Profile of Nosocomial Sepsis in a Neonatal Intensive Care Unit of Tertiary Care Hospital in Eastern Part of Nepal

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ABSTRACT

Introduction: Nosocomial sepsis constitutes a global health problem. They lead to significant morbidity and mortality in both developed and resource-limited countries. The objective of the study was to describe the profile of nosocomial sepsis in neonatal intensive care unit (NICU).

Methods: This was a prospective descriptive study conducted in a teaching and referral NICU. All neonates in NICU who did not have any sign of infection at admission and remained hospitalized for at least 48 hours were observed. Profile of nosocomial infection was analyzed with descriptive statistics. P value of < 0.05 was considered significant wherever applicable.

Results: The incidence rate and density of nosocomial sepsis were 47.3% and 39.3 infections per 1000 patient-days respectively. Blood stream infection was the commonest nosocomial infection. Pseudomonas aeruginosa was the most commonly isolated agent in blood cultures of patients with nosocomial sepsis.

Conclusions: This study revealed a high incidence of nosocomial sepsis. Hence, there is urgent need to adopt policies to prevent these infections.

Key words: Nosocomial sepsis; Profile
INTRODUCTION

Neonates admitted to Neonatal Intensive Care Unit (NICU) have a substantial risk for acquiring nosocomial infections. The overall rates of infection in neonates vary from two to 18 infections per 100 admissions up to 42/100 admissions in the group of infants with birth weight < 1500 g.1-4 Blood stream infection is the most frequent infection type, followed by respiratory tract infection.1

The reported incidence of nosocomial sepsis in neonates is variable all over the world. In India, the incidence ranges from 1.5% to 37%.5,6 In contrast, surveillance reports from the USA have reported a rate of 0.9% to 7%.7-10 In our country, various studies have reported the incidence of nosocomial sepsis of around 10%.11,12 In resource limited set ups like Nepal and India, the incidence is higher.13-15 This is due to poor infection control practices, lack of supervision and inappropriate use of limited resources and overcrowding of hospitals.5 Various risk factors like prematurity, LBW, IUGR, low Apgar score, application of mechanical ventilation and exposure to central venous catheter are also important risk factors for higher nosocomial infections, especially in resource limited regions.16

In view of variable prevalence of neonatal sepsis, we conceptualized this research to describe the profile of nosocomial sepsis in a NICU of tertiary care hospital in eastern part of Nepal, and to compare these findings with international data. The study should enable us to point out strategies for future surveillance and potential intervention. It is essential to conduct the research on nosocomial infection, incidence and risk factors in order to control and minimize the infection.

METHODS

The study was conducted in a sixteen bedded NICU of Nobel Medical College Teaching Hospital (NMCTH), Biratnagar, which is a teaching hospital and tertiary care referral center situated in the Eastern part of Nepal. This study was conducted over a period of eight months from May to Dec 2020 in NICU of NMCTH. This was a prospective descriptive study. All neonates admitted to the NICU without any sign of infection during the study period, who remained hospitalized for at least 48 hours were eligible for inclusion. Out born neonates, neonates with severe congenital malformations, and the babies who died or were discharged or transferred to other department within 48 hours after being admitted in NICU were excluded.

Ethical clearance was received from Institutional Review Committee (IRC) of NMCTH and written informed consent in the local language was taken from the parents and / or guardians before the commencement of study. The details were prospectively collected after admission and recorded on standardized form until discharge from the hospital or death. All neonates included into the cohort were closely followed during their hospital stay for clinical signs of infection. For each patient, data on birth weight, adequacy for gestational age, gender, Apgar score at five minutes, absolute neutrophil count, micro-ESR, C-Reactive Protein (CRP), immature to total neutrophil ratio (I/T ratio), blood cultures, lumbar puncture, X-ray chest, medical devices used (central venous catheter, umbilical catheter, percutaneous catheter, mechanical ventilation), other relevant medical conditions and length of stay were collected. Nosocomial infection was defined as an infection not present and without evidence of incubation at the time of hospitalization and it was diagnosed according to the criteria of CDC.17 The diagnosis was based on clinical symptoms, laboratory findings and positive blood cultures. In all suspected cases, blood cultures were taken. When needed, urine and tracheal aspirate cultures were added. Lumbar puncture and CSF culture were performed in all patients who had bacterial growth in blood culture or clinical signs of meningitis. Nosocomial infection was considered to be present if onset of infection was beyond 48 hr of life with either (a) culture of sterile body fluids (blood, CSF, urine) yielding a recognized bacterial pathogen; (b) a tracheal aspirate culture yielding a pure growth of known bacterial pathogen in a neonate on ventilatory support with respiratory deterioration and radiographic pneumonia, or (c) clinical examination revealing a soft tissue infection. Neonates who had clinical features suggestive of infection appearing after 48 h of birth but not
yielding bacterial pathogens on culture of body fluids or tracheal aspirate were defined as having nosocomial infection if they had a positive sepsis screen. All neonates suspected to have sepsis and meningitis were screened by National Neonatology Forum (NNF) guidelines, India.\(^\text{18}\)

