

Original Research Article

Clinical and bacteriological profile of neonatal sepsis with emerging resistance patterns

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ABSTRACT

Background: The present study was designed to evaluate the clinical spectrum, bacteriological profile, antibiotic sensitivity pattern and mortality due to neonatal septicemia in neonates admitted in neonatal units attached to the SMS Medical College, Jaipur.

Methods: In born and out born babies of postnatal age up to 28 days who were bacteriological proven cases of septicemia were subjected to history, clinical examination and laboratory evaluation and data were analyzed statistically.

Results: Out of 150 cases 67.33% neonates were preterm and 77.33% were low birth weight neonates. Gram negative organisms were most common cause of septicemia (66.6%), Both the Gram negative and Gram positive organisms were sensitive to piperacillin-tazobactam, linezolid, fosfomycin, teicoplanin, polymyxin B, colistin, ofloxacin. Both the Gram negative and Gram positive organisms were resistant against cephalosporins, ampicillin, Amoxyclav, cotrimoxazole. Gram negative isolates were most sensitive to Polymyxin B (70%) and had the highest resistance to cefepime (36%). Gram-positive organisms were most sensitive to vancomycin (84%) and linezolid (82%). Highest resistance was noted from Amoxyclav (52%).

Conclusions: Preterm (<37 week) and low birth weight (<2500gm) neonates are considered as major susceptible causes of neonatal sepsis. Proper hygiene and hand washing, early detection of sepsis and judicious use of antibiotics to prevent multidrug resistance is needful in our setup.

Keywords: Microbial sensitivity patterns, Multidrug resistance, Neonatal sepsis, Septicemia

INTRODUCTION

Neonatal septicemia is a clinical syndrome of bacteremia characterized by systemic signs and symptoms in first four week of life.¹ It is more common in developing countries compared with developed countries due to poor hygiene and suboptimal practices for infection control and is an important/chief cause of neonatal mortality and morbidity globally.² Incidence of neonatal sepsis according to the data from National Neonatal Perinatal Database (NNPD) is 3 per 1000 live births.³ In most developing countries, gram negative bacteria remain the

major cause of neonatal sepsis.^{4,5} A significant proportion of these deaths are caused by multidrug-resistant pathogens. Neonatal sepsis can be classified into two categories depending on the onset of symptoms-

Early onset sepsis (EOS)

It presents within the first 72 hours of life. In severe cases the neonate may be symptomatic at birth. Infants with EOS usually present with respiratory distress and pneumonia. The source of infection is generally the maternal genital tract. Risk factors associated with

increased risk of early onset sepsis include low birth weight (<2500 grams) or prematurity, febrile illness in the mother with evidence of bacterial infection within 2 weeks prior to delivery, foul smelling liquor, rupture of membrane >24 hours (PROM), single unclean or >3 sterile vaginal examination(s) during labor, prolonged labor (sum of 1st and 2nd stage of labor >24 hours), perinatal asphyxia (Apgar score < 4 at one minute) etc.

Late onset sepsis (LOS)

It usually presents after 72 hours of age. The infection in LOS is either hospital-acquired or community-acquired. Neonates usually presents with septicemia, pneumonia or meningitis. The risk factors for nosocomial sepsis include low birth weight, prematurity, admission in intensive care unit, mechanical ventilation, invasive procedures and central lines, administration of parental fluids and use of stock solutions. Factors that increase the risk of community acquired LOS include poor hygiene, poor cord care, and bottle feeding and prelacteal feeds. This study was aimed to assess the clinical spectrum, bacteriological profile, antibiotic sensitivity pattern and mortality due to neonatal septicemia in neonates admitted in neonatal units attached to the SMS Medical College, Jaipur.

METHODS

This Descriptive type of observational study was conducted after getting prerequisite clearance from the research review board. In born and out born babies of Postnatal age up to 28 days who were bacteriological proven cases of septicemia were included in the study. Babies with postnatal age more than 28 days or having contaminants grown on blood culture or fungal growth in blood culture were excluded.

