

## NEONATAL NOSOCOMIAL INFECTION: PROFILE AND RISK FACTORS

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**Objective:** To determine the incidence and risk factors for neonatal nosocomial infections.

**Design:** Cohort study. **Setting:** Tertiary care Teaching Hospital. **Methods:** Hospital born neonates transferred to the neonatal unit after birth and available in the unit 48 hours later comprised the cohort for the surveillance. Detailed maternal, intrapartum and neonatal variables were recorded. Risk factors for nosocomial infection were analyzed by both univariate and multiple logistic regression methods. **Results:** One hundred and thirty-four neonates were enrolled in the cohort. The overall nosocomial infection rate was 16.8/1000 patient days. Device associated infection rate was 11.9/1000 device days. Multidrug resistant *Klebsiella* species was the commonest organism causing nosocomial septicemia and pneumonia followed by *Pseudomonas aeruginosa*. The risk factors detected to be significantly associated with infection on multiple logistic regression analyses were a birth weight < 1500 g (OR 3.3) and assisted ventilation >72 h (OR 14.2). **Conclusions:** Very low birth weight (VLBW) neonates, especially those undergoing interventions such as mechanical ventilation are at the greatest risk for infection and death. Therefore, strict protocol for asepsis must be adhered to when handling these high risk infants.

**Key words:** Low birth weight, Mechanical ventilation, Nosocomial infection, Preterm.

NEONATAL nosocomial infections are an important cause of neonatal morbidity and mortality. However, its reporting in this country has been non-uniform. 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). In the absence of surveillance reports from India, neither reliable infection rates nor the contributory risk factors in the Indian setting are available to us. The present study was undertaken to determine the profile and risk factors for neonatal nosocomial infection.

### Subjects and Methods

Hospital born neonates transferred to the neonatal unit after birth and available in the unit for at least 48 hours comprised the cohort for the infection surveillance which was carried out over a period of six months. All neonates included into the cohort were closely followed during their hospital stay for clinical signs of infection. Those who did not manifest signs of infection during their stay in the unit were followed upto 72 hours after discharge (hospital recall visit on 4th post-discharge day) for clinical signs of infection to ensure de-

tection of cases who may be incubating an infection at the time of discharge from the unit.

### Definition

*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 were screened by total leukocyte count (abnormal-  $<5000/\text{cumm}$  or  $>20,000/\text{cumm}$ ), immature/total polymorphs (abnormal-  $>0.2$ ), micro-ESR (abnormal  $>10$  mm 1st h) and C-Reactive Protein (CRP). The sepsis screen was considered positive if at least two tests were positive (6,7). In all suspected cases with sepsis, CSF examination was done to detect meningitis.

Neonates presenting with infection beyond 48 h but under 7 days of life, but with maternal predisposing factors such as premature rupture of membranes, maternal fever and foul vaginal discharge were not considered to be nosocomial in origin.

Detailed baseline information with regard to maternal (premature or prolonged rupture of membranes, infections), intrapartum and neonatal (resuscitation, duration of stay, weight, gestation, morbidities, interventions such as vascular catheters and ventilation, outcome) variables were recorded.

### Statistical Analysis

Overall nosocomial infection rates were expressed as number of nosocomial infection/1000 patient days. Device associated infection rates were expressed as number of nosocomial infections/1000 device days (device being ventilator or indwelling vascular catheters). The risk factors for nosocomial infection were analyzed by both univariate and multiple logistic regression methods using appropriate parametric (Student-t test) and non-parametric tests (Mann-Whitney-U and Chi-square). A probability of 5% was considered significant.

### Results

#### Profile

During the study period, there were 2800 livebirths. There were 219 (7.8%) transfers to the neonatal unit, and amongst these 134 (61.2%) neonates became eligible for inclusion into the cohort. There were 22 (of 134 neonates) who developed nosocomial infections. In 21 a diagnosis of septicemia was made, with 11 having associated pneumonia and 4 having associated soft tissue infection. None of the neonates had meningitis or urinary tract infection. In 16 (76%) of these neonates, both sepsis screen and blood culture were positive; in 4 only the sepsis screen was positive and in 1 only the blood culture was positive. In the one case with only oral thrush, both sepsis screen and culture were negative. None had multiple episodes of infection. Multiresistant *Klebsiella* species (68%) was the commonest organism causing nosocomial septicemia and pneumonia followed by *Pseudomonas aeruginosa* (13%).

The overall nosocomial infection rate was 16.8/1000 patient days and device associated infection rate was 11.9/1000 device days. *Table I* provides the profile of neonates included in the cohort. Neonates

who developed nosocomial infection were significantly lower in their birth weights and gestation. The median age at diagnosis of infection was 184 h (range 52-824 h). There were no differences with regard to maternal chorioamnionitis, resuscitation procedures at birth or birth asphyxia, fetal growth retardation, sex and malformations. A significantly larger number of neonates with infection had delivered vaginally. The two groups had comparable morbidities such as transient tachypnea of newborn, meconium aspiration and hypothermia, but significantly more neonates in the infection group had hyaline membrane disease (HMD). Neonates with infection had a significantly higher mortality and stayed longer in hospital (contributed by the lower birth and higher morbidity).

