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Original Article

The Study of Nosocomial Infections in Neonatal Intensive Care Unit: A Prospective Study in Northwest Iran

Mohamad Bagher Hoseini[1], *BabakAbdinia[2], Mohammad Ahangarzadeh Rezaee[3], Shahram Abdoli Oskouie[1]

[1]Associate Professor, Pediatric Health Resarch Center,Tabriz University of Medical Sciences, Tabriz, Iran.
[2]Assistant Professor, Pediatric Health Resarch Center,Tabriz University of Medical Sciences, Tabriz, Iran.
[3]Associate Professor, Department of Microbiology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.

Abstract

Background:
Nosocomial infections are an important cause of mortality in neonatal intensive care units (NICUs). Therefore, in this study, the incidence and prevalence of nosocomial infections were determined in NICUs of the three largest neonatal centers in northwest Iran, and the causative bacteria were identified in order to provide potential solutions to control the infections in these hospitals.

Materials and Methods:
This is a descriptive-prospective study in which the cases of nosocomial infections were examined in the three largest hospitals in Tabriz city in northwest Iran, during one year (from June 2012 to May 2013) based on clinical findings, medical and nursing reports of patients, and laboratory results.

Results:
Of the 3129 patients hospitalized in NICUs of the three hospitals, 208 patients were diagnosed with nosocomial infections. The incidence rate of nosocomial infections was 11.34% (per 100 patient-days) with: 52.4% bacteremia, 32.69% pneumonia, 5.77% urinary tract infections, 5.29% wound infections, and 3.85% necrotizing enterocolitis. There was a statistically significant relationship between invasive procedures (such as umbilical catheters, central venous catheters, surgery, and TPN) and sepsis (P=0.001).The relationships between urinary tract infection and urinary catheter (P=0.000), and aggressive procedures (such as suctioning and intubation) and pneumonia (P=0.001) were also statistically significant.

Conclusion:
Incidence of nosocomial infections in premature and low birth weight newborns is considered as a health threat. The findings of this research reiterate the importance of giving further attention to prevention and control of nosocomial infections in the NICU.

Keywords: Infections, Neonatal intensive care unit (NICU), Nosocomial.

***Corresponding Author:**
Dr. Babak Abdinia, Pediatric Health Resarch Center, Tabriz University of Medical Sciences, Tabriz, Iran.
Email: babdinia@yahoo.com
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Introduction

Nosocomial infections are a major problem for hospitalized patients due to increasing duration of hospitalization and costs of treatment (1). These infections make the treatment of patients difficult due to increasing mortality and morbidity particularly in NICUs (2,3). Nosocomial infections may involve any organ; however, blood, urinary tract, surgical wounds, and the lower respiratory tract are more frequently involved as compared with other organs. Various factors such as prematurity, low weight, prolonged hospitalization, use of broad-spectrum antibiotics, and particularly the use of invasive procedures such as intubation, ventricular shunt, intra-vascular catheter, and parenteral nutrition with fat emulsions facilitate the development of such infections, and increase their incidence (4-6). Prevention and control of nosocomial infections in NICUs will not be possible without identifying the current status of these infections and their predisposing factors. There are numerous reports from around the world, and also from each individual country's hospitals, on the status of these infections (7).An effective strategy should be implemented in every hospital to prevent nosocomial infection. This strategy should comprise of the following items: continuous care and monitoring of the infection and type of the organism, emphasis on careful hand washing, minimal use of central veins catheters, treatment of people carrying the disease, wise and prudent use of antimicrobial drugs (8), arranging training programs and providing feedback to staff, and adequate nursing (9). Therefore, to identify the current status of nosocomial infections, this study examined the incidence and prevalence of these infections in NICUs of the three largest neonatal centers in northwest Iran, and also identified the causative bacterial agents, in order to provide potential solutions to control the infections in these hospitals.

Materials and Methods

This is a descriptive-prospective study in which nosocomial infections were studied in the three largest hospitals in Tabriz (Children's, Al-Zahra, and Taleghani Hospitals) in northwest Iran during one year (from June 2012 to May 2013) based on Iranian national nosocomial infection surveillance (NNIS) system definitions (10), a collection of clinical findings, medical and nursing reports of patients, and laboratory results. Screening forms were completed for all newborns that were admitted in the NICU for 48 hours or longer, based on standard definitions for raised nosocomial infections. Screening forms were composed of four main parts:

1) Nosocomial infection is defined as a limited or diffuse infection following hospitalization, which is caused by infectious agents or toxic reactions, and the infection lasts for at least 48 hours after admission till the patient is discharged. Based on NNIS system definitions, nosocomial infections were divided into five groups, including bloodstream infections (BSI), pneumonia, urinary tract infections, surgery wound infections, and necrotizing enterocolitis.

