Bacteriological profile and its antibiogram of Neonatal sepsis in a Tertiary neonatal intensive care unit in North Karnataka: Record Based Case Series Study

Ramesh Rajesh Pol, Sandeep K S, Vijaykiran S, Raghavendra N Vanaki, Arun B Katti,
Department of Pediatrics, S. Nijalingappa Medical College, Bagalkot., Bagalkot, Karnataka, India

Introduction:

Sepsis is the commonest cause of morbidity and mortality in newborns, and accounts nearly 30-50% of all the total neonatal deaths in developing countries [1,2]. It is estimated that up to 20% of neonates develop sepsis and 1% of them die of sepsis and its related causes [2].The bacteriological pattern of sepsis is constantly under change with advances in the early recognition with advanced laboratory tests and treatment of sepsis, and the increased survival of tiny preterm babies.

Septicemia has been classified as early onset septicemia (EOS) and late-onset septicemia (LOS)[3]. The most common microorganisms associated with EOS include Coagulase negative Staphylococcus species (CONS), Group B Streptococcus (GBS), Escherichia coli (E. Coli), Haemophilus Influenzae and Listeria monocytogenes[4], whereas LOS is caused by CONS, Staphylococcus aureus, E. coli, Klebsiella, Pseudomonas, Enterobacter, Candida species, GBS, Serratia, Acinetobacter and anaerobes. The recent trends show an increase in infections due to CONS and Acinitobacter with multidrug resistant strains[4].

Sepsis related morbidity and mortality can be reduced with prevention of sepsis itself, timely recognition, rational antimicrobial therapy and aggressive supportive care. The knowledge of bacteriological profile and its antibiogram pattern is of immense help in reducing the mortality with septicemia[5]. Thus, this study was aimed to determine the bacteriological profile and antibiotic susceptibility pattern of neonatal sepsis in our Neonatal Intensive Care Unit (NICU), in order to frame a sepsis management protocol, based on adequate knowledge of the causative organisms and their antimicrobial sensitivity pattern.

Materials and Methods:

We retrospectively reviewed positive blood cultures obtained in the neonatal intensive care unit between 01 January 2020 and 31st October 2022 at S. Nijalingappa Medical College and HSK hospital, Bagalkot. All neonates, either born at the tertiary hospital or transferred from referral units, whether preterm or term regardless of diagnosis, who had a positive blood culture, were included.

Information on patient demographics, neonatal and maternal risk factors, dates when blood cultures were taken, organisms identified and antibiotic susceptibilities was collected. Data were entered into an Excel spreadsheet.

With aseptic precautions blood volumes of 1 mL-2 mL inoculated into one Paediatric blood culture bottle (BACTEC Peds Plus Culture bottle). The bottles remain in the instrument for 5 days after which they are removed if no growth occurs. The VITEK system (Vitek instrument for sensitivity testing, which uses the broth microdilution method) was used for organism identification and for ascertaining antibiotic susceptibility of recovered organisms.

The antibiotic policy with suspected infection or sepsis is as follows: first-line empirical therapy was Cefotaxime and or Amikacin; second-line antibiotics include Piperacillin-tazobactam, Levofloxacin or amikacin, which have broader spectrum cover against most Gram-positive and Gram-negative aerobic and anaerobic bacteria, and third-line treatment is meropenem, which has the broadest range of cover against Gram-positive and Gram-negative bacteria. Multidrug resistant organisms were started on either Colistin or Tigicycline. Antifungal therapy with fluconazole was included for premature neonates with persistent thrombocytopenia, positive for urinary

Address for Correspondence:
Dr Ramesh Rajesh Pol
Professor, Department of Pediatrics,
S. N. Medical college, Bagalkot, Karnataka, India
Email: rameshpol@ymail.com

fungal elements or who cultured positive for *Candida* species.

Neonatal sepsis was divided into early onset sepsis (EOS) and late onset sepsis (LOS). Early onset sepsis, defined as sepsis within the first 72 h of life, is often attributed to acquisition of infection during the peripartum period. Late onset sepsis, occurring after 72 h of life, is often attributed to acquisition of infection in the community or in the NICU (Hospital acquired).

Results

Altogether 2607 patients were admitted between 1st January 2020 and 31st October 2022. Out of which 2104 specimens were sent for culture and sensitivity testing, out of which 353 specimens were positive.

Table 1. Demographic profile of newborns with sepsis (n=353)

Characteristics	EOS (n=167)	LOS (n=186)	TOTAL (n=353)
Gender			
Male	84	94	178
Female	83	92	175
Mode of Delivery			
Vaginal delivery	103	132	235
LSCS	59	48	107
Assisted Delivery	5	6	11
Gestational Age			
Preterm	80	123	203
Term	81	60	141
Post Term	6	3	09
Birth Weight			
VLBW	21	27	48
LBW	70	60	130
Normal Weight	76	92	168
>3.5kg	0	5	5
not known	0	2	2
Place Of Delivery			
Inborn	86	75	161
Outborn	69	123	192

About 52.7% of babies were of early onset sepsis and about 47.3% of babies were of late onset sepsis. The sepsis rate was noted higher in neonates born through vaginal route, preterms and delivery at private hospitals. The demographic profile of newborns with sepsis is been shown in table 1.

