

Bacteriological profile of neonatal sepsis in a secondary care hospital in rural Tamil Nadu, Southern India

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ABSTRACT

Introduction: Neonatal sepsis is a leading cause of neonatal mortality and morbidity in the world. The objective of the current study was to detect the common causative microorganisms of neonatal sepsis and their antimicrobial resistance patterns in a rural secondary hospital in Tamil Nadu, India. **Materials and Methods:** Neonates (0–28 days) admitted to this newborn care unit from October 2013 to September 2015, with a diagnosis of probable sepsis were studied. All the enrolled babies had blood cultures taken and were followed up till final outcome, which was discharge or death, irrespective of culture result. Univariate analysis was performed for factors associated with culture positivity, generating odds ratios, and confidence intervals. **Results:** Among the 107 babies with a diagnosis of probable sepsis, 28 (26.2%) had shown bacteria in culture. The majority (94.4%) were of early-onset sepsis. The predominant organisms were *Staphylococcus aureus* (10/28) and *Klebsiella* (6/28). 100% of Gram-negative bacilli and 90% of *Staphylococcus* were resistant to Ampicillin. Gentamicin resistance among Gram-negative bacilli and *Staphylococcus* was 52.9% and 20%, respectively, while third-generation cephalosporin resistance was 31.2% and 20%, respectively. Among the neonates diagnosed as probable sepsis, idiopathic prematurity ($P = 0.007$) was found to have a statistically significant association with culture-positive sepsis. **Conclusion:** The culture positivity rate among the neonates with probable sepsis in the current study was 26%. An alarmingly high degree of antibiotic resistance observed calls for robust infection control practices and an urgent evaluation and development of individual and national antibiotic policies for neonatal sepsis.

Keywords: Antibiotic policy, antimicrobial resistance, neonatal septicemia, prematurity

Introduction

Neonatal sepsis is a leading cause of neonatal mortality in the world.^[1] It is also one of the common morbidities in neonatal units in India.^[2,3] Majority of neonatal sepsis occurs in developing countries.^[4]

Although risk factors attributable to neonatal sepsis, its causative organisms, and their antimicrobial resistance patterns are well described, such evidence is based predominantly on data from

tertiary hospitals.^[3-7] Good laboratory facilities, especially blood culture, are frequently unavailable in the rural healthcare setting, resulting in the nonavailability of relevant data on culture-proven neonatal sepsis. With progress achieved in the past two decades in promoting institutional deliveries among the rural population of India, research on neonatal sepsis in rural hospitals could be a useful addition to medical literature.

The objective of the current study was to detect the common causative microorganisms of neonatal sepsis and their antimicrobial resistance patterns in a rural secondary care hospital in Tamil Nadu, India.

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Materials and Methods

The study was done in the special newborn care unit of a secondary level rural hospital in Tamil Nadu. The hospital has a 55-bedded obstetrics unit and a 10-bedded Neonatal Intensive Care Unit (NICU) with predominant level II care.

Neonates (0–28 days) admitted to this newborn care unit from October 2013 to September 2015, with a diagnosis of probable sepsis were studied. Outborn babies and babies with gross congenital anomalies were excluded.

Babies with one or more of the following risk factors – maternal fever, prolonged rupture of the membranes for more than 24 h, foul-smelling or meconium-stained liquor, or frequent (>3) unclean vaginal examinations, and/or having severe prematurity, or birth asphyxia necessitating active resuscitation were considered at risk for sepsis and admitted to neonatal unit for observation. All such neonates were monitored daily for signs and symptoms of sepsis. A diagnosis of probable sepsis was made in the presence of a set of clinical signs as per the Young Infant Study Algorithm standard definitions of sepsis, adapted from National Healthcare Safety Network which included tachypnea, respiratory distress, prolonged capillary refill time, abnormal color, abdominal distension, poor sucking, irritability, convulsions, temperature abnormalities, lethargy, or apnea. Blood culture was done for all neonates with a diagnosis of probable sepsis.

Early-onset and late-onset of sepsis were defined as infection within the first 72 h of life and >72 h of life, respectively. Those babies with new onset symptoms and signs suggesting worsening of sepsis during the hospital course were subjected to subsequent blood culture. Detailed history was collected in a pro forma. All the study participants were followed up till final outcome, which was discharge or death, irrespective of culture result.

BACTEC system was used for blood culture. Bottles were incubated in the bactec9050 incubator. After the bottles were flagged positive, Gram-stain was performed from the broth for preliminary identification of the type of organisms isolated. Subcultures were made in blood agar and MacConkey agar and incubated at 37°C for 18–24 h. Organisms were processed for identification. Susceptibility testing was also performed using AST-GP67 card for Gram-positive cocci and AST GN25/N090 for Gram-negative bacilli. Processing was done as per manufacturer's instructions. Cards were loaded onto the VITEC 2 compact (biomerieux) instruments. Culture was reported sterile if there was no growth in 7 days.

