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Neonatal Infections: a 5-Year Analysis in a Neonatal Care Unit in North East of Iran

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Abstract

Background: Neonatal infections are one of the major causes of death in Iran. Since identifying the risk factors, types, site, bacterial causes, and case fatality rate of an infection can be effective in selecting preventive and therapeutic methods, and appropriate supportive measures, this study aimed to investigate the aforementioned factors in the neonatal intensive care unit (NICU) of Ghaem Hospital in Mashhad- Iran during a 5-year period.

Materials and Methods: This cross-sectional study was conducted from Jan 2010 to Jun 2016 on 221 infants diagnosed with infections (positive blood, cerebrospinal fluid, or urine cultures, and radiographic evidence of lung infection as well as laboratory and clinical evidence of infection). Data collection tools consisted of a researcher-made questionnaire including maternal and neonatal characteristics and clinical and laboratory evaluation. Moreover, the infants were followed up until hospital discharge or death. Data were analyzed using SPSS-16.

Results: The incidence of neonatal infection was 11.6%. About 70% of the infants were born preterm and 52% of the infected infants were born by cesarean. The most common pathogens of sepsis were gram-negative bacteria (55%), coagulase-negative staphylococci (35%) and other gram-positive bacteria (10%). There were three main causes of infection of central nervous system (CNS): Klebsiella (66%), Escherichia coli (17%), and Acinetobacter (17%). Infant mortality rate due to infection was 28.1%. The causes of death included meningitis (60%), sepsis (27%), and UTI (16%).

Conclusion: According to our study, the prevalence of infection and mortality rate in our ward is higher compared to developed countries. The most common cause of infections was gram-negative bacteria, but coagulase-negative staphylococci become more prevalent and needs more attention.

Key Words: Iran, Neonatal infections, Neonatal intensive care unit, Mortality, Sepsis.

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1- INTRODUCTION

Neonatal infection is a serious disease with high mortality rate which is usually a major challenge for neonatologists due to non-specific symptoms as well as lack of an early definitive diagnostic test (1). According to the World Health Organization (WHO), infant mortality rate is about 5 million per year, 98% of which occurring in developing countries. Based on these statistics, the most common causes of infant mortality are asphyxia, prematurity, and infection. Proper pre-birth care for the mother, sanitary control of the equipment in labor rooms, observing hygiene principles by hospital staff, proper infection prevention, and appropriate use of antibiotics are among the important factors determining the prevalence of neonatal infection (2). Neonatal intensive care unit (NICU) is one of the critical units in hospitals in terms of hospital-acquired infections which are often difficult to control (3). The prevalence of hospital-acquired infections and types of pathogens are different in various NICUs (4).

Hospital-acquired infection is an infectious disease that is acquired after hospitalization or birth in the hospital. The one suffering from had not been infected before hospitalization or birth, and he/she had not been in the incubation period. Since the average incubation period is 2-3 days, hospital-acquired infections appear during the first 48-72 hours after hospitalization (5). Hospital-acquired infections increase length of hospital stay and treatment costs, so are the major problems hospitalized that patients are faced with (6). According to the declaration of the WHO in October 13, 2005, more than 1.4 million people suffer from hospital-acquired infections every year. Currently, the incidence rate of hospital-acquired infections is estimated to be 5-15% and 25% in developed and developing countries, respectively (7).

Prematurity is the most important predisposing factor for neonatal infection during the first 7 days after birth. The other factors include male gender, low Apgar score, mother's age, the number of mother's live births, pre-birth care for the mother, chorioamnionitis, mother's urinary tract infection, premature rupture of membrane (PROM) more than 18 hours before birth (8), low weight, prolonged hospital stay, taking broad-spectrum antibiotics, and specially using invasive procedures such as endotracheal tube, ventricular shunt, intravascular catheter, parenteral nutrition with lipid emulsions, and changes in the skin and mucous membranes (7, 9, 10). Bacteremia is the most common form of hospital-acquired infection (11). The incidence rate of neonatal sepsis is 1-4 per 1000 live births in developed countries (7). Sepsis is one of the major causes of neonatal mortality which accounts for about 25% of all neonatal deaths in our NICU (12).

