Bacteriological study of neonatal sepsis and antibiotic susceptibility pattern of isolates in Kathmandu, Nepal

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ABSTRACT

Bloodstream infections in neonates are life-threatening emergencies. Identification of the common bacteria causing such infections and their susceptibility patterns will provide necessary information for timely intervention. This study was done to determine the prevalence of neonatal septicaemia, identify the bacterial isolates and study their antimicrobial susceptibility pattern in neonates admitted to the neonatal intensive care unit of Nepal Medical College Teaching Hospital (NMCTH), Kathmandu, Nepal. This descriptive-analytical study was conducted in NMCTH from July 2011 to January 2012. Blood culture of all neonates who were suspected for neonatal sepsis was performed. Bacterial isolation, identification and antimicrobial susceptibility testing were done by standard microbiological method. Out of 120 neonates suspected of having neonatal sepsis, 30.8% (37/120) were blood culture positive (i.e. prevalence = 30.8%). The most common causative agents of neonatal sepsis was *Staphylococcus aureus* (56.8%; 21/37) followed by *Klebsiella pneumoniae* (21.7%; 8/37), *Pseudomonas aeruginosa* (13.4%; 5/37) and others. Neonatal sepsis was more frequent in male neonates (32.5%) while (26.5%) in female neonates in the ratio of 1.2:1 ($p > 0.05$). Neonatal sepsis was significantly higher (58.3%) in low birth weight (LBW) (< 2.5kg) neonates compared with good birth weight (GBW) (23.9%) (<0.05). Prevalence was higher in preterm neonates (57.8%; 11/19) as compared with term-babies (25.7%) (P=0.05). Generally, all of the isolates were sensitive to most of the antibiotics used as the first line drugs like amikacin, gentamicin, cefotaxime and ampicillin except *Acinetobacter baumannii*. This organisms was only sensitive towards cotrimoxazole, azithromicin, cefotaxime and ceftazidime.

Keywords: Neonate, sepsis, aetiological agents, antimicrobial susceptibility.

INTRODUCTION

Neonatal bacterial sepsis (NBS) remains an important cause of mortality and morbidity among neonates. It is estimated that 20% of all neonates develop sepsis and it is responsible for about 30-50% of total neonatal deaths.[1,2] About 99% of the approximate 1 million annual neonatal deaths from life-threatening invasive bacterial infections occur in developing countries, at least 50% of which are from home births or community settings.[3] Low birth weight is an important indirect cause of death. Premature babies present with early and fulminant disease. About 450 newborn children die every hour, mainly from preventable causes, which is unconscionable in the 21st century.[4]

Neonatal sepsis is a disease of infants who are younger than one month of age are clinically ill and have positive blood culture.[5] When pathogenic bacteria gain access into the blood stream, they may cause overwhelming infection without much localization termed as septicaemia or may get predominantly localized to the lungs resulting in pneumonia or the meninges causing meningitis.[6]

Depending on the onset of symptoms, neonatal sepsis is of two types: early onset of sepsis, infection acquired within 72 hours of age and late onset of sepsis, infection acquired after 72 hours of age. Differentiation into early and late onset neonatal sepsis is important because of probable differences in the pathophysiology and pathogens associated with early onset and late onset neonatal sepsis in prevention and treatment.[7] Consequently, early onset and late onset neonatal sepsis are also associated with different distributions of pathogens. Bacterial agents implicated in early onset of sepsis include group B *Streptococcus* (GBS), *Escherichia coli*, coagulase-negative *Staphylococcus* (CoNS), *Haemophilus influenzae* and *Listeria monocytogenes*[8] whereas the organisms commonly associated with late-onset sepsis include CoNS, *Staph. aureus*, *Kl. pneumoniae*, *E. coli*, *Enterobacter* species, *Ps. aeruginosa* and *Acinetobacter* species.[9] As neonatal septicaemia is a life-threatening emergency and delays in diagnosis and treatment may have adverse consequences, surveillance is needed to identify the common symptoms and signs as well as the antibiotic sensitivity pattern for the agents.[10]

MATERIALS AND METHODS

The study was carried out prospectively in Nepal Medical College Teaching Hospital (NMCTH), Kathmandu, Nepal from July 2011 to January 2012. A total of 120 neonates suspected of having neonatal sepsis were included in this study. 1–2 ml of blood was drawn aseptically before starting antimicrobial treatment 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 method.[11] The antimicrobial susceptibility testing was done by Kirby-Bauer disk diffusion technique that is recommended by Clinical Laboratory Standards Institute (CLSI) recommendations.[12] The various antimicrobials that were used for susceptibility testing are as follows: amikacin, ampicillin, cefotaxime, ceftriaxone, chloramphenicol, ciprofloxacin, gentamicin, cotimoxazole, ofloxacin, piperacillin and tobramycin manufactured by Hi-media.

RESULTS

Of the total 120 blood samples collected from neonates suspected of neonatal sepsis, the prevalence was found to be 30.8% (37/120). The most common causative agents of neonatal sepsis detected in our study was *Staph. aureus* (56.8%) followed by *Kl. pneumoniae* (21.7%), *Ps. aeruginosa* (13.4%) and others also has been shown (Table-1).

