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Original Research Article

Bacterial profiling, sensitivity and resistance pattern of neonatal sepsis in neonatal intensive care unit of tertiary care hospital

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ABSTRACT

Background: This study aimed to identify the distribution of pathogens and their antimicrobial resistance patterns in the neonates admitted to the NICU of a tertiary care hospital in northern India.
Methods: After obtaining written informed consent, neonates with confirmed or suspected cases of neonatal sepsis (n=167) aged 0-28 days were included. As soon as the baby arrived, all the clothes were removed and kept in a pre-heated warmer. Before administering I/V antibiotics, all the routine and culture samples were taken. The clinical data were collected and analysed using SPSS.
Results: Most of the neonates were from lower middle class, out-born, LSCS, early preterm, and low birth weight (LBW). 167 neonates had culture-confirmed infections [blood culture positive (13.8%) and sepsis screen positive (86.2%)]. Gastric aspirate cytology was positive in 61.7% of patients. Maximum cytology-positive cases were seen in neonates with EOS. The most common risk factors were birth asphyxia. 142 individuals were discharged, with 72.5% diagnosed with EOS and 89% with LOS. There was a significant difference in gastric aspirate cytology when associated with expiry and discharge. Out of 167 neonates, 13.77% were culture-positive for neonatal sepsis. Out of 23 organisms, 82.6% were resistant, while, 17.4% were not. Staph aureus was the major causative organisms. Among the Gram Positive and Negative bacteria, the highest sensitivity was observed for imipenum. All gram-positive bacteria were resistant to cotrimazole, tobramycin, and erythromycin.
Conclusions: Implementation of effective preventive strategies to combat the emergence of antibiotic resistance is urgently needed.

Keywords: Bacterial profiling, Sensitivity, Resistance pattern, Neonatal sepsis, Tertiary care hospital

INTRODUCTION

The daily risk of mortality in the first 4 weeks of life is ~30-fold higher than the post-neonatal period, that is, from 1 month to 59 months of age.[1,2] Every year, nearly 2.8 million newborns worldwide pass away before they have reached their first month of life. India accounts for one-fifth of all yearly child births and more than a quarter of all neonatal deaths worldwide. India's neonatal mortality rate steadily decreased from 83.6 deaths per thousand live births in 1971 to 20.3 deaths per thousand live births in 2020.[3] Prematurity, sepsis, and perinatal asphyxia are the leading causes of morbidity and mortality among neonatal fatalities in India. Neonatal sepsis (NS) is defined as "a clinical syndrome characterised by systemic signs and symptoms and

bacteremia during the first month of life". It is further subdivided into early onset neonatal sepsis (EONS) if signs and symptoms of sepsis appear within the first O-3 day of life and late onset neonatal sepsis (LONS) if clinical features of sepsis appear after the first week of life, up to 28 days or 1 month.[4] The information regarding etiologic agents is mixed. Group B Streptococcus is the most prevalent cause of EONS in developed countries, Enterobacteriaceae is the most common cause in developing countries.[5-7] Neonatal sepsis is a worldwide problem that poses a management challenge to neonatal and infant care groups. Antibiotic resistance against the most frequent bacterial infection has exacerbated the issue. It has been stated that neonates are the most vulnerable to bacterial sepsis, with an incidence of 1 to 10 per 1000 live births globally.[8] According to published data, sepsis accounts for 10% of all maternal fatalities and 26% of all neonatal deaths.[9] Over the last two decades, sepsis mortality has grown by around 13.7% every year.[10] According to hospital-based research in India, the frequency is 30 per 1000 live births, with approximately 20% dying in the hospital; for those with culture positive sepsis, the rate jumps to up to 50%. They not only have a greater mortality rate, but they also have longer hospital stays, use more resources, and are at a higher risk of severe neurodevelopmental outcomes.