Infection surveillance was consistently conducted according to the National Infection Surveillance System (NNIS / CDC / Atlanta) definitions,\(^\text{17}\) which consider all neonatal infections, whether acquired during delivery or hospitalization, as nosocomial, unless evidence indicates transplacental acquisition. Sepsis was defined as isolation of at least one positive peripheral blood culture (except coagulase negative Staphylococcus aureus, for which isolation of two positive blood cultures were required) with clinical signs and symptoms. Sepsis was broadly divided in two types. They were laboratory confirmed sepsis and clinical sepsis (CSEP). Blood stream infections were considered as clinical sepsis when clinical and laboratory findings of infection were present, without positive cultures, and as laboratory confirmed when positive cultures were also present. The incidence rate of nosocomial infection was calculated as number of infections per 100 patients admitted, and incidence density as number of infections per 1000 patient-days. Descriptive statistics was performed for all the studied variables. Some of them were then categorized according to the frequency analysis. The level of statistical significance adopted was \(p < 0.05\) wherever applicable. SPSS for Windows 20.0 software was used for all statistical analysis.

### RESULTS
Total 450 neonates were admitted to NICU during the study period. One hundred twenty neonates were excluded for the following reasons: 20 died, 92 transferred to nursery or neonatal ward within 48 hours and eight were out born. One hundred eight neonates developed 156 episodes of nosocomial infections and 84 infants developed 94 episodes of nosocomial sepsis. Total length of hospital stay in NICU was 3960 days. The incidence rate and the incidence density were 47.3% and 39.3 infections per 1000 patient-days. Blood stream infection was the commonest nosocomial infection as shown in Table 1. Pseudomonas aeruginosa was the most commonly isolated agent in blood cultures of patients with sepsis (Figure 1), which was sensitive to amikacin, ceftazidime and ciprofloxacin as shown in Table 2.

### DISCUSSION
Nosocomial infection is recognized as one of the most significant causes of morbidity and mortality among hospitalized newborns especially in NICU.\(^\text{19}\)

### Table 1. Nosocomial infection site distribution

| Localization            | N  | Percent |
|-------------------------|----|---------|
| Bloodstream infection   | 94 | 60.25%  |
| With positive cultures  | 28 | 29.78%  |
| Clinical sepsis         | 66 | 42.30%  |
| Meningitis              | 32 | 20.52%  |
| Pneumonia               | 30 | 19.23%  |
| Total                   | 156| 100.0%  |

**Figure 1.** Etiological agents isolated from blood culture in laboratory confirmed sepsis

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However, the exact impact of this condition is difficult to point out, since there is a wide variation in infection rates reported in the literature, possibly due to differences in surveillance or study methods. This study adopted NNIS definitions to overcome this problem. Around the world, each NICU has unique characteristics that are reflected in the epidemiology of nosocomial infections. Hence it is extremely important to control the inherent aspects of each NICU, and to make it available to the local laborious body and the scientific community interested in epidemiological data. Unfortunately, this practice is still not universal, and there are not many published studies that portray the epidemiology and risk factors for infection in Nepalese NICUs.

In this study, the incidence rate and incidence density of nosocomial infection were 47.3% and 39.3 infections per 1000 patient-days. Incidence of nosocomial infection was reported to vary between 6.2 and 50.7 infections per 100 admissions, and between 4.8 and 62 infections per 1000 patient days at various centers in the previous studies.20,21 A study conducted by Edison Nagata et al in Brazil has reported the similar incidence of nosocomial infection, but their study has reported much higher incidence density of 62 infections per 1000 patient-days as compared to our study.18 Similarly, C. Auriti et al also reported 32.2% of hospital acquired infections (HAIs) in their study of 280 infants of which 55 neonates had 90 episodes of HAIs.21 However, studies from Turkey and Saudi Arabia have reported much lower incidence rate of 16.2% - 19.2% and incidence density of 10.3 - 13.7 infections per 1000 patient-days.21,22 Sarvikivi E et al has also reported the similar incidence of HAI in their study.23 It is stated that this discrepancy of incidence rate and density of hospital acquired infection between neonatal units could be due to underlying differences in patient populations studied, care practices, surveillance methods and study designs.22-24