Sample size was calculated at 95 percent confidence interval assuming 8.9 percent neonates having positive blood culture. At 3 percent absolute allowable error, 500

suspected cases of neonatal septicemia were taken as sample size in the present study. These selected patients were subjected to history, clinical examination and laboratory evaluation. Samples for blood culture obtained from neonates under strict asepsis, in blood culture bottle. All investigations were done in SMS Medical College. The entire data were collected in a pre-tested proforma, collected data were analyzed statistically using statistical package for social science (SPSS) version 12.0.

RESULTS

Out of 500 neonates 385 (77%) had early onset sepsis and 115 (23%) had late onset sepsis. 316 (63.2%) were male and 184 (36.8%) were female neonates with a male to female ratio of 1.7:1. 150 (30%) of 500 participants had positive blood culture. Birth weight distribution suggested that 71% LBW babies were included in the study. 174 babies were having birth weight <2500 gm (34.8%), 130 babies had birth weight <1500 gm (26%) and 51 babies (10.2%) were extremely low birth weight out of 355 LBW babies (Figure 1).

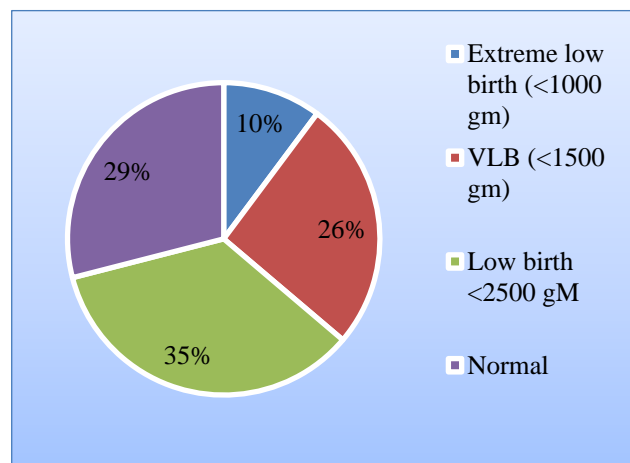


Figure 1: Distribution of neonates according to birthweight.

Table 1: Distribution of culture proven septic neonates according to onset of sepsis, gestational age, birth weight, sex and mortality.

Category	Total number of cases		GA (Wks)				Weight (gm)				Male		Female		Mortality	
			Term (>37)		Preterm (<37)		AGA >2500		LBW <2500		No.	%	No.	%	No.	%
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Early onset	117	78.0	39	26.0	78	52.0	29	19.33	88	58.67	77	51.33	40	26.67	26	17.33
Late onset	33	22.0	10	6.67	23	15.33	5	3.33	28	18.67	22	14.67	11	7.33	2	1.33
Total	150	100.0	49	32.67	101	67.33	34	22.67	116	77.33	99	66.00	51	34.00	28	18.67

Observation regarding gestational age revealed that 314 (62.8%) babies were preterm and 186 (37.2%) were full term. Assessment of antenatal risk factors in neonates of

suspected sepsis suggested that PROM was major contributing risk factor (62.68%) in suspected neonates of sepsis followed by MSL (31.34%), BPV (2.98%) and

PIH (1.49%). Majority of newborns, 400 (80%) were vaginally delivered in the present study and 100 through LSCS. Birth history of neonates of suspected sepsis depicted immediate cry after birth in 426 (85.2%), delayed cry in 50 (10%) and no cry after birth in 24 (4.8%) (Table 1).

