Original Article

Nosocomial Sepsis and its Risk Factors: A Cross-Sectional Study in a Neonatal Intensive Care Unit

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Abstract

Introduction: Nosocomial sepsis is a common and serious infection of neonates who are admitted in intensive care unit. They lead to significant morbidity and mortality in both developed and resource-limited countries. The neonatal intensive care unit (NICU) is a suitable environment for disseminating the infections and, hence, needs preventive intervention. The study was carried out to determine the risk factors for nosocomial sepsis in neonatal intensive care unit.

Material and Methods: This was a cross-sectional study conducted in a seven bedded teaching and referral hospital 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. Nosocomial sepsis was diagnosed according to the CDC criteria. Risk factors for nosocomial sepsis were analyzed with Chi-square test and Logistic regression model. P-value of <0.05 was considered significant.

Results: Low birth weight (both preterm and IUGR) and mechanical ventilation were found to be related with nosocomial sepsis.

Conclusions: Low birth weight and mechanical ventilation were the most important risk factors for nosocomial sepsis.

Key words: Nosocomial sepsis, Neonatal intensive care unit, 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 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 usually emanate from the patient's own body (endogenous flora), or from contact with hospital staff, contaminated devices and consumables (cross-contamination) and from the hospital environment (exogenous flora).[4]

There are various risk factors for nosocomial sepsis. Prematurity, low birth weights, IUGR, low Apgar score, application of mechanical ventilation and exposure to central venous catheter are the risk factors for nosocomial infection.[5]

According to the various studies,[6,7] the infection rate in NICU of Nepal varied from 7-11.6%.[8] However, the risk factors, such as prematurity, low birth weight, length of hospitalization, application of gastric tube and ventilation

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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 nosocomial infection in NICU.[9,10,11] Since Nepal's health care system, regulation procedure, efficiency and socioeconomic situation are unique, it is essential to conduct the research on nosocomial infection, incidence and risk factors in order to control and minimize the infection.

Material and Methods

The study was conducted in a seven bedded NICU of an Institute which is a teaching hospital and tertiary care referral center. This study was conducted over one year period from September 2015 to September 2016 in NICU. The study was a hospital based cross-sectional study. All neonates admitted to NICU without any sign of infection, which remained in NICU for at least 48 hours were eligible for inclusion. Sample size was calculated by using the formula.

$n= Z^2 PQ/L^2$ (Z= 1.96 for 95% CI, P= Incidence of infection, Q= 1-P, L= 0.05).

*Inclusion Criteria***:**

1) All neonates admitted to neonatal intensive care unit during the study period
2) Inborn neonates
3) Duration of stay in NICU ≥ 48 hrs.

*Exclusion criteria***:**

1) Neonates who died or were discharged or transferred to other department within 48 hours 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 enrollment in the 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 hours would comprise the cohort for the infection surveillance which was carried out over a period of one 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 five minutes, absolute neutrophil count, micro-ESR, CRP, immature to total neutrophil 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.[12] 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 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 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 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.[13]

Infection surveillance was consistently conducted according to the National Infection Surveillance System (NNIS/CDC/Atlanta) definitions,[12] 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 in two types. They were laboratory confirmed sepsis and clinical sepsis (CSEP). 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 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. 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 in order to identify independent risk factors for sepsis. The level of statistical significance adopted was $p<0.05$. SPSS for Windows 16.0 software was used for all statistical analysis.

Results

A total of 225 patients were admitted to NICU during the one year period. Sixty were excluded for the following reasons: 10 died, 46 transferred to nursery or neonatal ward within 48 hours and four were out born. Fifty four infants developed 78 episodes of nosocomial infections 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.

The variables associated with nosocomial sepsis according to the univariate analysis were: birth weight ($p <0.001$), Apgar ≤6 at 5min ($p= 0.02$) 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 ≤1500gm (p<0.001; OR 54.6 (0.002 – 0.147) and mechanical ventilation (p<0.0001; OR 74.9 (8.47 – 663.9) as shown in Table 1.

Table 1: Potential risk factors for nosocomial sepsis among patients admitted in NICU in Univariate and Multivariate analysis model (N= 165)

Variables	Number exposed		Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
	NI +ve (%) N= 54 (32.7)	NI -ve (%) 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)						
≥ 16	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 (gm)						
≤ 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 minute						
≤ 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			

Discussion

Nosocomial sepsis is recognized as one of the most significant causes of morbidity and mortality among hospitalized newborns especially in neonatal intensive care unit.[14] 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.

In this study, the incidence rate and incidence density of nosocomial infection were 47% and 39 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.[15-18] A study conducted by Edison Nagata et al in Brazil has reported the similar incidence of nosocomial infection.[19] 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,[20-23] although different from some Brazilian reports,[24] 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 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.[20,21,22,25]

Birth weight, mechanical ventilation and Apgar at 5min were associated with nosocomial infection in the univariate analysis but multivariate analysis identified birth weight (1501-2500gm) and mechanical ventilation as independent risk factors for nosocomial infection in NICU.

Birth weight has been consistently considered as a strong and independent predictor of adverse outcomes, including nosocomial infections.[14,20,24,26] In this study, while the odds ratio of infants whose birth weights were 1501-2500gm was 0.183 (0.071-0.469) which is in accordance with previously published data.[26] Those newborns whose birth weights are ≤1500gm are often more severely ill, the majority of them die before the nosocomial infection 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.[24,26] In this study, the exposure to mechanical ventilation independently increased the risk for neonatal nosocomial infections. Umbilical catheterization was observed to be the most important risk factor for the development of hospital-acquired infection in various studies.[27-29] Yet, we observed that mechanical ventilation had the highest calculated risk for developing nosocomial sepsis.

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 nosocomial infections in our institution. Furthermore, the knowledge of prognostic factors for nosocomial infection allows a precise stratification of the population at risk and the implementation of more efficient and tailored therapeutic strategies.

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