Institutional Analysis of Bacteriological Profile and Antibiotic Susceptibility of Neonatal Sepsis in Eastern Nepal

Abstract

Introduction: In developing nations, neonatal sepsis account for the larger portion of neonatal morbidity and mortality. Blood culture is considered as the gold standard for the diagnosis. Both the conformation and management is difficult for clinicians in resource limited nations like Nepal.

Method: It is a prospective observational study conducted at one of the tertiary care hospital in eastern Nepal over a year.

Result: Incidence of neonatal sepsis was 12.9%. The incidence of blood culture positive neonatal sepsis was 15%. Coagulase Negative *Staphylococcus aureus* and *Escherichia coli* were two most predominant organism isolated. All of the isolated *Klebsiella* and *Pseudomonas* showed resistance to Ampicillin whereas Coagulase Negative *Staphylococcus aureus* showed sensitivity to Vancomycin.

Conclusion: Bacteria are showing resistance to multiple antibiotics. This is an alarming moment for the pediatrician. Antibiotics should be used judiciously and continuous surveillance should be done to monitor the changing epidemiology of organisms and antibiotic sensitivity as the emergence of resistance to commonly used antibiotics is high.

Keywords

Neonatal sepsis, antibiotics, blood culture, resistance

Introduction

Septicemia in neonates refers to generalized bacterial infection documented by positive blood culture. It is a clinical syndrome characterized by the systemic sign of infections accomplice by bacteremia[1]. Septicemia in neonates can lead to sepsis. Delay in diagnosis and commencement of appropriate treatment may result in high morbidity and mortality rates. Changing bacterial flora and emergence of resistant strains leads to the problem thus neonatal septicemia requires accurate and timely clinical and laboratory diagnosis and proper management for a better outcome[2].

Some commonly found risk factors leading to neonatal sepsis are low birth weight, preterm delivery, maternal infection within two weeks of delivery, meconium stained liquor and premature rupture of membrane for more than twenty-four hours.

The presence of foul-smelling liquor or three of the abovementioned risk factors warrants initiation of antibiotic treatment. Infants with two risk factors should be investigated and then treated accordingly[3]. The incidence of sepsis among preterm neonates is six times greater than of full-term infants which can be attributed to the more immature immune system of preterm infants and their prolonged periods of hospitalization which increase the risk of nosocomial contracted infection[4].

According to Nepal Demographic and Health Survey 2016, the national neonatal mortality rate was 21/1000 live births. Infections including sepsis contributed to 16% of neonatal mortality[1]. Currently, the emergence of multidrug-resistant bacteria imposes challenges in the treatment of neonatal sepsis[5]. The incidence is higher in late preterm than in term infants. The reported incidence of early and late-onset sepsis in late preterm neonates were 4.4 and 6.3 per 1000 respectively[6]. Though the exact incidence of early-onset neonatal sepsis in Nepal is not available, studies have shown that neonatal sepsis accounts for 17% of total neonatal admission and 5% of death in neonates. Neonates are immunocompromised and defend weakly against bacterial infections. Despite the advance in health care, neonatal sepsis is burden for developing

countries. The bacterial agents implicated in early-onset sepsis include *Group B Streptococcus* (GBS), *Escherichia coli*, *coagulase-negative Staphylococcus*, *Haemophilus influenza,* and *Listeria monocytogenes*. The organisms commonly associated with late-onset sepsis include *coagulase-negative staphylococci (CONS), Staphylococcus aureus, Klebsiella pneumonia, Escherichia coli*, *Enterobacter spp.*, *Pseudomonas aeruginosa*, *and Acinetobacter* species[7]. Clinical presentation of neonatal sepsis varies and there are no pathognomonic features[8]. Most observed clinical signs and symptoms are decreased feeding, lethargy, inactivity, fast breathing, hyperthermia or hypothermia, etc. Surveillance is needed to identify the common pathogens of the disease as well as the antibiotic susceptibility profile of the pathogens in a particular area. The objective of this study is to find the common bacteriological profile and antibiotic resistance for neonatal sepsis in eastern Nepal.

Methods

This study was done to determine the prevalence of neonatal septicemia, identify the bacterial isolates and study their antimicrobial susceptibility pattern in neonates admitted to the neonatal intensive care unit of Nobel Medical College and Hospital, Biratnagar, Nepal. This descriptive study was done over a one-year duration from (Jan2018 -Jan2019). Blood culture of all neonates who were suspected of neonatal sepsis was performed. Bacterial isolation, identification, and antimicrobial susceptibility testing were done by the standard microbiological method.

All clinically suspected cases of neonatal sepsis admitted in NICU of Nobel medical college were enrolled in the study. Cases with major congenital malformation, birth weight <1Kg were excluded from the study. Ethical approval was taken from the Institutional Ethical Review Board of Nobel Medical College and Hospital, Biratnagar, Nepal.

