

Neonatal Sepsis: Bacteriological Profile and Antibiotic Sensitivity Pattern in Nepal Medical College

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ABSTRACT

Neonatal sepsis is one of the important causes of mortality in the newborn. If treated early with the appropriate antibiotics it is possible to prevent most of the neonatal deaths due to sepsis. This study was conducted in the neonatal intensive care unit, Nepal Medical College Teaching Hospital, Kathmandu, Nepal over a period of 2 years from April 2012 to March 2014. This was a prospective study conducted to determine the prevalence of neonatal sepsis, identify the bacterial isolates and their antimicrobial sensitivity pattern among the newborns admitted for suspected neonatal sepsis. Out of 285 cases of suspected neonatal sepsis, blood culture was positive in 26.0% (75/285). The most common causative organism was *Staphylococcus aureus* 36.0% (27/75), followed by *Klebsiella pneumoniae* 24.0% (18/75) and *Acinetobacter spp* 14.6% (11/75). Most of the organisms showed good sensitivity to quinolones and aminoglycosides and high degree of resistance to most penicillins. There is an increasing trend of antibiotic resistance to the commonly used first line drugs. Continuous surveillance for antibiotic susceptibility is needed to ensure proper empirical therapy.

Keywords: Antibiotic sensitivity, bacteriological profile, neonatal sepsis.

INTRODUCTION

Every year 4 million babies die in the first 4 weeks of life. Various conditions are responsible for neonatal mortality among which neonatal sepsis accounts for about 26% of neonatal deaths.¹ If diagnosed early and treated aggressively with appropriate antibiotics, it is possible to save most cases of neonatal sepsis.²

Neonatal sepsis can be sub-typed into early onset sepsis (EOS) if the onset of symptoms is before 72 hours of life or late onset sepsis (LOS) if it appears later. Usually the early onset sepsis are caused by organisms prevalent in the maternal genital tract and the late onset sepsis by the organisms thriving in the external environment.²

Causative organisms of neonatal sepsis varies from place to place and age of the neonate. In the west early onset infections are mostly caused by *Group B streptococci* (GBS) and *E coli*, while in our nursery most cases are due to Gram negative organisms, especially *E coli*, *Klebsiella* and *Enterobacter spp*.³ Trends in the bacteriological profile of sepsis vary to some extent by institution and may be influenced by local obstetrical practices as well as by local

variation in indigenous bacterial flora.⁴

Neonatal sepsis manifests as asymptomatic bacteremia, generalized sepsis, pneumonia or meningitis. Less specific signs of sepsis include irritability, lethargy, temperature instability, poor perfusion and hypotension. Suspected cases are treated with empirical antibiotic therapy, usually B-lactam antibiotics and aminoglycosides; third generation cephalosporins are added for critically ill infants.⁴ However, resistance to first line antibiotics and cefotaxime among both gram negative and gram positive isolates is emerging and is a major concern in neonatal intensive care unit.⁵

Due to the changing bacteriological profile and increasing antimicrobial resistance, the appropriateness of the empirical therapy using the first line drugs has been challenged. Knowledge of common organisms causing neonatal sepsis in a particular area and their antibiotic sensitivity pattern

MATERIALS AND METHODS

This is a prospective study conducted in the neonatal unit, Nepal Medical College Teaching Hospital (NMCTH), Kathmandu, Nepal over a period of two years from April 2012 to March 2014. All the neonates admitted in the neonatal unit and suspected to have neonatal sepsis were included in the study. Written informed consent was obtained from the parents of the neonates involved in the study. The neonates who presented with fever, hypothermia, lethargy, poor feeding, abdominal distension, vomiting, bulging fontanel, respiratory distress etc were suspected to have neonatal sepsis. The neonates who were born with the maternal risk factors like maternal fever, chorioamnionitis, prolonged rupture of membrane (more than 18 hours) were also suspected to have neonatal sepsis and included in this study. A detailed antenatal, natal and post natal history was taken. The birth weight, sex and day of onset of sepsis were noted.

