Type of Article: Original Article Research

CORRELATION OF SEPSIS SCREENING AND BLOOD CULTURE & SENSITIVITY IN CLINICALLY SUSPECTED CASES OF NEONATAL SEPSIS AND THEIR ANTIBIOTIC SUSCEPTIBILITY PATTERNS

Chithra S[1]*, Aryama Aniruddhan. V. J[2], Thota Chakradhar Reddy [3]

[1]Assistant Professor, [3]Senior Resident, [3]3rd Year PG, Dept of Paediatrics, Meenakshi Medical College & Research Institute, Kanchipuram India

Corresponding Author: Dr. Chithra S

Assistant Professor, Dept of Paediatrics, Meenakshi Medical College, Kanchipuram, India.

Abstract

Background: The definition of neonatal Septicemia is "a syndrome characterized by systematic signs and symptoms due to generalized bacterial Infection with a positive blood culture, in the first 28 days of life after birth.

Objective: to correlate Blood culture results with the Sepsis Screen to form an idea about the usefulness of investigations in early diagnosis and treatment of Neonatal Septicemia.

Methods: This study was conducted in the Department of Pediatrics, Meenakshi Medical College & Research Institute, Kanchipuram from February 2022 to March 2023. Blood samples were collected from 125 clinically suspected cases of Neonatal Septicemia admitted to the Neonatal Intensive Care unit in the Department of Pediatrics..

Results: Of the 64 culture positive cases, early onset septicemia was seen in75% of cases and late onset septicemia in 25% of cases. Septicemia was seen among 64% of Preterms,40.6% of very low birth weight neonates, 79.7% of neonates with spontaneous vaginal delivery and 62.5% of hospital inborn neonates. Unclean per vaginal examination prior to delivery, prematurity, low birth weight and birth asphyxia were the common risk factors seen in the culture positive cases. Majority of the culture positive cases i.e. 42.2% belonged to the high risk sepsis score group, followed by 40.6% in the moderate risk group and 17.2% of the cases in the low risk group. Gram negative organisms were the predominant causative agents of septicemia in 56.3% of cases compared to Gram positive organisms in 43.7% of cases.

Conclusion: In view of the ever changing spectrum of the causative agents of neonatal septicemia and their antibiotic sensitivity patterns from time to time and from one institute to another, a positive blood culture and the antibiotic susceptibility testing of the isolates are the best guide to the antimicrobial therapy

Keywords: Sepsis Screening, Blood Culture & Sensitivity, clinically suspected cases of neonatal sepsis, Antibiotic Susceptibility**.**

INTRODUCTION

Bacterial infections are the commonest causes of Neonatal morbidity and mortality in the Neonatal life. Fulminant and fatal outcomes may occur with complications such as shock, disseminated intra-vascular coagulation and consequent multi- system /organ failure. Early

diagnosis is the best option for intervention and preventing mortality in such conditions.

The National Neonatal Perinatal Database (NNPD) reports that the Neonatal Septicemia in tertiary care institutions has an incidence in the range of 0.1% - 4.5% and was 30 per 1000 live births contributing to 19% of all the mortalities among the neonates born in the Hospitals.[1]

The clinical presentation is tricky and mimics several other diseases causing difficulty inearly diagnosis. The presentation of cases in the clinics are subtle and nonspecific needing a high index of suspicion for early diagnosis and management. Certain perinatal risk factors have been evaluated as indicators for the prediction of Neonatal Septicemia for getting a objective score for the management.

The neonatal sepsis screening score consists six perinatal risk factors for evaluating the cases, to be used by the clinicians for screening and treating the Neonates for Septicemia

Neonatal septicemia is categorized into Two Groups as Early onset septicemia (before one week of Life) and Late Onset Septicemia (after one week of Life)[2]. But for the availability of advanced antibiotic therapy which can treat all Neonatal Septicemia cases successfully, the case fatality rate is very high. This stresses upon the need for early diagnosis and treatment[3]. The GOLD STANDARD for the diagnosis of the Neonatal Septicemia is a Positive Blood Culture[3]. Since culture results take 48-72 hrs. for definitive indication causing in delay of treatment, even when the culture results are awaited, an early protocol of diagnosis and rational therapy by way of certain rapid diagnostic tests such as Total WBC count, Absolute Neutrophil count, Immature and Total Neutrophil Count (I/T), Platelet count, C-Reactive protein, Micro ESR, Buffy Coat Smear Study can be used as screening tests for sepsis[4,5] in addition to the sepsis score [6] to initiate presumptive therapy.