Results

Total 1080 neonates admitted in NICU of Nobel medical college over one year of duration (January 2018 to January 2019) out of which 140 cases were neonatal sepsis were included in the study meeting the inclusion criteria. Out of 140 cases, 28(20%) cases were born outside the hospital and 112(80%) cases were born in the hospital maternity ward. Out of total cases, 35 (25%) were preterm and 105(75%) cases were term neonates. The most common clinical presentations in this study were tachypnea, lethargy, refusal to suck, and temperature instability.

In this study, out of 140 neonates, blood culture was positive in 21(15%) neonates and 119(85%) were culture negative.

Table 1: Frequency of growth in blood culture

Bacteria	**Frequency**	**Percentage**
Coagulase-negative *staphylococcus aureus*	6	28
Pseudomonas aerogenosa	3	14
Klebsiella pneumonia	3	14
Escherichia coli	4	19
Staphylococcus aureus	2	9
Citrobacterfruendi	1	5
Acenatobacteranitratus	1	5
Enterococcus faecalis	1	5
TOTAL	21	100%

Coagulase-negative *Staphylococcus aureus* (CONS) was found in 6(28%) as shown in table 1.

Table 2: Antibiotic sensitivity pattern for CONS

Antibiotic	Resistance Frequency	Sensitive Frequency
Cloxacillin	4(67%)	2(33%)
Vancomycin	0	6(100%)
Amikacin	0	6(100%)
Linezolid	0	6(100%)
Teicoplanin	0	6(100%)
Cotrimoxazole	3(50%)	3(50%)
Clindamycin	4(67%)	2(33%)
Penicillin	6(100%)	0
Chloramphenicol	1(17%)	5(83%)

Among CONS, 67% were resistant to Cloxacillin,100% were resistant to Penicillin,50% were resistant to Cotrimoxazole,67% were resistant to Clindamycin and 17% were resistant to Chloramphenicol. All were sensitive to Vancomycin, Amikacin, Linezolid, and Teicoplanin.

Table 3:Antibiotic sensitivity pattern for *Pseudomonas*

Antibiotic	Resistance Frequency	Sensitive Frequency
Ampicillin	3(100%)	0
Cefotaxime	2(67%)	1(33%)
Ceftazidime	1(33%)	2(67%)
Ciprofloxacin	0	3(100%)
Gentamicin	1(33%)	2(67%)
Amikacin	0	3(100%)
Tazobactum-pipperacillin	0	3(100%)
Meropenem	1(33%)	2(67%)

Pseudomonas aeruginosa counted for 14% of all organisms detected of which 100% were resistant to Ampicillin,67% were resistant to Cefotaxime,67% were sensitive to Ceftazidime,100% sensitive to Amikacin and Tazobactum-piperacillin,67% sensitive to Meropenem

Table 4: Antibiotics sensitivity pattern of *Escherichia coli*

Antibiotic	Resistance Frequency	Sensitive Frequency
Ampicillin	3(75%)	1(25%)
Cefotaxime	2(50%)	2(50%)
Ceftazidime	1(25%)	3(75%)
Ciprofloxacin	3(75%)	1(25%)
Cefuroxime	3(75%)	1(25%)
Gentamicin	0	4(100%)
Amikacin	0	4(100%)
Tazobactum-pipperacillin	1(25%)	3(75%)

19% of the detected organism in blood culture was *E.Coli* of which 75% resistant to Ampicillin, 50% resistant to Cefotaxime, 75% resistant to Ciprofloxacin, and Cefuroxime,75% were found sensitive to Ceftazidime and Tazobactum-piperacillin,100% sensitive to Gentamicin and Amikacin.

The outcome in neonatal sepsis:

At the time of admission, a sepsis screen was done for all the neonates enrolled and empirical antibiotic therapy with Ampicillin and Amikacin were administered intravenously. The neonates were periodically reviewed clinically and with laboratory results. Based on the organism grown in culture the antibiotic regimen was changed according to the sensitivity pattern. In this study, 28(20%) neonates expired and 112(80%) neonates recovered.

Discussion

Sepsis remains one of the most important causes hospital admission for neonates with bad outcomes despite considerable progress in infection control, the introduction of new antimicrobial agents, and advanced measures for early diagnosis and treatment[1]. Different hospitals have different bacteriological profile for neonatal sepsis. Similarly, the antibiotic resistance pattern also varies from institute to institute. Our institutional incidence of neonatal sepsis is 12.9% as per this study which is largely lower than the other tertiary care hospital (32%)[9].

