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

Abstract

Introduction: In the developing nations, neonatal sepsis account for the larger portion of the 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 the resource limited nations like Nepal.

Method: It is a retrospective 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 positivity in the neonatal sepsis was 15%. Coagulase negative *Staphylococcus species* and *Escherichia coli* were two most predominant organism isolated. All of the isolated *Klebsiella spp.* and *Pseudomonas spss.*showed resistance to ampicillin whereas 100% of Coagulase Negative *Staphylococcus spp.* showed sensitivity to vancomycin.

Conclusion: Isolated bacteria showed 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

Neonatal sepsis refers to an infection involving the bloodstream in newborn infants less than 28 days old [1]. 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]. Most common 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 above mentioned 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 advances in health care, neonatal sepsis is a burden for the developing countries. The bacterial agents implicated in early-onset sepsis include *Group B Streptococcus* (GBS), *Escherichia coli*, *coagulase-negative Staphylococcus spss. (CoNS),*

Haemophilus influenzae, 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 the 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 the neonates who were suspected of neonatal sepsis was performed. Blood culture bottles were prepared in the hospital lab and it was monitored manually. Antibiotic sensitivity was done by Kirby Baur technique.

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 body 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 S*taphylococcus spp.*	6	28
Pseudomonas aeruginosa	3	14
Klebsiella pneumoniae	3	14
Escherichia coli	4	19
Staphylococcus aureus	2	9
Citrobacter fruendi	1	5
Acinetobacter anitratus	1	5
Enterococcus faecalis	1	5
TOTAL	21	100%

Coagulase-negative *Staphylococcus spp.* (CONS) was found in 6(28%), *Escherichia coli* as 19% and others 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-Piperacillinspelling	0	3(100%)
Meropenem	1(33%)	2(67%)

Pseudomonas aeruginosa counted for 14% of all organisms detected of which 3 (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-Piperacillin	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 as per hospital policy. 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 cause 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 was largely lower than the other tertiary care hospital a Kathmandu (32%)[9]. The commonest clinical presentation in this study was 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 spp*. (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 the present 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 found in all organism 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] On the contrast,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 gentamicin. In another study in India, 33.3% and 16.6% of isolates were found sensitive to amikacin and gentamicin[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 pneumoniae a*ccounted for 20% of isolates[9]

Pseudomonas spss accounted for 14% of total blood culture in this present study which is almost equal (13.4%) to a another study documented at a tertiary hospital in Nepal[9]. In a study conducted in Peshawar, *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 edical 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, Acinetobacter anitratus*, and *Citrobacter freundii* have been isolated in 5% of cases of blood culture-proven sepsis. In a similar study conducted in Nigeria, 8% of isolates were *Enterococcus spp*. among blood culture-proven sepsis. In a study conducted in Chitwan medical college, Bharatpur[1], *Acinetobacte*r *spp*. accounted for 9.5% of blood culture positive.

Improper antenatal care and nutritional deficiencies, prematurity and low birth weight are some of the common and contributing factors of neonatal sepsis. So measures to improve maternal nutrition, health education,(remove comma) 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 spp.* were the most common organisms 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 showed resistance to multiple antibiotics. This is an alarming moment for the pediatrician.

References:

[1] AnsariSeale AC, Blencowe H, Manu AA, Nair H, Bahl R, Qazi SA, Zaidi AK, Berkley JA, Cousens SN, Lawn JE. Estimates of possible severe bacterial infection in neonates in sub-Saharan Africa, south Asia, and Latin America for 2012: a systematic review and meta-analysis. The Lancet infectious diseases. 2014 Aug 1;14(8):731-41.

[2] Ansari S, Nepal HP, Gautam R, Shrestha S, Neopane P, Chapagain ML. Neonatal septicemia in Nepal: early-onset versus late-onset. International journal of pediatrics. 2015 Nov 16;2015.

[3] Singh M, Narang A, Bhakoo ON. Predictive perinatal score in the diagnosis of neonatal sepsis. Journal of Tropical Pediatrics. 1994 Dec 1;40(6):365-8.

[4] Lamba M, Sharma R, Sharma D, Choudhary M, Maheshwari RK. Bacteriological spectrum and antimicrobial susceptibility pattern of neonatal septicaemia in a tertiary care hospital of North India. J Matern Neonatal Med. 2016 Dec 16;29(24):3993–8.

[5] Yadav NS, Sharma S, Chaudhary DK, Panthi P, Pokhrel P, Shrestha A, Mandal PK. Bacteriological profile of neonatal sepsis and antibiotic susceptibility pattern of isolates admitted at Kanti Children's Hospital, Kathmandu, Nepal. BMC research notes. 2018 Dec;11(1):1-6.

