 inborn neonates were selected on the basis of following criteria:

A. High risk factors: (Newborn with either 1 major or 2 minor are at risk for sepsis):

i. Major
- PROMs >18 h
- Maternal fever >38°C
- Chorioamnionitis and
- Sustained fetal heart rate > 160/min

ii. Minor
- PROMs >12 h
- Foul smelling liquor
- Maternal fever <38°C
- Maternal WBC >15000/mm^3
- Birth weight <2 kg
- Prematurity <37 weeks or
- Multiple gestations.

B. Clinical

i. Neonates with refusal of feed
ii. Lethargy
iii. Respiratory distress
iv. Off colored soles or
v. Temperature instability.

Neonates with life threatening congenital anomalies, metabolic disorders or outborn neonates were excluded from the study. On admission to NICU, neonates were stabilized with temperature maintenance, intravenous fluids and/or oral feeds. Pulse oximetry, NIBP, and blood sugar were monitored. Gestational age was estimated by New Ballard Score method and babies were stratified into three groups <34 weeks, 34-37 weeks, >37 weeks respectively. Baby was clinically monitored for respiratory distress, lethargy, refusal of feed, temperature instability, cry, tone and activity.

The following investigations as a part of septic screen were done: (1) Total leukocyte count (normal - 5000-24000/mm^3) <5000 or >24000 is significant, (2) ANC (normal >/1800/mm^3) <1750/mm^3 is significant, (3) platelet count (normal - 1.5-4 lakh/mm^3) <100000/mm^3 is significant, (4) peripheral smear for band forms immature/total (I/T) ratio (normal value is 0.16 for first 24 h and 0.12 after 24 h) >0.2 is suggestive of infection, (5) CRP (after 6 h) >6 mg/L, (6) Chest X-ray (after 6 h), (7) Gastric aspirate for polymorphs (>5/HPF is significant), (8) Micro ESR (normal Micro ESR = [Age in days +2] mm/h).

Any neonate with septic screen positive or those developing clinical sepsis within 72 h of birth was diagnosed to have an EOS. Samples for blood culture were collected from these neonates soon after birth with all aseptic precautions. Appropriate antibiotics were started according to prevailing antibiotic policy immediately after sending septic screening. Septic screen positive babies were correlated with gold standard test i.e., BACTEC for culture proven sepsis.

All inborn neonates satisfying inclusion criteria were selected for study. Data gathered was compared by using Pearson's Chi-square test for quantitative data. Significance was taken as $p<0.05$. All the statistical analysis mentioned above was done by software SPSS: 12 for windows.

RESULTS

Amongst the 51 babies included in the study, 61% were males and 39% were females. Out of total 51, 74.5% were shifted to NICU in <2 h of life, 13.7%, 7.8% and 3.9% were shifted 3-12 h, and 25-72 h respectively. Out of 51 babies, 2 (3.92%) were <1 kg, 7 (13.73%) were between 1 and 1.5 kg, 24 (47.06%) were between 1.5 and 2.5 kg and 18 babies (35.29%) were >2.5 kg. Total 9 babies (18%) were <34 weeks of gestation, 12 babies (24%) were between 34 and 37 weeks and 30 babies (58%) were >37 weeks. Total 48 (94%) mothers were antenatally registered, 17(33%) had PROM, 13 (25.5%) had leucocytosis, 4 (7.8%) had intrapartum fever, 3 (5.9%) had UTI and one (2%) mother had chorioamnionitis.

Amongst 51 babies, 21 (41.2%) had leucocytosis, 8 (15.7%) had leucopenia, 11 (21.6%) had thrombocytopenia and 2 (3.9%) had anemia. Total 44 babies (86.3%) had elevated CRP, 17 (33.3%) had abnormal Micro ESR and 28 babies (54.9%) had abnormal I/T ratio. 40 (80%) babies had normal chest X-ray, 18% babies had pneumonia and 2% babies had hyaline membrane disease. Amongst 51 babies, 33.33% babies had culture proven neonatal sepsis.

