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Bacterial Infections and Relevant Factors in Neonates Hospitalized at Intensive Care Unit

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ABSTRACT

Background: Among the most common causes of death in preterm infants are neonatal infections, which remain high despite antibiotic therapy and preservative measures. The control of hospital infections is now a global priority, and many factors contribute to the spread of these infections. This study aimed to determine the frequency of bacterial infections in neonates and identify the common causes of infection in neonates admitted to the neonatal intensive care unit (NICU) of Alzahra Hospital in Isfahan, Iran.

Methods: In this cross-sectional study, the population consisted of all neonates who were admitted to the NICU of Al-Zahra Hospital in Isfahan, Iran, from April 2017 to March 2018. Neonates who had a positive culture (blood, cerebrospinal fluid, urine, eye discharge, and tracheal tube secretions) were enrolled. The data were collected by a structured questionnaire, including maternal and neonatal information.

Results: In this study, 56 newborns admitted to the NICU of Alzahra Hospital in Isfahan were studied. Their age range was within 5-28 days (18.88±8.41). Thirty-two (57.1%) neonates were male, and 24 (42.9%) newborns were female. In total, 26 (46.4%) neonates had prematurity that was the most common reason for hospitalization. The most isolated microorganisms were *Staphylococcus epidermidis*, *Enterococcus*, *Klebsiella*, *Enterobacteriaceae*, *Candida* spp., *Acinetobacter*, *Streptococcus pneumoniae*, *E. coli*, and *Streptococcus viridans*, respectively.

Conclusion: According to the results of this study, the frequency of nosocomial infections in the NICU of Alzahra Hospital in Isfahan was 7.4%. The findings of this study highlighted the importance of paying more attention to controlling and preventing hospital infections in NICUs.

Keywords: Bacterial infection, Neonate, NICU

Introduction

Among the most common causes of death in premature newborns are neonatal infections, for which there is no effective antibiotic therapy. Preterm infants, especially at gestational age under 34 weeks have a relative immunodeficiency (2). The prevalence rate of bacterial infections in newborns is up to 10%, and in cases of prematurity, it is higher. Prolonged hospitalization and mechanical ventilation are risk factors for infection in premature neonates (2-4).

In developing countries, many deaths occur in newborns under 2 months, and almost all cases are due to acute pneumonia (5, 6). In developing countries, the most common causes of pneumonia in children are *Streptococcus pneumoniae* and other respiratory syncytial viruses (i.e., *pneumococcus*), *Hemophilus influenzae*, *Mycobacterium tuberculosis*, *Staphylococcus aureus*, and gram-negative bacteria (7-9).

The lack of opsonizing antibodies can lead to dangerous bacterial infections, such as group B *streptococcus*, *E. coli*, influenza type b, and

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Streptococcus pneumoniae, in a newborn. Humoral immune deficiency and the gestational age have an inverse association; accordingly, in neonates with a birth weight of 999-600 g, the risk of infection is higher than 86% in comparison to the newborns with a weight above 2500 g (10, 11).

The control of nosocomial infections is now a global priority, and many factors cause the spread of these infections. Worldwide, 4,000,000 neonates expire annually, 25% of which is due to sepsis (12). Among neonatal infections in the United States, the frequencies of bacteremia, respiratory infections, soft tissue ulcer infection, central nervous system infection, and genitourinary tract infection are 33.6%, 26.9%, 5.9%, 5.3%, and 4.1%, respectively. In the same country, the most common cause of septicemia is *Staphylococcus aureus* and *Streptococcus* (13).

In different regions, the infection pathogen varies. For example, in Pakistan, the most common cause of neonatal infections was *Klebsiella* in 1991, which is shown to cause a relatively lower incident of infection due to a 2003 study. However, the most common reported cause of infection in the United States was coagulase-negative *staphylococci* (14). In this regard, 11.4% of infections in Saudi Arabia were in the neonatal ward, and the most common cause was gram-negative microorganisms (15).

In a 2007 study in New York, the most common cause of infections in newborns was gram-positive bacteria (77.1%) (16). In another study, ventilator-induced pneumonia was associated with 8.8% to 32.3% of hospital infections and birth weight of the newborn (17). In a study conducted in Mashhad, Iran, in 2008, the most common bacterial pathogen causing hospital infection was mutated *Coagulase Staphylococcus aureus*, followed by *Klebsiella pneumoniae* (18). Also, Darvispour et al. in a study in 2010 investigated the cases of nosocomial infections and their associated factors in the neonatal intensive care unit (NICU). Among a total of 270 cases of hospitalization, 44 cases (16.29%) were diagnosed with nosocomial infections. Micro-organisms isolated from blood cultures were *Enterobacter* and *Klebsiella* spp. (19).

