Int J Biol Med Res. 2011; 2(1): 360-368

Contents lists available at BioMedSciDirect Publications

International Journal of Biological & Medical Research

Journal homepage: www.biomedscidirect.com

Original Article

Correlation of Blood culture results with the Sepsis score and the Sepsis screen in the diagnosis of Neonatal Septicemia.

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ARTICLE INFO

Keywords:
Blood culture,
Neonatal septicemia,
Sepsis score,
Sepsis screen

ABSTRACT

To isolate the organism responsible for neonatal septicemia from the blood and to correlate the blood culture results with the Sepsis score and the Sepsis screen parameters. Methods:This prospective study was done over a period of one year. Blood samples from 115 clinically suspected neonatal septicemia cases were subjected to aerobic culture and Sepsis screen tests like C-Reactive protein, micro-ESR, buffy coat smear study, total WBC count, Absolute neutrophil count, Immature/Total neutrophil count (I/T) ratio and platelet count. The culture results were correlated with the Sepsis score and the Sepsis screen tests. Results:Of the 115 cases studied, 50.4% were blood culture positive. 60.3% were males. 37.4% were preterm and 41.3% were very low birth weight neonates. High risk sepsis score was seen in 43.1% cases. Early onset septicemia was more common, seen in 77.6% of cases than late onset septicemia (22.4%) cases. Gram negative organisms accounted for 56.9% of the isolates than Gram positive organisms seen in 41.4% of cases. Klebsiella pneumoniae and Staphylococcus aureus were the commonest organisms isolated in 43.1% and 37.9% of cases respectively. Positive buffy coat smear was the single best reliable sepsis screen test with a high specificity (86.7%) but, the positive predictive value and specificity was high when two or more sepsis screen tests were combined. The mortality rate among the culture positive cases was 46.5% with maximum case fatality seen in the late onset septicemia cases (57.1%). Conclusion:The sepsis scoring system in predicting neonatal septicemia clinically needs further evaluation. Blood culture remains the gold standard for the diagnosis of neonatal septicemia. Combination of two or more sepsis screen parameters has better results in diagnosing neonatal septicemia compared to a single test while awaiting the blood culture results. KEYWORDS: Blood culture, Neonatal septicemia, Sepsis score, Sepsis screen.

1. Introduction

Neonatal septicemia refers to a clinical syndrome characterized by systemic signs and symptoms due to generalized bacterial infection with a positive blood culture in the first four weeks of life.[1] Bacterial infections are the commonest cause of morbidity and mortality during the neonatal period. Fulminant and fatal course of infection may result from complications such as shock, disseminated intravascular coagulation and multi-system organ failure, mandating early diagnosis of this life-threatening condition for a timely treatment and a favourable outcome.[1,2,3]

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In developing countries, sepsis is the commonest cause of mortality responsible for 30-50% of the 5 million total neonatal deaths each year. The reported incidence of neonatal sepsis varies from 7.1 to 38 per 1000 live births in Asia[4]. National Neonatal Perinatal Database (NNPD, 2002-2003) from India has reported an incidence varying from 0.1% to 4.5%. The database comprising of 18 tertiary care neonatal units across India found sepsis to be one of the commonest causes of neonatal mortality contributing to 19% of all neonatal deaths. Septicemia was the commonest clinical category with an incidence of 23 per 1000 live births[5]. Gram negative organisms are found to be more frequently responsible for septicemia than Gram positive organisms as evidenced by many Indian studies.[6]

The clinical presentation is often subtle or nonspecific and usually mimicked by several other disorder. A high index of suspicion is required for the early diagnosis and management of neonatal septicemia. Without treatment, the case fatality rate is high, Hence certain perinatal risk factors have been evaluated as indicators to predict neonatal septicemia and scored objectively to facilitate management. The scoring system by Takkar VP and Bhakoo ON [7] consisting of six perinatal risk factors, is one such valuable tool most commonly used by clinicians to screen and treat the neonates for septicemia. Several authors categorize neonatal septicemia into early onset septicemia (presents within the first 72 hours of life) and late onset septicemia (usually presents after 72 hours of life) for epidemiological and therapeutic purposes.[8]

