

Nosocomial infections in neonatal units in Turkey: epidemiology, problems, unit policies and opinions of healthcare workers

Turkish Neonatal Society, Nosocomial Infections Study Group

SUMMARY: Turkish Neonatal Society Nosocomial Infections Study Group. Nosocomial infections in neonatal units in Turkey: epidemiology, problems, unit policies and opinions of healthcare workers. *Turk J Pediatr* 2010; 52: 50-57.

The epidemiology of nosocomial infections in Turkish neonatal intensive care units (NICUs) shows that nosocomial sepsis is an important problem, especially for very low birth weight (VLBW) infants, and gram-negative agents, particularly *Klebsiella* species, are still the major causes of nosocomial infections. Sepsis frequency was 6.4%, ranging from 2.1 to 17%, in 16 centers in Turkey. Sepsis frequency was 22% in infants <1500 g, 6% in those 1500-2500 g, and 3% in those >2500 g. Sepsis-related mortality was 24.4 for 100 sepsis cases, ranging from 0 to 75 for 100 cases. Ventilator-associated pneumonia frequency was 1.7%, catheter-related infection frequency was 0.14% and urinary tract infection frequency was 3.7%.

Healthcare workers (HCWs) complain of the inadequacy of some basic facilities and of staffing; however, they are aware of the causes and solutions and are willing to overcome this major health problem. We conclude that Turkish neonatal HCWs are quite optimistic about preventing neonatal nosocomial infections.

Key words: nosocomial infection, newborn, epidemiology, infection control.

In the last two decades, the survival rates of very low birth weight (VLBW) infants increased with the broad use of exogenous surfactant and new ventilation techniques. These preterm infants are one of the most vulnerable groups of patients for nosocomial infections (NIs) due to their immature immune system, necessary medical treatments, mechanical ventilation, and invasive procedures performed in the neonatal intensive care unit (NICU). Prolonged hospital stay with the decreasing gestational age also carries the risk of introduction of resistant hospital pathogens¹⁻³. For the above reasons, as the survival rates of these infants increase, NIs become a greater concern in the NICU, with increased morbidity, mortality and treatment costs.

Nosocomial infection is an infection during hospitalization that was not present or in incubation at the time of admission⁴. The

most common hospital infections are blood stream infection (BSI) (32%-53%)^{5,6}, followed by pneumonia (12%-18%), ear, nose and throat infections (8%-21%), gastrointestinal infections and necrotizing enterocolitis (NEC) (5%-11%), and urinary tract infections (17%)^{7,8}.

While the majority of VLBW infants have only one episode of culture-proven sepsis during their NICU hospitalization, 20% have two events, 6% have three, and 2% have four. Multiple sepsis episodes are more common in the lowest birth weight categories, with almost 40% of infants with birth weights of <750 g having two or more episodes.

The epidemiology of NIs among neonates in NICUs has been investigated in many studies from different countries. However, epidemiological studies for NIs in NICUs from Turkey, which are few in number, represent single center experiences^{3,7,9-11}. This is the first

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multicenter study of the epidemiology of NIs in NICUs from Turkey.

Material and Methods

This study was performed in two different ways. First, an electronic questionnaire was sent to all certified neonatologists in Turkey via a special network. Neonatologists working in 16 centers who agreed to participate in this epidemiologic study provided their surveillance data regarding the NIs in their NICU in 2005. As all participating centers had infection control committees, which were doing active surveillance at the time of the study, data provided from these centers were considered reliable.

As a second part of the study, another questionnaire seeking the opinions of neonatal unit healthcare workers (HCWs) about the problems and prevention of NIs was given to congress participants (n=424) during the 14th National Congress of Neonatology in Turkey, and 108 replies were evaluated.

Statistical analysis was carried out with the SPSS for Windows 15.0 software package. Chi-square test was performed to determine differences between groups. Statistical significance was considered at $p < 0.05$.

