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Nosocomial infections in neonatal intensive care unit In Pediatric Assiut University Hospital: incidence and risk factors

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Abstract: Background: Nosocomial infections (NIs) have become a matter of major concern in neonatal intensive care units (NICUs). Nosocomial infections are the result of the interaction of several risk factors. **Objective:** to identify risk factors for nosocomial infections among neonates admitted to neonatal intensive care unit in Pediatric Assiut University Hospital (AUH). Knowledge of modifiable risk factors could be used to guide the design of interventions to prevent the problem. **Methods**: Incidence (surveillance) study for identification of new nosocomial infections for one year & 9 days from (17 of April 2007 to 26 of April 2008). The total population: All neonates attending NICU in pediatric AUH from the Obstetric Department of Maternal–Healthcare Assiut University Hospital. The target population is all neonates that developed nosocomial infections within 72 hrs of admission. The presence of risk factors was studied. A practical guide completed for each patient, which included: Demographic risk factors as age, birth weight, sex, single or multiple births, type of delivery, premature rupture of membranes, variables recorded daily as enteral feeding, parenteral feeding, mechanical ventilation and indwelling catheter. Differences between patients with and without NI for discrete variables were estimated by the chi-square test. The association between risk factors and the presence of NIs were estimated by relative risk. **Results:** from a total of 990 admitted neonates, the incidence rate and the incidence density rate were 16% and 24.45% infections per 1000 patient-days, respectively. Case fatality rate was 91.8%. The following risk factors were associated with NIs ($P < 0.05$): mechanical ventilation, umbilical catheter, prematurity, birth weight less than 1500 g, use of ryle, transport outside NICU, premature rupture of membrane & peripheral vascular catheter. **Conclusion**: The risk of NIs increases with increasing invasive devices, decreasing birth weight, and gestational age. There is an increased mortality rate associated with NI. Strategies to minimize the impact of risk factors must be identified.

INTRODUCTION

Nosocomial infection in the neonatal intensive care unit (NICUs) is the result of the interaction of several risk factors. Prematurity, multiple underlying diseases, immune system immaturity, exposure to broad-spectrum antibiotics, and the high likelihood of cross-infections due to close contact with a multidisciplinary team have all been related to the occurrence of

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nosocomial infections. Prolonged duration of NICU stay (probably a surrogate marker of the patient's severity of illness), and low birth weight have also been related to an increased risk of nosocomial infections. Intensive use of invasive medical devices (i.e., urinary catheters, central venous catheters [CVCs], and mechanical ventilators) for both diagnostic and therapeutic purposes probably account for the greater risk of nosocomial infections[1].

Nosocomial infection (NI) is a major cause of morbidity and mortality in neonatal intensive care nurseries[2,3] and affects the cost of medical care by increasing resource consumption and the duration of hospitalization in developed countries[4].

Major risk factors for NI include: low birth weight and gestational age, respiratory disease, mechanical ventilation, use of central catheters, use of naso-gastric tubes, and parenteral nutrition[2,3,5] thus, available data suggest that medical interventions are important risk factors for NI in neonates. The extent to which these findings apply to developing countries, in which financial resources for heath care are limited, is unclear[6].

Advanced medical technology such as the closed system of a central line and tracheal tube in the neonatal intensive care unit (NICU) has improved the quality and length of life of neonates born with prematurity and congenital defects. However, nosocomial infection risks are high in NICU babies due to their immature immune systems and the need for invasive diagnosis and treatment, causing high mortality and increases in medical costs[4,7,8,9].

The incidence of nosocomial infection ranges from 6% to 25%, with a large amount of variation by birth weight and treatment condition[2,10]. Nosocomial infections could be prevented by instituting careful bacteriologic surveillance, improving hand hygiene, and limiting

antibiotics and invasive procedures[11-16]. Therefore, it is very important to determine the incidence of nosocomial infection, to identify risk factors for NI that give Knowledge of modifiable risk factors for NI which would enable developing countries to implement interventions to decrease NI and associated complications.

In view of the limited literature and studies on NIs in pediatric ICU or neonatal ICU, in developing countries, this study was conducted in neonatal intensive care unit in Assiut Pediatric University Hospital (the first study), in order to know the size of the problem (NIs) among neonates and to identify risk factors for nosocomial infections among infants.

MATERIAL and METHODS:

Incidence study (the first study) prospective identification of new nosocomial infections (incidence surveillance) for one year & 9 days from (17 of April 2007 to 26 of April 2008).