The commonest clinical presentation in this study is tachypnea whereas another study found that the most common presenting clinical feature was respiratory distress followed by fever and feeding problems[10]. As compared to 15% of blood culture positive rate in this study,10.8% were noted in another study from Chitwan Medical College[11]. Also, in a study conducted in Nepal Medical College Teaching Hospital, Kathmandu, the positivity of the blood culture were 30.8%[12]. Coagulase Negative Staphylococcus aureus (CONS) was seen as the most common (28%) growth after 72 hours where as 46.6% growth were seen in a study conducted in Chitwan Medical college in 2013 [1]. Coagulase Negative Staphylococci were 17.4% where as Klebsiella were 16.11% in a tertiary care hospital in North India [4]. Regarding the antibiotics sensitivity pattern of CONS, 33% of isolates were found to be sensitive to Cloxacillin whereas, in a study conducted in Dhulikhel[12], 57.1% were found to be sensitive to Cloxacillin. In our study all of the isolated CONS were found to be sensitive to Vancomycin which is similar to the result of a study conducted in South India[1]. Sensitivity to Amikacin was 100% in this study and 88.9% in a study at Dhulikhel, Nepal[12]. All isolates of CONS were found to be 100% sensitive to Ampicillin, where as 40% were resistant to Ampicillin in a study at Dhulikhel [13]. Around 19% of *Escherichia coli* were isolated after 72 hours of growth. Bergin SP et al. showed 19.7% of

blood culture-proven sepsis were *Escherichia coli*[14]. Another study conducted showed Escherichia coli accounted for 15%[14]. Regarding sensitivity pattern, 14% of isolates were found sensitive to Ampicillin similar (16.6%) to other study [15] A study conducted in Paropakar Maternity and Women Hospital showed 42.85% were sensitive to Ampicilin [16].

In current study, 25% of isolates were found to be sensitive to Amikacin and 100% were found to be sensitive to Gentamicin whereas in a study conducted in Propakar Maternity and Women Hospital[16] 42.85% of isolates were found sensitive to both Amikacin and Gentamycin. In another study in India, 33.3% and 16.6% of isolates were found sensitive to Amikacin and Gentamycin [15].

After 72 hours of blood culture, *Klebsiella pneumonia* was isolated in 14%.

In a similar study, *Klebsiella* species accounted for 25% of isolates[17]. A study conducted at a tertiary hospital in Kathmandu, Nepal, Klebsiella pneumonia accounted for 20% of isolates[9]

Pseudomonas species accounted for 14% of total blood culture in this present study which is almost equal (13.4%) to a another study docnduted at a tertiary hospital in Nepal[9]. In a study conducted in Peshawar, Pakistan Pseudomonas was isolated in 13% of blood culture-proven sepsis[18][19]. In this study all the cases were found to be resistant to amikacin, and all cases were found to be sensitive to Tazobactum-piperacillin and Ciprofloxacin and 37% were found to be sensitive to Cefotaxime, and 67% were sensitive to meropenem. In a similar study conducted in Rama Medical College, 100% sensitivity was seen with Meropenem and Amikacin, and 66.6%were found to be sensitive to Cefotaxime and tazobactam-piperacillin[20].

Isolated *Staphylococcus aureus* were 9% in the present study which is similar to a study where it was 18%.[21] About half (50%) of cases were sensitive to Cloxacillin which is lower than studies conducted at Dhulikhel, Nepal which showed a sensitivity of 91.7%[13]. Whereas similar rate (40%) of growth was seen in a study conducted in Bayelsa state, Nigeria showed [22]. *Enterococcus, Acinito bacteranitratus,* and *Citrobacte rfruendi* have been isolated in 5% of cases of blood culture-proven sepsis. In a similar study conducted in Nigeria, 8% of isolates were Enterococcus species among blood culture-proven sepsis. In a study conducted in Chitwan Medical College, Bharatpur[1], *Acinetobacte*r species accounted for 9.5% of blood culture positive.

Improper antenatal care and nutritional deficiencies prematurity and low birth weight are some common factors. So measures to improve maternal nutrition, health education, and prevention of prematurity would bring down the mortality due to neonatal septicemia. Knowledge of the most commonly isolated bacteria in neonatal intensive care units or nurseries, along with the antimicrobial susceptibilities of these organisms are valuable in treating suspected cases of neonatal septicemia.

Conclusion

The incidence of neonatal sepsis was 12.9% in this study which is similar to most of the studies conducted in other institutions of Nepal and southeast Countries. Blood culture proven sepsis were 15% which is less than most of the studies from different institutions of Nepal. Coagulase Negative *Staphylococcus aureus* were the most common organism isolated followed by *Escherichia coli.* Gram-negative growth rate was higher than gram-positive growth. All of

isolated *Klebsiella* and *Pseudomonas* were found to be resistant to ampicillin. Bacteria are showing resistance to multiple antibiotics. This is an alarming moment for the pediatrician.

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