2) Information about demographic data of neonate.

3) Information about the patient's daily reports in the unit including any changes in vital signs, especially fever during hospitalization; underlying diseases and their severity; location of infection, nosocomial infection signs, timeframe for onset of infection after birth; types of manipulations performed on the infant during hospitali-zation, including catheterization, surgery, intubation, etc; and information about starting antibiotic treatments in the ward.

4) Information about laboratory findings including the type of isolated bacteria, antibiogram, date and place of sampling, and other experimental and paraclinical tests. Standard and similar methods were

used for the analysis and culture of specimens in the three hospitals. All personnel were trained for performing blood cultures and sending them from other parts. The same protocols were implemented in the three hospitals.

The supernatant was removed and the sediment was cultured on 5% sheep blood agar and chocolate agar plates using standard techniques and also used for Gram staining. All isolates were identified on the basis of their colony, morphology, culture characteristics, and their biochemical reactions according to standard procedures without culture for anaerobes. In order to prevent between contamination and true positive cultures, in the absence of clinical symptoms and laboratory findings conformity, samples culture was repeated.

All isolates were examined for resistance to routine antimicrobial agents by standard disk diffusion method using *Staphylococcus aureus* (ATCC 25923) and *Escherichia coli* (ATCC 25922) as control strains (11). The antibiotics tested were gentamicin, amikacin, ceftazidime, ceftizoxime, cefotaxime, ceftriaxone, imipenem, ciprofloxacin, co-trimoxazole, chloramphenicol, penicillin, oxacillin, ampicillin, vancomycin, rifampicin and erythromycin (Mast Company, Merseyside, UK).

The infection control team examined any clinical signs and all infection sites on a daily basis, and took culture samples by sterile aspiration from endotracheal tube discharges at the beginning of intubation, and also every week or whenever there were signs of suspected pneumonia. In cases of vascular catheters, culture samples were taken from blood and the catheter if suspected symptoms of sepsis were present. All infants until 48 hours after discharge, premature infants until completion of 44 weeks of gestational age, and in surgical cases 30 days post-operation with over 48 days after their admittance in the NICU were checked for nosocomial infections. After the infection was confirmed, detailed information of nosocomial infection cases was recorded and the prevalence and incidence of nosocomial infection in the NICU were identified monthly.

Nosocomial infections were divided into five groups, including BSI, pneumonia, urinary tract infections, surgical wound infections, and necrotizing enterocolitis. According to control practitioner and standard definitions, if the neonatal nosocomial infection did not fall under any of these five groups, it was excluded from the study. This study was conducted with parental consent and ethics committee approval. Data were analyzed using SPSS software version 13and ($P<0.05$) was considered to be statistically significant.

Results

During the study period, from a total of 3129 patients hospitalized in NICUs of the three hospitals, 208 patients were diagnosed with nosocomial infections.

The incidence rate of nosocomial infections was 11.34% (per 100 patient-days) in the present study. Of the 208 affected newborns, 134 patients (64.4%) were males and 73 patients (35.1%) were females and one patient's gender (0.5%) was unknown. 50 patients (24%) were delivered vaginally and 158 patients (76%) were born by cesarean section. Birth weight distribution was as follows: 20 patients (9.6%) were less than 1000 g, 52 patients (25%) were 1000–1500 g, 60 patients (28.8%) were 1501–2500 g, and 76 patients (36.5%) were over 2500 g.

Minimum and maximum gestational ages were 25 and 40 weeks, respectively with an average of (34.6 ±4.81) weeks. The lowest and the highest age of the newborns at the time of admission were one day and 40 days, respectively, with an average of 9.5 ± 5.8 days. 133 patients (63.9%) were discharged, and 75 patients (36.1%) had died (Table. 1).

Table 1: Demographic data of neonate with nosocomial infections.

