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Role of early indicators in the diagnosis and outcome of neonatal sepsis in tertiary care hospital

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ABSTRACT

Sepsis is the commonest cause of neonatal mortality. Septicemia was the commonest clinical category with an incidence of 23 per 1000 live births. Number of screening procedures like micro ESR ,band cell count, I/T ratio, gastric aspirate for polymorphs, C –Reactive protein, alpha haptoglobin, serum fibrinogen levels have been tested in their efficacy of predicting neonatal sepsis. Positive CRP was found to be the single most sensitive and specific test in diagnosis of neonatal septicemia. The present study 180 neonates with clinical suspicion of septicemia included to evaluate the usefulness of combination of tests in septic screen in predicting neonatal sepsis. CRP was positive in 94 cases (91.3%) of culture positivity with statistical significance. Case fatality rate was 26.1%.

Keywords : Sepsis , Septic Screen

INTRODUCTION

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life infections[1]. Sepsis is the commonest cause of neonatal mortality; it is responsible for about 30-50% of the total neonatal deaths in developing countries[2]. Sepsis related mortality is largely preventable with rational antimicrobial therapy and aggressive supportive care[3].

The incidence of neonatal sepsis according to the data from National Neonatal Perinatal Database (NNPD, 2002-03) is 30 per 1000 live births. Among intramural births, Klebsiella pneumoniae was the most frequently isolated pathogen (32.5%), followed by Staphylococcus aureus (13.6%). Among extramural neonates (referred from community/other hospitals), Klebsiella pneumoniae was again the commonest organism (27%), followed by Staphylococcus aureus (15%) and Pseudomonas (13%)[4].

A number of screening procedures like micro ESR ,band cell count, I/T ratio, gastric aspirate for polymorphs, C –Reactive protein, alpha haptoglobin, serum fibrinogen levels have been tested in their efficacy of predicting neonatal sepsis. Positive CRP was found to be the single most sensitive and specific test in diagnosis of neonatal septicemia.

Neonates were classified as Probable and possible sepsis based on protocols of National Neonatal Forum of India [4]

AIMS AND OBJECTIVES

- To study the role of early indicators in the diagnosis of sepsis.
- To study the bacteriology and antibiotic sensitivity pattern of neonatal sepsis.
- To study the outcome of neonatal sepsis.

MATERIALS AND METHODS

This study was a prospective study conducted in the Department of Pediatrics, S.V.R.R.G.G. Hospital, Tirupati. For a period of one year October 2010 to September 2011.After admission detailed history and clinical findings were recorded in the proforma. Empirical antibiotic therapy was started according to antibiotic guidelines.

INCLUSION CRITERIA

1) All Neonates admitted in our hospital from outside as well as neonates born at Government Maternity Hospital, Tirupati with the risk factors, symptoms and signs that were suspicious of septicemia were included

A. Perinatal risk factors(Low birth weight, Prematurity, Birth asphyxia, Home delivery, PROM more than 24 hours, Maternal fever, Instrumentation)

B. Clinical risk factors (Refusal to suck,Lethargy / Irritability, Vomiting / Diarrhea, Abdominal distension, Convulsions, Umbilical discharge / conjunctival discharge/abscess/pustules, Hyper /hypothermia, Respiratory distress, Jaundice, Sclerema, Bleeding, Tachycardia/ bradycardia, Tachypnea, Apnea, Pallor)[5]

Exclusion Criteria

1. Neonates who received antibiotics before admission, with congenital malformations and associated surgical conditions and with history of indigenous drug administration

The neonates were investigated as follows

1. Total leucocyte count was done by using Neubaur's chamber. Leucopenia with count < 5000cells/ mm^3 was considered positive for septicemia.
2. Peripheral smear prepared with a drop of blood from heel prick and stained with Leishman's stain.
    a. The neutrophil is about 10-12 microns in diameter. The cytoplasm contains fine pale violet granules and number of lobes increase with maturity.
    b. Toxic granules were identified as a coarse darkly stained granules.
3. A ratio of immature neutrophils to neutrophil count was obtained after identifying the immature forms on peripheral smear. A ratio of > 0.2 was suggestive of septicemia.
4. Micro –ESR is simple and inexpensive. It was obtained by collecting capillary blood in micro hematocrit tube. Value of > 15 mm at the end of 1^{st} hour was considered as suggestive of infection.
5. C – reactive protein : This test is done by using diagnostic kit for in-vitro detection of CRP in human serum by the rapid slide latex agglutination qualitative method supplied commercially by Omega Diagnostics Ltd[6].
6. Blood culture : In all neonates blood sample was collected from peripheral vein with all aseptic precautions, prior to administration of antibiotic therapy[7].

OBSERVATIONS

Sepsis screen test results were compared with the blood culture results as the gold standard. The "p" value of less than 0.05 was accepted as indicating statistical significance. Data analysis was carried out using MS excel, epi info, 3.5.1 version.

180 neonates with clinical suspicion of septicemia were included in the study.

