

## Original Research Article

# NEONATAL SEPSIS: CLINICAL SPECTRUM, BACTERIOLOGICAL PROFILE AND ANTIBIOTIC SENSITIVITY PATTERNS IN NEONATAL INTENSIVE CARE UNIT IN A TERTIARY CARE HOSPITAL OF A METROPOLITAN CITY

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### ABSTRACT

**Background:** Neonatal sepsis is the commonest cause of neonatal mortality. Surveillance of causative organisms and their antibiotic sensitivity pattern promotes rational use of antibiotics and antibiotic stewardship.

**Materials and Methods:** Blood cultures were performed for all clinically suspected neonatal sepsis cases for a period of 18 months. Identification of all pathogenic isolates was followed by antibiotic sensitivity testing.

**Results:** Of the 300 neonates with clinical suspicion of sepsis, 77 neonates had blood culture positive sepsis. Sepsis was predominant in females (53.25%). Low birth weight (85.67%) and prematurity (84.66 %) were important neonatal risk factors for sepsis. Early onset sepsis occurred in 63% of the cases. Gram-negative constituted 70.13 % of all isolates. The most frequently isolated organisms in blood was *Klebsiella pneumoniae* subspecies *pneumoniae* (28.57%). Gram negative organisms included *Klebsiella pneumoniae* subspecies *pneumoniae*, *Klebsiella aerogenes*, *Acinetobacter baumannii* complex, *Escherichia coli*, *Stenotrophomonas maltophilia*. Among Gram-positive organisms, Coagulase negative Staphylococcus (CONS) was most frequently isolated followed by *Staphylococcus aureus* and *Enterococcus faecium*. Gram negative organisms were most susceptible to carbapenems followed by aminoglycosides. Gram positive isolates were least resistant to vancomycin and linezolid.

**Conclusions:** Gram negative sepsis was the most common type of sepsis among the neonates.

**Keywords:** Neonatal sepsis, Blood culture, Antibiotic stewardship.

## INTRODUCTION

Neonatal sepsis is a critical health issue in newborns, presenting a range of symptoms that can vary in severity. This condition is one of the leading causes of neonatal morbidity and mortality worldwide,<sup>[1]</sup> particularly among very low birth weight preterm infants. It refers to infections that may or may not involve the presence of bacteria in the bloodstream, and can progress to serious conditions such as

septicemia, meningitis, or pneumonia.<sup>[2]</sup> The World Health Organization reports that neonatal infections contribute to approximately 1.6 million deaths each year, with a significant proportion occurring in developing nations like India.<sup>[1]</sup> The emergence of multidrug-resistant (MDR) organisms has exacerbated the situation. These organisms are characterized by resistance to at least three distinct classes of antibiotics that are typically effective against the specific pathogen.<sup>[3]</sup> However, many of

these deaths can be prevented with timely diagnosis and appropriate antibiotic therapy.<sup>[4]</sup>

Neonatal sepsis is broadly categorized into early onset sepsis (EONS) (occurs within first 72 h of life) and late onset sepsis (LONS) (occurs between 72 h to 90 days of life).<sup>[5]</sup> The source of the pathogen can be intrauterine or maternal flora, or hospital or community acquired. The bacterial organisms commonly associated with early-onset sepsis include group B Streptococcus (GBS), *Escherichia coli*, coagulase negative Staphylococcus species, *Haemophilus influenzae*, and *Listeria monocytogenes*.<sup>[5]</sup> In contrast, the bacteria most frequently responsible for late-onset sepsis are coagulase-negative Staphylococcus species (CoNS), *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Escherichia coli*, *Enterobacter* species, *Pseudomonas aeruginosa*, and *Acinetobacter* species.<sup>[4]</sup>

The bacteriological profile of neonatal sepsis is different in developed and developing countries. *Klebsiella pneumoniae* is the most common bacterial agent causing neonatal sepsis in developing countries, while group B Streptococcus and coagulase-negative Staphylococci (CoNS) are the common agents in developed countries.<sup>[6]</sup> There also exists a regional variation in the prevalence of the bacterial organisms causing neonatal sepsis in developing countries.