Results

Epidemiology

Neonatologists working in 16 out of 25 Turkish referral centers agreed to take part in the study. Data from 16 centers were pooled together and analyzed. The data of a total of 9,359 infants admitted to 16 centers in Turkey showed 601 culture-proven nosocomial sepsis cases. Sepsis frequency was 6.4% in all of the infants admitted to participating centers in 2005, whereas it varied widely from center to center, ranging from 2.1 to 17%. Distribution of nosocomial sepsis cases according to birth weight was available for 13 centers. Data from these 13 centers showed a sepsis frequency of 22% in infants < 1500 g, 6% in those 1500-2500 g, and 3% in those > 2500 g (Table I).

The most frequent microorganisms grown in blood cultures were *Klebsiella* spp. (7 centers), *Serratia* spp. (3 centers), coagulase-negative *Staphylococcus* (CoNS) spp. (3 centers), *Escherichia coli* (1 center), *Pseudomonas* spp.

(1 center) and *Staphylococcus aureus* (1 center).

Data provided from 13 centers showed that the median value for sepsis-related mortality was 24.39 for 100 sepsis cases, ranging from 0 to 75 for 100 sepsis cases in different centers. Mortality related to sepsis was higher in lower birth weight groups; median, minimum and maximum values (given in parenthesis) for infants < 500 g, 1500-2500 g and > 2500 g were 40/100 sepsis cases (0-100), 12.5/100 sepsis cases (0-100) and 0/100 sepsis cases (0-100).

Nosocomial ventilator-associated pneumonia (VAP) data was available from 9 centers, and VAP frequency was 1.7% (min 0.17, max 62.6). Nosocomial urinary tract infection (UTI) data was available from 12 centers, and UTI frequency was 3.7% (min 0, max 8.6). Catheter-related infection data was available from 6 centers, and frequency was 0.14% (min 0, max 15.7).

Unit Policies and Problems

Participating physicians from 16 different centers were queried in the electronic questionnaire regarding factors that are known to be important for infection control and possible problems in daily practice.

Infection control committees were performing active surveillance in all of the participating centers. Eight of 16 centers had written antibiotic prescription policies. Glycopeptides, carbapenem, piperacillin-tazobactam and ciprofloxacin were reserved antibiotics and used only according to the protocols and culture results in these centers.

The nurse-to-patient ratio was quite inadequate especially during night shifts. During day shifts, the mean number of infants per nurse was 3.66 ± 1.54 (2-7.75), while during night shifts this number was as high as 5.67 ± 1.85 (3.25-10.33) per nurse.

Overcrowding and understaffing in six centers, again lack of time in two centers, noncompliance of medical personnel in one center, and noncompliance of consultants from different departments such as pediatric surgery or radiology were reported as factors that negatively influenced hand hygiene.

Disinfectants were supplied without any

difficulty in most of the NICUs. One center declared that they rarely had difficulty in obtaining disinfectants, and 4 others stated that they sometimes had this problem. Seven of the 16 centers (44%) sometimes had difficulties in obtaining disposable materials.

The preferred way of hand disinfection was alcohol-based solutions in addition to liquid soap in 9 centers, chlorhexidine in 2 centers, and either liquid soap or chlorhexidine in 5 centers.

In all of the 16 centers, catheter care, aspiration and all invasive procedures were performed using sterile gloves. Only 3 centers were consistently using gloves for all patient contact. Two centers used gloves for contact with infected patients. One of the participating centers reported that they follow the guidelines of the Centers for Disease Control and Prevention (CDC).

Disinfection of washable devices was performed with chlorinated water, sodium dichloroisocyanurate and savlon solution. Medical devices unsuitable for washing were disinfected according to the manufacturers' recommendations. Incubators were disinfected in different ways in different centers. Quaternary ammonium compounds, sodium dichloroisocyanurate (precept disinfectant tablet), chlorhexidine, liquid detergents, clinox (concentrated surface disinfectant), and glutaraldehyde solutions were preferred according to the local infection control committee recommendations.