The various neonatal and maternal risk factors for neonatal sepsis were also analysed. The common neonatal risk factors noted were prematurity, low birth weight (LBW), birth asphyxia, meconium staining/ aspiration, central venous catheterization >10 days and continuous positive airway pressure use, where as maternal risk factors noted were difficult delivery (caesarean, forceps, vacuum), premature and also prolonged rupture of membranes (>18 hours), maternal fever, recurrent abortions, urinary tract infection, and chorio-amnionitis.

Table 2. Bacteriological profile and its drug sensitivity pattern.

Drug Name	CONS (n= 92)	Klebsiella (n=71)	Acinetobacter (n=40)	E.coli (n=39)	Enterococcus (n=24)	Enterobacter cloacae (n=21)	Sterptococcus (n=20)	Pseudomonas (n=19)	Staph Aureus (n=16)	Citrobacter (n=11)
Cefotaxime	NT	NT	NT	NT	NT	57%	NT	NT	NT	NT
Cefoperazone-Sulbactum	NT	46 (65%)	26 (65%)	26 (68%)	NT	21 (100%)	NT	6 (33%)	NT	4 (33%)
Ceftazidime	NT	29 (38%)	15 (38%)	27 (69%)	NT	NT	NT	17 (92%)	NT	3 (30%)
Gentamicin	64 (70%)	33 (46%)	20 (50%)	12 (31%)	17 (70%)	15 (72%)	20 (100%)	19 (100%)	12 (73%)	NT
Amikacin	59 (64%)	31 (43%0	21 (53%)	22 (56%)	15 (64%)	21 (100%)	NT	19 (100%)	11 (68%)	7 (68%)
Ciprofloxacin	43 (47%)	31 (43%)	19 (47%)	0	11 (47%)	15 (72%)	0	19 (100%)	7 (47%)	6 (57%)
Imipenem	NT	38 (53%)	24 (61%)	29 (75%)	NT	19 (90%)	NT	14 (75%)	NT	NT
Meropenem	72 (78%)	38 (53%)	23 (57%)	29 (75%)	18 (78%)	19 (90%)	NT	14 (75%)	13 (83%)	8 (78%)
Linezoid	74 (80%)	NT	NT	NT	19 (80%)	NT	18 (90%)	NT	13 (83%)	NT
Vancomycin	92 (100%)	NT	NT	NT	24 (100%)	NT	20 (100%)	NT	16 (100%)	11 (100%)
Oxacillin	0	NT	NT	NT	0	NT	0	NT	8 (50%)	0
Piperacillin/ Tazobctum	32 (35%)	29 (41%)	24 (61%)	22 (56%)	16 (65%)	16 (75%)	NT	14 (75%)	10 (65%)	7 (65%)
Colistin	NT	65 (92%)	34 (86%)	30 (78%)	NT	17 (81%)	NT	19 (100%)	NT	11 (100%)
Tigecycline	78 (85%)	71 (100%)	40 (100%)	39 (100%)	20 (85%)	21 (100%)	20 (100%)	19 (100%)	14 (85%)	11 (100%)
Trimethoprim / Sulfamethoxzole	92 (100%)	71 (100%)	32 (80%)	32 (81%)	24 (100%)	21 (100%)	0	19 (100%)	16 (100%)	11 (100%)

NT- Not Testsed

Among 353, Gram negative bacteria constituted of 53.8% (n = 190), of which Klebsiella species (38.94%) was the most predominant. Most common isolates were Coagulase negative Staphylococcus aureus 92/353 (26%), followed by Klebsiella 71/353 (20.11%) and Acinetobacter 40/353 (11.33%). Both Gram positive and Gram negative bacteria isolated showed high susceptibility to Tigecycline and Trimethoprim-Sulfamethoxazole. Gram Negative bacteria showed high susceptibility to Colistin and Carbapenems, while gram positive bacteria showed susceptibility to Linezolid and Vancomycin. Most of the organisms showed resistant to the commonly used antibiotics (Table 2).

Discussion:

Neonatal sepsis is an emergency of life-threatening nature and is a significant cause of morbidity and mortality in the newborns[6]. Despite advancement in hygiene, newer antimicrobial agents, and technology for rapid identification and treatment, neonatal sepsis remains the major causes of deaths in the newborns in developing countries[7]. Around 214,000 deaths each year are attributable to antimicrobial-resistant sepsis, and a large percentage (around 63%) of sepsis infections are resistant to first-line antibiotic drugs. Almost one in five of those infants with culture-positive sepsis die of sepsis.