Group B streptococcus (GBS), other streptococci, staphylococcus aureus, E. coli, staphylococcus epidermidis, and listeria monocytogenes are the microorganisms causing sepsis. In premature infants, the infection caused by coagulase-negative Staphylococci (CoNS) is prevalent. Group D streptococcus (GDS), Pseudomonas, and Klebsiella, are among the recently isolated pathogens (13). Of all neonatal sepsis cases, 18-78% are caused by gram-negative microorganisms (14, 15). Clinical presentation of neonatal sepsis can vary; in most studies symptoms include fever, respiratory distress, tachycardia, malaise, poor feeding and lethargy (3, 16, 17).

A study by Besharati et al. (2013) showed that CoNS and Klebsiella pneumoniae were the most common colonized bacteria that caused hospital-acquired infections, especially septicemia in infants hospitalized in NICUs. Moreover, mothers' hands and nipples, personnel's

hands, baby bottles, and expressed breast milk inside them consisted the most isolated coagulase negative staphylococci and Klebsiella pneumoniae and were the most important sources of bacteria in this unit (18). In a study by Qazvini et al. (2008), 32 out of 971 infants suffered from hospital-acquired infections. Coagulase-negative staphylococci (34.74%), Klebsiella pneumoniae (31.42%), and some other gram-negative bacilli were the most common bacteria isolated from these patients (19). Since neonatal infections are one of the major causes of death in Iran, identifying the risk factors, types, site, bacterial causes, and case fatality rate of such infections can be effective in selecting preventive and therapeutic methods, and appropriate supportive measures. Therefore, this study aimed to investigate the aforementioned factors in the NICU of Ghaem Hospital in Mashhad-Iran during a 5-year period.

2-MATERIALS AND METHODS

Infants admitted to the NICU at the Ghaem University Hospital between January 2010 and May 2016 were included in this study. Ghaem University Hospital is a teaching hospital that provides tertiary care in the northeast part of Iran. It has a level three NICU with a total of 25 beds. Each NICU nurse cares for 4 or 6 babies. There are 3 attending neonatologists, 2 neonatal fellows and also 2 pediatric residents and 2 intern doctors working in the NICU during each shift.

2-1. Study Design

1,900 neonates were admitted to the NICU. Of these, 221 neonates with definitive infection were included in this study. Infection is a condition that affects the host due to the invasion, growth, and proliferation of pathogens. Hospital-acquired infection is a localized or generalized infection caused by the pathogenic reactions related to the infectious agent or its toxic products, provided that it occurs at least 48-72 hours after the patient is admitted to the hospital. The infants with positive blood, cerebrospinal fluid, or urine cultures, or evident radiological evidence in chest X-ray as well as clinical signs were included in the study as the target group. The inclusion criteria were as follows:

* Clinical symptoms of sepsis developed after the third day following delivery, and
* Onset of clinical symptoms of sepsis not later than the seventh day after being discharged from NICU.

The participated infants were examined and completely evaluated in terms of having infection. Maternal, pregnancy, and delivery characteristics of these infants were also assessed. The type of infectious pathogen was determined according to laboratory report, and the infants were followed up until hospital discharge or death. Patients' clinical data and blood stream isolates were retrospectively reviewed for gestational age, birth weight, symptoms and signs, pathogen, need to ventilator, and mortality, using a researcher-made Questionnaire. The identification of blood isolates and antibiotics susceptibility testing were performed by microbiology laboratory using standard methods consistent with current Clinical and Laboratory Standards Institute (CLSI) recommendations. This study was approved by the Research Committee of Mashhad University, and written consents were obtained from the patients' parents before they were included into the study.