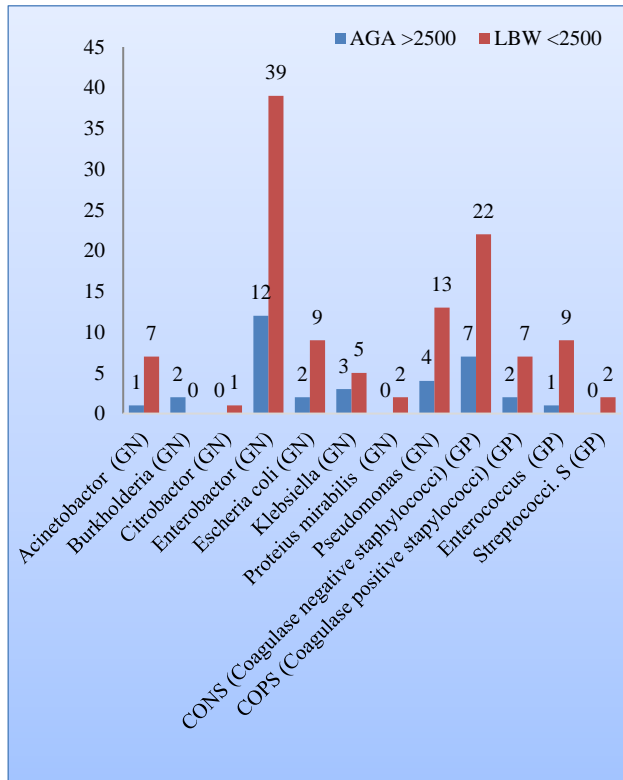


Figure 2: Causative organism according to birthweight.

Presenting symptoms of neonates of suspected sepsis at the time of admission

Difficulty in breathing was major symptom/complaint (71%) at the time of admission. Decreased oral acceptance (10.80%), abnormal body movement (7.4%), yellowish discoloration of body (5.8%), excessive cry after birth (1.2%), low birth weight, abdominal distention, bleeding PR, blood in stool, loose stool, fever, not gaining weight and not passing stool were other presentations. Early onset sepsis to late onset sepsis ratio was 2:1.

Distribution of bacterial isolates

Out of 500 neonates for suspected sepsis 150 neonates were culture proven sepsis. Out of 150 neonates, 78% were EOS and 22% were LOS. Out of 150 cases 67.33% neonates were preterm and 77.33% were low birth weight neonates. Among the isolated organisms, Gram negative organisms were present in 66.60% neonates.

Gram negative

Gram negative organisms were grown in blood culture of 100 (66.6%) neonates out of 150 blood culture positive neonates, in which preterm (<37 weeks) 68% and low birth weight (<2500 grams) 76% encountered. Gram negative organisms encountered in first 72 hours in decreasing order of frequency were *Enterobacter spp.* 51 (34%), *Pseudomonas* 17 (11.33%), *Escherichia coli* 11 (7.33%), *Acinetobacter spp.* 8 (5.33%), *Klebsiella* 8 (5.33%), *Proteius mirabilis* 2 (1.33%), *Burkholderia* 2 (1.33%) and *Citrobacter* 1 (0.66%). Gram negative organisms were encountered in 79% in EOS and 21% LOS.

Table 2: Characteristics of gestational age and birth weight in neonatal sepsis according to causative organism.

	GA (Wks)		Wt (gm)				Total			
	Term (>37)		Preterm (<37)		AGA >2500		LBW <2500		No.	%
	No.	%	No.	%	No.	%	No.	%		
<i>Acinetobacter (GN)</i>	1	0.67	7	4.67	1	0.67	7	4.67	8	5.33
<i>Burkholderia (GN)</i>	2	1.33	0	0	2	1.33	0	0	2	1.33
<i>Citrobacter (GN)</i>	1	0.67	0	0	0	0.00	1	0.67	1	0.66
<i>Enterobacter (GN)</i>	18	12.00	33	22.00	12	8.00	39	26.0	51	34.00
<i>Escheria coli (GN)</i>	2	1.33	9	6.00	2	1.33	9	6.00	11	7.33
<i>Klebsiella (GN)</i>	2	1.33	6	4.00	3	2.00	5	3.33	8	5.33
<i>Proteius mirabilis (GN)</i>	0	0	2	1.33	0	0	2	1.33	2	1.33
<i>Pseudomonas (GN)</i>	6	4.00	11	7.33	4	2.67	13	8.67	17	11.33
<i>CONS (Coagulase negative staphylococci) (GP)</i>	11	7.33	18	12.00	7	4.67	22	14.67	29	19.33
<i>COPS (Coagulase positive staphylococci) (GP)</i>	4	2.67	5	3.33	2	1.33	7	4.67	9	6.0
<i>Enterococcus (GP)</i>	2	1.33	8	5.33	1	0.67	9	6.00	10	6.66
<i>Streptococci. S (GP)</i>	0	0	2	1.33	0	0	2	1.33	2	1.33

