

Original Research Article

Blood culture positive sepsis and sensitivity pattern in a tertiary care neonatal centre in eastern India

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ABSTRACT

Background: The objective of this study is to evaluate sensitive pattern of causative organisms of neonatal sepsis with its clinical outcome in a tertiary neonatal care unit of eastern India.

Methods: This retrospective observational cohort study was done in a tertiary care hospital of Odisha. All the blood culture positive neonatal sepsis cases, excluding neonates with multiple congenital malformations, diagnosed during January 2017 to December 2018 were analysed using descriptive summary statistics.

Results: A total of 73 neonatal sepsis cases were diagnosed by BacT/Alert and VITEK-2 blood culture method. Among them, 50 (68%) babies had gram negative sepsis, 14 (19%) cases of gram-positive sepsis and nine (13%) cases of fungal sepsis. In present study 38 (52%) cases were early onset sepsis, 38 (52%) babies were term, 55 (75%) were male and 44 (60%) babies were out born. *Klebsiella pneumonia* and *Acinetobacter* were the most common organism in early onset and late onset sepsis respectively. Among gram negative organism (GNB), 66% were multi drug resistant. A fifty percent of gram-negative organism were sensitive to meropenem and 28% were sensitive to piperacillin/tazobactam. The sensitivity of GNB to colistin, ciprofloxacin, amikacin was 76%, 64% and 56% respectively. The sensitivity of gram-positive organisms to linezolid, vancomycin, teicoplanin and penicillin were 92%, 85%, 85% and 20% respectively. Survival rate among culture positive sepsis was 83%.

Conclusions: Multi drug organisms are emerging in modern neonatal care practice. Practice of antibiotic stewardship may save the babies from multidrug resistance organism in future.

Keywords: Multidrug resistance, Neonate, Sepsis

INTRODUCTION

Neonatal sepsis contributes to 20% of neonatal mortality in India.¹ The incidence of sepsis in hospital-based studies is 30 per 1000 live births and in community-based studies, the incidence is 2.7-17% of all live births.^{2,3} Based on onset of disease, neonatal sepsis is classified as early onset sepsis and late onset sepsis.

Organisms of early onset sepsis originate mostly from maternal genital tract. However, organisms of late onset sepsis are either nosocomial infection or community

acquired infection. Prolonged hospitalization of very low birth weight neonate, use of central lines, catheter and respiratory support for their survival lead to nosocomial infection. The increasing prevalence of multidrug resistance pathogens in neonatal intensive care unit (NICU) and slow introduction of newer antibiotics are real challenges in management of neonatal sepsis. Strict follow-up of antibiotics stewardship programmed will help to counteract the present and future problem of sepsis management. One step to antibiotic stewardship is regular monitoring of pattern of causative organisms and antibiotic resistance profile. The prevalence of organism

both in early and late onset neonatal sepsis differs from western world in our country.

Bacterial flora and their resistance pattern of a unit also changes from time to time. The present study was planned to evaluate causative organisms of neonatal sepsis in a tertiary care NICU and their sensitivity pattern.

METHODS

This retrospective observation cohort study was done in a tertiary care neonatal center of Odisha.

Patient case records of blood culture confirmed sepsis cases admitted to the new-born intensive care unit during January 2017 to December 2018 were examined using a pre-defined protocol for assessment.

Inclusion criteria

- All the blood culture positive neonatal sepsis cases admitted to NICU.

Exclusion criteria

- Neonates with multiple congenital malformation
- Neonates with complex congenital heart disease.

Statistical analysis

From the case records, gestational age, onset of disease in days, sex, birth weight, inborn/out born cases, identified organisms with sensitive pattern and survival outcome were recorded for analysis using Microsoft excel.

Descriptive summary statistics were used to describe demographic profile of cases, culture identified organisms, sensitive pattern and clinical outcome. Distribution of sensitive pattern by gram positive, and gram-negative status were also described. The distribution of multi drug resistance (MDR) among each gram-negative species were tabulated and described.

RESULTS

During the study period, 73 blood culture positive cases of neonatal sepsis were isolated by BacT/Alert and VITEK-2 blood culture method.

Out of 73 cases, 50 (68%) babies had gram negative sepsis, 14 (19%) babies had gram positive sepsis and fungal sepsis was diagnosed in nine (13%) neonates.

Among culture positive sepsis, 38(52%) cases were early onset sepsis. In our study 38(52%) babies were term, 55 (75%) babies were male, 44 (60%) babies were out born and 23 (32%) babies were very low birth weight (Table 1).

Table 1: Demographic profile of neonates.

