ORIGINAL ARTICLE

Profile and Risk Factors for Nosocomial Sepsis in a Neonatal Intensive Care Unit of BPKIHS

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ABSTRACT

Introduction: Nosocomial sepsis is a common and serious problem of neonates who are admitted for intensive care. With advancement of technologies in neonatal intensive care unit (NICU) worldwide, survival rates of newborns particularly low birth weight and premature babies are higher. This has led to longer duration of hospital stay predisposing these babies to nosocomial infections (NI). Hence, it is one of the main causes of morbidity and mortality in NICU. The objective of the study was to determine the profile and risk factors for nosocomial sepsis in NICU.

Materials and Methods: This was a prospective cohort study conducted in a seven-bedded 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 h were observed. Healthcare-associated Infections was diagnosed according to the Centers for Disease Control and Prevention criteria. Risk factors for NI were analyzed with Chi-square test and logistic regression model. $P < 0.05$ was considered statistically significant.

Results: The incidence rate and density of NI were 47% and 39.3 infections per 1000 patient-days, respectively. *Staphylococcus aureus* was the most commonly isolated agent in blood cultures of patients with nosocomial sepsis. Low birth weight and mechanical ventilation were found to be related with nosocomial sepsis ($P < 0.05$).

Conclusions: This study revealed the high incidence of nosocomial sepsis. Low birth weight and mechanical ventilation were the most important risk factors for sepsis.

Key words: Neonatal intensive care unit, nosocomial sepsis, risk factors

INTRODUCTION

Nosocomial sepsis constitutes a global health problem[1] and contributes to significant morbidity and mortality, longer duration of hospitalization, as well as increased the cost of treatment in both developed and resource-poor countries.[2]

Nosocomial sepsis has been defined by the US Department of Health and Human Services for Disease Control and Prevention as an infection occurring during hospitalization which was not present or incubating at the time of admission.[3] The organisms causing most nosocomial infections (NI) usually emanate from the patient's own body (endogenous flora) or contact with hospital staff, contaminated devices, and consumables (cross-contamination) and from the hospital environment (exogenous flora).[4]

The reported incidence of nosocomial sepsis in neonates from India ranges from 1.5% to 37%.[1-4] In contrast, surveillance reports from the USA have reported a rate of 0.9% to 7%.[5] A recent review from the WHO found that the prevalence of health-care-associated infection was 15.5/100 patients in developing countries, which was much higher than the prevalence reported from Europe and the USA.[6]

A study conducted by Shrestha *et al*. in Nepal has reported the incidence of nosocomial sepsis of 10.79%.[7] Similarly, its incidence in neonates from India ranges from 1.5% to 37%.[8-11] Nevertheless, NI remains a major cause of preventable morbidity and mortality in developing countries where infection rates are relatively higher due to poor infection control practices, lack of supervision, and inappropriate use of limited resources and overcrowding of hospitals.[2]

There are various risk factors for nosocomial sepsis. Prematurity, low birth weight, intrauterine growth restriction, low Apgar score, application of mechanical ventilation, and exposure to central venous catheter are the risk factors for NI.[12]

According to the published articles, the infection rate in neonatal intensive care unit (NICU) of Nepal varied

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from 7% to 11.6%.[13-15] However, the risk factors, such as prematurity, low birth weight, length of hospitalization, application of gastric tube, and ventilation associated with the nosocomial sepsis in NICU in Nepal are rarely reviewed and analyzed as most of the studies only discussed the epidemiological profile of NI in NICU.[14-18] Since Nepal's health-care system, regulation procedure, efficiency, and socioeconomic situation are unique, it is essential to conduct the research on NI, incidence, and risk factors to control and to minimize the infection.

MATERIALS AND METHODS

The study was conducted in a seven-bedded NICU of B.P. Koirala Institute of Health Sciences (BPKIHS) which is a teaching hospital and tertiary care referral center situated in the Eastern part of Nepal. This study was conducted over 1 year period between September 2014 and September 2015 in NICU of BPKIHS. This is a prospective cohort study. All patients admitted to the NICU without any sign of infection, who remained hospitalized for at least 48 h, were eligible for inclusion.

Inclusion Criteria

1. All neonates admitted to Neonatal intensive care during the study period
2. Duration of stay in NICU >48 h.

Exclusion Criteria

1. Neonates who died or were discharged or transferred to other department within 48 h after being admitted in NICU
2. Out born neonates
3. Severe congenital malformations.

Written informed consent in the local language was taken from the parents and/or guardians of all patients before the commencement of study. After admission to NICU, the details were prospectively collected and recorded on standardized form until discharge from the hospital or death.