The gold standard for the diagnosis of neonatal septicemia is a positive Blood culture.[1,8] Definitive culture results takes at least 48-72 hours resulting in treatment delays. Hence, certain rapid diagnostic tests such as C-reactive protein, Micro-erythrocyte sedimentation rate, Buffy coat smear examination, Total WBC count, Absolute neutrophil count, Immature/Total Neutrophil count ratio and Platelet count collectively termed as the 'Sepsis Screen'[9, 10] is used, in addition to the Sepsis Score[7] to diagnose septicemia early and initiate a presumptive treatment while awaiting culture report.

The present study was undertaken to isolate the organism responsible for Neonatal septicemia from Blood and correlate the Blood culture results with the Sepsis score and the Sepsis screen tests for the early diagnosis of Neonatal septicemia.

2. Materials and Methods

This prospective study was conducted at a teaching tertiary care hospital in Bangalore. 115 clinically suspected cases of neonatal septicemia admitted to the Neonatal Intensive Care Unit were studied. Informed consent was taken from the parents/ guardians of all patients. Detailed history and clinical findings were recorded in the proforma. All newborn babies aged 0-28 days presenting with one or more clinical features suggestive of septicemia and having one or more risk factors like prematurity, low birth weight, birth asphyxia, foul smelling liquor amnii, unclean per vaginal (PV) examination before delivery, prolonged rupture of membranes and prolonged labour, were included in the present study. Neonates with clinical features suggestive of septicemia receiving antibiotics were excluded from the study. A score was assigned to each of the risk factors and the neonates categorized into three groups based on this risk scoring (Sepsis score)[7]. Table.1 depicts the perinatal infection risk scoring of Takkar VP and Bhakoo ON and Table.2 shows the risk group categorization with suggested intervention strategy.

The investigations done were Blood culture, Buffy coat smear examination, C-Reactive protein (CRP) test, micro-Erythrocyte sedimentation rate (micro-ESR) estimation, Total leucocyte (WBC) count, Absolute neutrophil count (ANC), and Immature (band cells) count / Total neutrophil count ratio [I/T ratio]. The Blood cultures were processed and the isolates identified by standard microbiological procedures.[11,12] Cultures were reported as negative when they did not yield any growth at the end of 7 days. Buffy coat smear examination was done according to the technique described by Brooks and associates.[13] The CRP test was done by the rapid slide latex agglutination method using the diagnostic kit for the in-vitro detection of CRP in human serum supplied commercially by Span Diagnostics Ltd. The test was carried out as per the instructions described in the kit. micro-ESR estimation was done by using commercially available (Greiner Bio-one) standard heparinised micro-hematocrit capillary tubes. Blood was collected in the capillary tubes provided in the kit, from a heel prick of the neonate after disinfecting the area. One end of the tube was sealed with plasticin and the tubes were fixed vertically in an ESR stand. The rate of erythrocyte sedimentation was measured in millimeters at the end of one hour. The Total leucocyte count, differential count, ANC, I/T ratio and the Platelet count calculated as per standard haematological methods.[14]
The cut off values for the positive rapid screening tests in this study were as follows[10,15]:

1) C-Reactive protein (CRP)	: >1mg/dl.
2) Micro ESR (m-ESR)	:>15 mm in the 1st hour
3) Total leucocyte count (Leucopenia)	: < 5,000cells/cu.mm.
4) Absolute neutrophil count (Neutropenia)	:< 1,800cells/cu.mm.
5) Band cell count to total neutrophil count ratio (I/T ratio)	: ≥ 0.2
6) Platelet count (Thrombocytopenia)	: < 1.5 lakhs/cu.mm.

All the findings were recorded and comparisons drawn between blood culture results, sepsis score and the sepsis screen tests. Data was analysed using the SPSS software for Windows version 11 (Statistical Presentation System Software, SPSS Inc,1999, New York) and categorical tables, Chi-square values, probability coefficients, sensitivity, specificity, positive predictive values and negative predictive values of the three diagnostic methods derived and the results correlated. Conclusions were drawn from the tabulated results.