Septic screening was done which included total leukocyte count, differential count, erythrocyte sedimentation rate (ESR), C-reactive protein, chest x ray and blood culture. Lumbar puncture was performed in suspected cases of meningitis. Blood culture was done by drawing 1-2 ml of blood aseptically before starting antimicrobial agent and inoculated directly into Brain Heart Infusion broth (BHI) in a ratio of blood: BHI of 1:5. The processing of collected blood samples for culture and isolation was done by standard microbiological methods.⁶ The antimicrobial susceptibility testing was done by Kirby- Bauer disk diffusion technique that is recommended by Clinical Laboratory Standards Institute (CLSI) recommendations.⁷

RESULTS

In the study there were 285 cases of suspected neonatal sepsis. Blood culture was positive in 75 (26.3%) cases. There were 254 (89.1%) cases of early onset sepsis and 31(10.9%) cases of late onset sepsis. Culture positivity was seen in 65(25.6%) cases of early onset sepsis and 10 (32.2%) cases of late onset sepsis. Out of the total cases, 254(89.1%) neonates were born in NMCTH and 31(10.9%) were -born elsewhere. Blood culture was positive in 67(26.4%) neonates born in NMCTH and 8 (25.8%) neonates born elsewhere.

Neonatal sepsis was more common in male newborns 162(56.8%) compared to females 123(43.2%). Commonest organism isolated was *Staphylococcus aureus* 27(36.0%) followed by *Klebsiella pneumoniae* 18(24.0%) and *Acinetobacter spp* 11(14.6%). *Staphylococcus aureus* was the most common causative organism in the early as well as late onset sepsis. The etiological agents responsible for early and late onset sepsis are shown in Table 1.

Table 1: Bacterial isolates causing neonatal sepsis

S. No.	Bacterial Isolates	EOS	LOS	Total
1	<i>Staphylococcus aureus</i>	22	5	27 (36.0%)
2	<i>Klebsiella pneumoniae</i>	17	1	18 (24.0%)
3	<i>Acinetobacter anitarus</i>	10	1	11 (14.7%)
4	Coagulase negative staphylococcus (CONS)	8	-	8 (10.7%)
5	<i>Pseudomonas aeruginosa</i>	1	2	3 (4.0%)
6	<i>Escherichia coli</i>	2	1	3 (4.0%)
7	<i>Enterococcus spp</i>	2	-	2 (2.7%)
8	<i>Streptococcus spp</i>	1	-	1 (1.3%)
9	<i>Citrobacter furundi</i>	1	-	1 (1.3%)
10	<i>Salmonella typhi</i>	1	-	1 (1.3%)
	Total	65	10	75 (100.0%)

Staphylococcus was more susceptible to vancomycin 12(44.4%), ciprofloxacin 12(44.4%), ampicillin 11(40.7%) and gentamicin 11(40.7%) as compared to amikacin 5(18.5%), ampicillin 5(18.5%) and cefotaxime 4(14.8%) whereas none were sensitive to penicillin. *Klebsiella* was highly sensitive to ciprofloxacin 13(72.2%) followed by nalidixic acid 10(55.5%), ofloxacin 9(50.0%) and gentamicin 7(38.8%). Only 3(16.6%) cases were sensitive to cefotaxime and none were sensitive to ampicillin. Sensitivity of *Acinetobacter* was comparatively high to chloramphenicol 5(45.5%) and cotrimoxazole 5(45.5%) followed by ciprofloxacin 4(36.6%), ofloxacin 4 (36.6%) and cefotaxime 4(36.6%). It was less sensitive to ampicillin 2(18.8%) and amikacin 2(18.8%). None were sensitive to penicillin. The sensitivity pattern of all the organisms has been shown in Table 2 and 3.