Since nosocomial infections increase the mortality rate and duration of hospitalization in the NICU, it is one of the main problems of hospitalization, and its prevention and control require sufficient information on the epidemiology of these infections (18). This study aimed to determine the frequency of bacterial infections, in particular, the infections of the respiratory tract in neonates, and identification of its common causes in controlling and preventing infection in the infants admitted to the intensive care unit of Alzahra Hospital in Isfahan.

Methods

In this descriptive-analytic cross-sectional study, 759 newborns admitted to the NICU of Alzahra Hospital in Isfahan, Iran, from March 2017 to February 2018 were evaluated. A total of 56 neonates (i.e., 32 boys and 24 girls with the mean age of 8.41±18.88 days) with a positive culture in their body fluids were identified as hospital infection. The inclusion criteria were newborns who were hospitalized and up to 48-72 h later diagnosed with nosocomial infections in any body fluid sample cultures (blood, cerebrospinal fluid, urine, eye discharge, and tracheal secretion), aged between 5 and 28 days.

The data of these newborns, such as gender, prematurity, type of birth (i.e., cesarean section or vaginal delivery), polygamy, birth weight, duration and cause of hospitalization, physical findings, initial diagnosis, and treatment measures, were evaluated.

Statistics

The statistical data was extracted using SPSS software (version 24). Qualitative and quantitative variables were presented based on the number (i.e., percentage) and mean±standard deviation, respectively. Data analysis was performed with the Chi-Square test and analysis of variance.

Results

Out of 56 patients, 14 cases (25%) were born by vaginal delivery. There was no significant difference between the boys and girls in term of age and delivery type (P>0.05). The mean scores of gestational age, maternal age, neonatal weight at birth, and duration of hospitalization were 227.88±24.57 days, 5.71±30.21 years, 711.02±1802.16 g, and 19.07±31.30 days, respectively. There was no significant difference between the boys and girls in terms of mean scores of gestational age, maternal age, neonatal weight at birth, and duration of hospitalization (P>0.05).

The mean scores of the duration of using IV-line, nasal continuous positive airway pressure (NCPAP), urinary catheter, oxygen hood, nasogastric tube (NGT) (20), and intubation were 14.42±21.41, 2.88±3.41, 0.77±2.44, 4.35±5.02, 0.86±2.86, and 1.79±4.59 days, respectively. There was no significant difference between the boys

and girls in terms of the mean scores of the duration of using IV-line, NCPAP, urinary catheter, oxygen hood, NGT, and intubation (P>0.05). The mean scores of the duration of antibiotic treatment and surgical interventions were 7.80±3.49 and 9.32±2.75 days, respectively. There was no significant difference between the boys and girls in terms of the mean scores of the duration of antibiotic treatment and surgical interventions (P>0.05).

The most observed congenital malformation was patent ductus arteriosus (PDA) associated with 6 cases (10.7%). Other malformations observed in the face and skull, chromosomal problems, and vague genitals were reported with one case. Also, the premature rupture of the amniotic membrane has been reported in 8 (14.3%) patients. The amniotic fluid of 9 (16.1%) cases was contaminated with meconium. In the evaluation of maternal medical history, the prevalence of hypothyroidism was the highest observed in 12 (21.4%) cases, followed by pregnancy-induced hypertension (PIH) in 7 cases (12.5%; Table 1). There was no significant difference between the boys and girls in terms of congenital malformation, premature rupture, meconium amniotic fluid, and maternal medical history (P>0.05).

Oxygen hood and NCPAP were the most frequently used devices in 43 (76.8%) and 42 (75%) subjects, respectively. Twelve newborns (21.4%) were intubated, 6 cases had a urinary catheter (10.7%), and one patient (1.8%) had a central venous catheter. The reasons for hospitalization were premature delivery in 26 (46.4%) cases with the highest frequency, followed by respiratory distress syndrome in 10 (17.9%) subjects, and cyanosis or respiratory disease in 7 (12.5%) patients.

The interventions included colostomy, quantic atresia surgery, chest tube insertion, computed tomography angiography, inguinal hernia surgery, and thoracentesis, each of which was performed on a newborn. The most frequent sampling sites were the blood and eye in 14 (25%) and 13 (23.2%) cases, respectively (Table 2). There was no significant difference between the boys and girls in terms of these characters (P>0.05).