Table.1 : Perinatal infection risk score.

Perinatal factor	Risk Score
Foul smelling liquor	2
Unclean vaginal examination done before delivery	2
Duration of labour exceeding 24 hours	2
One minute Apgar score of 0 -6	2
Duration of rupture of membrane before delivery > 24 hours	1
Birth weight 2 kgs or less and / or gestation less than 37 wks	1
Total	**10**

Table.2 Risk Score And Risk Group Category With Suggested Intervention

Total Sepsis Score	Risk Group	Intervention Suggested
(0 – 3)	Low Risk	Withhold antibiotics
(4 – 5)	Moderate Risk	Investigate for presence of infection; give antibiotics if circumstantial evidence of infection is present.
(6 - 10)	High Risk	Start Antibiotics immediately

Table. 3: Shows The Distribution Of Perinatal Risk Factors Among Cases

	CLINICALLY SUSPECTED CASES		CULTURE POSITIVE CASES		
RISK FACTORS	**EOS NO(%)N=95**	**EOS NO(%)N=20**	**EOS NO(%)N=45**	**EOS NO(%)N=13**	**P VALUE**
Foul Smelling Liquor Amnii (FSLA)	35 (36.8%)	6 (30.0%)	18 (40.0%)	4 (30.8%)	0.77
Unclean Vaginal Examination Before Delivery (UPV)	83 (87.4%)	20 (100%)	42 (93.3%)	13 (100%)	0.25
Prolonged Labour > 24 Hrs	29 (30.5%)	3 (15.0%)	15 (33.3%)	2 (15.4%)	0.84
One Minute Apgar <6 (apgar<6)	58 (61.1%)	5 (25.0%)	29 (64.4%)	4 (30.8%)	0.79
Prolonged Rupture Of Membranes >24 Hrs	45 (47.4%)	7 (35.0%)	16 (35.6%)	5 (38.5%)	0.26
Gestational Age <37wks And/ Or Birth Wt ≤ 2kgs	60 (63.2%)	16(80.0%)	31 (68.9%)	10 (76.9%)	0.54

Table. 4: Shows The Sensitivity, Specificity, Positive Predictive Value And Negative Predictive Value Of Sepsis Score In Culture Positive Cases

SEPSIS SCORE TOTAL =10	SENSITIVITY (%)	SPECIFICITY (%)	POSITIVE PREDICTIVE ACCURACY (%)	NEGATIVE PREDICTIVE ACCURACY (%)
LOW RISK (0-3)	40.0%	46.7%	17.2%	73.7%
MODERATE RISK (4-5)	39.7%	68.4%	56.1%	52.7%
HIGH RISK (6-10)	43.1%	57.9%	51.0%	50.0%

Table. 5: Shows The Correlation Of Sepsis Screen Parameters With The Blood Culture Status

SEPSIS SCREEN PARAMETER	CULTURE POSITIVE N=58 NO (%)	CULTURE NEGATIVE CASES N=57 NO (%)	TOTAL N=115 NO (%)	P VALUE
A) Single Tests:				
C-reactive Protein (Positive : >1mg/dl)	53 (91.4%)	49 (86.0%)	102 (88.7%)	0.359
Leucopenia (TLC <5,000 Cells/mm^3)	7 (12.1%)	4 (7.0%)	11 (9. 6%)	0.055
Neutropenia (ANC <1800 Cells/mm^3)	2 (3.5%)	2 (3.5%)	4 (3.5%)	0.679
I/T Ratio≥0.2	48 (82.8%)	44 (77.2%)	92 (80.0%)	0.456
Thrombocytopenia (PL <1.5 X 10^5 Cells/mm^3)	23 (39.7%)	17 (29.8%)	40 (34.8%)	0.268
M-ESR >15 mm in the1st hour	19 (32.8%)	7 (12.3%)	26 (22. 6%)	0.009
Buffy Coat Smear (shows presence of Microorganisms)	52 (89.7%)	18 (31.6%)	70 (60. 9%)	<0.0001
[B]. Two or More Tests Positive	57 (98.3%)	46 (80.7%)	103 (89.6%)	0.002
[C]. Three or More Tests Positive	51 (87.9%)	27 (47.4%)	78 (67.8%)	<0.0001