Gram Negative bacteria contributes more to septicemia (65%-85%) than the Gram Positive bacteria which contributes (15%) as evidenced by the studies in India [7]. There has been a constant change in the organisms isolated and their drug sensitivity [7] due to several factors like Gestational Age, Birth Weight, Maternal Risk factors, place and mode ofdeliveryamong others. The abuse of antibiotics has further complicated the scenario the by rise of drug resistant strains of bacteria with fatal consequences. This scenario emphasizes the need for constant review of causative organisms and their antibiotic susceptibility and to use antibiotics responsibly.[7,8]

In this study an attempt is made to correlate Blood culture results with the Sepsis Screen to form an idea about the usefulness of investigations in early diagnosis and treatment of Neonatal Septicemia. The bacteria that are responsible for neonatal septicemia are also isolated and identified from blood with their antibiotic susceptibility pattern being determined to guide therapy

MATERIALS AND METHODS

This study was conducted in the Department of Pediatrics, Meenakshi Medical College & Research Institute, Kanchipuram from February 2022 to March 2023.. Blood samples were collected from 125 clinically suspected cases of Neonatal Septicemia admitted to the Neonatal Intensive Care unit in the Department of Pediatrics.

Inclusion criteria

1. Newborn babies in the age group of 0-28 days presenting with one or more clinical features suggestive of Septicemia were included in the present study.

2. Neonates with septicemia having one or more risk factors such as Prematurity, Low Birth Weight, Birth Asphyxia, foul smelling Liquor Amnii, unclean per vaginal examination before delivery, prolonged rupture of the membranes and prolonged labor, were included in the study

Exclusion criteria

Neonates with clinical features suggestive of Septicemia already receiving Antibiotics were excluded from the study.

METHODS: In the present study the following investigations were adopted to achievethe objectives of the study.

- Buffy coat smear examination.
- C- Reactive protein assay.
- Total leucocyte count.
- Absolut eneutrophil count.
- Band cell count
- Immature/Total neutrophil count ratio (I/Tratio).
- Blood culture
- Antibiotic susceptibility testing of the isolated pathogen from the blood.

Sample collection:

An area of approximately 5 cm over the venipuncture site was disinfected with 70% alcohol rubbing vigorously and allowed to dry.

Blood culture:

About 1 ml of blood was drawn aseptically and inoculated into a blood culture bottle making

a dilution of 1 in 10 to nullify the natural bacteriostatic/bactericidal activity of blood.

Antibiotic susceptibility testing:

Antibiotic susceptibility testing was done for all the isolates. The following antibiotics were tested for susceptibility:

Buffy coat smear examination:

Buffy coat smear examination was done by taking 1 ml of venous blood into a sterile bottle containing EDTA in the concentration of 2 mg/ml and mixed well.

C-reactive protein assay:
The sensitivity of the antigen in the kit for a visible agglutination is 6µg/ml. So in this study, a CRP value of >6µg/ml was taken as a positive test.

Other haematological tests: The Total leucocyte count, differential count, Absolute neutrophil count, Band cell count, I/T ratio and the Platelet count were calculated as per standard hematological methods.
The cut off values of the positive rapid screening tests in this study are as follows: C-Reactive protein (CRP): >6µg/ml. Total leucocyte count (Leucopenia): < 5,000cells/cu.mm. Absolute neutrophil count (Neutropenia):<1,500cells/cu.mm. Band cell count to total neutrophil count ratio (I/Tratio):>0.2 Platelet count (Thrombocytopenia): < 1.5 lakhs/cu.mm.

Statistical analysis:

The statistical analysis was done using the results of the present study. Sepsis score and Sepsis screen test results were compared with the blood culture results as the Gold standard. The number of True positives (TP), False positives (FP), True negatives (TN) and False negatives (FN) results were determined and Sensitivity, Specificity, Positive predictive accuracy and Negative predictive accuracy and the p-value for significance of the screening tests were calculated.

RESULTS

Of the 125 cases studied, 64 cases yielded a positive blood culture giving a success rate of 51.2%**.**
Out 125 cases studied, 84(67.2%) were males and41 (32.8%) were females.
Out of the76 male neonates, 39(60.9%) were blood culture positive and, of the 41female neonates, 25 (39.9%) were blood culture positive.
Majority i.e. 103 (82.4%) neonates were less than one week old, of which 50 (78.1%) cases yielded a positive growth in blood culture. The mean age of newborns in our study population is 4.16days.