The results of the cultures based on the indication of hospitalization showed that the highest percentage of *Staphylococcus epidermidis* (9 cases) was in premature neonates and the highest frequencies of *Enterococcus* were in prematurity and respiratory distress syndrome (3 cases). The highest bacterial resistance observed in antibiotics was ceftazidime in 15 (26.8%) cases, tetracycline and penicillin each in 11 (19.6%) subjects, oxacillin in 9 (16.1%) cases, and clindamycin and erythromycin each in 6 (10.7%) subjects.

Table 1. Congenital malformations and maternal history

Variable		Patients n (%)
Congenital malformations	Patent ductus arteriosus	6 (10.7)c
	Ambiguous genitalia	1 (1.8)
	Craniofacial	1 (1.8)
	Chromosomal disorder	1 (1.8)
	18 trisomy	1 (1.8)
	Intrauterine growth restriction	1 (1.8)
	Other	1 (1.8)
Premature rupture of amniotic membrane (more than 18 h)		8 (14.3)
Meconium contaminated amniotic fluid		9 (16.1)
Maternal disease history	Hypothyroidism	12 (21.4)
	Pregnancy-induced hypertension	7 (12.5)
	Gestational diabetes	4 (7.1)
	Hypothyroidism and Pregnancy-induced hypertension	2 (3.6)
	Hypothyroidism and Gestational diabetes	1 (1.8)
	Hypothyroidism, Pregnancy-induced hypertension, and Gestational diabetes	2 (3.6)

Table 2. Bacterial type based on sampling source

Variable		*Staphylococcus epidermidis*	*Streptococcus pneumoniae*	*Acinetobacter*	*Escherichia coli*	*Enterobacteriaceae*	*Enterococci*	*Klebsiella*	*Candidate species*	*Streptococcus viridans*	P-value
		n (%)									
Sampling site	Eye	6 (40.0)	1 (100.0)	0 (0.0)	1 (100.0)	2 (66.7)	1 (14.3)	2 (50.0)	0 (0.0)	0 (0.0)	0.001>
	Tracheal or endotracheal tube	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (33.3)	2 (28.6)	1 (25.0)	0 (0.0)	0 (0.0)	
	Blood	9 (60.0)	0 (0.0)	2 (100.0)	0 (0.0)	0 (0.0)	2 (28.6)	0 (0.0)	0 (0.0)	1 (100.0)	
	Urine	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (28.6)	1 (25.0)	3 (100.0)	0 (0.0)	
All samples		15 (40.5)	1 (2.7)	2 (5.4)	1 (2.7)	3 (8.1)	7 (18.9)	4 (10.8)	3 (8.1)	1 (2.7)	

The most commonly used antibiotics were ampicillin + gentamicin in 18 (32.2%) subjects, as well as ampicillin + gentamicin + cefotaxime, ampicillin + amikacin + cefotaxime, ampicillin + amikacin, and ampicillin + gentamicin + cefotaxime each one in 6 (10.7%) cases. There was a significant difference between the bacterial type and sampling site (P<0.001)

Discussion

The present study aimed to determine the frequency of hospital infections in the NICU of Alzahra Hospital in Isfahan and identify the underlying factors to provide strategies for controlling nosocomial infections in the hospital. During this study, 759 patients were admitted to the NICU. Hospital infections in the NICU, which had positive blood, urine, eye discharge, or positive tracheal secretions cultures were 56 cases, and the frequency of hospital infection was 7.4%. The evaluation of studies carried out at different geographical points indicates that the prevalence of nosocomial infections in different regions is different.

In a study conducted by Gaynes et al. (21), the incidence of hospital infections in NICUs in the United States has been reported in the range of 12-6% patients. The results of a study carried out by Sharon et al. (16) also showed that the incidence of infection in the intensive care unit is 7%. In a study conducted in Iran, Ghazvini et al. reported the incidence rate of hospital infections as 3.29% in the NICU of Ghaem Hospital in Mashhad.

Also, Brock et al. (22) reviewed the prevalence rate of hospital infections by 9.3% in the evaluation of neonates in the Pediatric Medical Center and Bahrami Hospital in Tehran. Hospital infections are associated with a variety of factors, including premature birth, low birth weight, premature rupture of amniotic sac, respiratory distress syndrome, respiratory failure, seizure, cyanosis, type of birth, multiple infections, uterine infections, long hospitalization period, use of antibiotics with a wide spectrum and maternal diseases, as well as the use of invasive procedures, such as intravascular catheters, intubation, intravenous feeding with fatty emulsions, and ventricular shunt (19).