Demographic data	
All	n=208
Gender	Male: n=134 (64.4%) Female: n=73 (35.1%)
Out Come	Dischargen=133 (63.9%) Death: n=75 (36.1%)
Age	Min: 1 day Max: 40 days Mean: 9.5 ± 5.8 day
Birth weight	<1000 g: n=20 (9.6%) 1000-1500 g: n=52 (25%) 1501-2500g: n=60 (28.8%) >2500 g n=76 (36.5%)
Reproductive age	< 25 w >40 W Mean: 34.6±4.81
Delivery Type	Cesarian: n=158(76%) NVD*n=50(24%)

* Normal vaginal delivery

Among the study patients, 67 patients (32.2%) had urinary catheters, 171 patients (82.2%) were intubated, 92 patients (44.2%) had central venous catheters, 57 patients (27.4%) had umbilical catheters, 154 patients (74%) received parenteral alimentation, and 91 patients (43.8%) underwent surgery.

Bacteremia, pneumonia, urinary tract infections, wound infections, and necrotizing enterocolitis were observed in 52.04%, 32.69%, 5.76%, 5.28%, and 3.84% of the patients, respectively (Table 2).

Table2: Frequency of microorganisms isolated from neonates with nosocomial infections

Frequency of microorganisms isolated in neonates with bloodstream infections		
microorganisms	Frequency	percent
Coagulase-negative Staphylococcus	41	19.7%
klebsiella	36	17.3%
Candida	11	5.3%
Staphylococcus aureus	4	1.9%
E. coli	3	1.4%
S. Viridans	2	1%
Gram-negative bacilli	2	1%
Enterobacter	2	1.4%
Frequency of microorganisms isolated in infants with urinary tract infection		
Candida	7	3.4%
E. coli	3	1.4%
Gram-negative bacilli	3	1.4%
klebsiella	2	1%
Frequency of microorganisms isolated in infants infected with pneumonia		
psudomonas	11	5.35
klebsiella	14	6.7%
Acinetobacter	20	9.6%
E. coli	5	2.4%
Candida	3	1.4%
Serratia	1	0.5%
Gram-negative bacilli	1	0.5%
Frequency of microorganisms isolated from neonates with surgical wound infection		
Enterobacter	1	0.5%
klebsiella	1	0.5%

There was a statistically significant relationship between the invasive procedures (such as umbilical catheter, central venous catheter, surgery, and TPN) and sepsis (P=0.001). Also, there was a significant relationship between urinary tract infection and urinary catheter (P=0.000), and between invasive procedures (such as suctioning and intubation) and pneumonia (P=0.001). Incidences of sepsis and

pneumonia in newborns weighing 1000–2500 g were 54.5% and 37.3%, respectively, which was statistically significant (P=0.001).

The organisms isolated most commonly from blood cultures of patients were 41 cases (19.7%) of *coagulase-negative staphylococcus*, 36 cases (17.3%) of *Klebsiella pneumoniae*, 11 cases (5.3%) of *Candida*, and four cases (1.9%) of *Staphylococcus aureus*. Organisms isolated from urine cultures included seven cases (3.4%) of *Candida*, three cases (1.4%) of *Escherichia coli* and non-fermentative gram-negative bacilli. Organisms isolated from cultures of endotracheal secretions were 20 cases (9.6%) of *Acinetobacter*, 14 cases (6.7%) of *Klebsiella*, and 11 cases (3.5%) of *Pseudomonas*. According to (Table 3), the highest antibiotic resistance was seen against erythromycin, oxacillin, clindamycin, and gentamicin in gram-positive bacteria, and against gentamicin, cephalexin, ceftazidime, ceftriaxone, ceftizoxime, cefotaxime, and cefixime in gram-negative bacteria. The most effective antibiotics were imipenem, ciprofloxacin, and vancomycin for gram-positive bacteria, and imipenem, ciprofloxacin, and chloramphenicol for gram-negative bacteria (Table. 4).

Table3: Antibiotic susceptibility of bacteria isolated from blood cultures.