DISCUSSION

The incidence of neonatal bacterial sepsis varies from 1-4 cases per 1000 live births in developed countries, with considerable fluctuation over time and with geographic location. Documentation of a positive blood culture is the first diagnostic criterion that must be met for sepsis. However, it is important to note that some patients with bacterial infection may have negative blood cultures (clinical infection) and other approaches to identification of infection are needed.⁸ Though other investigations are available, blood culture is still irreplaceable at present, since pure isolates are essential for antimicrobial drug susceptibility testing.⁹ In our study the incidence of blood culture positive sepsis was 26.0%. A similar study conducted in this hospital by RK Shrestha et al showed the prevalence of sepsis at 30.8%.¹⁰ The culture positivity rate in the other studies from Nepal ranged from 20.0 to 47.9%.¹¹⁻¹⁴ Studies done in the other countries also showed similar culture positivity rates ranging from 19.5 to 47.1%.^{15,16}

Table 2: Antibiotics sensitivity pattern of blood cultures in neonates presenting with sepsis

Antibiotics	Staphylococcus aureus	Klebsiella pneumoniae	Acinetobacter anitarius	Coagulase negative staphylococcus	Pseudomonas aeruginosa
Clindamycin	2 (7.4%)	NT*	NT	NT	NT
Piperacillin/Tazobactam	NT	1 (5.5%)	NT	NT	1 (33.3%)
Cloxacillin	11 (40.7%)	NT	NT	4(50.0%)	NT
Penicillin	0 (0%)	NT	0 (0%)	NT	NT
Ampicillin	5 (18.5%)	0 (0%)	2 (18.2%)	NT	NT
Cefotaxime	4 (14.8%)	3 (16.6%)	4 (36.4%)	1(12.5%)	2 (66.6%)
Vancomycin	12 (44.4%)	NT	NT	2(25.0%)	NT
Ciprofloxacin	12 (44.4%)	13 (72.2%)	4 (36.4%)	4(50.0%)	2 (66.6%)
Ofloxacin	4 (14.8%)	9 (50.0%)	4 (36.4%)	1(12.5%)	1 (33.3%)
Ceftriaxone	7 (25.9%)	1 (5.5%)	1 (9.1%)	3(37.5%)	2 (66.6%)
Amikacin	5 (18.5%)	6 (33.3%)	2 (18.2%)	3(37.5%)	3 (100.0%)
Nalidixic Acid	2 (7.2%)	10 (55.5%)	2 (18.2%)	1(12.5%)	1 (33.3%)
Azithromycin	10 (37.0%)	8 (44.4%)	4 (36.4%)	1(12.5%)	NT
Cotrimoxazole	6 (22.2%)	4 (22.2%)	5 (45.5%)	1(12.5%)	NT
Chloramphenicol	6 (22.2%)	4 (22.2%)	5 (45.5%)	2(25.0%)	2 (66.6%)
Cefixime	3 (11.1%)	0 (0%)	4 (36.4%)	0 (0%)	1 (33.3%)
Gentamicin	11 (40.7%)	7 (38.8%)	1 (9.1%)	1(12.5%)	1 (33.3%)
Amoxycillin	4 (14.8%)	1 (5.5%)	NT	3(37.5%)	1 (33.3%)
Meropenem	NT	1 (5.5%)	1 (9.1%)	NT	NT
Tobramycin	1 (3.7%)	NT	1 (9.1%)	1(12.5%)	1 (33.3%)

*NT: Not Tested

Table 3: Antibiotics sensitivity pattern of blood cultures in neonates presenting with sepsis