Neonatal sepsis is caused primarily by Gram-positive and Gram-negative bacteria, with a few instances caused by fungus such as Candida species. In underdeveloped nations, Gram-negative organisms are the most common pathogens causing newborn sepsis.[11] In contrast to neonatal intensive care units (NICUs) in industrialised nations, where gram-positive organisms continue to be the most common pathogens in both early and late-onset sepsis, the pathogen spectrum infecting newborns in NICUs in poor countries is quite different. The pathogen mix in early onset sepsis (EOS) did not vary from late onset sepsis (LOS) in a recent multi-center cohort research from India, with gramme negative bacteria accounting for nearly two-thirds of isolates. Klebsiella pneumoniae is a major pathogen of both community-acquired and nosocomial neonatal infections, with case fatality rates ranging from 18% to 68%. Drug-resistant K. pneumoniae has emerged as a significant pathogen in recent years, with substantial consequences due to restricted antibiotic options, higher hospital spending, and poor neonatal outcome.[12] Cephalosporin resistance has previously been observed at a high proportion (47%).[13] In developing countries, there has recently been an increase and spread of infection owing to resistance organisms. Advances in sepsis diagnosis and management can significantly reduce sepsis complications and improve outcomes, particularly in preterm infants. The increased frequency of NS in recent years may be attributable to the growing usage of invasive procedures and the emergence of resistant organisms. Bacterial resistance to routinely used antibiotics has evolved, complicating NS treatment. Antimicrobial resistance (AMR) has emerged as a global hazard to healthcare, causing morbidity and death to rise. AMR is responsible for an estimated 31.0% of newborn sepsis fatalities.[14] This is secondary to antibiotic abuse, over-the-counter and parallel market access, and counterfeit or low-quality medications, all of which are mixed with poor hygiene and living circumstances. Isolated bacteria in a recent multi-center cohort research from India demonstrated a significant level of antimicrobial resistance, not only to frequently used antibiotics but also to so-called reserve antibiotics such as extended-spectrum cephalosporins and carbapenems. Because of fluctuating patterns of microbial flora and antibiotic susceptibility, neonatologists who manage NICU always have a difficulty in controlling neonatal infections. Periodic surveillance of organisms causing NS that varies not only from one location to another but also over time, as well as their antimicrobial sensitivity and resistance pattern, can guide the proper empirical therapy and avoid the establishment of resistant flora. While this vital information is consistently gathered and updated in wealthy nations, data from underdeveloped countries, where the bulk of neonatal fatalities due to sepsis occur, is limited. Therefore, this study was carried out to identify the distribution of pathogens and their antimicrobial resistance patterns in the neonates admitted to the NICU of a tertiary care hospital of northern India.

METHODS

This observational prospective study was conducted at the Neonatal Intensive Care Unit, Pediatric Department, Nehru Hospital, Baba Raghav Das Medical College, Gorakhpur (Uttar Pradesh, India), a tertiary-care hospital in northern India during January 2020 to August 2021. Neonates (n=167) with confirmed or suspected cases of neonatal sepsis aged 0–28 days of age are included in the study after written informed consent was obtained from parents. Patient's age was more than 28 days of life, less than 1000 gm newborn, and with other serious complications were excluded from the study. As soon as the baby arrived, all the clothes were removed and kept in a pre-heated warmer. A quick RBS and IV line were to be secured. Weight of the baby is taken. Before administering IV antibiotics, all the routine and culture samples were taken. The clinical data were collected and entered in the proforma. The study was approved by the ethics committee of BRD Medical College, Gorakhpur.

Laboratory evaluation

Blood culture**:** The area where the sample is to be taken will be cleaned and sterilized with spirit and betadine.1-2 ml of blood is collected and mixed in the blood culture vial. The culture vial is sealed again. It is future sent to Regional Medical Research Center, Gorakhpur. Serum procalcitonin: Samples were taken in a plain vial. Then it was sent to the pathology within 30 mins. It was centrifuged for 10 min at 3000rpm for the desired serum collection. Gastric aspirate: Gastric Aspirate is taken by the nasogastric tube in a sterile syringe. It was transferred to the microbiology department within 4hrs. If more time

is required, it should be stored in the refrigerator at 2-8 degrees. Confirmed Neonatal sepsis: TLC less than 5000 cells/mm^3; ANC less than 2 cells/mm^3; C reactive protein more than 6 mg/l; Micro ESR; I/T ratio more than 2; Procalcitonin level more than 2-2.5; Gastric aspirate neutrophil count of more than 5 cells; and Blood culture positive. Out of the above 5 criteria, and 2 findings suggest sepsis screen positive, and criteria no. 8 is confirmed positive.

Suspected neonatal sepsis

Regardless of whether there is a clinical symptom or not, the presence of sepsis risk factors in the baby or findings suggesting sepsis in follow-up.

Statistical analysis

The collected data were statistically analysed using SPSS version 21. Interferential analysis for quantitative variables was done using an independent t test, whereas analysis for qualitative data was done using the Chi-square test. Statistical significance was set at $p<0.05$.

RESULTS

This hospital-based prospective study was conducted on a total of 167 neonates, females (53.9%) outnumbered males (46.1%).