In total of 17 culture positive patients, 11 babies (64.7%) were <37 weeks of gestation. It indicates that as maturity decreases, culture positivity increases. As weight of the baby is increases, number of culture positive patients decreased. Therefore, comparison of birth weight with culture positivity is statistically highly significant. Comparison between PROM and culture positivity is statistically highly significant indicating that PROM is major risk factor for development of EOS.

Relation of leucopenia and culture positivity is statistically highly significant. Positive Micro ESR test for diagnosis of neonatal sepsis is statistically highly significant. Out of 51 babies, 28 babies (54.9%) had abnormal I/T ratio and out of 17 culture proven cases, 12 cases (70.6%) had abnormal I/T ratio. CRP was positive in all 17 (100%) babies which is highly statistically significant. In our study of 51 babies, two babies died. Two babies who died were both culture positive. It indicates that comparison of culture positivity and mortality is statistically significant.

Table 1: Relation of culture positivity with neonatal and maternal risk factors (n=51)

Risk factors	Total culture positive		Total (%)	Sensitivity (%)	Specificity (%)
	No (%)	Yes (%)			
Gestational age in weeks					
<34	4 (44.4)	5 (55.6)	9 (100.0)	70.59	11.76
34-37	6 (50.0)	6 (50.0)	12 (100)	70.59	11.76
>37	24 (80)	6 (20)	30 (100)	35.29	29.41
Birth weight (in kg)					
<1 kg	1 (50)	1 (50)	2 (100)	94.12	2.94
1.5-2.5 kg	16 (66.7)	8 (33.3)	24 (100)	58.82	5.88
>2.5 kg	16 (88.9)	2 (11.1)	18 (100)	11.765	52.94
PROM					
No	28 (82.4)	6 (17.6)	34 (100)		
Yes	6 (35.3)	11 (64.7)	17 (100)		
Total	34 (66.7)	17 (33.3)	51 (100)	64.71	82.31

PROM: Premature rupture of membrane

Table 2: Correlation of culture positivity with laboratory investigations (n=51)

Laboratory investigations	Total culture positive		Total (%)	Sensitivity (%)	Specificity (%)
	No (%)	Yes (%)			
Leucopenia					
No	32 (94.1)	11 (64.7)	43 (84.3)		
Yes	2 (5.9)	6 (33.3)	8 (15.7)	35.29	94.12
Micro ESR					
No	27 (79.4)	7 (20.6)	34 (100)		
Yes	7 (41.2)	10 (58.8)	17 (100)	58.82	79.41
CRP					
No	7 (20.6)	0	7 (13.7)		
Yes	27 (79.4)	17 (100)	44 (86.3)	100	20.59

ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein

Table 3: Chi-square tests of various parameters

Pearson Chi-square	Value	Df	Asymp. Sig. (2-sided)
Gestational age	5.900 (a)	2	0.052
Birth weight	12.893 (a)	3	0.005
PROM	11.294(b)	1	0.001
Leucopenia	7.413 (b)	1	0.006
Micro ESR	7.456 (b)	1	0.006
CRP	4.057 (b)	1	0.044

PROM: Premature rupture of membrane, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein

DISCUSSION

A prospective descriptive study was carried out in the NICU of our hospital to study maternal risk factors, neonatal risk factors and evaluate efficacy of septic screen in diagnosis of EOS in tertiary care unit. Neonatal sepsis was diagnosed on the basis of blood culture positivity which is gold standard for diagnosis of sepsis but for better outcome and survival, simple and rapid diagnostic tests are required for early and effective initiation of treatment of the septic newborns.

Total 51 inborn babies were included in our study. Amongst 51 patients, 74.5% patients were admitted in NICU within 2 h of life and total of 96.1% patients were admitted within 24 h of life and found to have septicaemia. Movahedian et al. [10] has studied 1680 newborns and found to have early onset septicemia in 77.5% cases. We found that in EOS, sepsis is more common in first 24 h of life which is correlating with the reports from other studies.