Antibiotics	E coli	Enterococcus	Streptococcus	Citrobacter	Salmonella typhi
Ampicillin	0 (0%)	NT	NT	0 (0%)	NT
Cefotaxime	0 (0%)	0 (0%)	NT	NT	NT
Vancomycin	NT	2 (100.0%)	NT	1 (100.0%)	NT
Ciprofloxacin	2(66.6)	0 (0%)	1 (100.0%)	1 (100.0%)	1 (100.0%)
Ofloxacin	0 (0%)	1 (50.0%)	NT	NT	NT
Ceftriaxone	1(33.3)	0 (0%)	1 (100.0%)	1 (100.0%)	NT
Amikacin	2(66.6)	1 (50.0%)	1 (100.0%)	NT	1 (100.0%)
Nalidixic Acid	1(33.3)	NT	NT	0 (0%)	NT
Azithromycin	NT	0 (0%)	NT	NT	NT
Cotrimoxazole	0 (0%)	NT	0 (0%)	0 (0%)	1 (100.0%)
Chloramphenicol	NT	NT	0 (0%)	0 (0%)	1 (100.0%)
Cefixime	0 (0%)	0 (0%)	0 (0%)	1 (100.0%)	1 (100.0%)
Gentamicin	2(66.6)	NT	1 (100.0%)	NT	NT
Amoxycillin	NT	0 (0%)	1 (100.0%)	NT	1 (100.0%)
Tobramycin	1(33.3)	1 (50.0%)	NT	NT	NT

In the present study incidence of sepsis was more common among males (56.8%). Term male infants have an approximately two fold higher incidence of sepsis than term females.¹ In our study, the most common causative organism was *Staphylococcus aureus* (37.0%). The previous study done in this hospital also revealed *Staphylococcus aureus* as the most common organism (56.8%).¹⁰ *Staphylococcus aureus* has also been reported by other investigators from Nepal as the most common pathogen causing neonatal

sepsis.^{11,12} It was seen as the most common causative organism causing both early and late onset sepsis in this study. Its greater prevalence in neonatal septicemia could be explained by the fact that *Staphylococcus aureus* is a common hospital acquired organism and there is a high chance of transmission of this organism to neonates from health care workers and relatives.¹⁶ Early onset infections are caused by organisms prevalent in the maternal genital tract or in the delivery area.² The most common organisms

in the female genital tract are *Group B streptococci (GBS)*, *Enteric organisms*, *Gonococci* and *Chlamydiae*.⁸ But *GBS* was not isolated from any of the neonates in the present study. This may be due to the use of intrapartum antibiotics to reduce vertical transmission of *GBS* after preterm rupture of membrane.⁸ *Klebsiella pneumoniae* was the second most common causative organism in our study. Whereas, in a study conducted in South India it was seen as the most common organism causing neonatal sepsis.¹⁵ *Klebsiella pneumoniae* is one of the agents that commonly cause nosocomial infections.⁸ The third most common organism in our study was *Acinetobacter spp* (14.6%). One of the studies showed *Acinetobacter spp* as a potential pathogen in neonatal septicemia, which accounted for 35.7% of blood culture positive sepsis.¹⁷

In our study almost all the isolates were resistant to penicillin and ampicillin. Cefotaxime shows low sensitivity to most of the isolates followed by gentamicin. Ampicillin resistance was seen in this hospital in the previous study also.¹⁰ Low sensitivity to first line antibiotics for neonatal sepsis like ampicillin and gentamicin was also observed by the other authors.^{18,19,20} A study done in one of the centers in Nepal also showed a high degree of resistance of gram positive organisms to most penicillins and cephalosporins and there was a high incidence of resistance noted with most third generation cephalosporins and aminoglycosides amongst most gram negative organisms.¹² In our study the highest sensitivity was noted with ciprofloxacin and amikacin which is similar to another study which also showed quinolones as the most potent antibiotics in neonatal sepsis.²¹ High sensitivity to amikacin was seen in other studies as well, which concurs with our findings in this study.^{15,19}

The two areas of concern seen in this study were the varying microbial patterns of neonatal sepsis with the emergence of *Acinetobacter spp*, a non-fermenting Gram negative bacillus as the causative organisms and the high degree of resistance observed for the commonly used antibiotics. Periodic review of neonatal sepsis for the knowledge of the pathogens and their antibiotic susceptibility would be a useful guide in antibiotic therapy. Steps should be taken to control the emergence of resistant strains. Indiscriminate use of antibiotics should be discouraged. The empirical regimen should be modified based on the antibiogram of the isolates. Infection control policies like hand hygiene practice, barrier nursing and promotion of clean deliveries should be implemented to reduce the load of neonatal sepsis.

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