Table : 1 : Distribution of place of delivery

Place of delivery	Number	Percentage (%)
Extra mural	122	67.8
Intra mural	58	32.2
Total	**180**	**100.0**

➢ Septicemia was more among extramural babies than intramural babies.

Table No. 2 : Distribution according to TLC and culture

TLC range	Culture		Total
	Positive	Negative	
<5000	39(37.8%)	32(41.5%)	71
>5000	64(62.2%)	45(58.5%)	109
Total	**103**	**77**	**180**

χ^2 = 0.25; p=0.61; NS

- Leukocytosis was noticed among 64 cases (62.2%) with culture positivity compared to leucopenia found in 39 cases(37.8%).

Table No.3 : Distribution according to toxic granules and culture

Toxic granules	Culture		Total
	Positive	Negative	
Present	86(83.5%)	27(35.1%)	113
Absent	17(16.5%)	50(64.9%)	67
Total	**103**	**77**	**180**

χ^2 = 44.2;P<0.001; S

- Toxic granules in peripheral smear were found in 86 cases (83.5%) with culture positivity with statistical significance.

Table No.4 : Distribution according to I : T ratio and culture

IT ratio	Culture		Total
	Positive	Negative	
>0.2	78(75.7%)	23(29.8%)	101
<0.2	25(24.3%)	54(70.2%)	79
Total	**103**	**77**	**180**

χ^2=38.2; P<0.001;S

- I : T ratio was > 0.2 in 78 cases (75.7%) of culture positivity.

Table No. 5 : Distribution according to micro ESR and culture

micro ESR	Culture		Total
	Positive	Negative	
>15mm at end of 1st hr	76(73.8%)	4(5.2%)	80
<15mm at end of 1st hr	27(26.2%)	73(94.8%)	100
Total	**103**	**77**	**180**

χ^2= 83.9; P<0.001; S

- micro ESR was >15mm at the end of 1st hr in 76 cases (73.8%) of culture positivity.

Table No.6 : Distribution according to CRP and culture

CRP	Culture		Total
	Positive	Negative	
Positive	94(91.3%)	5(64.5%)	99
Negative	9(8.7%)	72(93.5%)	81
Total	**103**	**77**	**180**

χ^2 = 127.9; P<0.001; S

- CRP was positive in 94 cases (91.3%) of culture positivity with statistical significance.

Table No. 7 : Combination of two tests CRP and microESR

CRP (positive) and microESR(>15mm)	Culture		Total
	Positive	Negative	
Yes	76(73.8%)	3(3.9%)	79
No	27(26.2%)	74(96.1%)	101
Total	**103**	**77**	**180**

χ^2 = 87.4; P<0.001; S

- Sensitivity of the combination – 73.8% ; Specificity of the combination – 96.1%

Table No. 8: Combination of two tests CRP and toxic granules

CRP positive and toxic granules present	Culture		Total
	Positive	Negative	
Yes	79(76.7%)	4(51.2%)	81
No	24(23.3%)	73(94.8%)	97
Total	**103**	**77**	**180**

χ^2=90.6; P<0.001;S

- Sensitivity of the combination – 76.7%; Specificity of the combination – 94.8%

Table No. 9: Comparison of two tests toxic granules and microESR

Toxic granules (present) microESR(>15mm)	Culture		Total
	Positive	Negative	
Yes	65(63.1%)	2(2.6%)	67
No	38(36.9%)	75(97.4%)	113
Total	**103**	**77**	**180**

χ^2= 90.6

- Sensitivity of the combination – 63.1%; Specificity of the combination – 97.4%

Table No.10 :Distribution according to culture organism isolated by age range

Organism isolated	Age range		
	< 7days	> 7days	Total
Staph. Aureus	18	17	35
Klebsiella	18	15	33
Proteus	8	4	12
CONS	8	2	10
E .coli	6	2	8
Pseudomonas	2	0	2
Acinetobacter	0	1	1
Citrobacter	0	1	1
Moraxella	1	0	1
Negative	74	3	77
Total	**135**	**45**	**180**

χ^2 = 43.6; P<0.001; S

- Staphylococcus aureus, Klebsiella, Proteus, CONS were the common organisms isolated in early onset sepsis.
- Staphylococcus aureus, Klebsiella were more common among late onset sepsis.

Table No.11: Comparison of Sensitivity, Specificity, Positive Predictive value, Negative Predictive value, Accuracy and Kappa Statistic of Combination of any Two Tests

Combination of test	Sensitivity	Specificity	PPV	NPV	Accuracy	Kappa statistic
CRP + microESR	73.8%	96.1%	96.2%	73.3%	83.3%	0.67(substantial agreement)
CRP + toxic granules	76.7%	94.8%	95.2%	75.2%	84.4%	0.69(substantial agreement)
Toxic granules+ microESR	63.1%	97.4%	97.0%	66.4%	77.8%	0.57(moderate agreement)

- Specificity and positive predictive value were increased at the cost of sensitivity when combination of tests were done.