- Majority. 48 (38.4%) neonates were in the Very low birth weight category, of which
- The mean birth weight of our study population was 2.10 kgs.

26 (40.6%) were culture positive.

- Of the 125 cases, 71 (56.8%) were preterm babies, 44 (35.2%) were term neonates and 10 (8%) were post term neonates.
- Among culture positive cases, 41 (64.0%) were preterm, 19 (29.7%) were term, while only 4 (6.3 %) were post term neonates. Maximum culture positive cases were seen among the preterm neonates.
- Out of the 125 cases 101 (80.8%) of the neonates had spontaneous vaginal delivery while 5 (4.0%) were delivered by assisted instrumental vaginal delivery and 19 (15.2%) were delivered by caesarean section.
- The proportion of culture positive cases was high among neonates delivered by spontaneous vaginal delivery constituting about 51 (79.7%) of the cases.

- Of the 125 neonates, 68 (54.4 %) were inborn babies, of which 40 (62.5%) were culture positive whereas 51 (40.8%) were hospital out born babies with 23 (35.9%) being culture proven cases.
- Maximum culture positive cases were from the hospital inborn neonates.

Table 1: Distribution of perinatal risk factors among cases

RISK FACTORS	CLINICALLY SUSPECTED				CULTURE POSITIVE			
	EOS(100)		LOS(25)		EOS(48)		LOS(16)	
	NO.	%	NO.	%	NO.	%	NO.	%
FSLA	38	38	7	28	21	43.8	5	31.3
UPV	87	87	25	100	45	93.6	13	81.3
PL	30	30	3	12	16	33.3	2	12.5
1min.APGAR <6	61	61	5	20	31	64.6	4	25
PROM	46	46	10	40	16	33.3	6	37.5
GA <37W / B.WT<2KG	63	63	19	76	33	68.7	12	75

- Among the clinically suspected cases, 78 (87%) of EOS and all the LOS cases 25 (100%) had the major risk factor of unclean per vaginal (PV) examination prior to delivery.
- In the culture positive cases, 45 (93.6%) of EOS had an unclean PV examination; while 13 (81.3%) LOS cases had a history of unclean PV examination. The difference observed was statistically not significant in either the clinically suspected or the culture positive cases.
- Gestational age <37 weeks and / or a Birth weight ≤ 2 kgs was the second majorriskfactor seen among 63 (63.16%) and 19 (76%) of the clinically suspected cases of EOS and LOS respectively. Among the culture positive cases, 33 (68.7%) of EOS cases and 12 (75%) of LOS cases had this risk factor. The difference observed was statistically not significant in

both the groups.

 The third major risk factor seen among the clinically suspected cases was a One- minute Apgar score<6 among61 (61%)of EOS cases and 5 (20%) of LOS cases. Among the culture positive cases, 31(64.6%) of EOS cases and 4(25%) of LOS cases had this risk factor. The difference observed was statistically not significant in both the groups.

Table 2: Distribution of sepsis score among the cases

SEPSIS SCOREOUT OF 10	CLINICALLY SUSPECTED						CULTURE POSITIVE					
	EOS		LOS		TOTAL		EOS		LOS		TOTAL	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
LOWRISK 0-3	20	20	9	36	28	22.4	6	12.5	5	31.2	11	17.2
MODERATE RISK4-5	35	35	10	40	46	36.8	19	39.6	7	43.8	26	40.6
HIGHRISK 6-10	45	45	6	24	51	40.8	23	47.9	4	25	27	42.2
TOTAL	100	80	25	20	125	100	48	75	16	25	64	100

 Of the clinically suspected cases, 45 (45%) belonged to the high risk group, followed by the moderate risk group 35 (35%) while only 20 (20%) belonged to the low risk group.

 Among the culture positive cases, 27 (42.2%) belonged to the high risk group, followed by 26 (40.6%) cases in the moderate risk group and only11 (17.2%) cases in the low risk group. 53 (82.8%) of the cases belonged to both the moderate and high risk groups.