Variable		N (%)
Gestation	Term	38 (52)
	Preterm	35 (48)
Inborn/ Outborn	Inborn	29 (40)
	Out born	44 (60)
Birth weight	>2500g	25 (34)
	1500-2499g	25 (34)
	<1500g	23 (32)
Sex	Male	55 (75)
	Female	18 (25)

Among 50 Gram negative organism, *Klebsiella pneumoniae* was isolated in 16 cases, followed by *Acinetobacter boumani* in 10 cases (Table 2).

Table 2: Distribution of Gram-negative organisms.

Organism	No. of cases	EOS	LOS
<i>Klebsiella</i>	16	11	05
<i>Acinetobacter</i>	10	02	08
<i>Enterobacter</i>	04	0	4
<i>Burkholderella</i>	06	04	02
<i>E. coli</i>	05	02	03
Other Gram-negative bacilli	09	08	01
Total	50	27	23

Out of 14 Gram positive organism, five cases were Coagulase negative staphylococcus (CONS), followed by three cases *Staphylococcus aureus*, three cases of Group B *Streptococcus* (GBS) and three cases of enterococcus (Table 3).

Table 3: Distribution of Gram-positive organisms.

Organism	No. of cases	EOS	LOS
CONS	5	03	02
<i>S. aureus</i>	3	0	03
<i>S. agalacti</i>	3	03	0
Enterococcus	3	01	02
Total	14	07	07

Klebsiella was the predominant organism in early onset sepsis (EOS) and *Acinetobacter* was the leading cause of late onset sepsis (LOS). Fifty percent of gram-negative organism were sensitive to meropenem and 28% were sensitive to piperacillin and tazobactam. However sensitive to colistin, ciprofloxacin, amikacin was 76%, 64% and 56% respectively.

Majority (96%) of gram-negative organisms were resistant to ampicillin and among cephalosporins, cefoperazone and sulbactam was sensitive only in 30% of gram-negative organism (Table 4).

Out of 20 carbapenem resistant GNB, 18(90%) organisms were sensitive to colistin and the sensitivity to

ciprofloxacin and amikacin were 55% and 50% respectively. Twenty-eight percent of gram-positive organism were sensitive to benzyl penicillin and ciprofloxacin. The sensitivity to linezolid, vancomycin

and teicoplanin were 92%, 85%, 85% respectively. Out of eight *Staphylococcus* organisms (CONS and *S. aureus*), six (75%) were resistant to oxacillin (Table 5).

Table 4: Sensitivity of Gram-negative organism.

Antibiotics	Sensitive	Intermediate sensitive	Resistance
Meropenem	25 (50%)	5	20
piperacillin -tazobactam	14 (28%)	0	36
Amikacin	28 (56%)	2	20
Ciprofloxacin	32 (64%)	3	15
Colistin	38 (76%)	0	12
Cephalosporin- sulbactam	15 (30%)	3	28
Ampicillin	2 (4%)	0	48

Table 5: Sensitivity of gram-positive organism.

Antibiotics	Sensitive	Intermediate	Resistance
Penicillin	4	0	10
Ciprofloxacin	4	1	9
Linezolid	13	0	1
Vancomycin	12	2	0
Teicoplanin	12	1	1

In present study, 33(66%) gram negative organisms were multi drug resistant. An 81% of *Klebsiella* spp, 60% of *Acinetobacter* spp. and (6/6)100% *Burkholderia cepacia* were multi drug resistant (Table 6).

Table 6: Distribution of MDR gram negative organism.

Organism (N)	Frequency of MDR organism n (%)
<i>Klebsiella</i> sp. (16)	13 (81)
<i>Acinetobacter</i> sp. (10)	06 (60)
<i>Burkholderia</i> sp. (06)	06 (100)
<i>Enterobacter</i> sp. (04)	03 (75)
Others GNB (14)	05 (35)
Total GNB (50)	33 (66)

Out of 73 babies three babies died and nine neonates were left the unit before completion of treatment. Survival incidence in culture positive sepsis was 61/73(83%). Only one neonate with gram negative sepsis and two babies with fungal sepsis had died during the study period.