The total population: All neonates attending NICU in Pediatric AUH from the Obstetric Department of Maternal – Healthcare Hospital.

The target population is all neonates that developed nosocomial infections within 72 hrs of admission according to the Centers for Diseases Control and Prevention (CDC)/National Nosocomial Infection Surveillance (NNIS) definitions for NIs for infants ≤12 months [17].

- Inclusion criteria: All neonates admitted to NICU who born in the obstetric department of Maternal – Healthcare Hospital.
- Exclusion criteria: if neonates developed infections before or within 48 hrs of admission were generally considered maternally acquired and neonates born outside AUH.

Practical guide was constructed to be the tool of data collection. Using a practical guide, one form was completed for each neonate.

The guide included two parts:

The first part was used for all admitted inborn neonates in NICU and included:

Demographic risk factors:

- Age (gestational age): <37 ws = preterm.
- Birth weight category : <1000 g,1000 - ,≥1500 (<1500 g = premature).
- Single or multiple births.
- Type of delivery (caesarian section or vaginal).
- Premature rupture of membranes (>24 hs before delivery).
- Presence of meconium stained amniotic fluid.

Time dependant variables were recorded daily:

- Presence or absence of enteral feeding
- Presence or absence of parentral feeding with pre-prepared (TPN→ Amino-venous) or prepared in the Neonatal Intensive Care Unit.
- Mechanical ventilation
- Indwelling catheter (peripheral vascular catheter & umbilical catheter).
- Transport out side the NICU.
- Outcome.

The second part of the practical guide was used for neonates who developed nosocomial infections and included:

- Date of onset of infection.
- Microorganisms isolated and antimicrobial susceptibility.

Data were obtained from hospital records, nursing notes and oral communication with the attending physicians.

- Blood samples were taken from cases of NI for blood cultures, and complete blood count.

Data revision, computer data entry & statistical analysis:

All data were revised, coded, and were subjected to computer entry and analysis to fulfill the objectives. The advanced

Statistical Package for Social Sciences (SPSS) version 11 were used for statistical analysis. Description of the population (descriptive studies), frequency of risk exposure and infection rates were calculated as overall infection rate (per 100 admissions and 1000 patient-days). Denominators used to calculate the incidence of NI were daily number of admissions, and number of patient-days.

Differences between patients with and without NIs were estimated by the chi-square test. The association between risk factors and the presence of NIs were estimated by relative risk (RR) and their corresponding 95% CI. The significance level used was p less than 0.05.

The birth weights of the babies were classified into 3 groups: ≥1, 500g, 1,000- and less than 1,000 g. The incidence of infections was determined in the birth weight groups.

RESULTS

Study population:

Total 990 neonates were admitted during the duration of surveillance from 17th of April 2007 to 26th of April 2008, total patient days were 6463 days.

Maximum weight for neonates was 5049 g and minimum weight was 527 g with the mean weight 1944 $\pm$ 842 g.

Table (1) shows the characteristics of study subjects. Males were 62.4% of total admitted while females were 37.6%. 36.7% of neonates were less than 1500 g, 77.6% were premature (preterm), 71% of births were single and 53.7% of neonates were born by caesarean section. Premature rupture of membranes was present in 19% of cases.

Enteral feeding was used in 55.2% of neonates, of them 73.8% naso-gastric tubes were used. Mechanical ventilation was used in 52.6% of neonates, the use of peripheral vascular catheter was used in 63.1% of neonates and the use of central line (umbilical catheter) was used in 57% of cases. 24.9% of neonates were

transported outside the NICU. 58.8% of admitted neonates were died (table 1).

Table (2) shows the incidence of nosocomial infection. One hundred and fifty eight (158) developed nosocomial infections within 72 hrs after admission. The cumulative incidence rate was 16 per 100 admitted neonates, incidence density was 24.45 neonates per 1000 patient days and the case fatality rate was 91.8%.

The risk factors most closely associated with the development of NIs were mechanical ventilation (RR 4.4; 95%, CI 2.9-6.5), parentral feeding (amino venous) (RR 4.2; 95%, CI 3.08-5.85), umbilical catheter (RR 2.5; 95%, CI 1.8-3.5), prematurity (2.4; 95%, CI 1.5-3.9), weight less than 1500 g (RR 1.86; 95%, CI.0-2.08) and vaginal delivery (1.4; 95%, CI 1.04-1.85) use of naso-gastric tube (Ryle) (RR 1.3, 95%, CI 0.99-1.8), Transport outside NICU (RR 1.3, 95%, CI 0.97-1.8), (table3).

