Asian Journal of Clinical Pediatrics and Neonatology Original Article

Pattern and antimicrobial susceptibility of organisms causing blood stream infection in a Neonatal Intensive Care Unit (NICU) from India

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Abstract

Background: Globally infections are the single most common cause of neonatal deaths. A report from India (National Neonatal-Perinatal Database - NNPD: 2002-03) showed incidence of sepsis was 30/1000 live births (LB). Pattern and antimicrobial susceptibility of organisms have kept on changing in the NICU. Objective: To identify common bacterial pathogens associated with neonatal sepsis in a tertiary care NICU and to determine their antibiotic susceptibility pattern. Design/Methods: Prospective descriptive study. Blood culture reports of culture positive neonatal sepsis admitted to Level III NICU in South India during January 2011-June 2012 were analyzed. Demographic data of the babies was collected. Results: Total 1924 blood cultures were done for in total 1924 blood cultures were done for babies with suspected clinical sepsis. The yield rate was 9.3% (n=179/1924). The incidence of culture proven sepsis was 24/1000 live births. Of all, 82% (n=148) were Gram-negative organism, 11% (n=20) were Gram-positive organism and 7 % (n=11) were fungal organism. Over all, Klebsiella pneumoniae was the most common organism (45%) in both early onset sepsis (EOS) and late onset sepsis (LOS) followed by Acinetobacter species. The overall drug resistance to first and second line antibiotics like Ampicillin (100%), Gentamicin (91%), Amikacin (47%) and Piperacillin plus Tazobactum (45%) were high. Conclusions: The incidence of sepsis was similar to NNPD data 2002-2003, not changed much since a decade. Acinetobacter species are important emerging and drug resistant organism in newborn sepsis. It is alarming to note that the drug resistance among organisms causing both early and late onset neonatal sepsis.

Keywords: Neonatal sepsis, Gram positive organisms, Gram negative organisms, Antibiotic sensitivity.

INTRODUCTION

An estimated 4 million neonatal deaths occur around the world every year. About one third of these deaths are caused by infections.[1] These mortalities are mainly happening in developing countries and India is the home to the highest number of newborn deaths in the world of which 52% are due to infections [2]. Numerous factors such as lack of antenatal care, unhygienic and unsafe delivery practices, and prematurity and low birth weight contribute to the high morbidity and mortality [3]. Neonatal sepsis is a life-threatening clinical emergency that demands urgent diagnosis and treatment. High rate of antibiotic resistance against common bacterial pathogens has further worsened the situation. Bacterial pathogens responsible for this serious condition vary with geographical area and time [4]. Hospital surveillance at regular intervals regarding antibiotic policy in the institution should be reviewed.

The present study was conducted to show the recent pattern of organisms causing blood stream infection and their antimicrobial susceptibility in a neonatal intensive care unit (NICU) and to provide information to pediatricians and neonatologists regarding choice of antibiotics in the management of neonatal sepsis.

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MATERIAL AND METHODS

This was a prospective descriptive study. An analysis was conducted of reports of all blood cultures obtained from the neonates who had suspected clinical sepsis admitted in the NICU at a tertiary care hospital for 18 months from January 2011 to June 2012. The unit is a 40-bedded NICU serving both inborn (predominantly, more than 90 % of total admissions) and out born neonates. All neonates with suspected clinical sepsis were included in the study. Detailed records of the gestational age, birth weight, age at onset of clinical signs and symptoms, and blood culture results, and if positive, organism and its antibiogram were noted in a proforma. Blood culture was taken in all suspected clinical sepsis babies before starting or changing antibiotics. Clinical sepsis in this study was defined as presence of any one of the signs suggestive of sepsis such as, lethargy, apnea (if apnoea is not physiological as assessed by attending physician), tachypnea, tachycardia, hypotension, temperature instability, symptomatic hypoglycemia, change in oxygen requirement, poor perfusion, abdominal distension plus positive septic screen.[5]