Table 1: Demographic profile of neonates with sepsis (n=167).

Parameters		N	%
Age	<72 hrs	27	16.2
	72 hrs to 5 days	30	18.0
	>5 days	110	65.9
Sex	Male	77	46.1
	Female	90	53.9
Outborn/inborn	Inborn	52	31.1
	Out born	115	68.9
Rural/urban	Rural	141	84.4
	Urban	26	15.6
Mode of delivery	LSCS	86	51.5
	NVD	81	48.5
Socio-economic status	Upper lower	8	4.8
	lower middle	159	95.2
Term	Early	51	52.0
	Full	41	41.8
	Late	6	6.1
Preterm	Extremely	2	2.9
	Very early	14	20.3
	Early	39	56.5
	Late	14	20.3
Birth weight	ELBW	4	2.4
	VLBW	32	19.2
	LBW	86	51.5
	Normal	45	26.9

The majority of the neonates had aged more than five days (65.9%), followed by 72 hours to 5 days (18%) and age <72 hours (16.2%). The most of the neonates were from rural areas (84.4%), lower middle class (95.2%), out-born (68.9%), LSCS (51.5%), the early term (52%), early preterm (56.5%), and low birth weight (LBW) (51.5%) (Table 1).

The most frequently observed signs and symptoms were lethargy, followed by respiratory distress, refusal to feed, abnormal body movement, fever, anemia, yellowish discoloration of the body, abdominal distention, comatose, pustule, and others. In the present study, 167 neonates had culture-confirmed infections; blood culture positive (13.8%) and sepsis screen positive (86.2%). 15% of patients were found with EOS, and 10% with LOS in blood culture positivity, while in sepsis screen positivity, 85% were found with EOS, and 90% were with LOS. Gastric aspirate cytology was positive in 61.7% of patients and negative in 38.3%. Maximum cytology-positive cases were seen in neonates with EOS compared to neonates with LOS.

The most common risk factors were birth asphyxia (55.7%), followed by prematurity (38.9%), leaking PV for less than 24 hr (29.3%), leaking PV for more than 24 hr (23.4%), top feed (9%), bleeding PV (4.8%), and pre-lacteal feed (6%).142 subjects were discharged, while 25 expired. Of 142 discharged subjects, 72.5% were diagnosed with EOS, and 89% with LOS while out of 25 expired subjects, 27.5% were diagnosed with EOS, and 11% with LOS. Among the discharge and expiry patients, the mean SPO2 at room air was 89.87±6.00 and 89.80±5.80, HR was 151.67±16.07 and 158.12±16.34, RR was 61.89±8.63 and 63.16±6.87 and temp was 37.34±0.79, and 37.80±0.68, respectively. In 142 discharged study subjects, most had abnormal procalcitonin (59.2%), followed by leucopenia (48.6%), abnormal IT ration (42.3%), abnormal ESR (38%), abnormal ANC (39.4%), abnormal gastric aspirate cytology (49.3%), increased CRP (21.8%), anemic (4.2%), and leukocytosis (2.1%).

In 25 expiry subjects, most had leucopenia (72%), followed by abnormal procalcitonin (56%), abnormal ANC (56%), abnormal gastric aspirate cytology (28%), increased CRP (24%), abnormal ESR (24%), abnormal IT ration (24%), and anemic (12%). There was significant difference found in gastric aspirate cytology when associated with expiry and discharged (Table 2). In the case of gastric aspirate cytology, 89.3% had sepsis screen positive, 85.4% had outcome discharge, 14.6% had outcome expiry, and 11.7% had blood culture positive. In expired neonates, 52% of the neonates were LBW (Table 3).

Out of 167 neonates, there were 23, 13.77% found culture positive from neonatal sepsis. Out of 23 organisms, 19, 82.6% were resistance while 4, 17.4% were not (Table 4).

Table 2: Comparison of lab parameters of neonatal sepsis with outcome.