Table 3: Distribution of sepsis screen parameters among the cases

SEPSIS SCREENING	CULTURE POSITIVE(64)		CULTURE NEGATIVE(61)		TOTAL(125)	
	NO.	%	NO.	%	NO.	%
CRP+VE	58	90.6	52	85.2	110	88
-VE	6	9.4	9	14.7	15	12.1
WBC<5000	8	12.5	5	8.2	13	10.4
5000-20000	53	82.8	44	72.1	97	77.6
>20000	3	4.7	12	19.7	15	12.0
ANC<1800	2	3.1	3	4.9	5	4.0
>1800	28	43.8	23	37.7	51	40.8
>5500	34	53.1	35	57.3	69	55.2
I/T>/=0.2	51	79.7	47	77.0	98	78.4
<0.2	13	20.3	14	22.9	27	21.6
PLT<150000	27	42.1	18	29.5	45	36.0
>150000	37	57.8	43	70.4	80	64.0
SMEARGRAM+V	24	37.5	10	16.4	34	27.2

E	34	53.1	9	14.7	43	34.4
GRAM–VE SMEAR-VE	6	9.3	42	68.9	42	33.6

C- Reactive protein was positive in 110 (88.0%) of 125 cases of which 58 (90.6%) were culture positive and 52 (85.2%) were culture negative.

Leucopenia was seen in 13 (10.4%) of the 125 cases. Of this 8 (12.5%) were culture positive while 5 (8.2%) were culture negative. 97 (77.6%) cases had normal WBC counts, of which 53 (82.8%) were culture positive. Leukocytosis was seen in 15 (12.0%) of the125 cases, of which 3 (4.7%) cases were culture positive.

Neutrophiliawas seen in 69 (55.2%) of the 125 cases, this included 34 (53.1%) culture positive and 35 (57.3 %) of culture negative cases, while Neutropenia was seen in only 5(4%) of the 125 cases; of which 3 (4.9%) were culture positive. The rest 51 (40.8%) of the 125 cases had a normal Absolute Neutrophil count, out of which 28 (43.8%) cases being culture positive.

I/T ratio ≥ 0.2 was seen in 98 (78.4) of the 125cases; of these 51 (79.7%) were culture positive and 47 (77.0%) were culture negative.

Thrombocytopenia was seen in 45 (36.0%)of 125 cases, 27(42.1%) were culture positive Where as 18 (29.5%) were culture negative. 80 (64.0%) of the 125 cases had normal platelet counts.

Buffy coat smear study showed Gram positive cocci in 34(27.2%) of 125 cases, out of which 24 (37.5%) cases were culture positive. Gram negative bacilli was seen in 43 (39.4%) of 125 cases, 34 (53.1%) cases were culture positive. 42(33.6%) of 125 cases showed no organisms on buffy coat smear study, but 6 (9.34%) of these cases were culture positive.

Table 4: Blood culture results among the cases

CULTURE STATUS	CASES				TOTAL	
	EOS		LOS		NO.	%
	NO.	%	NO.	%		
POSITIVE	48	75	16	25	64	51.2
NEGATIVE	52	85.2	9	14.8	61	48.8
TOTAL	100	80	25	20	125	100

Of the 125 clinically suspected septicemic cases, 64 (51.2%) were culture positive and 61 (48.8%) were culture negative.

Of the 64 culture positive cases, early onset septicemia was seen in 48 (75.0%) cases and 16 (25.0%) cases showed late onset septicemia.

Table 5: spectrum of bacterial isolates

BACTERIAL	CULTURE POSITIVE	TOTAL

ISOLATES	EOS		LOS		NO.	%
	NO.	%	NO.	%		
S.aureus MRSA	6	75.0	2	25	8	28.6
S. aureus MSSA	13	63.2	3	18.8	16	57.2
CONS	1	5.3	3	75.0	4	14.3
TOTAL	20	71.4	8	28.6	28	43.7
KLEBSIELLA	20	74.0	7	25.9	27	77.1
E.coli	3	75.0	1	25.0	4	11.4
P.aeuruginosa	4	100	0	0	4	11.4
P.vulgaris	1	100	0	0	1	2.8
TOTAL	27	77.1	8	22.9	36	56.3

- Majority i.e. 36 (56.3%) of the isolates were Gram negative organisms, Klebsiella pneumoniae being the commonest isolated in 27 (42.2%) of the 64 culture positive cases, followed by Escherichia coli 4 (6.2%).
- The other organisms isolated were Pseudomonas aeruginosa 4(6.2%),Proteusvulgaris1 (1.6%).
- Gram positive organisms were obtained in 28 (43.7 %) out of 58 cases.