Early Onset Sepsis (EOS) and Late Onset Sepsis (LOS) is defined as clinical evidence of sepsis within 72 hours or after 72 hours after birth respectively and blood culture grew an organism. Same organism grown repetitively in a single baby was counted as single positive culture. Babies with blood culture contaminants were not included in the study. Blood culture was considered to be negative when no growth was seen even after 5 days for bacteria and 14 days for fungus. During the study period, Ampicillin and Gentamicin were used as first line, Amikacin and Piperacillin plus Tazobactum as second line for EOS. Piperacillin plus Tazobactum and Amikacin used as first line in LOS. Antibiotics were changed

according to the blood culture results.Blood culture sample included a single sample collected from a peripheral vein under aseptic conditions. The local site was cleansed with povidone iodine (1%) and allowed to dry followed by 70% alcohol based antiseptic and allowed to dry. Blood volume of 1 ml was taken for each blood culture. Blood cultures were done either by BACTEC 9120 or Brain Heart agar. In BACTEC 9120 isolates were identified by automated identification and Microscan 96 performed antibiotic susceptibility. In Brain Heart agar, isolates were identified by conventional biochemical tests and antibiotic susceptibility was performed by disk diffusion method.[6]

RESULTS

Total numbers of live births during the study period were 5410. 2720 babies were admitted to NICU, and more than 90% of these were inborn. The majority were premature babies, low birth weight babies and babies born to high-risk mothers with antenatal risk factors. Culture proven sepsis occurred in 4.9% babies (n=134) of all NICU admissions with a rate of 24/1000 LB. Overall neonatal mortality rate was 7.7/1000 LB (n=42) and of these, 42% (n=18) of neonatal deaths were due to sepsis. Neonatal mortality due to EOS (25%) was higher than that due to LOS (11%).

Table 1: Gram Negative Organisms Sensitivity and Resistant pattern

Antibiotic	Sensitivity	Resistant
Amikacin	53%	47%
Cefaperazone with Sulbactum	73.5%	26.5%
Cefepime	27.5%	72.5%
Cefepime with Tazobactum	43%	57%
Piperacillin with Tazobactum	55%	45%
Ciprofloxacin	62%	38%
Imepenam	84%	16%
Meropenam	71%	29%
Polymyxin	97.5%	2.5%
Colistin	98.5%	1.5%
Tobramycin	25%	75%
Ceftazidime	20%	80%
Ceftriaxone	11%	89%
Cephataxime	30%	70%
Aztreonam	7%	93%
Gentamycin	9%	91%
Levofloxacin	25%	75%
Cotrimaxazole	10%	90%
Ticarcillin + Clavulonic acid	11%	89%
Ampicillin	0%	100%
Ampitum	0%	100%

During the study period, 1924 blood cultures were analyzed. Out of which 179 samples yielded growth, positivity rate being 9.3%. Of the culture positive cases, 82% (n=148/179) samples had Gram-negative bacteria, while 11% (n=20) grew Gram-positive bacteria and 7% (n=11) had fungal growth. The various organisms grown in blood culture are shown in Figure 1. Overall, Klebsiella pneumoniae was the most common organisms causing blood stream infection (n=78/148) in our setup. Acinetobacter species were the second most common (27/148). Among Gram-positive organisms (n=20/179), Staphylococcus aureus (n=8/20) was the most common. Half (n=4/8) of them were Methicillin Resistant Staphylococcus aureus (MRSA).

Thirty six babies (n=36/134) (26%) had EOS and ninety eight babies (n=98/134) (74%) had LOS. In both EOS and LOS, Gram-negative organisms were more common (75% each) pathogen (EOS: n=28/36, LOS: n=75/98). Gram-positive infection in EOS and LOS was 25% (n= 8/36), and 13% (n=12/98) respectively. In patients with LOS, incidence of fungal sepsis was 12% (n=11/98). Incidence of sepsis was higher (75%) in preterm (<37 weeks) and low birth weight (<2500 g) babies. (Figure 2a, 2 b). A high degree of resistance to common first and second line antibiotics was observed. Antibiotic susceptibility and resistant pattern for both gram positive and Gram-negative organisms were shown in Table 1 and 2.