Lab parameters		Outcome				P value
		Discharge (n=142)		Expiry (n=25)		
		N	%	N	%	
ANC	Abnormal (<2)	56	39.4	14	56.0	0.122
	Normal	86	60.6	11	44.0	
CRP	Normal	111	78.2	19	76.0	0.810
	Increased (>6)	31	21.8	6	24.0	
Procalcitonin	Normal	60	42.3	11	44.0	0.827
	Abnormal (>0.2)	82	57.7	14	56.0	
Anemia	Anemic (<10)	6	4.2	3	12.0	0.112
	Normal	136	95.8	22	88.0	
TLC	Leucopenia	69	48.6	18	72.0	0.088
	Normal	70	49.3	7	28.0	
	Leukocytosis	3	2.1	0	.0	
ESR	Abnormal (>15)	54	38.0	6	24.0	0.178
	Normal	88	62.0	19	76.0	
IT Ratio	Abnormal (>0.20)	60	42.3	6	24.0	0.085
	Normal	82	57.7	19	76.0	
Gastric Aspirate cytology	Abnormal (>5)	70	49.3	7	28.0	0.049
	Normal	72	50.7	18	72.0	

Table 3: Association of sepsis screen, blood culture and outcome of neonatal sepsis with gastric aspirate cytology.

Parameters		Gastric aspirate cytology				P value
		Positive		Negative		
		N	%	N	%	
Sepsis screen	Positive	91	88.3	53	82.8	0.313
	Negative	12	11.7	11	17.2	
Outcome	Discharge	92	89.3	50	78.1	0.049
	Expiry	11	10.7	14	21.9	
Blood culture	Positive	12	11.7	11	17.2	0.313
	Negative	91	88.3	53	82.8	

Table 4: Presence of resistance and sensitive pattern of neonatal patients.

Parameters	Resistance		Sensitive	
	Frequency	%	Frequency	%
Yes	19	82.6	23	100
No	4	17.4	0	0
Total	23	100	23	100

Table 5: Association between sepsis type, isolates and gram staining status.

Parameters	Isolates	EOS, N (%)	LOS, N (%)	N	%
Gram positive	*S. aureus*	15 (78.9)	3 (75)	18	78.3
	Streptococcus	2 (10.5)	1 (25)	3	13.0
Gram negative	*E. coli*	2 (10.5)	0 (0)	2	8.7
Total		19 (100)	4 (100)	23	100.0

P value of gram positive vs. negative =1.000; applied Fisher exact test

S. aureus, *E. coli*, and streptococcus were the major causative organisms in this study. In EOS-diagnosed neonates, 17 gram-positive neonates (15, 78.9% were *S. aureus* and 2, 10.5% were streptococcus) while two were gram-negative (*E. coli* 2, 10.5%). While in LOS-diagnosed neonates, four gram-positive neonates (3, 75% were *S. aureus* and 1, 25% were streptococcus) (Table 5).

In the present study, among the gram-positive bacteria, the highest sensitivity was observed for imipenum, streptomycin, tetracycline, doxycycline meropenum, vancomycin, pipracillin/tazobactum, and tigecyclin. Among Gram-negative bacteria, the highest sensitivity was observed for imipenum, streptomycin, tetracycline, doxycycline, meropenum, vancomycin, pipracillin/tazo-bactum, and tigecyclin.

Table 6: Association between antibiotics, its sensitivity with gram positive and negative isolates.

Parameters	Sensitive (n=23)		Gram positive	Gram negative
	Frequency	%	Frequency	Frequency
Cotrimazole	5	21.74	5	-
Imipenum	22	95.65	21	1
Tobramycin	5	21.74	5	-
Streptomycin	22	95.65	21	1
Erythromycin	5	21.74	5	-
Tetracycline	22	95.65	21	1
Amoxiclav	18	78.26	18	-
Doxycycline	22	95.65	21	1
Ampicillin/sulbactam	18	78.26	18	-
Cefpodoxime	18	78.26	18	-
Cefpirome	18	78.26	18	-
Meropenum	22	95.65	21	1
Vancomycin	22	95.65	21	1
Pipracillin/tazobactum	22	95.65	21	1
Tigecyclin	22	95.65	21	1

Table 7: Association between antibiotics, its resistance with gram positive and negative isolates (n=19).

Parameters	Total resistance		Gram positive	Gram negative
	N	%	N	N
Cotrimazole	18	94.74	18	-
Imipenum	1	5.26	-	1
Tobramycin	18	94.74	18	-
Streptomycin	1	5.26	-	1
Erythromycin	18	94.74	18	-
Tetracycline	1	5.26	-	1
Amoxiclav	5	26.32	5	-
Doxycycline	1	5.26	-	1
Ampicillin/Sulbactam	5	26.32	5	-
Cefpodoxime	5	26.32	5	-
Cefpirome	5	26.32	5	-
Meropenum	1	5.26	-	1
Vancomycin	1	5.26	-	1
Pipracillin /tazobactum	1	5.26	-	1
Tigecyclin	1	5.26	-	1

Table 8: Resistance patterns of multi-drug resistant bacteria to second line of antibiotics.