Since delay in the treatment of neonatal sepsis is associated with increased mortality, empirical therapy is of utmost importance in the treatment of neonatal sepsis. However, the appropriateness of the empirical therapy is being challenged in the current circumstances by changes in bacteriological profile and increase in antimicrobial resistance posing challenges in the optimal management of suspected and confirmed cases of sepsis. Knowledge of common organisms causing neonatal sepsis in a particular area and their antibiotic sensitivity pattern should be taken into consideration before setting guidelines for empirical therapy.<sup>[7]</sup>

Therefore, there is a need for surveillance to understand the trends in pathogens causing neonatal sepsis and the antibiotic susceptibility profile of the pathogens in a particular area.<sup>[2]</sup>

The purpose of this study was to investigate the clinical presentation, bacterial etiologies, and antimicrobial susceptibility profiles of neonatal sepsis in the NICU of a tertiary care hospital of a metropolitan city, with the goal of developing an effective antimicrobial strategy for managing neonatal sepsis.

## MATERIALS AND METHODS

A prospective study of 300 neonates with clinical suspicion of sepsis was conducted at tertiary care hospital in Mumbai, Maharashtra. The study was conducted from December 2022 to May 2024 after obtaining Institutional Ethics Committee approval (IEC/460/22). Neonates between the age of 0–28

days admitted to NICU with suspected neonatal sepsis were included in the study. Neonates older than 28 days of life, those with congenital abnormalities, and those who had already been administered antibiotics were excluded from the study. Clinical and demographic data were collected in a predesigned set of questionnaires before which consent was taken from the mother/guardian. Sepsis was suspected based on the presence of one or more clinical signs such as respiratory distress, refusal to feed, lethargy, fever, seizures, jaundice and hypothermia. Among others, low birth weight (< 2500 g), history of bag-mask ventilation, rupture of amniotic membrane for more than 18 h (PROM), increased capillary refill time >3 sec, antepartum fever, foul-smelling liquor and repeated ( $\geq 3$ ) unclean per vaginal examinations were considered as risk factors for neonatal sepsis. For all neonates suspected of having sepsis, a laboratory evaluation was conducted using C-reactive protein (CRP) testing. Blood samples for culture were collected prior to initiating antibiotic treatment, following strict aseptic techniques by the neonatologist, and sent to the microbiology laboratory for analysis. Blood culture sample included a single sample collected from a peripheral vein or artery under aseptic conditions in an automated blood culture bottle or a conventional blood culture bottle depending on the availability. The local site was cleansed with 70% alcohol and povidone-iodine (1%), followed by 70% alcohol again. For automated blood culture bottle, about 2ml of blood was inoculated into Bact/ALERT® PF Culture Bottles and processed using the Bact/ALERT® 3D 240 Microbial Detection System. Similar amount of blood was introduced aseptically in a conventional blood culture bottle, whenever used. Conventional blood culture bottles received were incubated aerobically in an incubator at 37°C and were examined daily for 7 days for evidence of growth, indicated by turbidity, hemolysis, gas production and presence of any discrete colonies. Conventional blood culture bottles were subcultured on MacConkey agar, 5% Sheep blood agar and Chocolate agar after 24 hours, 3rd and 5th day after receipt of the specimen in laboratory. For automated blood culture bottles, positively identified bottles were subjected to gram's stain and subculture on 5%sheep blood agar, chocolate agar and, Mac Conkey agar plates and put for overnight incubation at 37°C. Antibiotic sensitivity testing was performed on Mueller-Hinton agar (MHA) plates by the modified Kirby-Bauer disk diffusion method as per the Clinical Laboratory Standard Institute (CLSI) guidelines 2022. Minimum inhibitory concentration (MIC) testing of colistin was done by microbroth dilution testing. Bacterial isolate was subjected to various dilutions of antibiotics. The highest dilution of antibiotic that inhibit the growth of bacteria was considered as MIC. Additional investigations were carried out as needed. Empirical antibiotic treatment was initiated for neonates with suspected sepsis. The AST results were informed to the treating clinician.

## Statistical Analysis

Data was entered into an excel sheet and statistical analysis was done using the EPI INFO 7.2.5 application for Windows software. Statistical analyses were done by Chi square test and Fischer's exact test. P value <0.05 was statistically significant.