DISCUSSION

Neonatal infections are an important cause of mortality and morbidity worldwide.[2] Incidence of sepsis in NNPD (2002-

Table 2: Gram Positive Organisms Sensitivity and Resistant pattern

Antibiotic	Sensitivity	Resistant
Amoxyclac	33.75%	66.25%
Ampicillin	40%	60%
Chloramphenicol	70%	30%
Clarithromycin	45%	55%
Clindamycin	63.5%	36.5%
Cotrimaxazole	43.5%	50.5%
Erythromycin	50%	50%
Gentamycin	61.5%	38.5%
Levofloxacin	55%	45%
Linezolid	100%	0%
Moxifloxacin	85%	15%
Netilmycin	75%	25%
Oxacillin	33.75%	66.25%
Penicillin	33.75%	66.25%
Teicoplanin	97.5%	2.5%
Tertracycline	82.5%	17.5%
Vancomycin	100%	0%
Rifamycin	100%	0%

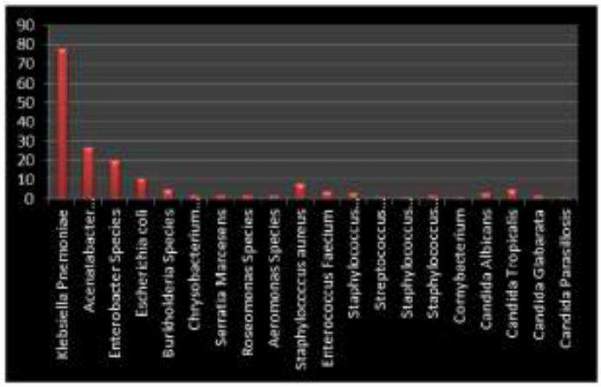

Figure 1: Pattern of microbial organism in the study

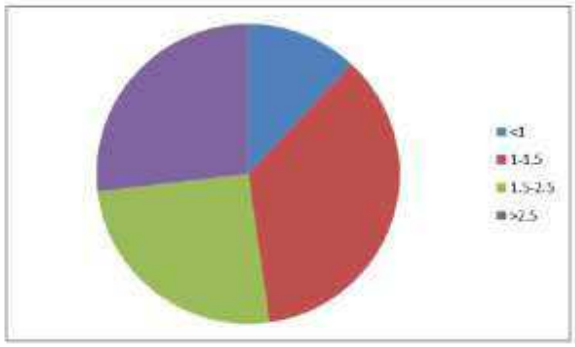

Figure 2 b: Culture positive sepsis according to birth weight (in kilograms)

2003) was 30/1000 live births [5]. A study of 17 level III units in Asia showed that incidence of sepsis varied from 3.0 to 15 per 1,000 live births [7]. The incidence of sepsis in the present study was 24/1000 live births. The most common etiological agents of early and late onset sepsis in the present study were gram-negative organisms. It could be because infections may have been horizontally acquired even in the first few days of life. Zaidi et al reported a similar picture in a review of etiology of neonatal sepsis in developing countries [8].

Klebsiella pneumoniae was the most common pathogens noted in the present study. This was in keeping with work done previously from Eastern India [9] as well as generally reported from the low and middle-income countries [10]. Interestingly, non-fermenting gram negative bacilli like Acinetobacter species was emerged as the second most common organism in our study. This is similar to the trend shown by a study conducted at a tertiary care center in northern India [11]. Mortality due to Acinetobacter sepsis was 33% in comparison to 10% mortality in babies with non-Acinetobacter sepsis. It was a grave consequence as these organisms are often intrinsically resistant to several common antibiotics and also tend to persist in the nosocomial environment, which could subsequently become a reservoir of infection.