Out of 17 culture positive patients, 11 patients (64.7%) were <37 weeks of gestation as seen in Table 1. This indicates that EOS is most commonly seen in premature babies, which is compatible with results of other studies. Cohen-Wolkowiez et al. studied EOS and LOS in late preterm infants and found that prematurity is an important risk factor in developing early and LOS [7]. In our study, we found that out of 17 culture positive patients, total 15 (88.24%) were low birth weight babies (<2.5 kg) seen in Table 1. Hornik et al. studied early and LOS in very-low-birth-weight infants from a large group of NICU and concluded the same results [6].

In our study, out of 51 mothers, 48 were antenatally registered, 17 had PROM, 4 had intrapartum fever, 3 had UTI, 13 had leukocytosis and 1 had chorioamnionitis. Amongst 17 cultures proven sepsis patient, 11 (64.7%) babies had PROM >12 h depicted in Table 1. Shah et al. [11] have done study in Nepal and found to have 46% of neonatal sepsis in PROM patients. Udani et al. [12] found neonatal sepsis in 24.03% cases of PROM and Saxena et al. [13] in 31.63% found the PROM

as predisposing factor to septicemia. In our study, other risk factors like antenatal registration, intrapartum fever, urinary tract infection, leukocytosis and chorioamnionitis were not significantly associated with EOS.

Amongst 8 babies with leucopenia, 6 (75%) were culture positive which indicates that when leucopenia is present chances of development of EOS are high. In our study, we found leucopenia had a sensitivity of 35.29% while specificity of 94.12%, as mentioned in Table 2 very similar to the study done by Bhale et al. [14] Kim et al. [15] has retrospectively evaluated 61 cases of neonatal sepsis and reported leucopenia as a significant diagnostic laboratory finding for neonatal sepsis. These include the ratio of either band cells or all immature neutrophils (e.g. bands, metamyelocytes, and myelocytes) to total neutrophil count [16] Out of 17 culture proven cases, 12 cases (70%) had abnormal I/T ratio which is comparable to other studies. Speer et al. [17] demonstrated that I/T ratio was more than 0.2 and was consistently abnormal (60% of the cases) than total counts of white blood cells, neutrophils or immature neutrophils.

Amongst 17 babies who had abnormal Micro ESR, 10 babies (58.8%) were culture positive which indicates that Micro ESR can be used as septic parameter for diagnosis of EOS as seen in Table 2. In our study, Micro ESR had sensitivity of 58.82% while specificity of 79.41% as depicted in the study by Vinay et al. [18] Micro ESR can be used as good bed side test for diagnosis of sepsis. The minimal requirement of blood and its simplicity enhances its utility in neonatal care [14]. The response was not elevated or influenced by antibiotics; therefore, the test is useful in the evaluation of the patients whose culture results are infected by concurrent antibiotic therapy. In our study, out of 51 babies, 44 babies (86%) were CRP positive; out of 17 culture positive babies, CRP was positive in all 17 (100%) babies which are statistically significant seen in Table 3 showing that CRP has 100% sensitivity as a septic marker. Bhale et al. confirmed that CRP is highly significant in evaluating EOS [14].

CONCLUSION

PROM is the most common maternal risk factor for EOS while prematurity and low birth weight is common neonatal risk factors. In the presence of above factors, the neonate should be screened and observed for the development of sepsis and considered for early institution of appropriate antibiotics. Leucopenia, CRP and Micro ESR are associated with culture proven sepsis. Micro ESR, Total leucocyte count and CRP are easy, quick and cost effective screening tools for diagnosis of EOS. CRP is a good sensitive marker while Micro ESR and leucopenia being more specific markers in diagnosis of the same.

ACKNOWLEDGMENT

We are grateful to Dr D Y Patil Hospital and Research centre for giving us the permission to publish the study.