Hospital born neonates transferred to NICU after birth and available in the unit for at least 48 h would comprise the cohort for the infection surveillance which was carried out over a period of 1 year. 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 5 min, absolute neutrophil count, micro-erythrocyte sedimentation rate, C-reactive protein, immature to total neutrophil ratio, blood cultures, lumbar puncture, X-ray chest, medical devices used (central venous catheter, umbilical catheter, percutaneous catheter, and mechanical ventilation), other relevant medical conditions and length of stay were collected.

NI 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 Centers for Disease Control and Prevention (CDC).[19] The diagnosis of infection 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 cerebrospinal fluid (CSF) culture were performed in all patients who had bacterial growth in blood culture or clinical signs of meningitis.

NI was considered to be present if onset of infection was beyond 48 h 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 NI if they had a positive sepsis screen. All neonates suspected to have sepsis and meningitis were screened by the National Neonatology Forum guidelines, India.[20]

Infection surveillance was consistently conducted according to the National Infection Surveillance System (NNIS/CDC/Atlanta) definitions,[19] 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, for which isolation of two positive blood cultures were required) with clinical signs and symptoms. Sepsis was broadly divided into two types. They were laboratory confirmed sepsis and clinical sepsis. Bloodstream 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 NI 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. Chi-square test was performed for the association between potential risk factors and nosocomial sepsis. The variables with $P < 0.20$ in the univariate analyses were included in multivariate logistic regression model to identify independent risk factors for sepsis. The level of statistical significance adopted was $P < 0.05$. SPSS for Windows 20.0 software was used for all statistical analysis.

This study was approved by the Institutional Ethics Review Board of BPKIHS.

RESULTS

A total of 225 patients were admitted to NICU during the 1 year period. Sixty were excluded for the following reasons: 10 died, 46 transferred to nursery or neonatal ward within 48 h, and four were out born. Fifty-four infants developed 78 episodes of NIs and 42 infants developed 47 episodes of nosocomial sepsis. Total length of hospital stay in NICU was 1980 days. The incidence rate and the incidence density were 47% and 39 infections per 1000 patient-days. *Staphylococcus aureus* was the most commonly isolated agent in blood cultures of patients with sepsis [Table 1]. Most of the organisms were sensitive to ciprofloxacin as shown in Table 2.

The variables associated with NI according to the univariate analysis were Birth weight ($P < 0.001$), Apgar ≤6 at 5 min ($P = 0.02$), and mechanical ventilation ($P < 0.0001$). The variable (umbilical catheterization) although not statistically significant ($P = 0.18$), were included in the multivariate analysis ($P < 0.20$). The multivariate analysis identified two independent risk factors for nosocomial sepsis in the NICU: Birth weight ≤1500 g ($P < 0.001$; odds ratio [OR] 54.6 [0.002–0.147]), and mechanical ventilation ($P < 0.0001$; OR 74.9 [8.47–663.9]) as shown in Table 3.

DISCUSSION

NI is recognized as one of the most significant causes of morbidity and mortality among hospitalized newborns, especially in neonatal NICU.[21] 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 NIs. Obviously then, 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.

Table 1: Etiologic agents isolated from blood cultures in laboratory-confirmed sepsis

Microorganisms	*n* (%)
S. aureus	8 (4.84)
K. pneumoniae	2 (1.21)
P. aeruginosa	1 (0.60)
Enterococcus species	1 (0.60)
E. coli	1 (0.60)
Enterobacter	1 (0.60)
No growth	151 (91.51)
Total	165 (100)

S. aureus: Staphylococcus aureus, K. pneumoniae: Klebsiella pneumoniae , P. aeruginosa: Pseudomonas aeruginosa, E. coli: Escherichia coli

Table 2: Antibiotic susceptibility pattern

Microorganisms	Sensitive to
S. aureus	Ciprofloxacin, cefotaxim, azithromycin, vancomycin, amikacin, gentamycin
K. pneumoniae	Ciprofloxacin, levofloxacin, meropenem, amikacin, gentamicin, imipenem
P. aeruginosa	Ciprofloxacin, ofloxacin, cefotaxime, ceftazidime, gentamicin, imipenem, piperacillin, tobramycin
Enterococcus species	Vancomycin
E. coli	Ciprofloxacin, amikacin, imipenem
Enterobacter	Ciprofloxacin, amikacin, imipenem

S. aureus: Staphylococcus aureus, K. Pneumoniae: Klebsiella pneumoniae, P. aeruginosa: Pseudomonas aeruginosa, E. coli: Escherichia coli

In this study, the incidence rate and incidence density of NI were 47% and 39 infections per 1000 patient-days. Incidence of NI 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.[22-25] A study conducted by Nagata *et al*. in Brazil have reported the similar incidence of NI.[26] It is stated that this discrepancy between neonatal units could be due to underlying differences in patient populations studied, care practices, surveillance methods, and study designs.