Gram positive

The Gram-positive organisms were grown in blood culture of 50 (33.33%) neonates out of 150 blood culture positive neonates, in which preterm (<37 weeks) 66% and low birth weight (<2500 grams) 80% encountered. Gram positive organisms encountered in first 72 hours, in decreasing order of frequency were CONS 29 (19.33%), *Enterococcus* 10 (6.66%), COPS 9 (6%), *Streptococcus* 2 (1.33%). Gram positive organisms encountered in 38% EOS and 12% LOS.

Characteristics of gestational age and birth weight in neonatal sepsis according to causative organism

Out of 150 cases 67.33% neonates were preterm and 77.33% were low birth weight neonates (Figure 2). Among the isolated organisms, Gram negative organisms were present in 66.60% neonates. Enterobacter spp. were most common (34%) among the Gram negative isolates while CONS were most common (19.33%) among Gram positive isolates. Gram negative organisms were detected in 79% in EOS and 21% LOS (Table 2).

Antibiotic sensitivity/resistance pattern of bacterial isolates (in Gram negative)

The antibiotic sensitivity pattern depicted that Gram negative organisms had a high degree of resistance to commonly used antibiotics like ampicillin, gentamycin, amikcin, cefotaxime, ceftriaxone, cefepime and Amoxycylav. These isolates were most sensitive to Polymyxin B (70%) and had the highest resistance to cefepime (36%). In the Gram-negative group, the best overall sensitivity was to Polymyxin B (70%), Piperacillin-Tazobactam (53%), Meropenam (44%), Ofloxacin (40%) and Fosfomycin (39%). Overall resistance was from cefepime (36%), cefotaxime (24%), amikcin (22%), ceftriaxone (19%), gentamycin (13%), Amoxycylav (10%). Sensitivity from cefuroxime and amoxicillin were not tested.

Antibiotic sensitivity/resistance pattern of bacterial isolates (in Gram positive)

As a group, the Gram-positive organisms were sensitive to vancomycin (84%) and linezolid (82%) followed by Sensitivity to teicoplanin (58%), piperocillin-tazobactam (42%), and fosfomycin (40%). Highest resistance was noted from Amoxycylav (52%) followed by azithromycin (34%), ciprofloxacin (32%), cefotaxime (30%), cefoxitin (28%), cotrimoxazole (24%).

Both the Gram negative and Gram positive organisms show sensitivity to piperacillin-tazobactam, linezolid, fosfomycin, teicoplanin, polymyxin B, colistin, ofloxacin. Both the Gram negative and Gram positive organisms were resistant against cephalosporins, ampicillin, Amoxycylav, cotrimoxazole. Gram negative isolates were most sensitive to Polymyxin B (70%) and had the highest

resistance to cefepime (36%). Gram-positive organisms were most sensitive to vancomycin (84%) and linezolid (82%). Highest resistance was noted from Amoxycylav (52%). Both the Gram negative and Gram positive organisms show sensitivity from piperacillin-tazobactam, linezolid, fosfomycin, teicoplanin, polymyxin B, colistin, ofloxacin.