In the present study, hospital infections were higher in males (57.1%), compared to those in females. The highest number of infections in newborns with the second birth rank was 30 (53.6%), and the majority of deliveries were cesarean section (n=42; 75%). The most congenital malformation seen in neonates with positive culture was PDA. Also, 14.3% of neonates had an amniotic sac rupture more than 18 h. Amniotic fluid was also observed in 16.1% of patients contaminated with meconium.

The most commonly reported disease in mothers was hypothyroidism (21.4%), followed by PIH (12.5%). Also, in 7.2% of mothers, these two conditions were present simultaneously. In the case of aggressive procedures carried out in this study, tracheal tubes were the most frequent procedures (21.4%). In 10.7% of the patients, the urinary catheter was used, and NGT was also utilized with the same frequency. One of the known risk factors for nosocomial infections is the use of gastric acid-reducing agents, such as H2 blocker, or proton pump inhibitors, and in our study, 7.1% of the patients used an H2 blocker. Also, the most common reason for admission was prematurity (46.4%), followed by respiratory problems (30.4%).

The most common offspring isolated from culturing patients were *Staphylococcus epidermidis* (40.5%), *Enterococcus* (18.9%), *Klebsiella* (10.8%), *Enterobacteriaceae* (8.1%), and *Candida* species (8.1%), respectively. As it is evident, in most cases, positive cultures are negative for *coagulase staphylococci*. On the other hand, gram-negative bacilli also played a major role in hospital infections. In the United States, the most common pathogenic bacteria reported in this regard were negative *coagulase staphylococci* with 48% of the cases being isolated from bloodstream infections (23).

In this study, 37.8% of the positive cultures were related to the blood samples of the patients. Also, in a study conducted by Qazvini et al., the most commonly isolated organisms from culture are *Staphylococcus coagulase* negative, *Klebsiella*, *Escherichia coli*, *Pseudomonas*, *Staphylococcus aureus*, and *Acinetobacter*. In a study conducted by Yogaraj et al. (24) on patients admitted to pediatric intensive care units, the most commonly detected cases were coagulase-negative *Staphylococcus aureus*, followed by *Enterobacteriaceae*, *Pseudomonas*, *Klebsiella*, *Serratia*, *Escherichia coli*, and *Acinetobacter*. Moreover, the most common type of hospital infection is septicemia.

In a study conducted by Hosseini et al. (25), the most common isolated microorganisms were *Staphylococcus coagulase negative*, *Klebsiella*, *Candida*, *Staphylococcus aureus*, *Escherichia coli*,

Enterobacteriaceae, and *Streptococcus viridans*. In a study carried out by Wellness et al. (26), the highest frequency was reported with *Enterobacteriaceae*, *Staphylococcus aureus*, *Klebsiella*, *Escherichia coli*, and *Staphylococcus epidermidis,* respectively. In a study performed by Barak et al., the highest frequency of pathogens was related to *Pseudomonas*, *Klebsiella*, and *Enterobacteriaceae*.

In the present study, it was found that the patients with positive cultures had an average intravenous catheter use of over 20 days, and about three-fourths of the patients needed oxygen support for ventilation, which can be a potential risk factor for hospital infection. In several studies, the incidence rate of hospital infection in patients with a long-term intravenous catheter has been reported to be 96.87% (27) despite the consideration of hygiene.

In an antibiogram study, the highest bacterial resistance was observed in the antibiotics of ceftazidime (26.8%), tetracycline and penicillin (19.6%), oxacillin (16.1%), and clindamycin and erythromycin (each on 10.7%). In a study conducted by Qazvini et al., the highest levels of bacterial resistance were related to antibiotics penicillins, ceftazidime, and cefotaxime. In a study carried out by Hosseini et al., the most bacterial resistance was related to erythromycin, oxacillin, clindamycin, and gentamicin in gram-positive bacteria and against gentamicin, cephalexin, ceftazidime, ceftriaxone, cefotaxime, and cefixime in gram-negative bacteria.

Conclusion

According to the results of our study, the frequency of nosocomial infections in newborns admitted to the intensive care unit of Alzahra Hospital of Isfahan was 7.4%. Our findings highlighted the importance of paying more attention to controlling and preventing hospital infections in the NICU. The attention and accuracy of the treatment staff in this domain are important, especially the observation of personal hygiene, and most importantly the regular cleaning of hands and use of sterile gloves. It was also required to follow all sterile conditions when installing intravenous catheters inside the patient's body.

Limitations

One of the limitations of this study, which is inherent in all retrospective studies, was a bias in terms of the quality of collecting the original information. The impossibility of identifying a number of infectious pathogens and the sample size were other limitations of this study. The patient's records in the study period included in the study may not have enough power to apply to all population.

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Conflicts of interests

No conflict of interests is declared by the authors in this study.

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