Nosocomial sepsis was the most prevalent infection in this study, with clinical sepsis accounting for the majority of cases, and nosocomial meningitis was the second most prevalent one. This distribution is similar to that reported by other authors,[27-30] although different from some Brazilian reports,[21,26] which describe pneumonia as the most common infection. The proportion of sepsis in this study (60.2%) is definitely worrisome since neonatal sepsis carries on 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.[27-29,31]

Birth weight, mechanical ventilation, and Apgar at 5 min were associated with NI in the univariate analysis; however, multivariate analysis identified birth weight

Table 3: Potential risk factors for NI among patients admitted in NICU in univariate and multivariate analysis model (*n*=165)

Variables	Number exposed		Unadjusted OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
	NI positive (%) *n*=54 (32.7)	NI negative (%) *n*=111 (67.3)				
Gender						
Female	29 (53.7)	52 (46.8)	1.31 (0.68–2.52)	0.41		
Male	25 (46.3)	59 (53.2)	Ref			
Length of hospitalization (days)						
≥6	10 (18.5)	21 (18.9)	1.2 (0.36–4.06)	0.73		
6–15	37 (68.5)	78 (70.3)	1.2 (0.44–3.37)	0.68		
≤5	7 (13.0)	12 (10.8)	Ref			
Gestational age (weeks)						
<32	12 (22.2)	15 (13.5)	0.50 (0.19–1.25)	0.13		
32–37	22 (40.7)	46 (41.4)	0.83 (0.40–1.72)	0.62		
>38	20 (37.1)	50 (45.1)	Ref			
Birth weight (g)						
≤1500	25 (46.3)	42 (37.8)	1.5 (0.67–3.58)	0.001	54.6 (0.002–0.147)	0.0002
1501–2500	13 (24.1)	53 (47.7)	0.24 (0.10–0.57)	0.30	9.1 (0.01–0.93)	0.0426
>2500	16 (29.6)	16 (14.5)	Ref		Ref	
Apgar at 5 min						
≤6	19 (35.2)	60 (54.1)	0.46 (0.23–0.90)	0.02		
≥7	35 (64.8)	51 (45.9)	Ref			
Mode of delivery						
Vaginal	34 (62.9)	62 (55.9)	1.34 (0.68–2.61)	0.38		
Cesarean section	20 (37.1)	49 (44.1)	Ref			
Mechanical ventilation						
Yes	15 (27.8)	7 (6.3)	5.7 (2.16–15.06)	0.0001	74.9 (8.47–663.9)	0.0001
No	39 (72.2)	104 (93.7)	Ref			
Umbilical catheterization						
Yes	3 (5.6)	2 (1.8)	3.2 (0.51–19.78)	0.18		
No	51 (94.4)	109 (98.2)	Ref			

NICU: Neonatal intensive care unit, NI: Nosocomial infection, OR: odds ratio, CI: Confidence intervals

(1501–2500 g) and mechanical ventilation as independent risk factors for NI in NICU.

Birth weight has been consistently considered as a strong and independent predictor of adverse outcomes including NIs.[21,26,27,32] In this study, while the OR of infants whose birth weights were 1501–2500 g was 0.183 (0.071–0.469) which is in accordance with previously published data.[32] Those newborns whose birth weights were ≤1500 g are often more severely ill, the majority of them die before the NI is documented or even before it really happens. This may explain the apparent paradox of the statistical result. It also underlines the limited ability of our NICU in changing the outcome of these extremely low birth weight newborns.

It is well known that devices are part of the advances in medical therapy that have resulted in significant improvement in neonatal survival. On the other hand, it is well recognized that these same beneficial tools can also place the newborn at a considerable higher risk of health-care associated infections.[21,26,27,32] In this study, the exposure to mechanical ventilation independently increased the risk for neonatal NIs.

Umbilical catheterization was observed to be the most important risk factor for the development of hospital-acquired infection in various studies.[33-35] Yet, we observed that mechanical ventilation had the highest calculated risk for developing nosocomial sepsis. The umbilical catheterization was found to be the least risky intervention. This difference may be attributed to the sterile practices during catheter insertion, the microenvironment, or colonization of NICU and the infant, presence of comorbidities, and duration of catheter use but especially to our principle of early shifting from

umbilical catheter to percutaneous catheter whenever possible and assigning a well-educated and experienced team which is responsible for insertion and optimal care of the catheter.

CONCLUSIONS

This study showed that low birth weight and exposure to mechanical ventilation are independent risk factors for nosocomial sepsis. These results raise two important matters: First, the necessity of providing a better antenatal care and avoid the occurrence of complications secondary to low birth weight and prematurity; second, the implementation of protocols for judicious use of invasive procedures on NICUs. We believe that these actions together will definitely decrease the incidence of neonatal NIs in our institution. Furthermore, the knowledge of prognostic factors for NI allows a precise stratification of the population at risk and the implementation of more efficient and tailored therapeutic strategies.

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