Bacteria	Mero-penem, Amikacin	Strep-tomycin	Tetra-cycline	Doxy-cycline	Tobra-mycin	Cotri-mazole	Erythr-omycin	Amox-iclav	Ampi-cillin/ Sulba-ctam	Cefpo-doxime	Cef-pirome
S. aureus	0	0	0	0	18	18	18	5	5	5	5
E. coli	1	1	1	1	0	0	0	0	0	0	0
Streptococcus	0	0	0	0	0	0	0	0	0	0	0

In our study, among Gram-negative bacteria, the highest resistance was observed for imipenum, streptomycin, tetracycline, doxycycline meropenum, vancomycin, pipracillin/ tazobactum, and tigecyclin (Table 6). All Gram-positive bacteria were resistant to cotrimazole, tobramycin, and erythromycin. All gram-negative bacteria were sensitive to polymixin band colistin (Table 7, 8).

DISCUSSION

This hospital-based prospective study was conducted at Nehru Hospital, BRD Medical College, Gorakhpur (UP), in the Neonatal Intensive Care Unit of the pediatric department over one year, on 167 neonates, females outnumbered males. In contrast to our study, Mehar et al and Ingale et al reported that infections were more

common in males.[15,16] The male preponderance in neonatal septicemia may be linked to X-linked immune regulatory genes resulting in susceptibility to infections in males. Most of the neonates had aged more than five days (65.9%), followed by 72 hours to 5 days (18%) and age <72 hours (16.2%) in our study. Getabelew et al found out that age of neonates was significantly associated with neonatal sepsis.[17] In our study, most of the neonates were from rural areas, lower middle class, out-born, LSCS, the early term, early preterm, and low birth weight (LBW).

Preterm and low birth weight neonates are more susceptible to infection due to underdeveloped innate immunity and fragile, easily damaged skin. These neonates depend on survival on therapeutic interventions and thus acquire infections.[18] In contrast to our study, Mehar et al reported that most infected neonates were born vaginally (81.9%), indicating vertical transmission from the maternal genital tract. The majority of neonates were inborn (74.5%).[15] In this study, the infections were more common in neonates with low birth weight. When associated with sepsis type, 40 had EOS, and 127 had LOS; most EOS and LOS had LBW, followed by very low birth weight and extremely low birth weight. This finding is consistent with studies done in Afghanistan, Sweden and Spain.[19-21] This may be due to low-birth-weight newborns are mostly premature, have immature immune system, unable to feed, easily lose their heat, low store of glucose and more likely risk to develop hypoglycemia may increases the likelihood of neonatal infections. In the present study, 167 neonates had culture-confirmed infections; blood culture positive (13.8%) and sepsis screen positive (86.2%). 15% of patients were found with EOS, and 10% with LOS in blood culture positivity, while in sepsis screen positivity, 85% were found with EOS, and 90% were with LOS. However, in other studies from India, the culture positivity rate was 13-22%.[22,23]

The most frequently observed signs and symptoms in study were lethargy, followed by respiratory distress, refusal to feed, abnormal body movement, fever, anemia, yellowish discoloration of the body, abdominal distention, comatose, pustule, and others. Similar findings were noted in studies from KIST Medical College, Nepal (54%) and Beni Suef University Hospital, Egypt (36%).[24,25] Gastric aspirate cytology was positive in 61.7% of patients and negative in 38.3%. Maximum cytology-positive cases were seen in neonates with EOS 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 labor room. Immature immunological responses of the neonates in the first week of life make them more susceptible to infections in this period. Other authors made similar observations in the studies.[26] The most common risk factors were birth asphyxia, followed by prematurity, leaking PV for less than 24 hr, leaking PV for more than 24 hr, top feed, bleeding PV, and pre-lacteal feed, which is similar to that reported in other studies, such as Mehar et al and West & Tabansi, reported similar risk factors.[15,27] In this study, 142 subjects were discharged, while 25 expired which is similar to other studies.[28,29] Of 142 discharged subjects, 72.5% were diagnosed with EOS, and 89% with LOS. While out of 25 expired subjects, 27.5% were diagnosed with EOS, and 11% with LOS. Ballot et al have reported higher case fatality rate in LOS infection (19.6%) as compared to EOS infection (6.3%). However higher mortality rate in EOS infection was reported by Sabeeh Jumah & Hassan et al.[30,31]