WHO recommended first line antibiotics for early onset neonatal sepsis - Ampicillin and Gentamicin, showed alarming resistance rates in the present study. Our unit's policy was to use Piperacillin plus Tazobactum and Amikacin as the first line antibiotics in late onset sepsis and second line antibiotics for early onset sepsis. In the present study, gram-negative organisms

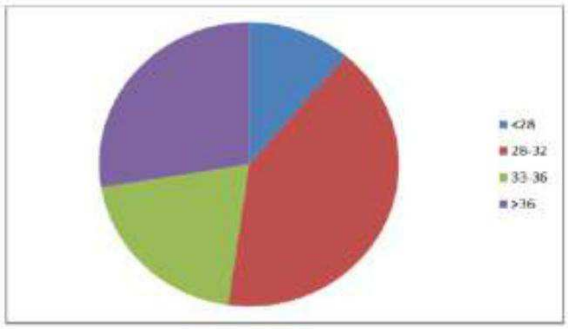

Figure 2 a: Culture positive sepsis according to Gestational age (in weeks)

were moderately susceptible to Amikacin, Piperacillin plus Tazobactum and Ciprofloxacin and highly susceptible to Cefaperazone plus Sulbactum, Carbapenems and Colistin. An increase in resistance for Piperacillin plus Tazobactum may have possibly been sparked by an increase in its usage in the unit.

The current scenario suggests the need to stringently monitor the use of antibiotics and perhaps bring about an effective antibiotic cycling policy. The importance of drawing a blood culture before starting antibiotics cannot be overemphasized. It is essential to ensure the availability of quality microbiology service as well as to encourage the treating physician's reliance on reports. The present study has its own limitations as the sample size was small and the present study was limited to one center only. A multicentric study across the country would reveal the pattern of organisms and antibiotic susceptibility in the NICUs.

CONCLUSION

This study describes the profile of neonatal sepsis in a level III NICU in southern India. Klebsiella was the most common organism and Acinetobacter species were the second most common and emerging multi drug resistant organisms causing newborn sepsis. This study suggests that periodic review of the choice of empirical antibiotics in EOS and LOS in every NICU in the country should be done.

REFERENCES

1. Lawn JE, Cousens S, Zupan J; Lancet Neonatal Survival Steering Team. 4 million neonatal deaths: when? Where? Why? Lancet. 2005;365(9462):891-900.
2. National Neonatology Forum & Save the Children (2 0 0 4) . S t a t e o f I n d i a ' s N e w b o r n s . N e w Delhi/Washington, DC: National Neonatology Forum & Save the Children/US.
3. Thaver D, Zaidi AK. Burden of neonatal infections in developing countries: a review of evidence from community-based studies. Pediatr Infect Dis J. 2009;28(1 Suppl):S3-9.
4. Mahmood A, Karamat KA, Butt T. Neonatal sepsis: high antibiotic resistance of the bacterial pathogens in a neonatal intensive care unit in Karachi. J Pak Med Assoc. 2002;52(8):348-50.
5. NNPD (2005). National Neonatal-Perinatal Database Report 2002–2003. India: National Neonatology Forum.
6. Clinical and Laboratory Standards Institute.

Performance standards for antimicrobial susceptibility testing; eighteenth informational supplement. CLSI document M100-S18. Wayne, PA: Clinical and Laboratory Standards Institute; 2008.

7. Tiskumara R, Fakharee SH, Liu CQ, Nuntnarumit P, Lui KM, Hammoud M, et al; Asia-Pacific Neonatal Infections Study. Neonatal infections in Asia. Arch Dis Child Fetal Neonatal Ed. 2009;94(2):F144-8.

8. Zaidi AK, Thaver D, Ali SA, Khan TA. Pathogens associated with sepsis in newborns and young infants in developing countries. Pediatr Infect Dis J. 2009;28(1 Suppl):S10-8.

9. Mahapatra A, Ghosh SK, Mishra S, Pattnaik D, Pattnaik K, Mohanty SK. Enterobacter cloacae: a predominant pathogen in neonatal septicaemia. Indian J Med Microbiol. 2002;20(2):110-2.

10. Kuruvilla KA, Pillai S, Jesudason M, Jana AK. Bacterial profile of sepsis in a neonatal unit in south India. Indian Pediatr. 1998;35(9):851-8.

11. Agnihotri N, Kaistha N, Gupta V. Antimicrobial susceptibility of isolates from neonatal septicemia. Jpn J Infect Dis. 2004;57(6):273-5.