The knowledge of current bacteriological profile of sepsis and patterns of antibiotic sensitivity in a geographic area is the basis of deciding empirical treatment of neonatal sepsis. In earlier days, the common pathogens implicated in neonatal sepsis were E. coli, Group B streptococci, Listeria monocytogenes, and Enterococcus species especially in the early onset sepsis. However, recent studies from developing countries show different findings with a shift towards Gram negative bacteria like E. coli, Klebsiella, S. aureus and CONS in both early and late onset neonatal sepsis[8-10]. Also there are considerable local variations in microbial flora and drug susceptibilities.

Blood culture positivity rate varies from center to center and time to time. In our study, blood culture positivity rate among the neonates with probable sepsis was 16.77%, similar to the studies reported by Bhat YR et al[11] (17.8%), Jyothi P et al[12] (19.2%), Srinivasa S et al[13] (19.2%) and Mehar V et al[14] (22.1%). The variation of blood culture positivity rate depends on differences in blood culture techniques, collection of blood sample after administration of antibiotic therapy, intrapartum antibiotic use, low grade bacteremia and infection with anaerobes decide culture positivity rate.

The occurrence of EONS in India ranged from 10.4% to 75.0%[15]. In our study found that LOS (52.7%) was more common than EOS (47.3%). Similar results were also reported by Goyal M et al[16]. In our study, the most common organism causing sepsis in newborns were gram negative bacteria (Klebsiella, Acinitobacter and E. Coli),which accounts for 53.8%. Similar results were also reported by different studies from India[11-14,17]. In contrast to present study, gram positive bacteria was the predominant pathogens in the few studies from India[15]. Klebsiella pneumonia (20.1%) followed by Acinetobacter Baumannii (11.3%) were predominant gram negative bacteria isolated in our study, which is similar to Nayak S et al., study[17]. Similar results were also reported by Delhi Neonatal Infection Study (DeNIS) where 75% of isolates were gram negative bacilli[18].

Anti-Microbial Resistance (AMR) is a global problem and it is surging rapidly in India. Most of gram negative bacteria causing neonatal sepsis are now multidrug resistant. In our study, antibiogram found that majority of gram negative bacilli and cocci were highly resistant to first line antibiotics such as 3rd generation cephalosporins, flouroquilones and aminoglycosides. That was similar to various studies from India, where the gram negative organisms showed a high degree of resistance to commonly used antibiotics[15-18]. In our study, Tigicycline, Colistin and Meropenem were found to be most sensitive antibiotics for gram negative sepsis, while for gram positive sepsis, Linezolid and Vancomycin were found to be most sensitive antibiotics. Almost similar antibiotics sensitivity patterns were also reported by various studies from India[9,12-18]. Zakariya BP et al[9], reported that Klebsiella Pneumoniae was resistant to most of the antibiotics tested except for amikacin and meropenem. Srinivasa S et al[13], studied that gram positive bacteria showed good sensitivity to higher antibiotics such as vancomycin, linezolid and poor sensitivity to ampicillin, while gram negative bacteria showed good sensitivity to amikacin, gentamycin. Recently, a large cohort was reported by DeNIS collaboration high degree of Anti-Microbial Resistance (AMR), not only to commonly used antibiotics but also to reserve antibiotics such as extended spectrum cephalosporins and carbapenems[18]. Now-a-days, this situation is alarming because these are only few reserve antibiotics. If rational antibiotics stewardshippolicy are not followed and continue using these reserve antibiotics (meropenem, colistin, linezolid, vancomycin, Tigicycline), chances of multi drug resistance organisms will naturally develop against these antibiotics. There are certain risk factors for emergence of AMR such as irrational use of broad

spectrum antibiotics, poor infection control practice, lack of antibiotics stewardship policy, lack of nurse patient ratio and overcrowding. Hence, in any NICU, it is very essential to have annual review to define the current bacteriological profile and their sensitivity pattern. For prevention of neonatal infection, strict infection control practices and rational antibiotics policy of NICU should be followed.

Conclusion:

Gram negative organisms were the most common neonatal sepsis with higher degree of resistant to commonly used drugs. The management of neonatal sepsis depends on the microbes involved and their antimicrobial susceptibility pattern. As organisms evolve, drug resistance changes- that is why clinical guidelines for neonatal sepsis need constant adaptation. Updating guidelines relies on recent and good evidence, so this observational study is a significant step towards better treatment. So, early identification of high risk newborns, strict infection control practice, with regular monitoring of antibiotic susceptibility pattern with judicial use of antibiotics can decrease the resistance and also reduce the morbidity and mortality.

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Conflict of interest: Nil
Source of funding: Nil

Date received: 23rd Nov, 2022
Date accepted: 30th Mar, 2023