2-2. Statistical analysis

The results were expressed as the mean ± standard deviation [SD] or as a proportion of the total number of patients or isolates. For continuous variables, mean values were compared using two sample t-tests for independent samples. Differences in proportions were compared using a Chi-square test or Fisher's exact test, as

appropriate. All tests of significance are 2-tailed; all statistical analyses were done using SPSS software version 16. P-value less than 0.05 were significant.

3- RESULTS

3-1. Incidence

The incidence of infection was 11.6% among all NICU infants. The birth weight of neonates with sepsis was 1901 ± 0.930 grams, the age at onset was 12.5 ± 3.85 days, gestational age was 33.1 ± 2.44 weeks, Apgar score at first minute was 6.56 ± 2.1 and at fifth minute was 7.46 ± 1.8. The mean duration of hospitalization was 18.4 ± 4.19 days. Fifty five percent of neonates were male and 45% of them were female. Among infected neonates, 49 neonates (31.2%) were born term and 112 (68.8%) were born preterm. Thirty four percent of infected babies needs to resuscitation in the delivery room, and mode of delivery for 52% of them were cesarean section.

About 40% of them had history of premature rupture of membranes (PROM) and 36% did not have proper care during pregnancy. Among these neonates, 39% of them born from mothers who have had problems such as hypertension, preeclampsia, eclampsia, diabetes and history of infertility.

Sixty eight patients had respiratory distress as underlying problems and 48 of whom needed intubation, 8 patients (3.6%) had congenital heart disease, 12(5.4%) had thrombocytopenia, 3 (1.4%) had coagulopathy, 6 (2.7%) had congenital anomalies, 4(1.8%) patients had renal failure, Two renal vein thrombosis, 3(1.4%) cases of brain problem (two cerebral hemorrhage, one Myelomeningocele), two congenital metabolic disease, one infant had addicted mother.

Investigation of the prevalence of different types of infection shows that sepsis, pneumonia, conjunctivitis, urinary tract infection, and meningitis are the most common definite infections. Sepsis was the most common type of confirmed infection followed by pneumonia, conjunctivitis, urinary tract infection (UTI), and meningitis (**Figure.1**).

3-2. Distribution of pathogens

In infants with sepsis, Gram negative (55.1%) was the major causative pathogen, followed by coagulase-negative staphylococci (35.4%) and others gram positives cocci (9.5%). Overall, gram-positive microorganisms accounted for 44.9% of cases of neonatal infection and gram-negative microorganisms (55.1%) (**Table.1**). In this survey, 66% of infection of Central nervous system (CNS) was caused by Klebsiella, 17% by E-coli and 17% by Acinetobacter. Urinary Tract Infection (UTI) was caused by Klebsiella (5 infant), E-coli (4 infant), Coagulase Negative Staphylococci (4 infant), and other pathogens (5 infant). Staphylococcus epidermis, Pseudomonas aeroginosa and Enterococci were the most common cause of conjunctivitis.

3-3. Mortality and morbidity

In total, 52 (28.1%) of the infants died. Overall, the infection-related fatality rate was 60% for meningitis, followed by 27% and 16% for sepsis and UTI, respectively (**Table.2**). 53 cases of infection-related fatality occurred in preterm neonates and only 7 cases were observed in full-term neonates (P=0.000).Weight, age, Apgar score and gestational age among dead and alive neonates were compared in **Table.3**.

The infants in the deceased group were older than the ones in the discharged group; however, they had lower birth weight, 1-minute and 5-minute Apgar score, and gestational age.