Staphylococcus aureus was the commonest isolate 24 (42.9%); of which methicillin sensitive Staphylococcus aureus accounted for 16 (25.0%) cases, followed by methicillin resistant Staphylococcus aureus in 8 (12.5%) cases.

Table 6: Antibiotic susceptibility pattern of the gram positive bacterial isolates

ANTIBIOTICS	S.AUREUS–MRSA		S.AURUES-MSSA		CONS	
	NO.	%	NO.	%	NO.	%
AMP	0	0	2	13.3	0	0
AMK	3	37.5	13	86.7	1	25.0
GM	2	25.0	8	53.3	0	0
P	0	0	2	13.3	0	0
E	0	0	4	26.7	0	0
AMC	1	12.5	10	66.7	2	50.0
CIP	1	12.5	1	66.7	0	0
CTX	0	0	12	80.0	2	50.0
OFX	6	75.0	15	100	3	75.0
OX	0	0	10	67.0	0	0
CN	0	0	12	80.0	0	0
CFR	1	12.5	11	73.3	2	50.0
CFZ	0	0	13	86.7	1	25.0
MET	0	0	16	100	2	50.0
VA	8	100	16	100	4	100

showing 100% susceptibility to Ofloxacin, Methicillin and Vancomycin, while more than 80%

 Methicillin sensitive Staphylococcus aureus (MSSA) was the major gram positive isolate were susceptible to Amikacin, Cephalexin and Cefazolin.

 MRSA was 100% susceptible to Vancomycin (100%),followed byOfloxacin (75.0%).

 All the CoagulaseNegative Staphylococci were susceptible to Vancomycin, and 75 % were susceptible to ofloxacin while 50% of them were susceptible to Amoxyclav,Cefotaxime, Cefadroxil, Cefazolin and Methicillin.

 All the Gram positive isolates in the present study were 100% susceptible to Vancomycin.

Table 7: antibiotic susceptibility pattern of the gram negative bacterial isolates

ANTIBIOTIC	KLEBSIELLA		E.COLI		P. AERUGINOSA		P.VULGARIS	
	NO	%	NO	%	NO	%	NO	%
AMP	1	3.7	0	0	0	0	0	0
AMK	5	18.5	1	25.0	2	50.0	0	0
GM	2	7.4	1	25.0	2	50.0	0	0
OFX	20	74.0	3	75.0	4	100	0	0
AMC	3	11.1	1	25.0	0	0	0	0
CTX	5	18.5	0	0	1	25.0	0	0
CAZ	7	25.9	2	50.0	4	100	0	0
CTR	3	11.1	0	0	3	75.0	0	0
CFX	7	25.9	1	25.0	3	75.0	0	0
CZX	18	66.6	2	50.0	3	75.0	0	0
CB	1	3.7	1	25.0	4	100	0	0
CN	0	0	1	25.0	1	25.0	0	0

 The major Gram negative isolates were Klebsiella pneumoniae (27),of these 20 (74%) were susceptible to Ofloxacin and 18 (66.6%) were susceptible to Ceftizoxime.

 3(75%) of E.coli were susceptible to ofloxacin, 2 (50%)oftheEscherichiacoliisolates weresusceptible to ceftazidime, ceftizoxime.

 All the Pseudomonas aeruginosa were susceptible to Ofloxacin, Ceftazidime, carbenicillin while only 50% of the isolates were susceptible to Amikacin, Gentamicin, and 75 % to Ceftriaxone, Cefuroxime and Ceftizoxime.

 Proteus vulgaris was resistant to all the antibiotics.

Table 8: Correlation of sepsis screen parameters with the blood culture status

SCREENINGTESTS	CULTURE POSITIV	CULTURE NEGATIVE	TOTAL	P-VALUE

	E						
	NO.	**%**	**NO.**	**%**	**NO.**	**%**	
CRP+VE	58	90.6	52	85.2	100	88.0	0.359
LEUKOPENIA	8	12.5	5	8.2	13	10.4	0.434
NEUTROPENIA	2	3.1	3	4.9	5	4.0	0.612
I/TRATIO>0.2	51	79.7	47	77.0	98	78.4	0.722
THROMBOCYTOPENIA	27	42.2	18	29.5	45	36.0	0.154
BUFFYCOAT SMEAR	58	90.6	61	100	119	95.2	**<0.0001**

- C-Reactive protein and buffy coat smear had the best correlation with blood culture positivity, 58 (90.6%) of the 64 blood culture cases were CRP and buffy coat smear positive.
- Thiswas followed bytheI/ Tratio ≥ 0.2in 51(79.7%) cases.
- The parameter that was statistically significant in our study was the buffy coat smear study.