In 142 discharged study subjects, most had abnormal procalcitonin, followed by Leucopenia, abnormal IT ration, abnormal ESR, abnormal ANC, abnormal gastric aspirate cytology, increased CRP, anemic, and Leukocytosis. In 25 expiry subjects, most had Leucopenia, followed by abnormal procalcitonin, abnormal ANC, abnormal gastric aspirate cytology, increased CRP, abnormal ESR, abnormal IT ration, and anemic. There was significant difference found in gastric aspirate cytology when associated with expiry and discharged, which is similar to that reported in other studies.[32] In our study, 17.4% of 167 patients tested positive for serum procalcitonin, whereas 82.6% tested negative. According to the kind of sepsis (EOS & LOS), 13.4% of patients tested positive for EOS, and 30% tested positive for LOS in serum procalcitonin. This relationship was found to be significant. This is in contrast to another study, such as Chaurasiya et al who reported that 47 (97.9%) out of 48 cases with early onset sepsis had positive procalcitonin level, while 30 (93.75%) out of 32 patients with LOS had positive procalcitonin value.[33]

In the case of gastric aspirate cytology, 89.3% had sepsis screen positive, 85.4% had outcome discharge, 14.6% had outcome expiry, and 10.7% had blood culture positive. In expired neonates, 52% of the neonates were LBW. Among 167 neonates in the study population, 23 positive blood cultures were isolated. *S. aureus*, *E. coli*, and streptococcus were the major causative organisms in this study. In EOS-diagnosed neonates, 17 gram-positive neonates (15, 78.9% were staph aureus and 2, 10.5% were streptococcus) while two were gram-negative (*E. coli* 2, 10.5%). While in LOS-diagnosed neonates, four gram-positive neonates (3, 75% were staph aureus and 1, 25% were streptococcus). This is similar to reports by Akindolire et al in Ibadan, Nigeria, who reported *S. aureus* as the major organism causing both EOS and LOS, and Jatsho et al in Bhutan who reported CoNS as the major organism in both EOS and LOS. Uwe et al also reported *S. aureus* and CoNS were the major causative organisms in both EOS and LOS.[35,36] In the present study, among the gram-positive bacteria, the highest sensitivity was observed for imipenum, streptomycin, tetracycline, doxycycline meropenum, vancomycin, pipracillin /tazobactum, and tigecyclin. Among Gram-negative bacteria, the highest sensitivity was observed for imipenum, streptomycin, tetracycline, doxycycline,

meropenum, vancomycin, pipracillin/tazobactum, and tigecyclin. In our study, among Gram-negative bacteria, the highest resistance was observed for imipenum, streptomycin, tetracycline, doxycycline meropenum, vancomycin, pipracillin/tazobactum, and tigecyclin.

All Gram-positive bacteria were resistant to Cotrimazole, Tobramycin, and Erythromycin. Ingale et al reported that among Gram negative bacteria, highest resistance was observed for, third generation Cephalosporins; Ceftazidime (81.1%) and Cefotaxime (60.3%).[16] All Gram-negative bacteria were sensitive to Polymixin Band Colistin. Aurangzeb et al also showed high resistance to Ceftazidime (71.6%), Cefotaxime (55.2%) and Gentamicin (43.2%).

Ingale et al reported that the Gram-positive bacteria, the highest resistance was observed for Penicillin and Ampicillin (91.3%) followed by Amoxicillin-clavulanic acid (82.6%) Methicillin resistance was observed in 91.6% of CoNS.[16,37] All Gram-positive bacteria were sensitive to Vancomycin and Linezolid. Shaw et al have reported a high degree resistance to Penicillins and Cephalosporins however glycopeptides and monobactum as effective antimicrobial agents.[15,38]

Limitations

This study has some limitations. The database consists only of data from patients treated at the Neonatal Intensive Care Unit, Pediatric Department, Nehru Hospital, Baba Raghav Das Medical College, Gorakhpur (Uttar Pradesh, India). Therefore, it is important to recognize that it does not represent data for all patients.

CONCLUSION

S. aureus, *E. coli*, and streptococcus were the major causative organisms. A significant proportion of the isolates were multidrug resistant strains, which pose a great threat to neonatal survival, and thereby, warrant modification of existing empirical therapy. Implement-ation of effective preventive strategies to combat the emergence of antibiotic resistance is urgently needed. We recommend a combination of imipenum, streptomycin as the first line therapy and combination of tobramycin and cotrimazole as the second line empirical therapy in our NICU.

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