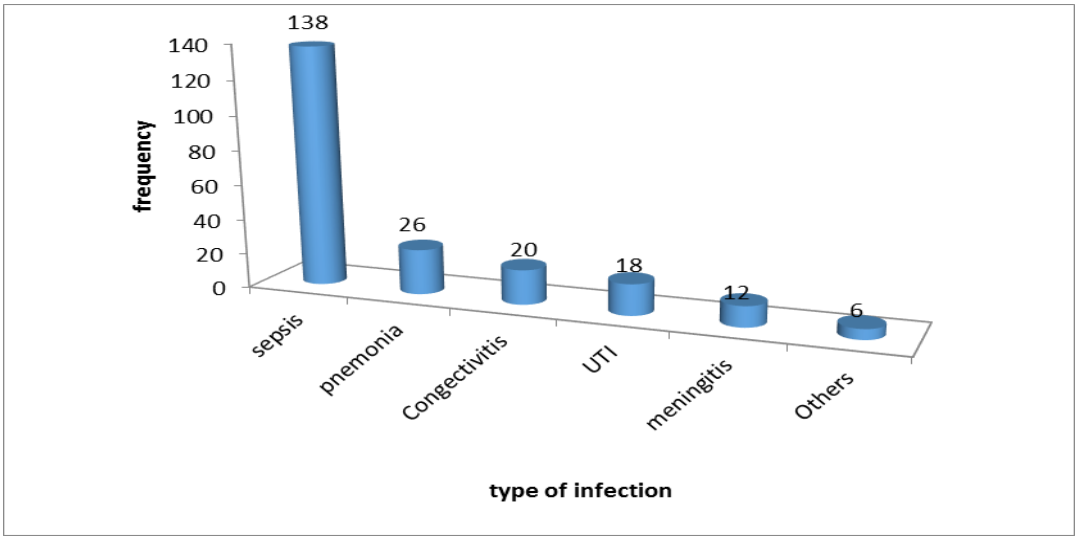

Fig.1: Frequency Distribution of Different Types of Infection in NICU

Table 1: Frequency of microbial causes of infection

Microorganism	Frequency	Percent
Coagulase Negative Staphylococcus	45	35.4
Klebsiella species	33	26.0
Enterobacter species	13	10.2
E.coli	12	9.4
Staphylococcus aureus	7	5.5
Pseudomonas species	5	3.9
Acinetobacter species	4	3.1
Enterococcus species	3	2.3
Gram-negative bacilli	2	1.5
Citrobacter	1	0.7
Gram positive cocci	1	0.7
Streptococcus species	1	0.7
Total	127	100

Table-2: The mortality rates for the major infections in patients with late-onset sepsis

Infection type of prognosis	Sepsis	Meningitis	Omphalitis	UTI	Pneumonia
Discharge	92(72.5%)	5(41.7%)	1(50.0%)	15(83.3%)	20(76.9%)
Death	35(27.5%)	7(58.3%)	1(50.0%)	3(16.7%)	6(23.1%)

UTI: urinary tract infection.

Table 3: Comparison of infant deaths or discharge due to infection

Variables	Discharge	Death	P- value (t-test)
Weight	2166±855	1439±879	0.393
Age	12±8.7	14±13	0.001
First Apgar score	7.19±1.6	5.23±2.3	0.000
Fifth Apgar score	8.03±1.3	6.29±2.0	0.000
Gestational Age	34.89±4.3	30.15±4.4	0.034

4- DISCUSSION

According to our study, the prevalence of infection in our setting is still high, but compared to other studies we reported in our country better situation, but they also have a significant mortality rate. The prevalence of infection was approximately 11.6% of admitted patients.The prevalence of neonatal sepsis is different from one hospital and society to another and depends on the underlying conditions of sepsis (20). Darvishpour et al. reported the prevalence of infections 16.9% (3) which is higher than our study. This higher prevalence could be because of the difference in ward setting or sample size. Ghahramani and colleagues investigated the incidence of infection in infants and reveal that 23% of admitted neonates have positive culture (7). Asghari and colleagues investigated the most common bacterial causes of neonatal sepsis in a hospital in Uromia, the incidence of sepsis was 8.9% which is very close to our study, which was 7.7% (21).