Opinions of HCWs about Neonatal Nosocomial Infections

In the second part of the study, a questionnaire regarding the opinions of HCWs about neonatal NIs was distributed to participants of the National Neonatology Congress in April 2006. One hundred and eight of 424 congress participants completed the questionnaire. Most of the HCWs who responded were from university hospitals (Table II). Positions of the questionnaire respondents are shown in Table III.

Most of the HCWs (72.2%) stated that they believed that NIs can be controlled and another 16.7% stated that the rates can be decreased, although there was no alternative box given

for this reply in the questionnaire (Table IV). When HCWs were grouped as nurses and doctors, there were no differences in their opinions about the problems pertaining to hospital infections and preventive measures ($p: 0.25$) (Table IV).

According to the Turkish neonatal HCWs who believed that NIs are preventable or at least can be reduced, the most important methodologies to control NIs were considered to be hand hygiene and ensuring sufficient numbers of HCWs in every shift, work with aseptic technique, education, rational antibiotic use, and minimal handling (Table V). It is quite interesting that only one HCW mentioned the importance of financial support. These answers again highlight the importance of high awareness of handwashing, preservation of optimal patient/nurse ratio, maintenance of supplies, and continuous education.

The most important problems leading to NIs were given as overcrowding, understaffing, inadequate basic conditions, lack of education, not working with aseptic technique, usage of broad spectrum antibiotics, and prolonged hospitalization.

Discussion

NICU infection rates have increased worldwide during the past decade. The increasing number of technology-dependent infants is the primary determinant in the increase in NIs^{1,2,12}. VLBW, gestational age < 29 weeks, birth outside the reference hospital, duration of mechanical ventilation and parenteral nutrition, and central catheters (umbilical artery/vein catheter, central venous catheter [CVC], percutaneous CVC) are reported as the risk factors in NIs^{9, 13-15}.

The incidence varies from 6% to 32% in the United States and from 8% to 10% in Europe-based studies^{1,2,5,6,12,16}. Neonatal infection rates are 3-20 times higher in developing countries than in developed countries¹⁷.

Data from 17 Canadian NICUs showed that at least one episode of NI developed in 23.5% of infants < 1500 g and in 2.5% of infants ≥ 1500 g. Over 95% of episodes were due to nosocomial bacteremia. Mortality was more strongly associated with NI versus in those without for infants ≥ 1500 g, but not for infants < 1500 g¹⁴. In fact, sepsis accounts

Table I. Sepsis Frequency in Different Birth Weight Groups

Birth weight group (g)	Number of infants with nosocomial sepsis	Number of infants admitted	%	p
< 1500	207	958	22	p: 0.001
1500-2500	98	1770	6	
> 2500	89	2903	3	

Table II. Workplaces of the Questionnaire Respondents

Type of hospital	Number	%
University	41	37.9
Community	26	24
Private	13	12
Not specified	28	25.9
TOTAL	108	100

Table III. Positions by the Questionnaire Respondents

Position	Number	%
Nurse	26	24
Resident	14	12.9
Pediatrician	35	32.4
Neonatologist	11	10.18
Professor	20	18.5
Clinical chief	2	1.8
TOTAL	108	100

Table IV. Responses to the Question "Do You Think That Hospital Infections Can Be Prevented?"