Discussion

In this section we discuss our results and compare them with some studies done by different authors in the past few decades.

- Maximum culture positive cases were seen in neonates less than one week of age (early onset septicemia) as compared to neonates aged more than one week (late onset septicemia)in the present study.
- The mean age of onset of septicemiain the present study was 4.81years.

females in the present study, n showing a ratio of1.56 : 1.

Tallur et al.,[9] and Roy et al.,[8] reported similar findings in their studies. The cause of ascending infection could be due to the rupture of membranes or during the passage of the baby through the infected birth canal or at the time of resuscitation in the labor room.

G. Karthikeyan et al.[10] reported an equal proportion of EOS and LOS cases in their study, while the study by R.S. Jaswal et al.,[11] shows a higher proportion of LOS cases than EOS cases. These findings could suggest a nosocomial source of infection and the geographical variation in the infecting organism.

The reason for the higher proportion of EOS could be the immature immunological responses in the newborns during the first week of life, making them more susceptible to infections in this period.

 In this study the proportion of culture positive septicemic cases were higher among the very low birth weight neonates when compared with the Low and Normal birth weight neonates.
 The mean birth weight of the neonates in this study was 2.24± 0.5kgs.

 The results of the present study are comparable with the studies conducted by Tallur et al.[9] and Zawar et al.[12]
 The proportion of culture positive septicemia cases was higher among the preterm neonates in this study.

 This was comparable to the results reported by Betty Chackoet al.,[13]

 Tallur et al.[9] showed a higher proportion of cases among term neonates compared to preterm neonates. These variations are probably due to differences in the population characteristics and the occurrence of the predisposing factors among them.
 Preterms are more susceptible to infections due to inherent deficiencies of both humoral and cellular defense mechanisms.
 Maximum (79.31%) number of cases was seen in neonates delivered by spontaneous vaginal deliveryin the present study.

 The result of this study was comparable with the observations in the other studies.
 The higher rates of septicemia in vaginally delivered neonates could be due to the surface colonization of the neonate with the microbiota of the vagina during delivery.

 The present study showed a bigger proportion of culture positive cases among the inborn neonates compared to neonates delivered and referred from other hospitals.

Examination before delivery (90.6%ofculture positive cases), low gestational age or birth weight (70.3%) and 1 minute APGAR </=6(54.6%) as the most common risk factors.

 This is comparable with the study conducted by Takkar et al.,[6] who found a higher rate of septicemia among cases having unclean PV before delivery and prolonged labor for >24 hrs.
 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 were among the high risk group, followed by

 Sriram R [14] reported a sensitivity of 40%, 39.7%, 43.1% respectively for a low, moderate and high risk sepsis score categories.

 In the present study, Klebsiella pneumoniae was the predominant isolate, followed by S. aureus.

 Gram negative organisms were the predominant isolates as compared to Gram positive organisms (56.3%vs43.7%respectively) in the present study.

 Similar observations were made by Tallur et al.,[9] Royet al.,[8]and

 G.Karthikeyan et al.,[10] R.S Jaswaletal.,[11] reported S.aureus as the commonest isolate, while P. aeruginosa was the commonest isolate in the study by Betty Chacko et al.[15].

 An Absolute Neutrophil count of <1,800 cells/cu.mm was taken as the diagnostic criteria for detecting neonatal septicemia in our study.

 Low sensitivity, specificity and negative predictive value of 3.1%, 5%, 46.6% respectively was observed. However, the test had the highest positive predictive value of 60% among the sepsis screen parameters studied. Contrasting reports were shown by Sriram R et al , Bhale et al and Lakhey. A et al negative predictive value. The variations in results shown in the different studies may be due to differences in the sampling time, infection severity, the diagnostic criteria that was followed, age of the neonates and reduced sensitivity of this test after the first week of life.

 In the present study with an I/T ratio ≥ 0.2 as the criteria for detecting neonatal septicemia, the sensitivity, specificity were at 79.6%, 77% respectively, while the positive predictive value was comparatively low at 48% in diagnosing septicemia and a negative predictive value of 51.9%. Sonawane et al[15]reported a sensitivity and specificity of 62.5% and 56.25 % respectively and A lakheyet al [16]reported a sensitivity of 73% and a positive predictive value of 63.8%.