## RESULTS

During the study period a total of 300 neonates admitted in NICU were suspected with clinical septicaemia. Among them, 126 (42 %) were female babies and 174 (58 %) were male babies. The overall rate of male to female ratio in clinical sepsis is 1.3:1. Out of 300 neonates, blood culture was positive in 77 (25.67 %) cases.

CRP value of more than 10 mg/dL was seen in 34.67 % (104/300) of neonates. Amongst these 74.03 %

(57/104) had culture confirmed sepsis. The above finding was found to be statistically significant ( $p < 0.001 < 0.05$  by Chi square test)

As seen in table 1, 257/300 (85.66 %) babies had low birth weight while 254/300 (84.67 %) were preterm babies. 189 (63 %) neonates presented with early onset sepsis (EOS) and the rest of the neonates presented with late onset sepsis (LOS). The most common risk factor in this study was low birth weight (< 37 weeks), which was more common in babies with Early onset sepsis (86.24 %). The significant neonatal risk factors were history of meconium stained amniotic fluid ( $p < 0.001$  by Fischer's exact test), history of perinatal asphyxia (suggested by low appgar score) ( $p = 0.0001$  by Fischer's exact test), NICU admission and invasive procedure ( $p < 0.001$  by Chi square test). History of prolonged rupture of membranes (>24 hours) was a significant maternal risk factor ( $p < 0.001$  by Fischer's exact test).

**Table 1: Demography and risk factors of the neonatal sepsis cases**

Variable	EOS (n=189)	LOS group (n=111)	Total (n=300) (%)	P value (Test)	Level of Significance
<b>Neonatal parameters</b>					
<b>Gestational age</b>					
Preterm (<37 weeks)	163 (86.24 %)	91 (81.98 %)	254 (84.67%)	0.32*	Not significant
Term (>37 weeks)	26 (13.76 %)	20 (18.01 %)	46 (15.33%)		
<b>Birth weight</b>					
< 2500 g	161(85.18%)	96(86.48 %)	257(85.67 %)	0.75*	Not significant
≥ 2500 g	28(14.82%)	15(13.52%)	43 (14.33%)		
<b>Maternal parameters</b>					
History of Maternal fever	4(2.11 %)	0(0 %)	4(1.33 %)	0.12#	Not significant
Rupture of membrane >18 h	43(22.75 %)	00(0 %)	43(14.33 %)	<0.001#	Significant
Foul smelling liquor	7(3.70 %)	2(1.80 %)	9(3 %)	0.35#	Not significant
<b>Neonatal-care-related parameters</b>					
NICU admission	9 (4.76 %)	107 (96.39 %)	116 (38.66 %)	<0.001*	Significant
<sup>§</sup> Invasive procedure insertion of endotracheal tube, central line or peripherally inserted central catheter.	9 (4.76 %)	96 (86.48 %)	105 (35 %)	<0.001*	Significant

\*CHI SQUARE TEST; #FISCHER EXACT TEST

Respiratory distress (30.66%) was the major presenting symptom, followed by refusal of feeds (28%), lethargy (26.66%) and hypothermia (25%). Fever, seizures, neonatal jaundice, vomiting, cyanosis and hypoglycemia were the other presenting symptoms (Table 2). In the EOS group, the most

important clinical presentations were respiratory distress 50(26.45%), refusal to feed 41 (21.69%) and lethargy 40 (21.16%) (Table 2). In the LOS group, the major clinical presentations were refusal to feed 43 (38.73%), difficulty in breathing 42 (37.83 %), hypothermia 41 (36.93%) and fever 26 (23.42%).

**Table 2: Clinical Presentation of Neonatal Septicaemia**

Clinical signs and symptoms	Onset of sepsis		Total (%) (n=300)
	EOS (n= 189)	LOS (n=111)	
Difficulty in breathing	50 (26.45%)	42 (37.83%)	92 (30.66 %)
Refusal to feed	41 (21.69%)	43 (38.73%)	84 (28 %)
Lethargy	40 (21.16%)	40 (36.03%)	80 (26.66 %)
Hypothermia	34 (17.98%)	41 (36.93%)	75 (25 %)
Fever	19 (10.05%)	26 (23.42%)	45 (15 %)