[6] Cohen-Wolkowiez M, Moran C, Benjamin DK, Cotten CM, Clark RH, Benjamin Jr DK, Smith PB. Early and late onset sepsis in late preterm infants. The Pediatric infectious disease journal. 2009 Dec;28(12):1052.

[7] Zakariya BP, Bhat V, Harish BN, Arun Babu T, Joseph NM. Neonatal sepsis in a tertiary care hospital in South India: Bacteriological profile and antibiotic sensitivity pattern. Indian J Pediatr. 2011 Apr;78(4):413–7.

[8] Mhada T V., Fredrick F, Matee MI, Massawe A. Neonatal sepsis at Muhimbili National Hospital, Dar es Salaam, Tanzania; Aetiology, antimicrobial sensitivity pattern and clinical outcome. BMC Public Health. 2012;12(1).

[9] Chapagain RH, Acharya R, Shrestha N, Giri BR, Bagale BB, Kayastha M. Bacteriological Profile of Neonatal Sepsis in Neonatal Intermediate Care Unit of Central Paediatric Referral Hospital in Nepal. Journal of Nepal Health Research Council. 2015 Sep 1;13(31):205-8.

[10] Lakhey A, Shakya H. Role of sepsis screening in early diagnosis of neonatal sepsis. Journal of Pathology of Nepal. 2017 Mar 30;7(1):1103-10.

[11] Thapa S, Sapkota LB. Changing trend of neonatal septicemia and antibiotic susceptibility pattern of isolates in Nepal. International journal of pediatrics. 2019 Feb 6;2019.

[12] Raghubanshi BR, Sagili KD, Han WW, Shakya H, Shrestha P, Satyanarayana S, Karki BM. Antimicrobial resistance among neonates with bacterial sepsis and their clinical outcomes in a tertiary hospital in Kathmandu valley, Nepal. Tropical Medicine and Infectious Disease. 2021 Jun;6(2):56.

[13] Shrestha S, Shrestha NC, Singh SD, Shrestha RP, Kayestha S, Shrestha M, Thakur NK. Bacterial isolates and its antibiotic susceptibility pattern in NICU. Kathmandu university medical journal. 2013;11(1):66-70.

[14] Bergin SP, Thaden J, Ericson JE, Cross H, Messina J, Clark RH, Fowler Jr VG, Benjamin Jr DK, Hornik CP, Smith PB. Neonatal Escherichia coli bloodstream infections: clinical outcomes and impact of initial antibiotic therapy. The Pediatric infectious disease journal. 2015 Sep;34(9):933.

[15] Vaniya HV, Patel NM, Agrawal JM, Trivedi HR, Dhanani JV, Balat JD. Antimicrobial culture sensitivity pattern in neonatal sepsis in a tertiary-care hospital. International Journal of Medical Science and Public Health. 2016;5(4):661-5.

[16] Khanal R, Manandhar S, Acharya GP. Bacteriological Profile of Neonatal Sepsis in a Tertiary Level Hospital of Nepal. Journal of Nepal Paediatric Society. 2014 Sep 1;34(3).

[17] Zaidi AK, Thaver D, Ali SA, Khan TA. Pathogens associated with sepsis in newborns and young infants in developing countries. The Pediatric infectious disease journal. 2009 Jan 1;28(1):S10-8.

[18] Rijal KR, Adhikari B, Ghimire B, Dhungel B, Pyakurel UR, Shah P, Bastola A, Lekhak B, Banjara MR, Pandey BD, Parker DM. Epidemiology of dengue virus infections in Nepal, 2006–2019. Infectious diseases of poverty. 2021 Dec;10(1):1-0.

[19] Ullah O, Khan A, Ambreen A, Ahmad I, Akhtar T, Gandapor AJ, Khan AM. Antibiotic sensitivity pattern of bacterial isolates of neonatal septicemia in Peshawar, Pakistan. Archives of Iranian medicine. 2016 Dec 1;19(12):0-.

[20] Sharma CM, Agrawal RP, Sharan H, Kumar B, Sharma D, Bhatia SS. "Neonatal sepsis": bacteria & their susceptibility pattern towards antibiotics in neonatal intensive care unit. Journal of clinical and diagnostic research: JCDR. 2013 Nov;7(11):2511.

[21] Kalathia MB, Shingala PA, Parmar PN, Parikh YN, Kalathia IM. Study of umbilical cord blood culture in diagnosis of early-onset sepsis among newborns with high-risk factors. Journal of Clinical Neonatology. 2013 Oct;2(4):169.

[22] Peterside O, Pondei K, Akinbami FO. Bacteriological profile and antibiotic susceptibility pattern of neonatal sepsis at a teaching hospital in Bayelsa State, Nigeria. Tropical medicine and health. 2015.