DISCUSSION

Blood culture remains the gold standard investigation for the diagnosis of neonatal sepsis. To know the bacteriological profile and antibiogram, the present study was conducted retrospectively in blood culture positive neonatal sepsis. In the present study gram negative

organism were isolated in 68% of all culture positive sepsis, followed by 19% gram positive sepsis. Fungal sepsis was isolated in 13% babies. Interestingly three cases of GBS were isolated among early onset sepsis. Similar pattern of bacteriological profile i.e.69% gram negative organisms and 26% gram positives bacteria were found in Pinaki et al which was conducted on microbiological pattern in rural India and the most common organism were *Klebsiella* sp, followed by *Staph aureus*.⁴ In Delhi cohort study conducted in multiple tertiary care centres, 64% isolates were gram-negative including *Acinetobacter* (22%), *Klebsiella* (17%), and *Escherichia coli* (14%).⁵ Study conducted in South India tertiary care hospital by Bambala et al, found that *Klebsiella pneumoniae* was isolated from 66% of culture positive cases followed by Coagulase-negative staphylococci in 12% of cases.⁶ Another study conducted in a tertiary care centre of western India also found that *Klebsiella pneumoniae* (35.4%) was leading cause of neonatal sepsis among the gram-negative pathogens and *Staphylococcus aureus* (22.9%) was the predominant among gram-positive pathogen.⁷ Bacteriological profile in northern, southern, western and eastern India (our study report) tertiary care centres were almost similar i.e. gram negative organism were the predominant microbiological agent in both early and late onset neonatal sepsis. *Klebsiella* sp. was the leading cause of early onset sepsis and *Acinetobacter* sp. was the commonest organism in late onset sepsis in our study. In NNPD Network, *Klebsiella* spp. (32%) were the leading pathogens, with the proportion of *Acinetobacter* spp. being a low 3%.² Now a days there was increasing incidence of *Acinetobacter* spp infections in tertiary neonatal units of India.⁵ The mortality in neonatal sepsis in advanced intensive care era is secondary to emergence of multi drug resistance bugs. Early isolation of organism and antibiogram guided treatment can help in survival of the septic neonates. In our study, the sensitivity of GNB to meropenem, piperacillin and tazobactam were 50% and 28% respectively. The antibiogram of *Klebsiella* spp in Pinaki et al, were sensitive to amikacin (84%),

gentamicin (86%), ciprofloxacin (73%), imipenem (100%), and cephalosporin (56%).⁴ In South India study majority of the *Klebsiella pneumoniae* isolates were resistant to all the antibiotics except amikacin and meropenem and 32% of them were ESBL producers.⁶ In Delhi cohort study the prevalence of carbapenem resistance among *Klebsiella spp.*, *Acinetobacter spp.* were 38% and 78% respectively.⁵ In our study the carbapenem resistance GNB were sensitive to colistin, ciprofloxacin and amikacin in 90%, 55% and 50% neonates respectively. In the present study 66% of gram-negative organism were multi drug resistant (MDR). Gram-negative isolates resistant to any three of five antibiotic classes (extended-spectrum cephalosporins, carbapenems, aminoglycosides, fluoroquinolones, and piperacillin-tazobactam) is defined as multidrug resistant. Eighty-one percent *Klebsiella spp.*, 60% *Acinetobacter spp.* and all isolated *Burkholderia cepacia spp.* were multidrug resistant. High rates of multidrug resistance were also observed in 82% *Acinetobacter spp.*, 54% *Klebsiella spp.* and 38% *Escherichia coli* in Delhi cohort study.⁵ Vrishali et al, described increased emergence of ESBL producers among *Klebsiella pneumoniae* (29.4%) and *E. coli* (25%).⁷ High proportion of resistance to common first and second line antibiotics like ampicillin (98.5%), gentamicin (84.4%), amikacin (65.6%) and cefotaxime (81.3%) were also noticed in study by Viswanathan et al.⁸ The rising prevalence of nosocomial infections in NICU are due to prematurity, low birth weight and increased duration of hospital stay.⁹ The emergence of high rates of multidrug resistant bugs is threatening for the Indian NICUs and its aetiologies are multifactorial.¹⁰⁻¹² In present study, 75% of staphylococcus spp. was resistant to oxacillin. Most of the gram-positive organism were sensitive to vancomycin and linezolid. The sensitivity of gram-positive organism to benzyl penicillin was 28%. Similar pattern of methicillin resistance prevailed in 61% of coagulase-negative staphylococci and 38% of *Staphylococcus aureus* isolates in Delhi cohort study.⁵ As per NNPD data, most of the *Staphylococcus aureus* isolates were sensitive to vancomycin (63.6%) and amikacin (39.7%), but not to penicillin (9.1%).² Despite high prevalence of MDR gram negative bacteria and methicillin resistance gram positive staphylococci, the survival of culture positive neonatal sepsis in present study was 83%. Nine (13%) babies were discharged against medical advice before completion of treatment and mortality rate was 4% in present study.

CONCLUSION

Multi drug resistant organisms are emerging in modern neonatal care practice. Antibiotics like colistin, ciprofloxacin and amikacin may be used in carbapenem resistance gram negative organisms. Practice of strict antibiotic stewardship may save the babies from multidrug resistant organism in future.

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