	Have no idea		No		Can be reduced		Yes	
	#	%	#	%	#	%	#	%
Nurse	-	-	3	11.5	2	7.7	21	80.8
Doctor	4	4.9	5	6.1	16	19.5	57	69.5
TOTAL	4	3.7	8	7.4	18	16.7	78	72.2

Table V. The Most Important Measures for Prevention of NIs in Two Different Groups of HCWs

	Yes, NIs can be prevented (n:78)	%	NIs can be reduced (n: 18)	%	TOTAL (n: 96)	%
Handwashing	62	79	6	33.3	68	70.8
Sufficient number of HCWs	33	42.30	5	27.77	38	39.58
Provision of minimal operational requirements (NICU design and maintenance of supplies)	31	39.74	3	16.66	35	36.45
Implementation of aseptic techniques	29	37.17	4	22.22	33	34.37
Education	25	32	2	11.11	27	28.12
Rational use of antibiotics	21	26.92	2	11.11	23	23.95
Minimal handling	16	20.51	2	11.11	18	18.75
Coordinated work with infection control committees	5	6.41	1	5.55	6	6.25
Limitation of entrance to NICUs	5	6.41	1	5.55	6	6.25
Human milk feeding	4	5.12	1	5.55	5	5.20
Optimal antenatal follow-up	2	2.56	0	0	2	2.08
Early enteral feeding	2	2.56	0	0	2	2.08
Financial support	1	1.28	0	0	1	1.04

for approximately half of all deaths beyond the second week of life in VLBW infants^{18,19}. From developing countries, the few studies on the VLBW population reported sepsis rates as 20-41%, reaching 68% when other types of infections were included. Infants <1000 g may not even be resuscitated in these countries¹⁷.

Our data of a total of 9,359 infants admitted to 16 centers in Turkey in 2005 showed 601 cases with culture-proven sepsis, with a mean nosocomial sepsis frequency per 100 admissions of 6.4. Sepsis-related mortality for the whole group was 24.3%. Incidence and mortality of sepsis were inversely proportional to birth weight.

The variation between the reports from different countries and centers results from not only the different healthcare practices and specific environment but also the nonstandard definitions of NIs and from differences in patient populations with respect to mean gestational age, birth weight and severity of the underlying illness, which significantly affect the incidence of NIs⁸. A national surveillance system reporting BSI, pneumonia and NEC and calculating device-related infection and patient infection days helps to realize and solve the problems early²⁰.

However, the comparison of device-related infection rates is more difficult because of the limited data from developing countries. In our study, VAP frequency was 1.7%, catheter-related infection frequency was 0.14% and UTI frequency was 3.65%.

The major pathogens of neonatal infections differ not only from country to country and from nursery to nursery but also change within years in the same nursery^{1,2}. During the last 20-25 years, a shift in etiology towards gram-positive bacteria, especially CoNS, for early and late sepsis and NIs with CoNS and *Candida* spp., has become a substantial problem in neonatal care^{15,18,21}. Gram-positive organisms were found to be responsible in 70.2% of infections in VLBW infants; the remaining infections included 17.2% gram-negative infections and 12.2% fungi⁸. On the other hand, *Klebsiella pneumoniae*, other gram-negative rods and staphylococci are the major pathogens, and antimicrobial resistance is a major problem in developing countries.

Neonatal *K. pneumoniae* infection varies from 4.1 to 6.3 per 1000 live births, and the case fatality rate is 18-68%. Assuming conservatively that *Klebsiella* is responsible for 20% of the estimated 1.6 million sepsis-related deaths in the developing world, *Klebsiella*-related neonatal deaths could amount to 320,000 neonatal deaths annually^{17,22}. Infections with multidrug-resistant organisms and *Candida* are also increasing in incidence¹.

Multidrug-resistant *K. pneumoniae* was reported as the leading cause of bacterial infections and sepsis-related mortality in neonates in Turkish NICUs in the 1990s⁹⁻¹¹. Nowadays, *S. aureus* and *S. epidermidis* and candidal infections are also increasing due to the increased survival of VLBW infants and as a result of increased use of invasive devices and broad spectrum antibiotics, at least in some of our units⁷.

In this study, the most frequently isolated microorganism in BSIs was *Klebsiella* spp. in 7 centers, *Serratia* spp in 3 centers, CoNS spp. in 3 centers, *E. coli* in 1 center, *Pseudomonas* spp. in 1 center and *S. aureus* in 1 center. This finding showed that gram-negative infections are still very important for our NICUs.