Blood stream infection was the most prevalent form of nosocomial infection in this study, with clinical sepsis accounting for the majority of cases, and nosocomial meningitis was the second most prevalent one.25,26 This distribution is similar to that reported by other authors,27,28 although different from some Brazilian reports,19,28 which describe pneumonia as the most common nosocomial infection. The proportion of sepsis in this study (60.2%) is definitely worrisome, since neonatal sepsis carries on a particular increased mortality, prolonged length of hospital stay and slower growth among very low birth weight infants and our rates are higher than those usually observed.26,27,29 This study showed a relatively high prevalence of nosocomial sepsis (including laboratory-confirmed and clinical sepsis) in our NICU and this could be because of higher number of LBW babies and hence their sickness, surveillance definition used and study population in our set up. Regarding bacterial isolates in nosocomial sepsis, pseudomonas and klebsiella were common isolates. In various studies from different parts of the world, organisms vary but coagulase negative staphylococcus aureus (CoNS) and gram negative organisms were commonest.23,27 This variation could have been resulted due to different geographic, socioeconomic, demographic as well as cultural differences.

Our study has tried to elaborate upon the incidence and the characteristics of neonatal sepsis in Eastern Nepal. Although this is a single centric study conducted over a relatively short duration with smaller sample size, it does help to elucidate the topic of neonatal sepsis in a developing nation. We are hopeful that larger, multi centric researches in

| Micro-organisms       | Sensitive to                                                  |
|-----------------------|---------------------------------------------------------------|
| Staphylococcus aureus | Ciprofloxacin, Cefotaxim, Azithromycin, Vancomycin, Amikacin, Gentamycin |
| Klebsiella pneumoniae | Ciprofloxacin, Levofloxacin, Meropenem, Amikacin, Gentamycin, Imipenem |
| Pseudomonas aeruginosa| Ciprofloxacin, Ofloxacin, Cefotaxim, Ceftazidime, Amikacin, Imipenem, Piperacillin, Tobramycin |
| Enterococcus species  | Vancomycin                                                   |
| E. coli               | Ciprofloxacin, Amikacin, Imipenem                            |
| Enterobacter          | Ciprofloxacin, Amikacin, Imipenem                            |
this field would be conducted in the future and help us understand more upon this topic.

CONCLUSIONS

The study revealed the high burden of nosocomial sepsis in a neonatal intensive care unit in Eastern Nepal. Bloodstream infection was found to be the commonest nosocomial infection. *Pseudomonas aeruginosa* was the commonest organism grown. Hence we should implement policies for prevention of nosocomial sepsis so that we can reduce the morbidity and mortality in neonates.

REFERENCES

1. Saiman L. Preventing infections in the Neonatal Intensive Care Unit. In: Wenzel RP, editor. Prevention and control of nosocomial infections. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2003: 342–368.
2. Moore DL. Nosocomial infections in newborn nurseries and neonatal care units. In: Mayhall CG, editor. Hospital epidemiology and infection control. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 2004: 851–884.
3. Brodie SB, Sands KE, Gray JE, Parker RA, Goldmann DA, Davis RB, et al. Occurrence of nosocomial bloodstream infections in six neonatal intensive care units. Pediatr Infect Dis J 2000;19(1):56-65. DOI: 10.1097/00006454-200001000-00012
4. Stoll BJ, Hansen N, Fanaroff AA, Wright LL, Carlo WA, Ehrenkranz RA, et al. Late-onset sepsis in very low birth weight neonates: the experience of the NICHD Neonatal Research Network. Pediatrics. 2002;110(2):285-291. DOI: 10.1542/peds.110.2.285
5. Tikhomirov E. WHO Programme for the Control of Hospital Infections. Chemotherapia. 1987;6(3):148-151. PMID: 3607925
6. Haley RW, Culver DH, White JW, Morgan WM, Emori TG, Munn VP, et al. The efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals. Am J Epidemiol. 1985;121(2):182-205. DOI: 10.1093/oxfordjournals.aje.a113990
7. Reese C, Richard P, Robert W, Barry B, Pablo S, Daniel K, et al. Nosocomial Infection in the NICU: A Medical Complication or Unavoidable Problem? J Perinatol. 2004;24(6): 382–388. DOI:10.1038/sj.jp.7211120
8. Emori GT, Gaynes RP. An overview of nosocomial infections including the role of the microbiology laboratory. Clin Microbiol Rev. 1993;6(4):428-442. DOI: 10.1128/cmr.6.4.428
9. Martone WJ, Jarvis WR, Culver DH, Haley RW. Incidence and nature of endemic and epidemic nosocomial infections. In: Bennett JV, Brachman PS (eds) Hospital Infections, 3rd ed. Little, Brown and Co, Boston.1992; 577-596.
10. Allegranzi B, Nejad SB, Combesnure C, Graafmans W, Attar H, Donaldson L, et al. Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis. The Lancet. 2011; 377(9761):228-241. DOI: 10.1016/S0140-6736(10)61458-4
11. Shrestha S, Shrestha NC, Dongol SS, Shrestha RP, Kayestha S, Shrestha M, et al. Bacterial Isolates and its Antibiotic Susceptibility Pattern in NICU. Kathmandu Univ Med J. 2013;41(1):66-70. DOI: 10.3126/kumj.v11i1.11030
12. Gupta P, Murali MV, Faridi MM, Kaul PB, Ramachandran VG, Talwar V. Clinical profile of klebsiella septicemia in neonates. Indian J Pediatri. 1993; 60(4):565-572. DOI: 10.1007/BF02751435
13. Mondal GP, Raghavan M, Vishnu BB, Srinivasan S. Neonatal septicemia among inborn and out born babies in referral hospital. Indian J Pediatri. 1991; 58(4): 529-533. DOI: 10.1007/BF02750936
14. Sharma PP, Halder D, Dutta AK, Dutta R, Bhatnagar S, Bali A, et al. Bacteriological profile of neonatal septicemia. Indian Pediatri. 1987; 24(11):1011-7. PMID: 3450639
15. Singh M. Nosocomial bacterial infection amongst newborn babies. Indian J Pediatri. 1978;45(369):314-7. DOI: 10.1007/BF02749259
16. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. Am J Infect Control. 1988;16(3):128-140. DOI: https://doi.org/10.1016/0196-6553(88)90053-3