 The differences in the results of this parameter shown by the different studies may be due to the changes in the sampling time, infection severity, age of the neonates, diagnostic criteria used and reduced sensitivity of this test after the first week of life.

 Thrombocytopenia: Platelet counts < 1.5 lakhs / cu, mm was taken as a criteria for detecting neonatal septicemia in this study. The present study showed a 42%, 29%, 40% and 53% of sensitivity, specificity, positive predictive value and negative predictive value respectively . Whereas the study by Majumadar. A et al[17] showed a sensitivity of 70%, specificity of 80%, positive predictive value of 40%, negative predictive value of 95%.

 In the present study, Buffy coat smear positivity was the most sensitive 90.6% along with CRP positivity. It also has the highest negative predictive value 87.5% of all the tests considered for the study. Sriram R[14] reported a 74.3% sensitivity, 86.7% specificity, 89.7% positive predictive value and 68.4% negative predictive value.

 In the present study, majority of the isolates were Gram negative organisms accounting for 56.3% of the isolates, Klebsiella pneumoniae being the commonest, isolated in 27(42.2%) of

the 64 culture positive cases.

 Maximum isolates of Klebsiella pneumoniae were susceptible to Ofloxacin 20(74%) and Ceftizoxime18 (66.6%), ceftazidime(25.9%),cefuroxime(25.9%). Most of the isolates were resistant to ampicillin, gentamicin, Carbenicillin, while there was 100% resistance to cephalexin.

Susceptibility was high with the second generation fluoroquinolones like Ofloxacin and the Third generation Cephalosporins like Ceftizoxime in the present study.

 Tallur et al.,[9] reported in their study that Klebsiella was the commonest pathogen isolated and were more susceptible to gentamicin, amikacin and the third generation cephalosporins

 Madhu Sharma et al., 2002[18] in their study reported predominantly Gram negative organisms (88.8%), with Klebsiella (47.1%) being the commonest isolate. They found a combination of sulbactum/cefoperazone (97.4%) to be most sensitive, followed by ceftizoxime (66.47%).

Overall, all the gram negative organisms except Proteus vulgaris were most susceptible to Ofloxacin and the third generation cephalosporin like Ceftizoxime, while most of the isolates showed resistance to Ampicillin and Cephalexin.

Staphylococcus aureus was the major Gram positive organism isolated constituting 24 (43.85%) of the isolates, with Methicillin Sensitive Staphylococcus aureus (MSSA) beingthe major organism accounting for about 16 cases of S. aureus, while 8 isolates were Methicillin resistant strains of S. aureus (MRSA).

All the MSSA isolates were 100% susceptible to Ofloxacin, Methicillin and Vancomycin, while only amikacin and cephazolin showing sensitivity in more than 80%. Maximum number of MSSA cases belonged to the early onset septicemia group accounting for 13 (63.2%) of the isolates.

All the isolates of MRSA showed 100% susceptibility to Vancomycin, followed by Ofloxacin (75%), Amikacin (37.5%), while less than 15% of the isolates were susceptible to other drugs. Apart from Methicillin, these isolates were also resistant to penicillin, oxacillin, Cefotaxime, cephalexin and cefazolin. Majority of the MRSA (75%) were from the early onset septicemia cases.

 In the present study, CONS isolates constituted only 14.3% of the gram positive isolates. 100%weresusceptibletoOfloxacinandVancomycin, while 50% of them were susceptible to Amoxyclav, Cefadroxil and methicillin.

 Similar patterns of antibiotic susceptibility of the CONS isolates was reported by Anand et al[19] in their study. Jyothi. P et al[20] reported a high sensitivity to Linezolid 91% followed by Piperacillin 66%.

 Overall, all the Gram positive isolates in the present study were 100% susceptible to Vancomycin.

CONCLUSION

Neonatal septicemia is a leading cause of neonatal mortality and morbidity in developing countries like India. It is more common among males, LBW and preterm neonates.

It was also found to be more prevalent among in born neonates with spontaneous vaginal delivery. Most of the cases were early onset septicemia 48(75%) compared to late onset septicemia 16(25%). Gram negative organisms are the predominant causative agents in neonatal septicemia with K.pneumoniae at the top of the list.

S.aureus is the most common Gram positive bacteria causing neonatal septicemia. MRSA is a significant problem in neonatal nurseries.