Descriptive statistics including frequencies and percentages was done. Univariate analysis was performed for finding factors associated with culture positivity, generating odds ratios, and confidence intervals.

Results

There were 3114 live births during the study period. Total admissions to newborn unit during the study period were 1070. The study included 107 neonates who satisfied the inclusion and exclusion criteria. The details of neonatal admissions are shown as a flowchart in Figure 1.

Of the 107 babies with a diagnosis of probable sepsis, 63 (59%) were males, 27 (25%) were preterm babies, and nine (8.4%) had birth weight <2 kg. The basic characteristics of study neonates are shown in Table 1.

Among the 107 babies, 28 (26.2%) blood samples had shown bacteria in culture, 13.1% babies had their first culture positive, 13.1% babies had their subsequent culture positive while 73.8% of neonates showed no growth in blood culture. A total of 101 (94.4%) individuals were of early-onset sepsis and 6 (5.6%) individuals were of late-onset sepsis. The predominant organisms identified were *Staphylococcus aureus* (10/28) and *Klebsiella* (6/28). The details of organisms isolated are shown in Table 2.

100% of Gram-negative bacilli and 90% of *S. aureus* were resistant to Ampicillin. Gentamicin resistance among Gram-negative bacilli and *S. aureus* was 52.9% and 20%,

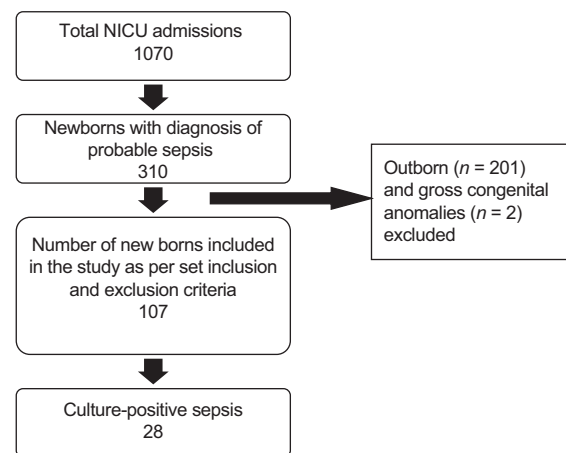


Figure 1: Details of Neonatal Intensive Care Unit admissions

Table 1: Characteristics of neonates with probable sepsis (n=107)

Characteristics	Categories	Frequency (%)
Gender	Male	63 (59)
	Female	44 (41)
Gestational age	Term	80 (75)
	Preterm	27 (25)
Birth weight (kg)	<1.5	4 (3.7)
	1.5-1.99	5 (4.6)
	2-2.49	30 (28)
	≥2.5	68 (63.5)

respectively. The prevalence of ciprofloxacin resistance was 20% among *S. aureus* and 12% among Gram-negative bacilli. None of the *S. aureus* but 17.6% of Gram-negative bacilli was resistant to Amikacin. In the study, 31.2% of Gram-negative bacilli and 20% of *S. aureus* were resistant to third-generation cephalosporins. The details of antimicrobial resistance are shown in Table 3.

Among the neonates with a diagnosis of probable sepsis, idiopathic prematurity ($P = 0.007$) was found to have a statistically significant association with culture-positive sepsis. Details of univariate analysis of factors associated with definitive sepsis are shown in Table 4.

Table 2: Details of organisms causing culture-positive neonatal sepsis

Organism identified	Frequency (%)
<i>Staphylococcus aureus</i>	10 (35.7)
Nonhemolytic streptococcus	1 (3.5)
<i>Klebsiella</i> spp.	6 (21.4)
<i>Escherichia coli</i>	3 (10.7)
<i>Pseudomonas aeruginosa</i>	1 (3.5)
Untyped Gram-negative	6 (21.4)
Nonfermenting Gram-negative	1 (3.5)

Table 3: Resistance pattern of organisms isolated to antibiotics

	Gram-negative bacilli, (%)	<i>Staphylococcus aureus</i> , (%)
Ceftriaxone/cefotaxime	05 (31.2)	02 (20)
Meropenem	2 (11.8)	0
Amikacin	3 (17.6)	0
Ciprofloxacin	2 (12)	2 (20)
Piperacillin	8 (47.1)	3 (30)
Gentamicin	9 (52.9)	2 (20)
Ampicillin	17 (100)	9 (90)
Cloxacillin	11 (64.7)	9 (90)
Linezolid	7 (41.2)	0