17. National Neonatology Forum, India; Evidence Based Clinical Practice Guidelines, October 2010.

18. Kawagoe JY, Segre CAM, Pereira CR. Risk factors for nosocomial infections in critically ill newborns: A 5-year prospective cohort study. Am J Infect Control 2001;29(2):109-114. DOI: 10.1067/mic.2001.114162

19. Brito DV, de Brito CS, Resende DS, Moreira do OJ, Abdallah VO, Gontijo FPP. Nosocomial infections in a Brazilian neonatal intensive care unit: a 4-year surveillance study. Rev Soc Bras Med Trop. 2010;43(6):633-637. DOI: 10.1590/s0037-86822010000600006

20. Tian LY, Hamvas A. Risk factors for nosocomial bloodstream infections in a neonatal intensive care unit. Zhongguo Dang Dai Er Ke Za Zhi. 2010;12(8):622-624. PMID: 20704794

21. Auriti C, Ronchetti MP, Pezzotti P, Marrocco G, Quondamcarlo A, Seganti G, et al. Determinants of nosocomial infection in 6 neonatal intensive care units: an Italian multicenter prospective cohort study. Infect Control Hosp Epidemiol. 2010; 31(9):926-933. DOI: 10.1086/655461

22. Sarvikivi E, Karki T, Lyytikainen O. Repeated prevalence surveys of healthcare-associated infections in Finnish neonatal intensive care units. J Hosp Infect 2010; 76(2):156-160. DOI: 10.1016/j.jhin.2010.03.020

23. Nagata E, Brito ASJ, Matsuo T. Nosocomial infections in a neonatal intensive care unit: Incidence and risk factors. Am J Infect Control. 2002; 30(1):26-31. DOI: 10.1067/mic.2002.119823

24. Pessoa-Silva CL, Richtmann R, Calil R, Santos RM, Costa ML, Frota AC, et al. Healthcare-associated infections among neonates in Brazil. Infect Control Hosp Epidemiol. 2004; 25(9):772-777. DOI: 10.1086/502475

25. Auriti C, Maccallini A, Di Liso G, Di Ciommo V, Ronchetti MP, Orzalesi M. Risk factors for nosocomial infections in a neonatal intensive-care unit. J Hosp Infect 2003; 53(1):25-30. DOI: 10.1053/jhin.2002.1341

26. Urrea M, Pons M, Serra M, Latorre C, Palomeque A. Prospective incidence study of nosocomial infections in a pediatric intensive care unit. Pediatr Infect Dis J. 2003; 22(6):490-494. DOI: 10.1097/01.inf.0000069758.00079.d3

27. Urrea M, Iriondo M, Thio M, Krauel X, Serra M, LaTorre C, et al. A prospective incidence study of nosocomial infections in a neonatal care unit. Am J Infect Control 2003; 31(8):505-507. DOI: 10.1016/S0196-6553(03)00077-4

28. Zaidi AK, Huskins WC, Thaver D, Bhutta ZA, Abbas Z, Goldmann DA. Hospital-acquired neonatal infections in developing countries. Lancet 2005; 365(9465):1175-1188. DOI: 10.1016/S0140-6736(05)71881-X

29. Brady M.T. Health care-associated infections in the neonatal intensive care unit. Am J Infect Control 2005; 33(5): 268-275. DOI: 10.1016/j.ajic.2004.11.006