Table No.12 : Distribution according to culture sensitivity and death

Culture sensitivity	Mortality		Total
	Yes	No	
Positive	35(74.5%)	68(51.1%)	103
Negative	12(25.5%)	65(48.9%)	77
Total	**47**	**133**	**180**

χ^2=7.72; P=0.005; S

- Mortality rate was 74.5 % in culture positive cases and 25.5 % in culture negative cases.

Table No. 13 : Distribution according to organism isolated and mortality

Organism	Mortality		Total
	Yes	No	
Staph.aureus	8	27	35
Klebsiella	13	20	33
Proteus	3	9	12
CONS	1	9	10
E.coli	5	3	8
Pseudomonas	2	0	2
Acinetobacter	1	-	1
Citrobacter	1	-	1
Moraxella	1	-	1
Negative organism	12	65	77
Total	**47**	**133**	**180**

χ^2 = 28.6; P<0.001; S

- Mortality rate was high in Klebsiella (27.6%) isolates followed by Staphylococcus aureus (17.1%) and E. coli (10.6%).
- Survival was more in Staphylococcus aureus isolates (20.3%), followed by Klebsiella (15.1%) Proteus and CONS (6.7%) respectively.

DISCUSSION

In the present study most of the babies with sepsis were extramural babies (67.8%). This could be because of more referrals from in and around places to our hospital. This is comparable to other studies [8-10].

Leucopenia with count < 5000 cells/mm^3 was considered positive for septicemia. In the present study leucopenia was noticed in 71 cases(39.4%) and leukocytosis was found in 109 cases(60.6%). In a study by Gerdes et al[11] leucopenia was noticed.

Toxic granules in the peripheral smear indicative of sepsis were found in 62.8% of cases and most of them were culture positive (47.8%) and has statistical significance in the present study Gerdes et al[11].

In the present study an I/T ratio > 0.2 is taken as the diagnostic criteria for detecting neonatal septicemia. I/T ratio >0.2 was found in 101(56.1%) cases of which culture positivity was seen in 78(77.2%) cases. This was comparable with other studies by Gerdes et al[11] and Khatua SP et al[12] and had statistical significance.

MicroESR > 15 mm at end of 1st hr was taken as positive test for neonatal septicemia. In the present study micro ESR >15mm was found in 80 cases and culture positivity was found in 76(95%) cases which is of statistical significance. These observations are consistent with other studies by Rekha Sriram et al[13] and Singh et al[14].

In the present study CRP was positive in 99 cases of which culture positivity was found in 94(94.9%) cases which has statistical significance and is consistent with other studies by Gerdes et al[11] and S. Datta et al[15].

In the present study combination of any two tests had more specificity and positive predictive value. In study by Gerdes et al[11] combination of tests had more of sensitivity and negative predictive value. Present study is consistent with Rekha Sriram et al[13] study.

Table No. 14: Comparision of different studies

Author	Year	Sensitivity	Specificity	PPV	NPV
Gerdes et al[11]	2004	100%	83%	27%	100%
Rekha Sriram[13]	2011	55.3%	91.3%	98.3%	19.3%
Present study	2012	71.2%	96.1%	96.2%	71.65

In a study by B.P Zakariya et al[16], out of 120 cases, 50 (41.66%) were culture positive. Klebsiella (66%) followed by CONS (12%) were more common. Klebsiella was the common pathogen in both early onset sepsis and late onset sepsis which is resistant to all the antibiotics tested except amikacin and meropenem and 32% of them were found to be ESBL producers.

In a study by S Begum et al[17] the most common etiologic agent was Klebsiella. In our study the most common etiologic agent was Klebsiella.

OUTCOME

In the present study 47 cases (26.1%) died out of 180 cases of neonatal sepsis. Thus the case fatality rate was 26.1%.In the present study out of 47 culture positive cases mortality was found in 35 (74.5%) cases which is statistically significant. Most common pathogen responsible for mortality was Klebsiella (27.7%) followed by staphylococcus aureus (17%). B.P Zakariya et al[16] in their study found Klebsiella as the common pathogen.

CONCLUSIONS

Culture positivity was found in 103 (57.2%) cases. Staphylococcus aureus (34%) followed by Klebsiella (32%) were the common pathogens isolated. Mortality was high in Klebsiella isolates. All sepsis screening parameters used were statistically significantly associated with culture proven sepsis. Sepsis screen has good specificity, sensitivity and positive predictive value and is a valuable aid in early diagnosis of neonatal septicemia. Sepsis screen is simple, cheap, less time consuming and easy to perform even at bedside. Combination of two tests had more specificity and positive predictive value. Mortality was higher in the culture proven cases35 (74.5%) which is statistically significant.

Limitations of the study

Small sample size need larger sample size, pathogens and antibiotic sensitivity vary with place to place .

Whats new

Combination of two tests had more specificity and positive predictive value so even peripheries where blood culture facilities are not there is useful for diagnosis and management of sepsis to decrease mortality.

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