*Risk Factors*

Several factors with a known risk for neonatal nosocomial sepsis were evaluated. On univariate analysis, it was observed that besides birth weight and gestation, other interventional factors significantly associated with infection were assisted ventilation and use of peripheral venous and umbilical vascular catheters (*Table II*). There were 21 (95.5%) in the infected group and 73 (65.2%) in the non-infected who had a peripheral venous access ( $p < 0.001$ ). Peripheral arterial access was present in 9(40.9%) infected and 10(8.9%) non-infected neonates ( $p < 0.01$ ). All durations and interventions presented in *Table II* pertain to the period before diagnosis of nosocomial infection. Prophylactic antibiotics were initiated in neonates mechanically ventilated

**TABLE I-Profile of Infected and Non-Infected Newborns**

Variables	Infection (n=22)	No infection (n=112)	Relative Risk (95% CI)
Birth Weight (g)* mean (SD)	1466.6 (581)	1947.2 (631)	—
Gestation (weeks)* mean (SD)	33.5 (3.4)	36.6 (3.0)	-
Small for dates (%)	16 (72.7)	62 (55.3)	1.3 (0.9,1.8)
Sex ratio (M : F)	1.18:1	1.2:1	
Vaginal birth (%)*	20 (90.9)	75 (67.0)	1.4 (1.1,1.6)
Resuscitation at birth (%)	5 (22.7)	29 (25.9)	0.9 (0.4,2.0)
<i>Neonatal Morbidities</i>			
HMD (%)*	6 (27.3)	4 (3.6)	4.7 (2.4,9.2)
Malformations (%)#	1 (4.5)	8 (7.1)	0.6 (0.1,4.8)
Duration of hospital stay (h) (median)	222.5	144	—
(25, 75 centile)	(136-872)	(76.5-288)	
Mortality (%)*	17 (77.3)	16 (14.3)	5.4 (3.3,8.9)

\*  $p < 0.05$

# Tracheo-esophageal atresia, intestinal/anal atresia, diaphragmatic hernia, open neural tube defects

HMD-Hyaline membrane disease.

**TABLE II-Interventional Risk Factors for Nosocomial Infection**

Variables	Infection (n=22)	No infection (n=112)	Relative Risk (95% CI)
Assisted ventilation (%)*	19 (86.3)	18 (16.0)	5.4 (3.4,8.5)
Duration of ventilation (h) (median) (25,75 centile)	105 (40-151)	33 (10-127)	-
Peripheral vascular catheterization (%)*,#	22 (100)	73 (65.5)	1.5 (1.3,1.8)
Duration of peripheral vein cannulation (h)* (median) (25, 75 centile)	210 (136-310)	60 (30-110)	
Umbilical vascular catheterization (%)+	5 (22.7)	9 (8.04)	2.8 (1.1,7.6)
<i>Prophylactic antibiotics</i>			
Ventilated neonates (%)	12 (63.2) (n=19)	11 (61.1) (n=18)	1.0 (0.6,1.7)
Other neonates (%)@	0 (n=3)	15 (15.9) (n=94)	—
Surgery (%)	0	4 (3.7)	—

\*  $p < 0.05$ ; +  $P=0.05$

# Includes both venous and arterial catheterization

@ Maternal chorioamnionitis, surgery, open neural tube defects

for indications other than infection, infants born to mothers with chorioamnionitis and those undergoing surgery for correction of malformations. The use of prophylactic antibiotic did not prevent infection occurrence between the groups when stratified by ventilation and other indications (in the case of nonventilated neonates, the lack of differences could be related to sample size).

To adjust for confounders, all factors observed to be significantly different in the two groups on univariate analysis (birth weight, gestation, mode of delivery, presence of HMD, mechanical ventilation, use of vascular access) were entered into a multiple logistic regression model. In the final model it was observed that a birth weight  $< 1500$  g (OR 3.3, 95% CI 1.2-9.7) and assisted ventilation  $> 72$  h (OR 14.2, 95% CI 4.4-46.2) were significantly ( $p < 0.05$ ) associated with a risk for nosocomial infection.

During the period of surveillance, the influence of nurse-patient ratios and handwashing techniques were also analyzed. It was observed that the nurse-patient ratio remained unchanged at 1:3 during the surveillance period. Medical and nursing personnel were observed at random for their handwashing techniques. One hundred and twenty-two observations were recorded. It was observed that 15-18% of nurses and residents did not adhere to adequate handwashing techniques.

## Discussion

There is a wide variation in the rates of neonatal nosocomial infections that have been reported. In the decade 1970-80, even in United States, there were wide differences in the incidence of nosocomial infection in neonatal intensive care units (NICU) (1.8% to 24.6%)(8-10). Several reasons

could be attributed for these differences, namely, proportion of very low birth weight neonates (< 1500 g); overcrowding in nurseries and proportion of surgical neonates handled by the unit. The pattern of reporting total episodes of infections amongst all at-risk babies fails to emphasize the importance of contributory risk factors such as duration of stay, use of devices like catheterization and ventilatory support towards the causation of nosocomial infection amongst the newborns. Current surveillance techniques suggest that the infection rates should be reported as patient days rate or device associated infection rate.

Low birth weight and prematurity have been reported to be important risk factors for neonatal sepsis (1,2,8). In neonates weighing <1500 g, infection rates have been reported to be as high as 56%(8). In the present study too, it was observed that the risk of neonatal sepsis amongst those <1500 g was 3 times greater than those weighing >1500 g. Other risk factors such as duration of stay, umbilical vascular catheterization, mechanical ventilation, male sex, surgery, total parenteral nutrition have been reported to be associated with neonatal nosocomial infections(8,10-13). In the present study it was observed that when adjusted for confounders, birth weight <1500 g and mechanical ventilation for >72 h were the only significant factors associated with neonatal nosocomial infections. There is need to stress upon strict adherence to aseptic protocols in neonatal units if infection rates are to be kept low.

There is a need for multicentric neonatal nosocomial infection surveillance systems using uniform definitions and reporting formats, to generate information on neonatal nosocomial infection rates and risk factors in our setting, so that appropriate preventive strategies can be adopted.

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