Busy NICUs, mismatch between the number of nurses and the number of critically ill patients, non-compliance with hand hygiene, lack of serious care for babies' skin, and long-term mechanical ventilation are the risk factors for hospital-acquired infections, which seem to play a major role in causing infection in our NICU. Therefore, it is recommended that nurses and physicians should be properly trained before working in the NICU and hand hygiene should be strictly monitored. Proper sterilization during venipuncture, specimen collection, catheterization, and intubation is strongly recommended. Fifty five percent of neonates were male and 45% of them were female. A study by Qazvini et al. (2008), also showed that hospital-acquired infections are more common in male infants. Although the prevalence of infections and mortality rate seem to be higher in male infants, its exact cause is not known (19).

Investigation of the prevalence of different types of hospital-acquired infections shows that sepsis, pneumonia, conjunctivitis, urinary tract infection, and meningitis are the most common definite infections, respectively. In a study by Qazvini et al. (2008), of 32 infants suffering from hospital-acquired infection, 27 (84.4%) had bloodstream infections, whereas 5 (15.62%) infants suffered from lower respiratory tract infections (19). In the present study, approximately 70% of the infected infants were premature and weighed less than 2,500 grams. Above mentioned parameter were shown to be associated with many risk complications including infection. The mean weight and gestational age of the neonates which survived was significantly higher than died one. A similar result was reported Asghari and Khaniki (21). Similarly in the study of Darvishpour and Asghari 73% and 69% of babies with infection were preterm babies (3, 21). Mutlu et al. (2011) reported that sepsis in premature infants was highly prevalent (66%) (22).

During the first seven days of life, the prevalence of sepsis in preterm infants is 6 times greater than term infants (23). Premature babies due to immune defects are prone to infection and also due to prolonged hospitalization and use of more invasive procedures, such as umbilical vein catheter, intubation receive long-term antibiotic than term infants are at higher risk of infection.In the study by Mutlu et al. (2011), sepsis was very common in infants weighing less than 1,500 grams (41%) (22). According to a study by Clark et al., infants, especially premature and low-birth-weight ones, are susceptible to hospital-acquired infections due to weakened immune system, prolonged hospital stay, using invasive procedures, and parenteral nutrition in NICUs (24). Incidence of PROM was high in infected neonates (40 cases) and so was strongly associated with infection. The mechanism

is the inflammation of the decidua listed chorion, a decrease in collagen membrane as a risk factor for premature rupture of fetal membranes considered several factors could be causing the problem. But there is a strong correlation between premature rupture of membranes and intrauterine infection and inflammation is probably the mother's genital tract infections important role in premature rupture of membranes and delivery of preterm (16, 25). In a study by Al-Riyami et al. (2013), PROM caused neonatal sepsis with a frequency of 50% (26). In another study (2011), PROM-related neonatal complications included meningitis (5.2%), sepsis (4%), and pneumonia (1.3%) (16).

The most common cause of neonatal infection in our study was Gram-negative bacilli (55%) and the second most common cause of neonatal infections was coagulase-negative staphylococci which cause approximately 36% of infections. Similarly at the study of Ghahramani and colleagues in Tabriz University, the most common bacteria which cause infection were Enterobacter and Klebsiella pneumoniae in 82.4% of cases, then coagulase negative Staphylococci (7%), Staphylococcus aureus (5.5%), Escherichia coli (3.5%), Pseudomonas aeruginosa (1%) and B hemolytic streptococci (0.5%) (27). In another study the most common organisms isolated from blood cultures were of Enterobacter (57%), Klebsiella sepsis (9%) and E.coli (2%) (28). Qazvini et al. (2008) reported that coagulase-negative staphylococci (43.74%), Klebsiella pneumoniae (31.42%), and some other gram-negative bacilli were the most common bacteria isolated from these patients, respectively (19).