REFERENCES

1. MacCraken GH Jr, Freji BJ. Acute infections. In: Avery GB, Fletcher MA, MacDonald MG, editors. Neonatology, Pathophysiology and Management of the Newborn. 4th ed. Philadelphia, PA: JB Lippincott Co.; 1994. p. 1088.
2. Jasani B, Kannan S, Nanavati R, Gogtay NJ, Thatte U. An audit of colistin use in neonatal sepsis from a tertiary care centre of a resource-limited country. Indian J Med Res. 2016;144(3):433-9.
3. Bryce J, Boschi-Pinto C, Shibuya K, Black RE; WHO Child Health Epidemiology Reference Group. WHO estimates of the causes of death in children. Lancet. 2005;365:1147-52.
4. Kumar M, Paul VK, Kapoor SK, Anand K, Deoraria AK. Neonatal outcomes at a subdistrict hospital in north India. J Trop Pediatr. 2002;48:43-6.
5. Gotoff SP. Neonatal sepsis and meningitis. In: Behrmanj RE, Klegman RM, Arvin AM, editors. Nelson Text Book of Pediatrics. 15th ed. Bengaluru, India: Prism Books Pvt., Ltd., WB Saunders Co.; 1996. p. 529.
6. Hornik CP, Fort P, Clark RH, Watt K, Benjamin DK Jr, Smith PB, et al. Early and late onset sepsis in very-low-birth-weight infants from a large group of neonatal intensive care units. Early Hum Dev. 2012;88 Suppl 2:S69-74.
7. Cohen-Wolkowiez M, Moran C, Benjamin DK, Cotton CM, Clark RH, Benjamin DK Jr, et al. Early and late onset sepsis in late preterm infants. Pediatr Infect Dis J. 2009;28(12):1052-6.
8. Adib M, Bakhshiani Z, Navaei F, Saheb Fosoul F, Fouladi S, Kazemzadeh -H. Procalcitonin: A reliable marker for the diagnosis of neonatal sepsis. Iran J Basic Med Sci. 2012;15(2):777-82.
9. Jain NK, Jain VM, Maheshwari S. Clinical profile of neonatal sepsis. Kathmandu Univ Med J. 2003;1(2):117-20.
10. Mohvehidian AH, Moniri R, Mosayebi Z. Bacterial culture of neonatal septicemia Indian J Public Health. 2006;35:84-9.
11. Shah GS, Budhathoki S, Das BK, Mandal RN. Risk factors in early neonatal sepsis. Kathmandu Univ Med J (KUMJ). 2006;4(2):187-91.
12. Udani RH, Vaze S, Reys M, Paul SS. Premature rupture of amniotic membranes and neonatal infection: Predictive value of bacteriologic cultures from different sites. Indian J Pediatr. 1980;47(385):137-40.
13. Saxena S, Anand NK, Saini L, Mittal SK. Bacterial infections among home delivered neonates. Clinical picture and bacteriological profile. Indian Pediatr. 1980;17:17-24.
14. Bhale CP, Kale AV, Kale SS, Mahajan M, Mulay SS. Utility of sepsis screen in the early diagnosis of neonatal sepsis. Indian J Neonatal Med Res. 2016;4(3):1001-7.
15. Kim SH, Hur KH, Kim SS, Chey MJ, Kim KH, Lee HS. Comparison between preterm and full term infants in neonatal sepsis. J Korean Pediatr Soc. 1993;36(11):1542-54.
16. Manroe BL, Weinberg AG, Rosenfeld CR, Browne R. The neonatal blood count in health and disease. I. Reference values for neutrophilic cells. J Pediatr. 1979;95(1):89-98.
17. Speer CP, Hauptmann D, Stubbe P, Gahr M. Neonatal septicemia and meningitis in Göttingen, West Germany. Pediatr Infect Dis. 1985;4(1):36-41.
18. 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 Appl Med Sci. 2015;3(2G):1005-10.

Funding: None; Conflict of Interest: None Stated.

How to cite this article: Kolhe S, Mahajan P, Siddiqui S, Sharma A, Rai R. Evaluation of efficacy of septic screen in diagnosis of early onset sepsis. Indian J Child Health. 2017; 4(3):405-408.