<b>Seizures</b>	18 (9.52%)	25 (22.52%)	43 (14.3 %)
<b>Jaundice</b>	9 (4.76%)	15 (13.51%)	24 (8 %)
<b>Vomiting</b>	4 (2.11%)	13 (11.71%)	17 (5.6 %)
<b>Cyanosis</b>	2 (1.05%)	8 (7.2%)	10 (3 %)
<b>Hypoglycemia</b>	4 (2.11%)	4 (3.6%)	8 (2.66 %)

Out of the 77 culture positive cases, female babies were predominant 41 (53.25%). Based on gestational age, 63 (81.81%) were preterm. 64 (83.11%) were

low birth weight (LBW) babies (Table 3). Only 01 (1.3%) was an out born baby. More than half of the neonates presented with early onset sepsis (59.74%).

**Table 3: Demography of culture positive septic neonates (n=77)**

<b>Demographic character</b>		<b>Number (percentage)</b>
Gender	Males	36 (46.75%)
	Females	41 (53.25%)
Birth weight	Low birth weight	64 (83.11%)
	Normal birth weight	13 (16.89%)
Gestational age	Preterm	63 (81.81%)
	Term	14 (18.19%)
Onset of sepsis	Early onset sepsis	46 (59.74%)
	Late onset sepsis	31 (40.26%)

Amongst the 77 (25.67 %) positive blood cultures, gram negative organisms predominated (70.13 %) indicating gram negative organisms to be the most frequent cause of septicaemia in this study. The most common isolated microorganism was *Klebsiella pneumoniae* (40.74 %), followed by *Klebsiella aerogenes* (25.92 %), *Acinetobacter baumannii* complex (22.23%), *Escherichia coli* (9.26%), *Stenotrophomonas maltophilia* (1.85 %). Among gram positive organisms, coagulase negative

staphylococci (CoNS) (78.94 %) was the most common organism isolated, followed by *Staphylococcus aureus* (10.53 %) and *Enterococcus faecium* (10.53 %). 04 candida species were also isolated, which were identified as non albicans candida. *Klebsiella aerogenes* was the most common cause of early onset sepsis (n=12/46,26.09%) and *Klebsiella pneumoniae* was the most common cause of late-onset sepsis (n= 11/31; 35.48%).

**Table 4: Distribution of the microbial flora in culture confirmed sepsis cases**

<b>Organisms</b>	<b>Types of sepsis</b>		<b>Total isolates (n=77) (%)</b>
	<b>Early onset sepsis (n=46)(%)</b>	<b>Late onset sepsis (n=31)(%)</b>	
<i>Klebsiella pneumoniae</i>	11 (23.91%)	11 (35.48 %)	22 (28.57%)
<i>Klebsiella aerogenes</i>	12 (26.09%)	02	14 (18.18%)
<i>Acinetobacter baumannii complex</i>	04	08 (25.80 %)	12 (15.6%)
<i>Escherichia coli</i>	04	01	5 (6.49%)
<i>Stenotrophomonas maltophilia</i>	01	00	01 (1.29%)
<b>Coagulase negative Staphylococcus species</b>	11 (23.91%)	04 (12.90 %)	15 (19.5%)
<b>Yeast</b>	01	03 (9.68 %)	04 (5.19%)
<i>Staphylococcus aureus</i>	01	01	02 (2.59%)
<i>Enterococcus faecium</i>	01	01	02 (2.59%)
<b>Total</b>	46 (59.74 %)	31 (40.25 %)	77

Overall Gram negative organisms were sensitive to carbapenems (43.39 %), followed by aminoglycosides (41.51 %), piperacillin-tazobactam (30.18 %) and fluoroquinolones and fourth generation cephalosporins (24.52 % each). A total of 30 multidrug resistant isolates were observed in this study, all of which showed intermediate susceptibility to colistin (100 %).