In another study about causes of bacterial infections E.coli (44.6%), Klebsiella sepsis (31%), coagulase negative staphylococci (10%) was the most common cause of neonate infection in our region among neonates with hyperbilirubinemia (29). The results of a study by Asghari Sana et al. (2011) showed that the most common microorganisms causing neonatal sepsis are coagulase-negative staphylococci (50%) and Klebsiella pneumoniae (19.4%)(30). Another study in Greece on hospital-acquired infections in NIUCs showed that coagulase-negative staphylococci are the most common cause of such infections in this group of patients (31). In a study by Kalman, the most common isolated microorganisms were coagulase-negative staphylococci, staphylococcus aureus, and beta-hemolytic streptococcus (32). In a study conducted in Turkey (2006), coagulase-negative staphylococci and Klebsiella pneumoniae were the most common organisms causing neonatal infections in NICUs (33).

Galanakis et al. (2002), reported that the most common pathogens of neonatal bacteremia in Greece were gram-negative bacilli (42%), coagulase-negative staphylococci (34%), and streptococci (17%) (31). In another study conducted in Georgia (2009), the most common organisms were Klebsiella pneumoniae and Enterobacter (15). Comparing the above results show that Gram-negative bacilli are still the most common infectious pathogen in neonatal units and the main risk factors for this is the crowded neonatal units, mismatch of nurses to patients and lack of hand washing in the areas of ours. Therefore, it is recommended to emphasis hand washing and other sterile conditions principles in contact with the baby and during invasive procedures such as venipuncture, intubation, installing umbilical vein catheter and even usual injections in order to be able to reduce the spread of this group of infections. Also, appropriate space and human resources required to reduce the incidence of gram-negative infections. In the study of the causes of meningitis, two thirds of cases of infected by Klebsiella sepsis and Escherichia coli accounted in 28% of the

cases, followed by Gram-negative bacilli other than E. coli (4%), other streptococci (4%), Neisseria meningitidis (3%), and Listeria monocytogenes (1.5%). In a study by Gaschignard et al. (2011), Group B strep (GBS) was the most common pathogen both in early-onset (77% vs. 18% for E. coli) and in late-onset meningitis (50% vs. 33% for E. coli). Among preterm infants, E. coli was more commonly isolated (45% vs. 32% for GBS), especially in very preterm infants (54%). GBS was more often involved in seizures than E. coli (41% vs. 25%) (34).

The most common pathogen that cause conjunctivitis were Staphylococcus epidermidis, Pseudomonas sepsis and Enterococcus. Amini et al. (2006) reported that the organisms responsible for causing neonatal conjunctivitis were staphylococcus aureus (31%), E. coli (23%), staphylococcus epidermidis (22%), Klebsiella (10%), Neisseria gonorrhoeae (3%), chlamydia trachomatis (2%), and pseudomonas aeruginosa (2%) (35).

The total mortality rate among our infants was approximately 28.1%, this rate was 60% for meningitis, 27% for sepsis and 16% for urinary tract infections. In the study by Mutlu et al. (2011), the mortality rate from hospital-acquired sepsis caused by gram-negative microorganisms was reported to be 16% (22). The mortality rate from neonatal bacteremia in Galanakis et al. (2002) study was 11% (31).

In the study by Qazvini et al. (2008), the mortality rate of infants suffering from hospital-acquired infections in NICUs was 3 cases (9.37%) (19). The results of the present study show that the infant mortality rate in Ghaem hospital in Mashhad- Iran, is high. Given that gram-negative organisms cause more severe diseases, the fact that gram-negative organisms were more common in the present study explains the difference in infant mortality rates.

5- CONCLUSION

According to our study, the prevalence of infection in our ward is similar to the country and is acceptable, but is much higher compared to developed countries. The mortality rate is also tripled comparing to developing countries which needs more emphasis on critical cares. The most common cause of infections was gram-negative bacteria, but coagulase-negative staphylococci become more prevalent and needs more attention

6- CONFLICT OF INTEREST

The authors had not any financial or personal relationships with other people or organizations during the study. So there was no conflict of interests in this article.