The incidence of nosocomial infections was high in the weight group 1000-less than 1500 (27.3%) & was 16.4% in females. The incidence of infections by both gender & birth weight was highest in both males & females in weight group 1000-less than 1500 (23.2% & 33%, respectively), (table 4).

The incidence of NIs was the highest in the preterm with (+) mechanical ventilation. As regard incidence of NIs by birth weight & mechanical ventilation, no difference in incidence between <1500 g (+) mechanical ventilation & those ≥1500 g (+) mechanical ventilation (25.4% & 24.9%), respectively (table 5).

Table (1): General results (characteristics) of admitted neonates at NICU in Pediatric Assiut University Hospital 2007-2008.

Characteristics	Number (990)	Percentage
Sex		
Male	618	62.4
Female	372	37.6
Weight (gm)		
< 1000	103	10.4
1000 -	260	26.3
≥ 1500	627	63.3
Preterm (premature)		
< 37 weeks	268	77.6
≥ 37 weeks	222	22.4
Number of births		
Single	703	71
Multiple	287	29
Type of Delivery		
Vaginal	458	46.3
Caesarean	532	53.7
Premature rupture of membranes (>24hs before delivery)		
Yes	188	19
No	802	81
Meconium stained amniotic fluid.		
Yes	29	2.9
No	961	97.1
Enteral feeding		
Yes	546	55.2
No	444	44.8
Ryle		
Yes	403	73.8*
No	143	26.2
Parentral feeding		
Yes	949	95.9
No	41	4.1
Mechanical ventilation		
Yes	521	52.6
No	469	47.4
Intravascular cannula (peripheral vascular catheter)		
Yes	624	63.0
No	366	37.0
Umbilical catheter		
Yes	563	56.9
No	427	43.1
Transport out side the NICU		
Yes	247	24.9
No	743	75.1
Out come		
Discharged	408	41.2
Died	582	58.8

* total=546

Table (2): Incidence of nosocomial infection

Incidence of nosocomial infection	
Total number of neonates included	990
Total patient days	6473
Neonates infected (Nosocomial infection)	158
Infected patients/100 neonates	16
Infected patients/1000 patient days	24.41

Table (3): characteristics of study neonates with or without nosocomial infection in NICU in pediatric AUH (2007-2008)

Characteristics (risk factor)	Nosocomial infections		Relative risk (95% CI)	
	Yes (n=158)	No. (n=832)		P
Gender				
Male	97 (61.4%)	521 (62.6%)	0.975 (0.71-1.28)	0.418
Female	61 (38.6%)	311 (37.4%)		
Preterm (prematurity)				
< 37	141 (89.2%)	627 (75.4%)	2.398 (1.48-.3.88)	0.000*
≥ 37	17 (10.8%)	205 (24.6%)		
Weight				
< 1500	82 (51.9%)	281 (33.8%)	1.86 (1.00-2.08)	0.000*
≥ 1500	76 (48.1%)	551 (66.2%)		
Number of birth				
Single	101 (63.9%)	602 (72.4%)	0.677 (0.47-.97)	0.02*
Multiple	57 (36.1%)	230 (27.6%)		
Type of delivery				
Vaginal	86 (54.4%)	372 (44.7%)	1.387 (1.04-1.85)	0.02*
Caesarean	72 (45.6%)	460 (55.3%)		
Premature rupture of membranes				
Yes	32 (20.3%)	156 (18.8%)	1.083 (0.76-1.54)	0.365
No	126 (79.7%)	676 (81.2%)		
Enteral feeding				
Yes	85 (53.8%)	461 (55.4%)	0.947 (0.71-1.26)	0.387
No	73 (46.2%)	371 (44.6%)		
Ryle				
Yes	75 (47.5%)	328 (39.4%)	1.316 (0.99-1.75)	0.04*
No	83 (52.5%)	504 (60.6%)		
Parentral feeding (amino venous)				
Yes	113(71.5%)	255 (30.6%)	4.224(3.08-5.85)	0.000*
No	45(28.5%)	577(69.4%)		
Mechanical ventilation				
Yes	131 (82.9%)	390 (46.9%)	4.368 (2.94-6.48)	0.000*
No	27 (17.1%)	422 (53.1%)		
Intravascular cannula peripheral vascular catheter				
Yes	102 (64.6%)	522 (62.7%)	1.068(0.79-1.44)	0.719
No	56 (35.4%)	310 (37.3%)		
Umbilical catheter				
Yes	121 (76.6%)	442(53.1%)	2.480 (1.76-3.51)	0.000*
No	37 (23.4%)	390 (46.9%)		
Transport outside NICU				
Yes	48 (30.4%)	199 (23.9%)	1.313 (0.97-1.78)	
No	110 (69.6%)	633 (76.1%)		0.05*
Outcome				
Discharged	13 (8.2%)	395 (47.5%)		0.000*
Died	145 (91.8%)	437 (52.5%)		