Table. 6: Shows The Sensitivity, Specificity, Positive Predictive Value And Negative Predictive Value Of Sepsis Screen Parameters

SEPSIS SCREEN P ARAMETERS	SENSITIVITY (%)	SPECIFICITY (%)	POSITIVE PREDICTIVE VALUE (%)	NEGATIVE PREDICTIVE VALUE (%)
A) Single Tests:				
C-reactive Protein Positive : >1mg/dl)	52.0%	61.5%	91.4%	14.0%
Leucopenia (TLC <5,000 CELLS/mm^3)	63.6%	51.0%	12.1%	93.0%
Neutropenia (ANC <1800 CELLS/mm^3)	50.0%	49.6%	3.5%	96.5%
I/T RATIO ≥ 0.2	52.2%	56.5%	82.8%	22.8%
Thrombocytopenia (pl <1.5 X 10^5 Cells/mm^3)	57.5%	53.3%	39.7%	70.2%
M-ESR >15 mm in the1st hour	73.1%	56.2%	32.8%	87.7%
Buffy Coat Smear (Shows presence of microorganisms)	74.3%	86.7%	89.7%	68.4%
B. Two or More Tests Positive	55.3%	91.7%	98.3%	19.3%
C. Three or More Tests Positive	65.4%	81.1%	87.9%	52.6%

3. Results

Of the 115 clinically suspected septicemic cases studied, 58 (50.4%) were culture positive and 57 (49.6%) were culture negative. 76 (66.1%) were males and 39 (33.9%) were females Among the culture positive cases, septicemia was more common among male neonates, seen in 35(60.3%) of the cases compared to female neonates 23(39.7%). Males were commonly affected compared to females with a ratio of 1.5:1. Majority i.e 95 (82.6%) of the neonates were less than one week old. The mean age of the neonates in the study was 4.7 days. Of the 58 culture positive cases, early onset septicemia (EOS) was more common, seen in 45(77.6%) of cases than late onset septicemia (LOS) seen in 13 (22.4%) of cases. The mean birth weight in the study population was 2.1kgs. Culture proven septicemia was more common among 43 (37.4%) of preterm neonates, 24 (41.4%) of very low birth weight neonates, 46 (79.3%) neonates with spontaneous vaginal delivery and 34 (58.6%) of the hospital inborn neonates.

Table.3 shows the distribution of perinatal risk factors among the clinically suspected and culture positive cases. Unclean per vaginal examination prior to delivery, prematurity, low birth weight and birth asphyxia were the most common perinatal risk factors seen among the culture positive cases. Majority of the culture positive cases i.e 25 (43.1%) belonged to the high risk sepsis score group, followed by 23 (39.7%) in the moderate risk group and 10 (17.2%) of the cases in the low risk group. The difference observed was statistically not significant ($p>0.05$). Table.4 shows the sensitivity, specificity, positive predictive and negative predictive values of the sepsis score in culture positive cases. High risk sepsis score had the highest sensitivity of 43.1%, moderate risk score had a high specificity of 68.4% and a positive predictive value of 56.1%, while the low risk sepsis score had a high negative predictive value of 73.7% in culture positive cases.

Majority of the blood culture isolates i.e 33 (56.9%) were Gram negative organisms, Klebsiella pneumoniae being the commonest isolated in 25 (43.1%) of the 58 culture positive cases, followed by Escherichia coli 3 (5.2%). The other organisms isolated were Pseudomonas aeruginosa 2 (3.6%), Enterobacter cloacae 1 (1.7%), Proteus vulgaris 1 (1.7%) and Salmonella typhi 1 (1.7%). Gram positive organisms were obtained in 24 (41.4%) out of 58 cases with Staphylococcus aureus being the commonest isolate in 22 (37.9%) cases followed by Staphylococcus epidermidis in 2 (3.5%) cases. Polymicrobial isolates i.e Klebsiella pneumoniae and Citrobacter freundii were obtained in only one case with early onset septicemia.