7- REFERENCES

1. Boskabadi H, Maamouri G, Afshari JT, Mafinejad S, Hosseini G, Mostafavi-Toroghi H, et al. Evaluation of serum interleukins-6, 8 and 10 levels as diagnostic markers of neonatal infection and possibility of mortality. Iranian journal of basic medical sciences 2013;16(12):1232.

2. Yalaz M, Çetin H, Akisu M, Aydemir S. Neonatal nosocomial sepsis in a level-III NICU: evaluation of the causative agents and antimicrobial susceptibilities. The Turkish journal of pediatrics 2006;48(1):13.

3. Darvishpour A, Hashemian H, Faal E, Fasihi M. Survey of Nosocomial Infection and Accompanied Factors in Neonatal Intensive Care Unit. Journal Of Guilan University Of Medical Sciences 2010;19(73): 37- 45.

4. Apostolopoulou E. Nosocomial Bloodstream infections in neonatal intensive care unit: excess of length of stay, extra costs of antibiotics. ICUs Nurs Web J 2004;19:1-7.

5. Larypoor M, Frsad S. Evaluation of nosocomial infections in one of hospitals of Qom ,2008. Iranian Journal of Medical Microbiology 2011;5(3):7-17.

6. Burke JP. Infection control-a problem for patient safety. New England Journal of Medicine 2003;348(7):651-6.

7. Kliegman R, Behrman RE, Nelson WE. Nelson textbook of pediatrics. Elsevier; 2016.

8. Wilson CB, Nizet V, Maldonado Y, Klein JO, Remington JS. Remington and Klein's Infectious Diseases of the Fetus and Newborn Infant: Elsevier Health Sciences; 2015.

9. Kawagoe JY, Segre CA, Pereira CR, Cardoso MFS, Silva CV, Fukushima JT. Risk factors for nosocomial infections in critically ill newborns: a 5-year prospective cohort study. American journal of infection control 2001;29(2):109-14.

10. Drews M, Ludwig A, Leititis J, Daschner F. Low birth weight and nosocomial infection of neonates in a neonatal intensive care unit. Journal of Hospital Infection 1995;30(1):65-72.

11. Jeong IS, Jeong JS, Choi EO. Nosocomial infection in a newborn intensive care unit (NICU), South Korea. BMC infectious diseases 2006;6(1):1.

12. Boskabad H, Moudi A, Parvini Z, Barati T. Evaluation of the cause and related factors of neonatal mortality in Qaem hospital 1388-89. The Iranian Journal of Obstetrics, Gynecology and Infertility 2012;14(7):21-6.

13. Taeusch HW, Ballard RA, Gleason CA, Avery ME. Avery's Diseases of the Newborn: Elsevier Health Sciences; 2005.

14. Kamath S, Mallaya S, Shenoy S. Nosocomial infections in neonatal intensive care units: profile, risk factor assessment and antibiogram. The Indian Journal of Pediatrics 2010;77(1):37-9.

15. Macharashvili N, Kourbatova E, Butsashvili M, Tsertsvadze T, McNutt L-A, Leonard MK. Etiology of neonatal blood stream infections in Tbilisi, Republic of Georgia. International Journal of Infectious Diseases 2009;13(4):499-505.

16. Boskabadi H, Maamouri G, Mafinejad S. Neonatal complications related with prolonged rupture of membranes. Macedonian Journal of Medical Sciences 2011;4(1):93-8.

17. Romero R, Chaiworapongsa T, Espinoza J. Micronutrients and intrauterine infection, preterm birth and the fetal inflammatory response syndrome. The Journal of nutrition 2003;133(5):1668S-73S.

18. Besharati R, Sadeshian A, Mamori GA, Lashkardoust H, Gholami S. Sources of bacteria causing nosocomial infections at NICU of Ghaem hospital in Mashhad, Iran. Journal of North khorasan University of Medical Sciences 2013;5(1):25-30.