Table 4: Univariate analysis of factors associated with culture-positive sepsis

Characteristics	Categories	Culture positive, (%)	Culture negative, (%)	P	OR (95% CI)
Idiopathic prematurity	Yes	07 (50)	72 (77.2)	0.032	3.31 (1.1-10.7)
	No	21 (22.8)	71 (77.2)		
Maternal fever	Yes	5 (22.8)	19 (79.2)	0.510	0.68 (0.2-2.0)
	No	23 (27.7)	60 (72.3)		
PROM >24 h	Yes	6 (20.7)	23 (79.3)	0.431	0.66 (0.2-1.8)
	No	22 (28.2)	56 (71.85)		
Birth weight <1.5 (kg)	Yes	3 (33.3)	6 (66.7)	0.436	1.4 (0.3-6.2)
	No	25 (25.5)	73 (74.5)		
Gender	Male	21 (33.3)	42 (66.7)	0.044	2.6 (1.0-6.9)
	Female	7 (15.9)	37 (84.1)		
Resuscitation at birth	Yes	3 (42.9)	4 (57.1)	0.263	2.25 (0.5-10.7)
	No	25 (25)	75 (75)		
MSAF	Yes	5 (23.8)	16 (76.2)	0.781	0.85 (0.2-2.6)
	No	23 (26.7)	63 (73.3)		

OR: Odds ratio; CI: Confidence interval; PROM: Premature rupture of membranes; MSAF: Meconium stained amniotic fluid

Discussion

The culture positivity rate among the neonates with probable sepsis in the current study was 26%. In previous studies done in India, it has ranged from 16% to 54%.^[3-8] The culture positivity might be an underestimation of actual status in our study, as anaerobic organisms were not tested in our institution. Outborn babies were excluded from our study due to difficulties in obtaining accurate antenatal and perinatal data.

Most common isolates in this study were *S. aureus* and *Klebsiella* spp. A review of studies on neonatal sepsis in India has found that *Klebsiella* species (15 studies), *Escherichia coli* (10 studies), and *S. aureus* (ten studies) were the most common isolates.^[8] Nonfermenting Gram-negative bacilli which are recently emerging in NICUs were few in number. One reason for this could be that the unit studied is of level II and interventions such as insertion of central vascular catheters were not performed in this unit. This study was characterized by the absence of Group B *Streptococcus* and coagulase-negative *Staphylococcus* (CONS). Infection with CONS is usually associated with the use of interventions, such as central vascular catheters, which was not prevalent in the unit studied.

The proportion of early-onset sepsis in other studies in India ranged from 10.4% to 85.0% of total neonatal sepsis. The incidence of late-onset sepsis might have been underestimated because the neonates were not followed up after discharge from the hospital. However, the high rate of early-onset sepsis and the apparent dominance of so-called nosocomial-type pathogens in early-onset sepsis could possibly be due to ultra-early horizontal transmission from delivery rooms and NICUs or vertical transmission from the maternal genital tract colonized with these pathogens after unhygienic personal and obstetric practices. The study warrants the need for further research to understand the pathogenesis of early-onset sepsis, including its association with obstetric and neonatal care practices around birth.

The results are consistent with a high degree of antibiotic resistance reported in other studies from India.^[8-12] The findings also underscore the need for action to contain the increasing problems of antimicrobial resistance.

Easy availability and widespread use of broad-spectrum antibiotics in the presumptive treatment of infections prevail in India. Blood culture facilities are not often available in most of the settings in rural areas. In such scenarios, clinicians have to depend on empirical antibiotic regimens. The high prevalence of resistance to Ampicillin makes it out of use in neonatal sepsis even in rural hospitals. The increasing resistance of Gram-negative organisms to extended-spectrum cephalosporins and carbapenems makes the choice of antibiotics difficult. Due consideration needs to be given to antistaphylococcal antibiotics in view of its high prevalence in both early-onset and late-onset neonatal sepsis.

Factor shown to be significantly associated with culture-positive sepsis was prematurity. None of the studied maternal factors had shown any significant association with culture-positive sepsis. Prematurity should be given more weightage in scoring systems assessing sepsis risk.

Conclusion

Data on culture-positive neonatal sepsis are limited from rural secondary care centers in India. *S. aureus* and *Klebsiella* spp. were the most common cause of neonatal sepsis in our setup. An alarmingly high degree of antibiotic resistance observed calls for an urgent evaluation and development of individual and national antibiotic policies and protocols for neonatal sepsis. Robust infection control practices in nursery and labor room, minimally invasive procedures, and restricting the use of aminoglycosides and quinolones as first-line antibiotics and carbapenems as second-line antibiotics are practical options to minimize mortality from sepsis.

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Conflicts of interest

There are no conflicts of interest.

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