Table.5 shows the correlation of the sepsis screen parameters with the blood culture status. Of the 58 culture positive cases, CRP was positive in 91.4% of the cases, leucopenia was noted in 12.1%, neutropenia in 3.5%, I/T ratio ≥ 0.2 in 82.8%, thrombocytopenia in 39.7%, m-ESR >15 mm in 32.8% and a positive buffy coat smear in 89.7% cases. Buffy coat smear study revealed no organisms in 10.3% of the culture positive cases. Table.6 shows the sensitivity, specificity, positive predictive and negative predictive values of the sepsis screen parameters in the culture positive cases. A positive buffy coat smear study was the single best reliable sepsis screen test to diagnose septicemia and the positive predictive value and specificity was high when two or more sepsis screen tests were combined.

The mortality rate was 46.6% (27/58) among the culture positive cases, while it was 34.8% in all the septicemic cases studied. Among culture negative cases, 13 cases out of 57 cases died giving a mortality rate of 22.8%. The overall mortality rate in this study was 34.8%.The difference between the mortality rates among the blood culture results was found to be statistically significant (p= 0.0075). Maximum case fatality rate of 57.1% was seen among the late onset septicemic cases and was associated with gram negative organisms.

4. Discussion

In this prospective study, of the 115 clinically suspected septicemia cases, 58 (50.4%) were culture positive and 57 (49.6%) were culture negative. The ratio of culture positive cases was higher among males than the females in the present study. These results are comparable with the observations made by other authors.[17,18] The male preponderance in neonatal septicemia may be linked to the X- linked immunoregulatory gene factor contributing to the host's susceptibility to infections in males.[19] Maximum culture positive cases were seen in neonates with EOS as compared to neonates with LOS in the present study. This could be due to ascending infection following rupture of membranes or through the infected birth canal or at the time of resuscitation of the newborn in the labour room. Immature immunological responses of the neonates in the first week of life makes them more susceptible to infections in this period.[16] Similar observations were made in the studies by other authors.[2,17,18]

The proportion of culture positive septicemia cases in this study was higher among the very low birth weight neonates as compared to the low and normal birth weight neonates. The rate of infection is inversely proportional to the birth weight, and low IgG levels due to impaired cellular immunity in the very low birth weight neonates contributes to the increased susceptibility to infections in these neonates [16]. Our results differ from some studies where a higher proportion of cases were reported in the low birth weight neonates [18] or among the normal birth weight neonates [20]. Culture positive septicemia cases were higher among the preterm neonates in the present study. Preterms are more susceptible to infections due to inherent deficiencies of both humoral and cellular defense mechanisms. It is suggested that the incidence of septicemia increases with the decreased gestational age of the neonates [16], thereby making preterms more vulnerable to infection. Studies by some authors showed a higher proportion of cases among the term neonates compared to the preterm neonates.[17] These variations probably reflect differences in the population characteristics and the presence of predisposing factors among them. Maximum number of cases (79.3%) was seen in neonates delivered by spontaneous vaginal delivery in the present study. The higher rates of neonatal septicemia in vaginally delivered neonates may be due to the surface colonization of the neonate with the microbial flora of the birth canal during vaginal delivery. In the present study, the higher proportion of culture positive septicemia among hospital inborn neonates points to a probable hospital acquired source of infection in them.