Antibiotics	Acinetobacter		Ecoli		Klebsiella		Staphylococcus aureus		CoNS	
	S	R	S	R	S	R	S	R	S	R
Erythromycin	-	-	-	-	-	-	۰	2 (100%)	1 (6.2%)	15 (93.8)
Oxacillin	-	-	-	-	-	-	۰	2 (100%)	1 (6.2%)	15 (93.8%)
Amikacin	۰	1 (100%)	2 (100%)	۰	44 (36.4%)	6 (54.5%)	1 (50%)	1 (50%)	5 (31.2%)	11 (68.8%)
Imipenem	1 (100%)	۰	۰	2 (100%)	10 (90.9%)	۰	۰	1 (%۵۰)	۰	۰
Penicillin	-	-	-	-	-	-	۰	2 (100%)	1 (6.2%)	13 (81.2%)
Gentamycin	1 (100%)	۰	۰	2 (100%)	1 (9.1%)	9 (81.8%)	۰	2 (100%)	2 (12.5%)	14 (87.5%)
Rifampin	-	-	-	-	1 (9.1%)	1 (9.1%)	1 (50%)	1 (50%)	8 (50%)	7 (43.8%)
Ceftazidime	۰	1 (100%)	۰	2 (100%)	1 (9.1%)	9 (81.8%)	-	-	۰	2 (12.5%)
Ceftriaxone	۰	1 (100%)	۰	2 (100%)	1 (9.1%)	9 (81.8%)	۰	2 (100%)	1 (6.2%)	14 (87.5%)
Ceftizoxim	۰	1 (100%)	۰	2 (100%)	1 (9.1%)	9 (81.8%)	۰	2 (100%)	1 (6.2%)	15 (93.8)
Cefotaxime	۰	1 (100%)	۰	2 (100%)	1 (9.1%)	9 (81.8%)	۰	2 (100%)	1 (6.2%)	15 (93.8)
Ciprofloxacin	1 (100%)	۰	۰	2 (100%)	11 (100%)	۰	۰	2 (100%)	6 (37.5%)	10 (62.5%)
Chloramphenicol	۰	1 (100%)	2 (100%)	۰	9 (81.8%)	1 (9.1%)	1 (50%)	1 (50%)	11 (68.8%)	5 (31.2%)
Clindamycin	-	-	-	-	-	-	۰	2 (100%)	۰	16 (100%)
Trimetoprim-sulfametoxazol	۰	1 (100%)	۰	2 (100%)	6 (54.5%)	4 (36.4%)	۰	2 (100%)	1 (6.2%)	15 (93.8)
Vancomycin	-	-	-	-	-	-	2 (100%)	۰	14 (87.5%)	1 (6.2%)

CoNS: *Coagulase-negative Staphylococcus*

Table4: Antibiotic susceptibility of bacteria isolated from the endotracheal tube.

Antibiotics	Ecoli		Acinetobacter		klebsiella		pseudomonas	
	S	R	S	R	S	R	S	R
Amikacin	2 (40%)	3 (60%)	13 (65%)	7 (35%)	2 (16.7%)	10 (83.3%)	8 (72.2%)	2 (18.2%)
Imipenem	.	5 (100%)	1 (5%)	16 (80%)	8 (66.7%)	4 (33.3%)	3 (27.3%)	6 (54.5%)
Tobramycin	.	.	.	2 (10%)	.	.	2 (18.2%)	6 (54.5%)
Gentamycin	.	4 (80%)	6 (30%)	14 (70%)	.	12 (100%)	3 (27.3%)	7 (63.6%)
Ceftazidime	.	5 (100%)	.	20 (100%)	.	12 (100%)	1 (9.1%)	9 (81.8%)
Ceftriaxone	.	5(100%)	.	20 (100%)	.	12 (100%)	1 (9.1%)	9 (81.8%)
Ceftizoxim	.	5 (100%)	.	20 (100%)	.	12 (100%)	.	9 (81.8%)
Cefotaxime	.	4 (80%)	.	20 (100%)	.	12 (100%)	.	10 (90.9%)
Ciprofloxacin	.	5 (100%)	1 (5%)	19 (95%)	7 (58.3%)	5 (41.7%)	4 (36.4%)	7 (63.6%)
Chloramphenicol	5 (100%)	.	1 (10%)	18 (90%)	10 (83.3%)	2 (16.7%)	1 (9.1%)	9 (81.8%)
Trimetoprim-sulfametoxazol	4 (80%)	1 (20%)	1 (5%)	19 (95%)	3 (25%)	9 (75%)	.	9 (81.8%)

Discussion

This study attempted to determine the incidence of nosocomial infections in NICUs of hospitals to identify their underlying causes, and provide guidelines for prevention of nosocomial infections within these hospitals.