Table (4): Incidence of nosocomial infection by birth weight, gender &both

Characteristics	(N)	Infections (N)	Incidence
Birth weight			
< 1000	103	11	10.7%
1000 –	260	71	27.3%
≥ 1500	627	76	12.1%
Gender			
Male	618	97	15.7%
Female	372	61	16.4%
Male			
Less than 1000	47	6	12.8%
1000 –	151	35	23.2%
≥ 1500	420	56	13.3%
Total	**618**	**97**	**15.7%**
Female			
Less than 1000	56	5	8.9%
1000 –	109	36	33%
1500	207	20	9.7%
Total	**372**	**61**	**16.4%**

Table (5): Incidence of nosocomial infection by preterm (prematurity) & mechanical ventilation

	Mechanical ventilation	Subjects	Infections (No.)	Incidence
<37 ws	+	449	117	26.1%
	-	319	24	7.5%
≥ 37 ws	+	72	14	19.4%
	-	150	3	2.0%
Total		**990**	**158**	**16%**

DISCUSSION

Our study shows that one hundred and fifty eight (158) neonates developed nosocomial infections within 72 hs after admission. The cumulative incidence rate was 16 per 100 admitted neonates, incidence density was 24.45 neonates per 1000 patient days and the case fatality rate was 91.8%.

The incidence rate and incidence density rate of NI observed in Colombia

were 8.4 and 6.2%, respectively[18]. The rate of NI was 74.3 infections per 100 admissions and 2.7 infections per 100 patient-days.[19].

The incidence rate and the incidence density rate were 50.7% and 62 infections per 1000 patient-days[20]. The incidence is high and may be due to the population at risk that stayed more than 24 hrs. The incidence of infected newborns was 14.4 per 100 newborns and 0.9/100 days of stay[5].

Cumulative incidence rate for NIs was 30.3 neonates out of 100 admissions. The incidence density average was 10.2 neonates per 1000 patient days. The subjects were 489 neonates who were admitted to the NICU, survived longer than 72 hour[21].

The overall NI incidence rate observed (34%)[22]. is approximately the mean of the recently reported Brazilian incidence rates (18.9%[23], 50.7%[24], and 22%[25].

Different rates in different studies might be due to different methodologies, different durations of studies & different infection control measures in different NICUs.

Nosocomial infections contribute to increased mortality rates. Systemic infections presenting with septic shock, hypotension, decreased tissue perfusion, profound acidosis, and end-organ failure can lead to death. Mortality rates are reported to be from 13% to 50% in infants who develop NIs, specifically those with blood stream infections and meningitis[26]. The NICHD Neonatal Research Network reported the mortality rate for infants with any NI to be 18% as compared with an overall NICU infant mortality rate of 7%[3].

Our study shows that the risk factors most closely associated with the development of NIs were: Mechanical ventilation (RR 4.4; 95%, CI 2.9-6.5), Parentral feeding (amino venous) (RR 4.2; 95%, CI 3.08-5.85), Umbilical catheter (RR 2.5; 95%, CI 1.8-3.5), prematurity (RR 2.4; 95%, CI 1.5-3.9), weight less than 1500 g

(RR 2.1; 95%, CI 1.5-2), vaginal delivery (RR 1.4; 95%, CI 1.04-1.85), use of naso-gastric tube (Ryle) (RR 1.3, 95%, CI .99-1.8), Transport outside NICU (RR 1.3, 95%, CI .97-1.8) & identified several modifiable risk factors associated with NIs, Mechanical ventilation, Parentral feeding (amino venous), umbilical catheter, use of naso-gastric tube (Ryle) & transport outside NICU.

Our study shows that mechanical ventilation was the most important risk factor. In pediatric populations, the pathogenesis of VAP is not well studied but because neonates have unique characteristics predisposing them to nosocomial infections. These patients' immature immune systems place them at increased risk for infection. Skin and mucous membranes are more permeable and are less effective barriers to infection. Abnormal granulocyte migration and bacterial digestion in these patients have been demonstrated.