The present study clearly shows a higher proportion of cases having unclean PV before delivery, prolonged rupture of membranes for >24 hrs and prolonged labour for >24 hrs as the commonest predisposing factors in developing definitive septicemia. It is also evident from the study that nearly an equal proportion of cases had a one minute Apgar score of <6, birth weight ≤ 2 kgs and / gestational age < 37 wks as risk factors for developing septicemia. Our results are comparable with other studies who found a higher rate of septicemia among cases having unclean PV before delivery and prolonged labour for >24 hrs [7]. Studies by some authors [20, 21] has shown a higher proportion of cases having a one minute Apgar score of <6 and birth weight ≤ 2 kgs and / gestational age <37 wks as risk factors for septicemia. These variations probably reflect differences in the rates of occurrence of the predisposing risk factors in the various studies. Maximum number of culture positive cases was seen among the high risk group, followed by the moderate risk group. Similar observations were made by other authors in their studies [7,22]. If

the recommendations of treatment based on the scoring system made by Takkar and Bhakoo.,1974 [7] were to be followed, antibiotics are to be withheld in the neonates belonging to the low risk group. This study clearly shows that 10 /115 (8.67%) cases that were culture positive belonged to the low risk group. Based on the recommendations of Takkar VP and Bhakoo O.N, these cases would not have received antibiotics even though they were culture positive, thus, emphasizing the need for blood culture in all clinically suspected cases of septicemia.

In the present study, 58 /115 cases studied were culture positive, giving a positivity rate of 50.4%. These results were comparable with the studies conducted by other authors [2,23,24] while, some authors showed a very low culture positivity rate (range = 25% to 42%) in their study [3,25,26].The low culture positivity in these studies may be due to intrapartum administration of antibiotics to mothers which can affect the blood culture results in neonates.[27] Gram negative organisms formed the majority of the isolates as compared to Gram positive organisms (58.6% vs 41.4% respectively) in the present study. Klebsiella pneumoniae (43.1%) was the predominant isolate, followed by S.aureus (37.9%). Similar observations were made in other studies.[2,17,19] However studies by few other authors showed S.aureus as the commonest isolate [23,24,26], while P.aeruginosa was the commonest pathogen isolated in another study.[3] NNPD data 2002-2003 shows that among the intramural births, Klebsiella pneumonia is the most frequently isolated pathogen (32.5%), followed by Staphylococcus aureus (13.6%) while, among the extramural neonates (referred from community/other hospitals); Klebsiella pneumonia is again the commonest organism isolated (27%), followed by Staphylococcus aureus (15%) and Pseudomonas (13%).[5]

The CRP test was least sensitive of the sepsis screen parameters but, had the highest positive predictive value in diagnosing septicemia. Various studies by other authors show variable results to this test.[26,28,27,29] The differences in the results of this parameter shown by the different studies is due to variations in the diagnostic criteria, the time of onset of infection (early or late) and different methods of CRP estimation. Neonatal septicemia is associated with leucopenia [15]. In the present study, Leucopenia i.e Total WBC counts <5000 cells/ cu.mm was taken as the diagnostic criteria for detecting neonatal septicemia. Leucopenia had a low sensitivity, specificity and positive predictive value but, a very high negative predictive value similar to the observation made by another study.[30] The differences in the results of this parameter in different studies may be due to variations in the blood sampling time, the severity of infection, the diagnostic criteria followed, the age of the neonates, and the reduced sensitivity of this test after the first week of life. ANC had the highest negative predictive value of 96.5% among the sepsis screen tests studied, which was similar to the observations seen in another study.[27] ANC varies considerably in the immediate neonatal period and normal reference ranges are available from Monroe's chart [31]. ANC below 1800 per cubic mm is believed to be the best predictor of sepsis, while neutrophilia does not correlate well [15].