As seen in table 5, only 22.72 % of the isolates of *Klebsiella pneumoniae* subspecies *pneumoniae* were sensitive to carbapenems. There were 17 multidrug resistant isolates which showed intermediate susceptibility to colistin. *Klebsiella aerogenes* showed good sensitivity to aminoglycosides, fluoroquinolones and carbapenems. Among the 12 *Acinetobacter* isolates, 10 isolates were multidrug resistant. All 10 isolates had intermediate sensitivity

to colistin and 6 (60%) isolates were sensitive to minocycline. *Escherichia coli* showed 40% sensitivity to carbapenems. There were 3 multidrug resistant isolates. None of the isolates of *Escherichia coli* were sensitive to the cephalosporins. Apart from *Acinetobacter baumannii* complex, the only non fermenter which grew in this study was *Stenotrophomonas maltophilia* which was sensitive to levofloxacin, minocycline and co-trimoxazole. Out of the 2 *Staphylococcus aureus* isolates, only one isolate was Methicillin resistant *Staphylococcus aureus* (MRSA) which was sensitive to vancomycin

and linezolid. None of the isolates showed inducible clindamycin resistance. The isolates of *Enterococcus faecium* were sensitive to linezolid, vancomycin, teicoplanin and none of them showed High level gentamicin resistance. As per the Standard operating procedures of the department, antimicrobial testing for coagulase negative *Staphylococcus* (CoNS) species is performed if grown simultaneously from 2 samples or consecutively from a repeat sample from the patient. Hence, AST of these isolates was not performed as repeat samples did not grow CoNS.

**Table 5: Antibiotic sensitivity pattern of isolates**

Antibiotics	Gram negative organisms					Gram positive organisms	
	<i>Klebsiella pneumoniae</i> subspecies <i>pneumoniae</i> (n= 22)	<i>Klebsiella aerogenes</i> (n= 14)	<i>Acinetobacter baumannii</i> complex (n= 12)	<i>Escherichia coli</i> (n= 5)	<i>Stenotrophomonas maltophilia</i> (n=1)	<i>Staphylococcus aureus</i> (n=2)	<i>Enterococcus faecium</i> (n=2)
Third generation cephalosporins	2/22 (9 %)	10/14 (71.42 %)	0/12 (0%)	0/5 (0%)	NT	NT	0/2 (0%)
Cefepime	2/22 (9 %)	10/14 (71.42 %)	1/12 (8.33 %)	0/5 (0%)	NT	NT	NT
Aminoglycosides	4/22 (18.18 %)	14/14 (100%)	3/12 (25 %)	1/5 (20 %)	NT	2/2(100%)	2/2(100%)
Carbapenems	5/22 (22.72 %)	14/14 (100%)	2/12 (16.66 %)	2/5 (40 %)	NT	NT	NT
Piperacillin tazobactam	2/22 (9%)	12/14 (85.71 %)	1/12 (8.33 %)	1/5 (20 %)	NT	NT	NT
Fluoroquinolones	1/22 (4.54 %)	14/14 (100%)	0/12 (0%)	1/5 (20 %)	1/1(100%)	0/2 (0%)	NT
Vancomycin	NT	NT	NT	NT	NT	1/1 (100 %)	2/2 (100 %)
Teicoplanin	NT	NT	NT	NT	NT	NT	2/2 (100 %)
Linezolid	NT	NT	NT	NT	NT	1/1 (100 %)	2/2 (100 %)
Minocycline	1/17 (5.88 %)	NT	6/10 (60 %)	NT	1/1(100%)	NT	NT
Cotrimoxazole	2/22 (9%)	13/14 (92.85%)	4/12 (33.33 %)	0/5 (0 %)	1/1 (100%)	2/2 (100 %)	0/2 (0%)

## DISCUSSION

The rise of antibiotic resistance has become a pressing concern in global health, posing serious challenges in the management of infectious diseases. Among the most vulnerable populations affected are neonates, particularly those in neonatal intensive care units (NICUs) in low- and middle-income countries. In recent years, there has been a disturbing increase in cases of neonatal sepsis caused by multidrug-resistant (MDR) organisms, leading to higher rates of morbidity and mortality. This trend underscores the urgent need for continuous monitoring of the bacterial pathogens responsible for neonatal infections and their evolving resistance patterns. Effective treatment of neonatal septicemia hinges on the prompt initiation of empirical antibiotic therapy, followed by tailored treatment based on culture and sensitivity results. Therefore, the accurate and timely identification of the causative microorganisms, along with a detailed understanding of their antimicrobial resistance profiles, is essential. This approach not only improves patient outcomes but also helps in

curbing the misuse of antibiotics, which is a key driver of resistance.