The risk factors were associated with NIs (P <0.05): birth weight, gestational age, mechanical ventilation, total parenteral nutrition & umbilical catheter[20] which concurs with our result.

The following factors were independently associated with sepsis: umbilical catheterization, both through the vein and the artery, mechanical ventilation; birth weight equal to or less than 2500 g; nasogastric tube & total parenteral nutrition[5].

The factors associated with NIs were birth weight less than 1500 g, and gestational age less than 32 weeks[21].

The onset of a HAI was strongly associated with a low gestational age and the presence of an intravascular catheter. HAIs frequently complicate hospitalization in NICUs and are associated with increased mortality[27].

The risk factors most closely associated with the development of NI were birth weight less than 1000 g (RR 1.8;

95% CI 1.0-2.1), umbilical arterial catheterization (RR 5.7; 95% CI 1.1-28.5), and parenteral nutrition (RR 2.4; 95% CI 1.2-4.6) [19].

Birth weight <1500 g and exposure to parenteral nutrition, percutaneous catheter, central venous catheter and mechanical ventilation are independent risk factors for NICU-acquired infections[22].

Use of central catheters is considered a major risk factor for NI[2,3,18].

Our observation that naso-gastric tube feedings are a risk factor for NIs concurs with[18]. Use of naso-gastric tubes for enteral nutrition may produce damage to the gastric mucosa directly, disrupting a natural barrier against infection. It is also possible that the apparent risk of feeding through a naso-gastric tube results from contamination of infant formulas with pathogens during their manual preparation. Owing to the higher cost of ready-to-administer infant formulas, as in our NICU prepared formulas manually using powdered milk. In Nurses not using sterile gloves and facemasks during the preparation of formulas; the potential for contamination secondary to human error still exist.

We conclude that variation in clinical practices, either because of the requirements of the patient population or because of choices made by care providers, is the major contributor to the variation in risk between institutions.

Our study shows that incidence of nosocomial infections was high in the weight group 1000-less than 1500 9 (27.3%) & was 16.4% in females.

The incidence of infections by both gender & birth weight was highest in both males & females in weight group 1000-less than 1500 g (23.2% & 33%), respectively. Numerous studies have indicated that the risk of nosocomial infection increases with decreases in birth weight, and that birth weight was the most important risk factor[2,10],[28],[29] and this concurs with our

study. However, the incidence of nosocomial infection is very different among these studies. For example, the incidence of infections in the birth weights groups. In the boys, the incidence of infections was 32.7% in the birth weight group of less than 1,000 g, 11.1% in the birth weight group of 1,000-1,499 g, and 4.2% in the birth weight group of more than 1,500 g. In the girls, it was 15.9% in the birth weight group of less than 1,000 g, 4.9% in the birth weight group of 1,000-1,499 g, and 3.1% in the birth weight group of more than 1,500 g. In both genders combined,it was 25.2% in the birth weight group of less than 1,000 g, 8.4% in the birth weight group of 1,000-1,499 g, and 3.7% in the birth weight group of more than 1,500 g[(29)].

Our study shows that the incidence of NIs was the highest in the preterm with (+) mechanical ventilation because preterm & mechanical ventilation were important risk factors.

As regard incidence of NIs by birth weight & mechanical ventilation, no difference in incidence between <1500 g (+) mechanical ventilation & those ≥1500 g (+) mechanical ventilation (25.4% & 24.9%), respectively.

CONCLUSION

In summary, this study has identified important modifiable risk factors for NIs. .Interventions aimed at reducing the effects of these risk factors may have the potential to decrease associated mortality, and costs of neonatal care.

Efforts to control the incidence of infection should be aimed at preventable factors, in many cases associated with external or invasive medical devices, principally through restricted use and early withdrawal, the use of adequate antiseptic techniques during insertion, manipulation, and maintenance, limiting parenteral nutrition, early feeding & decrease use of

ryle, and minimize transport outside unit.

Adopting a structured strategy that changes unit practices to address those risks, and evaluating the impact of the newly adopted strategies by tracking infection and organisms, the incidence of NIs in the neonatal population can be reduced.

The whole team in the NICU must follow infection control measures, our results strongly suggest the need to improve losing sight of the fact that the single most important and simplest of these measures is frequent hand washing.

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