Outcome of neonates admitted with suspected sepsis

Out of 500 neonates, 415 (83%) neonates were discharged in good condition after appropriate interventions were administered; including antibiotic therapies. 2 neonates were referred to pediatric surgery department during study period. Total deaths occurred in 83 (16.6%) out of the 500 neonates during study period. Out of 150 culture proven neonates 28 (18.66%) death occurred during study period, in which 17.33% were EOS and 1.33% were LOS. Gram negative organisms encountered in 24 (85.71%) deaths and Gram positive encountered in 4 (14.29%) deaths. Most common Gram negative organism encountered in culture proven deaths was Enterobacter species. Most common Gram positive organism encountered in culture proven deaths was CONS. The case-fatality rate was 18.66%. The findings of present study show that male to female ratio was >1, which is comparable with most of the studies Neonatal sepsis is common and contributes to mortality among neonates admitted in the neonatal units in Tertiary Care Centers in India, which is a developing country. This is similar with reports from studies in various tertiary care centers in India and other developing countries.⁶⁻¹⁰

DISCUSSION

In present study Gram negative organisms were most common cause of septicemia (66.6%), which is comparable with studies held in Bhubaneswar, India (84.39%), Delhi, India (66%), Pakistan (58.9%) and Thiruvananthapuram, India (70%). The case fatality rate was 18.66%, which is much lower than study in Delhi, India, where case fatality rate was 50.80%.¹¹ In other studies Gram-positive organisms were more common than Gram negative like Kerala, India (51.92%), Karnataka, India (80%), and Nepal (63.8%).¹² Gram-negative bacteria were responsible for 79% of the cases of early-onset neonatal sepsis which is comparable with study in Bhubaneswar, India (88.66%), Maharashtra, India (63.13%).¹³ The antibiotic sensitivity pattern varies from country to country, even state to state in the same country, because of poor antibiotic policies and unjustifiable use of antibiotics, especially in developing and poor countries.

In the present study in Gram-negative group, the best overall sensitivity was to Polymyxin B (70%), Piperacillin-Tazobactam (53%), Meropenam (44%), Ofloxacin (40%) and Fosfomycin (39%), which is similar to study in Thiruvananthapuram, India, which show 100% sensitivity from meropenem and 90% sensitivity

from piperacillin-tazobactam.¹⁴ Overall resistance was from cefepime (36%), cefotaxime (24%), ceftriaxone (19%) Amoxyclav (10%).

In present study Gram-positive organisms had most sensitivity to vancomycin (84%) and linezolid (82%), which is comparable with a study in Karnataka, India which depicted 100% sensitivity from vancomycin and linezolid.^{15,16} Sensitivity to teicoplanin (58%), piperacillin-tazobactam (42%), and fosfomycin (40%). Highest resistance was noted from Amoxyclav (52%). Resistance pattern from other antibiotics was azithromycin (34%), ciprofloxacin (32%), cefotaxime (30%), cefoxitin (28%), and cotrimoxazole (24%).

In the present study, there was an exceedingly high rate of resistance to ampicillin and cephalosporin for all micro-organisms. In present study culture proven sepsis neonates were 30%, which is comparable with study in Kerala, India (22.23%), Maharashtra, India (35.86%), Pakistan (21%), Nigeria (34%).¹⁷

In present study culture proven sepsis affected neonates were 30%, which is comparable with study in Kerala, India (22.23%), Maharashtra, India (35.86%), Pakistan (21%) and Nigeria (34%). Early-onset sepsis was more common (78%) than late onset sepsis (22%) which is comparable with similar studies in Bhubaneswar, India, Karnataka, India, Nigeria, Maharashtra, India.¹⁷ Preterm babies (67.33%) and low birth weight babies (77.34%) were more prone for sepsis, which is similar with reports from studies in various tertiary care centers in India and other developing countries.¹⁸

CONCLUSION

Preterm (<37 week) and low birth weight (<2500gm) neonates are considered as major susceptible causes of neonatal sepsis. Proper hygiene and hand washing, early detection of sepsis and judicious use of antibiotics to prevent multidrug resistance is needful in our setup.

Recommendations

According to the results of the present study preterm (<37 week) and low birth weight (<2500 gm) neonates are considered as major susceptible causes of neonatal sepsis. Proper hygiene and hand washing, early detection of sepsis and judicious use of antibiotics to prevent multidrug resistance is needful in our setup.

Guidelines on the reduction of emergence of drug resistance must be provided and implemented in new born units.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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