Risk factor based approach for management of neonates is one of the highly effective approaches for minimizing the mortality due to early onset neonatal sepsis in high income countries.<sup>[8]</sup> The risk factors can be either related to neonate or mother. In this study, the most common risk factor was low birth weight. Early onset sepsis cases were more common in preterm babies corresponding to that reported by Kishore et al.<sup>[9]</sup> All babies with perinatal asphyxia (low apgar score) presented as early onset sepsis in accordance to that reported by Pokhrel et al (7.3 %).<sup>[8]</sup> Kishore et al reported invasive procedures in 36 % of the babies.<sup>[9]</sup> As discussed by Cortese et al the risk of LOS was directly proportional to duration of central/umbilical catheters and ventilatory treatment.<sup>[10]</sup> Maternal History of prolonged rupture of membranes >24 hours (PROM) was similar to that reported by Investigators of Delhi Neonatal Infection Study (DeINS) collaboration (14.5 %).<sup>[11]</sup>

Respiratory distress was the major presenting symptom in the present study which was similar to studies done by Kurma et al (31.2 %), Charki et al

(37%), Das et al (26.8 %).<sup>[12,13,14]</sup> These authors have reported respiratory distress as the most common presentation in babies in the EOS group (29.4 %). The blood culture positivity in neonatal septicaemia were found to be similar to the prevalence rate of 23.6 % and 24.1 % reported by Yadav et al from Nepal and Das et al from West Bengal, respectively.<sup>[14,15]</sup>

Majority cases presented with early onset sepsis (EOS) which were in accordance with that of Kurma et al who found EOS in 65% of cases.<sup>[12]</sup> The incidence of sepsis was found to be more in preterm babies and low birth weight babies in the present study. This is in accordance with other studies that have been done previously in India.

Implementation of sepsis screens to identify true sepsis cases early can be helpful in the management of the sick babies.<sup>[16,17]</sup> In this study, only CRP was done and findings were similar to that reported by Rai et al and Bhatia et al (94.7 % and 81.25 %, respectively).<sup>[17,18]</sup> Amongst the suspected cases of neonatal sepsis, 78.92 % babies were sterile on blood culture as well as negative for CRP. A similar finding of high true negatives was also reported by Rai et al (87.1 %) and Lamachen and Mishra (84.4 %),<sup>[18,19]</sup>.

High percentage of Gram negative bacteria and low Gram positive bacteria was comparable with the studies done by Muley et al (70.8%), Kurma et al, Kedar et al and Gupta et al (68.3 % to 75.7 %) which also showed that gram-negative organisms were more common causes of neonatal sepsis.<sup>[4,12,20,21]</sup>

The bacterial flora causing neonatal sepsis in the developing world is more of gram negative organisms as compared to the developed world. During birth, the neonates are exposed to gram negative bacilli in mother's birth canal and immediate surrounding environment (skin of the neonate and healthcare personnel) which may lead to colonization with these bacilli.<sup>[22]</sup> Since the neonates have low levels of immunity, these colonizers can become opportunistic pathogens.<sup>[23]</sup> Four of the isolates were yeast which was similar to the study done by Charki et al from Karnataka (6%) and Alharbi et al (5%).<sup>[13,24]</sup>

As reported in studies done by Kurma et al and Kedar and Parekh et al, *Klebsiella pneumoniae* subspecies *pneumoniae* was the predominant isolate (34.7 % and 33.3 %, respectively).<sup>[12,20]</sup> *Acinetobacter baumannii* complex isolated was almost similar to that reported by Kedar and Parekh (18.18 %) from Pune.<sup>[20]</sup> Isolation of coagulase negative *Staphylococcus* species in neonatal blood cultures poses a great difficulty as these organisms may occur as contaminants or pathogens. The clinical significance was established after clinically correlating and discussion with the neonatologists. In this study, though coagulase negative *Staphylococcus* species was the major gram positive isolate (78.94 %), it was not reported as the pathogen in the first sample received. A repeat sample was requested in such cases wherein the repeat samples were found to be sterile.