Table-1: Distribution of pathogens in neonatal sepsis

Organisms	n (%)
Staphylococcus aureus	21 (56.8)
Klebsiella pneumoniae	8 (21.7)
Pseudomonas aeruginosa	5 (13.4)
Acinetobacter baumannii	1 (2.7)
E. coli	1 (2.7)
Salmonella Typhi	1 (2.7)
Total	**37 (100.0)**

Out of 120 neonates, 86 (71.7%) were male and 34 (28.3%) were female. Neonatal sepsis was more frequent in male neonates (32.5%) than in female neonates (26.5%) in the ratio of 1.2:1. But the association of culture positive and negative in male and female neonates is statistically insignificant ($p>0.05$). Neonatal sepsis was more common (58.3%) in low birth weight neonates (< 2.5kg). There was significant difference between birth weight and culture positive (p value 0.003).

Generally all of the isolates were sensitive to most of the antibiotics used as the first line drugs like amikacin, gentamicin, cefotaxime and ampicillin except *A. baumannii*. This organism was only sensitive towards cotrimoxazole, azithromicin, cefotaxime and ceftazidime. The sensitivity of the remaining organisms also has been shown (Table-2).

DISCUSSION

Neonatal sepsis remains a major clinical problem in neonatology with high morbidity and mortality rate especially, in developing countries like Nepal. In the present study, nearly one third (30.8%) of neonates had microbiologically confirmed sepsis. This finding was in agreement with the finding (28.3%) reported by previous study done in Nepal.[10] However, variable results have been reported by various studies from different parts of Nepal.[13-17] Administration of prior antibiotics from primary centre, infection with anaerobes or effective control in spread of nosocomial infection, might be the reasons for the variable results in different studies.[13]

In the present study, the most common causative agents of neonatal sepsis was *Staph. aureus* (56.8%) followed by *Kl. pneumoniae* (21.7%), *Ps. aeruginosa* (13.4%) and others. *Staph. aureus* as most common pathogen of neonatal sepsis has also been reported by other investigators from Nepal.[10,13,15-17] However, our finding was highest as compared to the findings reported by others from Nepal which ranged from 16.7% to 50.0%.[10,13,15-17] Its greater prevalence in neonatal septicaemia could be explained by the fact that, *Staph. aureus* is common hospital acquired organism which accounts for most of the infections and there is a high chance of transmission of *Staph. aureus* to neonates from health care workers and relatives.[18] For the same reason, it is possible that prevalence of this less fastidious organism is overestimated, and also due to comparative ease for its isolation.[19]

In the present study, neonatal sepsis was more frequent in male neonates (32.5%) while (26.5%) in female neonates in the ratio of 1.2:1.This may be due to the presence of single X-chromosome in male as compared to double chromosomes in female.[20] The reasons for increased number of male cases in these studies may be gender bias in presentation to hospital for care, place of study, sample and other factors.[21]

Table-2: Antibiotic resistance pattern of bacterial isolates (in percent) to various antibiotics

Antibiotics	*Staph. aureus* (n=21)	*Kl. pneumo niae* (n=8)	*Ps.aeruginosa* (n=5)	*A. baumannii* (n=1)	*E. coli* (n=1)	*S.* Typhi (n=1)
Amikacin	0	0	0	100	0	0
Gentamicin	9.5	0	0	100	0	0
Ampicillin	90.5	37.5	-	100	0	0
Ciprofloxacin	4.8	0	0	100	0	0
Cotrimoxazole	4.8	0	0	0	0	0
Azithromicin	61.9	37.5	0	0	0	0
Cefotaxime	23.9	-	0	0	0	0
Ceftazidime	-	-	0	0	0	0
Ofloxacillin	4.8	-	-	-	-	-
Cloxacillin	4.8	-	-	-	-	-
Piperacillin-tazobactem	-	-	0	-	-	-

Low birth weight is a strong risk factor for contributing to sepsis. In this study, neonatal sepsis was more common (58.3%) in low birth weight neonates (< 2.5kg) which was found to be statistically significant (p value = 0.05). This is in concordance with other studies where low birth weight was found to be important risk factor for sepsis.[10,21] There was greater chance of infection in preterm neonates 11 (57.8%).

Neonatal septicaemia is a life threatening emergency and rapid treatment with antibiotics is essential for a favorable outcome.[22] The knowledge of the aetiological organisms as well as their antimicrobial sensitivity profile is necessary for effective therapeutic intervention in neonatal sepsis.[23] Multi-drug resistance of the causative organisms of sepsis is a rapidly emerging and potentially disastrous problem. Infection with resistant organisms has been associated with treatment failure, higher morbidity and mortality, increased health costs and prolonged hospitalization.[24]

The present study shows a high degree of resistance of gram negative organisms to commonly used antibiotics ampicillin and gentamicin as well as third-generation cephalosporins. These results agree with many other studies too.[25,26]

To sum up, slow emergence of antibiotic resistance among bacterial isolates from neonatal sepsis warns Nepalese medical community for timely preparedness against this major health challenge. Proper antibiotic guidelines and its effective implementation will prove effective in antibiotic resistance control in Nepal.

From this study, the prevalence of neonatal sepsis in neonatal intensive care unit ward of NMCTH was found to be 30.8% which was confirmed by standard microbiological procedure. Present study indicated that, the most common aetiological agent of neonatal sepsis was *Staph. aureus* (56.8%) followed by *Kl. pneumoniae* (21.7%), *Ps. aeruginosa* (13.4%) and others. A low susceptibility to commonly used antibiotics like ampicillin is a cause for concern. The antibiotic susceptibility profiles suggested that, initial empirical choice of cefotaxime in combination with amikacin was the most rational.

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