Blood culture is still the "Gold standard" for the diagnosis of septicemia in neonates and should be performed in all suspected cases of septicemia prior to starting antibiotics.
Amikacin and Cefotaxime, the commonly used antibiotics as the first line therapy in our hospital were found to be a less effective combination.
Overall, all the isolates were most susceptible to Ofloxacin and the third generation cephalosporin like Ceftizoxime, which are the best alternatives for the first line therapy in neonatal septicemia.
In view of the ever changing spectrum of the causative agents of neonatal septicemia and their antibiotic sensitivity patterns from time to time and from one institute to another, a positive blood culture and the antibiotic susceptibility testing of the isolates are the best guide to the antimicrobial therapy.

REFERENCES

1. National Neonatal Perinatal Database. Report forthe year2002-03.National Neonatology Forum, India
2. ClohertyJP, Eichen wald EC,Stark AR.Manual of neonatal care.8thed.Philidelphia: Lippincott, Williams and Wilkins Publication; 2017
3. Gotoff SP,Behrman RE.Neonatal septicemia.J Pediatr.1970Jan;76(1):142–53
4. Paul VK,SinghM.Diagnosis and treatment of neonatal sepsis.Indian Pediatr.1986 Dec;23(12):1023–35.
5. GerdesJS,PolinR.Earlydiagnosisandtreatmentofneonatalsepsis.IndianJPediatr.1998 Jan-Feb;65(1):63–78
6. TakkarVP, Bhakoo ON, NarangA. Scoring system for the prediction of early neonatal infections. Indian Pediatr. 1974 Sep;11(9):597–600
7. Mathur NB.Neonatal sepsis. IndianPediatr.1996Aug; 33(8):663–74.
8. Roy I, Jain A, Kumar M, Agarwal SK. Bacteriology of neonatal septicaemia in a tertiary care hospital of northern India. Indian J Med Microbiol. 2002 Jul-Sep;20(3):156–9
9. Shashikala S. Tallur, Kasturi AV, Shobha D. Nadgir, Krishna BVS. Clinico- bacteriological

Study of Neonatal Septicemia in Hubli. Indian J Pediatr. 2000;67(3):169–74

10. Karthikeyan G, Premkumar K. Neonatal sepsis: staphylococcus aureus as the predominant pathogen. Indian J Pediatr. 2001 Aug;68(8):715–7
11. Raghavan M, Mondal GP, Bhat BV, Srinivasan S. Perinatal risk factors in neonatal infections. Indian J Pediatr. 1992 May-Jun;59(3):335–40
12. Zawar MP, Tambekar RG, Deshpande NM, Gadgil PA, Kalekar SM. Early diagnosis of neonatal septicemia by sepsis screen. Indian J Pathol Microbiol. 2003 Oct;46(4):610–2.
13. ChackoB,Sohi I.Earlyonsetneonatalsepsis.IndianJPediatr.2005Jan;72(1):23–6.
14. Arguedas A, Sierra H, Soley C. Fluoroquinolones in Pediatrics. Curr Drug Ther. 2006;1(1):117–25
15. Sonawane VB, Gaikwad SU, Kadam NN, Gavhane J. Comparative Study of Diagnostic Markers in Neonatal Sepsis. Journal of Nepal Paediatric Society. 2014 May 1;34(2).
16. Lakhey A, Shakya H. Role of sepsis screening in early diagnosis of neonatal sepsis. Journal of Pathology of Nepal. 2017 Mar 30;7(1):1103-10.
17. Majumdar A, Jana A, Jana A, Biswas S, Bhattacharyya S. Hematologic scoring system (HSS): A guide to decide judicious use of antibiotics in neonatal septicemia in developing countries. J Appl Hematol 2013;4:110-3
18. De A, Saraswathi K, Gogate A, Raghavan K. C-reactive protein and buffy coat smear in early diagnosis of childhood septicemia. Indian J Pathol Microbiol. 1998 Jan;41(1):23–6.
19. Christo GG, Shenoy V, Matthai J, Shivananda PG, Venkatesh A. Acinetobacter sepsis in neonates. Indian Pediatr. 1993 Dec;30(12):1413–6
20. Jyothi P, Basavaraj MC,Basavaraj PV. Bacteriological profile of neonatal septicemia and antibiotic susceptibility pattern of the isolates. Journal of natural science, biology, and medicine. 2013 Jul;4(2):306