I/T ratio is ≤ 0.16 at birth and declines to a peak value of 0.12 after 72 hours of age [8]. A ratio of ≥ 0.2 is a highly sensitive marker of neonatal septicemia.[15] In this study, I/T ratio had a very low sensitivity, specificity and the negative predictive values of 52.2%, 56.5% and 22.8% respectively while, the positive predictive value was comparatively high at 82.8%. Different studies have shown variable results in this parameter which may be due to the variations in the blood sampling time, the severity of infection, the age of the neonates, the diagnostic criteria followed and the reduced sensitivity of this test after the first week of life.[24,27,28] Thrombocytopenia was a poor predictor of neonatal septicemia in this study compared to the studies conducted by different authors.[24,27] This is because the platelet counts are significantly low in all neonates in the first week of life and only rise after this period.[27,32] micro-ESR had very low specificity and positive predictive value, but a higher specificity and negative predictive value in detecting septicemia in the study. Similar observations were made by the other authors. micro-ESR was a poor predictor of neonatal septicemia in our study compared to the studies conducted by other authors.[27,28,33] These variations are due to the fact that atleast four hours are required for hematological response to develop after the onset of infection and blood samples collected and analyzed before this will yield normal results.[27] High micro-ESR is a specific test but it has only moderate sensitivity. The value is spuriously high in neonates with haemolysis and low in babies with disseminated consumptive coagulopathy.[15]

Positive buffy coat smear was the most sensitive (74.3%) and specific (86.7%) parameter for screening septicemia which was comparable with the observations made by other authors in their study [24,34]. A positive buffy coat smear study, micro-ESR >15 mm in the 1st hour and leucopenia were the Sepsis screen tests in the decreasing order of significance in diagnosing neonatal septicemia in the present study.

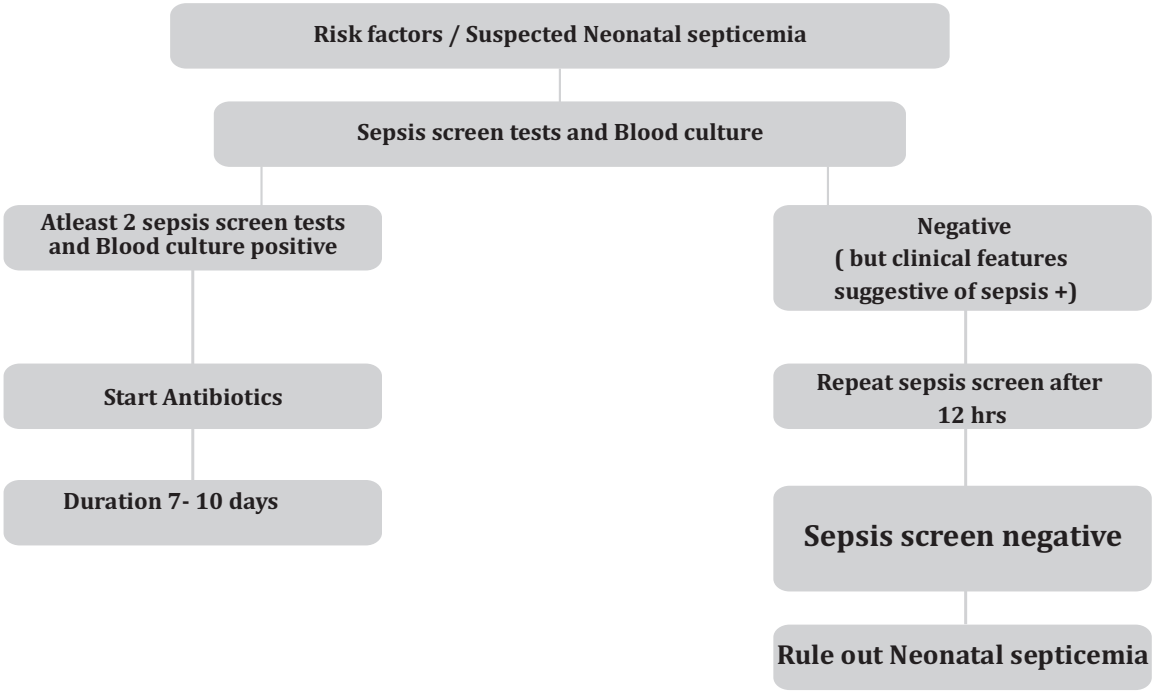
When two or more sepsis screen tests were combined together, the sensitivity and the negative predictive values decreased to 55.3% and 19.3% respectively, while the specificity and the positive predictive values increased to 91.7% and 98.3% respectively and was found to be statistically significant in detecting septicemia compared to the individual sepsis screen tests in this study. Similar observations were made by the other authors [4,28,27]. When three or more tests were considered together, the sensitivity and the negative predictive value increased to 65.4% and 52.6% respectively, but, the specificity and the positive predictive value decreased to 81.1% and 87.9%

respectively; compared to two or more tests being positive. Presence of two or more abnormal sepsis screen parameters is associated with a sensitivity of 93-100%, specificity of 83%, positive and negative predictive values of 27% and 100% respectively [4]. Similar observations were made by the other authors [27,35].