In this study, most of the gram negative isolates showed resistance to baseline antibiotics like third and fourth generation cephalosporins and beta lactam-beta lactamase inhibitor combination except *Klebsiella aerogenes*. Overall the gram negative bacteria exhibited lower sensitivity to commonly used antimicrobial drugs. The aminoglycoside sensitivity (41.51 %) was close to a study done by Gamit et al from Gujarat (45 % sensitivity to gentamicin and 55 % to amikacin).<sup>[25]</sup> The susceptibility of gram negative bacteria to third and fourth generation cephalosporins was 22.64 % and 24.52 %, respectively. The sensitivity of gram negative bacilli to fluroquinolones and piperacillin tazobactam combination in this study was only 24.52 % and 30.18 %, respectively which matched closely to a study done by Kishore et al from Patna (21 % and 37 %, respectively).<sup>[9]</sup> The carbapenem sensitivity of gram negative bacteria was found to be 43.39 % in this study which was almost similar to a study done by Nepal et al (46.2 %).<sup>[26]</sup> The high occurrence of carbapenem resistance depicts the evolving resistance pattern in the microorganisms along with inappropriate use of high end antibiotics.<sup>[27]</sup> Carbapenem resistance can be due to either production of a carbapenemase or production of beta lactamase along with porin channel mutation or production of efflux pumps. The genes producing carbapenemase enzyme are highly transmissible and can be associated with outbreaks in the hospital.<sup>[16]</sup> The variation in antibiograms of the different gram negative bacilli from different geographical areas may be due to the variations in the infection prevention and control (IPC) practices that are followed. Strengthening of IPC practices and promotion of antimicrobial stewardship programme can help in controlling antimicrobial resistance.

Out of the 2 isolates of *Staphylococcus aureus*, one isolate was Methicillin resistant *Staphylococcus aureus* (MRSA) based on the cefoxitin disc diffusion test, which was sensitive to vancomycin and linezolid. None of the *Staphylococcus aureus* isolates in this study were sensitive to penicillin which coincides with that reported by Kedar and Parekh from Pune.<sup>[20]</sup> Rai et al from Uttar Pradesh reported 82 % of the *Staphylococcus aureus* isolates susceptible to gentamycin which is little close to this study.<sup>[18]</sup> Amongst the two isolates of *Enterococcus faecium*, both were resistant to Penicillin and only one was sensitive to ampicillin, while no isolates of vancomycin resistant enterococci were reported. The 2 isolates of *Enterococcus faecium* were sensitive to linezolid corresponding to the study done by Chauhan et al, Dutta et al and Das et al who have reported 100 % sensitivity to both vancomycin and linezolid.<sup>[14,28,29]</sup> Strict adherence to contact precautions was advised to neonatologist caring for the neonate with MRSA in the blood culture.

## CONCLUSION

Sepsis is the most common cause of neonatal deaths worldwide and presents a challenge during management of these babies. In this study, 70.13 % of the culture confirmed cases improved clinically while approximately 8 % of the culture confirmed cases had complications. Only one neonate expired during the study period and was culture negative. The survivors of sepsis can have neurological sequelae. Regular antenatal care, special care of preterm and low birth weight babies, exclusive breast feeding, maintenance of hand hygiene along with early diagnosis with appropriate management remain the major pillars for controlling sepsis in neonates. Implementation of risk factor based approach along with the clinical presentations helps in the early management of suspected cases. Implementation of sepsis screens (C reactive protein, Procalcitonin, increased or decreased total leukocyte count, absolute Neutrophil count and micro ESR) can help in early identification of sepsis cases before the results of blood culture. The study depicts antimicrobial resistance in the gram negative flora. Rapid diagnostic tools to identify antimicrobial resistance as per the standards can be helpful in NICUs to monitor the treatment along with regular surveillance for AMR. A good antimicrobial stewardship programme with interdepartmental coordination for long term surveillance of antimicrobial susceptibility patterns is recommended for rational use of antibiotics in the facility. A standardized national and global surveillance programme for collection of neonatal antimicrobial resistance data is necessary for implementation of successful interventions.

**Limitation:** Due to the small sample size, the results of the study cannot be generalized to similar studies of the same region. The gram negative isolates showing resistance could not be tested for the resistance mechanisms by phenotypic or genotypic methods due to resource constraints. Understanding the resistance mechanisms can help in understanding the epidemiology of infection.

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