In this study, we found that the incidence of nosocomial infections in NICUs of three major hospitals in northwest Iran was 11.34%. In Tehran, this incidence was reported to be 9.3% in previous years by Barak et al (12). According to various studies (13) the incidence of infection varies based on birth weight, underlying diseases, medical facilities, and mode of care in different centers. According to reports from other parts of the world, the incidence of nosocomial infections differs within different regions. In the United States, the incidence of nosocomial infections in NICUs was 12%–26.5% based on patients' status (14). Studies conducted in NICUs in Europe have shown that 11.4% of patients were affected by one of the nosocomial infections, which included septicemia (bloodstream infections) (6/52%), lower respiratory tract infections (12.9%), ear, nose, and throat infections (8.6%), and urinary tract infections (8.6%), respectively(15,16) In general, the incidence of nosocomial infections depends on various factors, particularly characteristics of admitted patients such as prematurity, premature rupture of membrane, respiratory distress syndrome, respiratory failure, convulsions, cyanosis, and underlying diseases in mothers such as malnutrition. Additionally, infants who are given intravenous feeding, especially newborns with central venous catheters, are more

exposed to circulatory system infections (17,18). In this study, nosocomial infections were predominantly found in males. Furthermore, our study revealed a significant association between invasive procedures (such as umbilical catheter, central venous catheter, surgery, and total parenteral nutrition (TPN)) and sepsis; urinary catheter and urinary tract infection; and invasive procedures (such as suctioning and intubation) and pneumonia. Therefore, risk factors and invasive procedures are the main causes of neonatal infections. Among the microorganisms isolated from culture samples in our study, the most prevalent germs were Klebsiella pneumoniae, coagulase-negative staphylococcus, Acinetobacter, and Candida. Also, the most common organism isolated from blood was *coagulase-negative staphylococcus*. However, the most common bacterium causing nosocomial infections in NICUs varies greatly with time and in different parts of the world. For instance, in Pakistan a study showed that the most prevalent bacterium causing nosocomial infection in neonatal ward in 1991 was *Klebsiella*, but this bacterium was much lower in 2003, as reported in another study (18-20). While bacteria such as *Listeria monocytogenes* and *Streptococcus group B* were not reported in our study, these bacteria are listed as important pathogens in other countries except Iran (21-22). It is not clear whether these bacteria are prevalent in our country or they are not detected due to lack of suitable techniques required for their isolation from patients. In several studies on nosocomial infections in NICUs in hospitals, the most common causative bacterium of nosocomial infections was *coagulase-negative staphylococcus (*23). In the present study, among the commonly isolated germs, *coagulase-negative staphylococcus* and *S. aureus* were resistant to erythromycin, oxacillin, and clindamycin, and were highly sensitive to vancomycin, imipenem, and ciprofloxacin. Ni-Chung Lee et al. also reported that *S. aureus* and *coagulase-negative staphylococcus* were 95% resistant to oxacillin (24). Gram-negative bacteria were resistant to third-generation cephalosporins, cotrimoxazole, and amikacin, and were highly sensitive to imipenem, ciprofloxacin, and chloramphenicol, which is consistent with the results of studies conducted in Brazil and Tehran (25,26).

Conclusion

In this study, we found that the incidence of nosocomial infections in NICUs of three major hospitals in northwest Iran was 11.34%. The findings of this research show the importance of paying close attention to the control and prevention of nosocomial infections in NICUs, and emphasize on using more stringent methods by the personnel working in this ward, such as good personal hygiene, and more importantly, frequent hand washing, use of sterile gloves, and using aseptic conditions for invasive procedures and wound care. Incidence of nosocomial infections in wards, and in premature and low-weight neonates is considered to be a major health threat. Therefore, the programs and policies of the hospital-acquired infections care system should include: 1- Observation of hand hygiene principles, using aseptic techniques in invasive procedures, improving physical space, and observation of standard precautions. 2- Usage of human milk and initiation of oral feedings. 3-Reduction of laboratory testing that causes skin damage. 4- Development of a method to differentiate between contaminations and true-positive cultures. 5- Reduction of intubation days and usage of central lines. 6- Encouragement of teamwork to appreciate those responsible for outcomes. Moreover, due to the changing nature of

microbial agents and drug sensitivity patterns in different regions, an annual review would be helpful in determining the strains involved in nosocomial infections and the drug sensitivity patterns in order to facilitate selection of the appropriate antibiotic for experimental treatments.

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