From this study it can be derived that among the sepsis screen parameters studied, when single tests were considered, a positive buffy coat smear study was the most sensitive (74.3%) and specific (86.7%) test, CRP had the highest positive predictive value (91.4%), while Neutropenia had the highest negative predictive value (96.5%). When two or more sepsis screen parameters were considered together, the sensitivity and the negative predictive value decreased to 55.3% and 19.3% respectively, while the specificity and the positive predictive value increased to 91.7% and 98.3% respectively. When three or more tests were considered in combination, the sensitivity and the negative predictive value improved to 65.4% and 52.6% respectively, but the specificity and the positive predictive value decreased to 81.1% and 87.9% respectively. Overall, a positive buffy coat smear study was the best single reliable sepsis screen test to diagnose septicemia and the positive predictive value and specificity was high when two or more tests were combined together.

For early onset sepsis, it has also been suggested that documentation of polymorphs in the neonatal gastric aspirate at birth could serve as a marker of chorioamnionitis and it may be taken as one of the parameters of the sepsis screen [4,27]. The current protocol to be followed by the clinicians for the evaluation and management of neonates with risk factors / high clinical suspicion of septicemia is depicted in Fig.1.[8]

Maximum case fatality was seen in the late onset septicemia cases (57.1%) caused by gram negative organisms, while the case fatality was high among the early onset septicemia cases (44.4%) caused by gram positive organisms. Mortality was seen with Klebsiella pneumoniae in the LOS cases (50%), compared to EOS cases (47.4%). Similar observations were made by the some authors [17].The reported mortality rate in various studies from India ranges between 45% to 58% with most studies reporting a higher mortality rate (range =37% to 47%) among the EOS cases [3,15].



5. Conclusions

Neonatal septicemia is still a leading cause of mortality and morbidity in developing countries like India. It is more common among males, very low birth weight and preterm neonates. It is also found to be more common among the hospital inborn neonates with spontaneous vaginal delivery. Early onset septicemia is more common compared to late onset septicemia. Gram negative organisms are the predominant causative agents in neonatal septicemia. Hospital acquired infections are a major threat to the premature and low birth weight neonates with multidrug resistant microorganisms emerging as a major problem.

The objective scoring system suggested by Takkar VP and Bhakoo ON for the treatment protocol in clinically suspected cases

of neonatal septicemia had very low sensitivity and specificity which missed out 10 (17.24%) of the culture positive cases with a low risk score. Hence, this scoring system needs further evaluation in predicting neonatal septicemia on the basis of the presence or absence of the perinatal risk factors to decide upon the treatment regimen.

The value of the sepsis screen is more for excluding the diagnosis of neonatal septicemia which can be done reasonably if two screens 12-24 hours apart are negative. In a neonate who is stable otherwise or suspected of sepsis because of maternal risk factors, it is desirable to await results of sepsis screen before initiation of antibiotics. Since symptoms suggestive of sepsis may be caused by a variety of other illnesses, confirmation of sepsis by the sepsis screen tests may help in avoiding unnecessary antibiotic therapy.[15]

Blood culture is still the "Gold standard" for the diagnosis of septicemia in neonates and should be done in all cases of suspected septicemia. In view of the changing spectrum of the causative agents of neonatal septicemia and their antibiotic susceptibility patterns from time to time and from one hospital to another, a positive blood culture and the antibiotic susceptibility testing of the isolates are the best guide in choosing the appropriate antimicrobial therapy in treating neonatal septicemia.

Funding Sources- no funds have been received for this study or article.

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