19. Ghazvini K, Rashed T, Boskabadi H, Yazdan Panah M, Khakzadan F, Safaee H, et al. Neonatal intensive care unit nosocomial bacterial infections. Tehran University Medical Journal TUMS Publications 2008;66(5):349-54.

20. Amirsalari S, Kaveh Manesh Z, Sh A, Torkaman M. Evaluation of the most common clinical signs and laboratory finidings of neonatal sepsis in in Baqyatallah and Najmie Hospitals from 1380 to 1384. Journal Mil Med 2007;9(3):233-40.

21. Asghar SFS, Khaniki G. Determine the risk of bacterial blood infection common in babies Arefian Hospital of. New Molecular Biotechnology 2011;1(3):17-21.

22. Mutlu M, Aslan Y, Saygin B, Yilmaz G, Bayramoğlu G, Köksal I. Neonatal Sepsis Caused by Gram-negative Bacteria in a Neonatal Intensive Care Unit: A Six Years Analysis HK J Paediatr (new series) 2011;16(4):253-7.

23. Eicher DJ, Annibale DJ. Neonatal sepsis: evaluation and management. Journal of the South Carolina Medical Association (1975). 2002;98(3):106-12.

24. Clark R, Powers R, White R, Bloom B, Sanchez P, Benjamin DK. Nosocomial infection in the NICU: a medical complication or unavoidable problem? Journal of perinatology 2004;24(6):382-8.

25. Romero R, Chaiworapongsa T, Espinoza J. Micronutrients and intrauterine infection, preterm birth and the fetal inflammatory response syndrome. J Nutr 2003;133(5 Suppl 2):1668S-73S.

26. Al-Riyami N, Al-Shezawi F, Al-Ruheili I, Al-Dughaishi T, Al-Khabori M. Perinatal outcome in pregnancies with extreme preterm premature rupture of membranes

(Mid-Trimester PROM). Sultan Qaboos University medical journal 2013;13(1):51.

27. Ghahramani. blood infection in newborns hospitalized. Tabriz Tabriz University of Medical Sciences 1996; 35(52): 69-73.

28. Darvishpour A, Hashemian H, Faal E, Fasihi M. Survey of Nosocomial Infection and Accompanied Factors in Neonatal Intensive Care Unit. Journal Of Guilan University Of Medical Sciences 2010;19(73): 37- 45.

29. Boskabadi H, Maamuri G, Kiani M, Abdollahi A. Evaluation of urinary tract infections following Neonatal hyper-bilirubinemia. Journal of Shahrekord University of Medical Sciences 2010;12(2):95-101.

30. Asgharisana F, Gaibi S. study of the role of common bacterial etiology in neonatal sepsis in Urumiah Shahid. New Cellular and Molecular Biotechnology Journal 2011;1(3):17-21.

31. Galanakis E, Krallis N, Levidiotou S, Hotoura E, Andronikou S. Neonatal bacteraemia: a population-based study. Scandinavian journal of infectious diseases 2002;34(8):598-601.

32. Källman J, Kihlström E, Sjöberg L, Schollin J. Increase of staphylococci in neonatal septicaemia: a fourteen-year study. Acta paediatrica 1997;86(5):533-8.

33. Buyukyavuz BI, Adiloglu AK, Onal S, Cubukcu SE, Cetin H. Finding the sources of septicemia at a neonatal intensive care unit: newborns and infants can be contaminated while being fed. Japanese journal of infectious diseases 2006;59(4):213.

34. Gaschignard J, Levy C, Romain O, Cohen R, Bingen E, Aujard Y, et al. Neonatal Bacterial Meningitis: 444 Cases in 7 Years. The Pediatric infectious disease journal 2011;30(3):212-7.

35. Amini E, Ghasemi M, Zamani A. Prevalence and etiology of neonatal conjunctivitis in neonates hospitalized in Imam Khomeini hospital, Tehran. Iranian Journal of Pediatrics 2006;16(4):393-8.