Problems in Infection Control

In order to prevent and control infections, it is critical to perform active surveillance to monitor trends in pathogens and microbial susceptibility patterns. An active surveillance was being performed in all participating centers by an infection control nurse.

Antibiotic use in the NICU is around 4.4-10.5%, being much higher (42-60.4%) for preterms and 92% for VLBW infants¹⁵. Selection of antibiotic-resistant bacterial species and candida infections are mostly caused by this attitude²³. Administration of inadequate empiric antimicrobial therapy among NICU patients with nosocomial BSI was associated with higher mortality²⁴.

Our study showed that only eight centers had a written antibiotic prescription policy. Glycopeptides, carbapenem, piperacillin-tazobactam, and ciprofloxacin were the reserved antibiotics to be used only according to the protocols and culture results.

High-volume NICUs caring for the smallest and sickest infants have the highest mortality²⁵.

Adequate staffing as well as compliance to hand hygiene procedures are essential. The low compliance rate, rarely exceeding 40%, is due to the busy conditions of the NICU, urgent situations, responsibility for the same duty for two or more patients, forgetfulness, not perceiving the necessity, and hand dryness²⁶. Inconveniently located sinks or lack of sinks also lowers compliance.

The factors influencing hand hygiene reported in this study were overcrowding and understaffing in six centers, and similarly lack of time in two centers. However, in our total group, the nurse-to-patient ratio was quite inadequate, especially during night shifts. In NICUs caring for the smallest high-risk infants, 1-2 patients per nurse can be cared for with the lowest infection rates. However, we were unable to show the relation between nurse/patient ratio and NI rates. This is probably due to the low ratios in the total group and also because in the largest units with lower nurse-to-patient ratio, HCWs are caring for the relatively bigger and lower-risk infants in their units.

Availability of an alcohol solution can improve hand disinfection compliance, as shown by Maury et al.²⁷ Low compliance with handwashing sharply increased in Europe and the United States with the use of an alcohol rub. The mean number of direct touches by staff members and with clean hands was greater in NICUs using alcohol-based hand rub than in the NICU using antimicrobial soap²⁸. A waterless alcohol-based rub was significantly less costly than traditional handwashing because of the reduced time required, and was associated with significantly better quality²⁹. Alcohol-based solutions were used in all of the participating centers in addition to liquid soaps and/or chlorhexidine.

Disinfection protocols were different in different centers but they were quite acceptable according to the universal rules. However, some of the centers reported difficulty in obtaining disinfectants and disposable materials.

According to the CDC rules, gloving is necessary when in contact with blood or other potentially infectious material. All centers used sterile gloves in the catheter care and for aspiration and all invasive procedures as necessary. Practice of using non-sterile gloves was different in most of the centers. There were

centers in which gloves were used for every patient contact, while in others, gloving was limited to contact with infected patients.

Opinions of Health Care Workers about Neonatal Nosocomial Infections

In the second part of the study, the replies of neonatal HCWs to the second questionnaire were analyzed as shown in Table IV. Most of the HCWs (72.2%) replied that they believed that NIs can be controlled and another 16.7% stated that the rates can be decreased.

According to the Turkish neonatal HCWs who believed that NIs are preventable, the most important methodologies to control NIs were hand hygiene, ensuring sufficient numbers of HCWs for every shift, work with aseptic technique, education, rational antibiotic use, and minimal handling. These answers again show the importance of high awareness of handwashing and preserving the optimal patient/nurse ratio and maintenance of supplies. The most important problems leading to NIs were reported as overcrowding, understaffing, inadequate basic conditions, lack of education, not working with aseptic technique, usage of broad spectrum antibiotics, and prolonged hospitalization.

There were no differences in the opinions of Turkish nurses and doctors regarding the problems related with hospital infections and preventive measures.

Several studies have shown the positive effects of different interventions, such as increased compliance with hand hygiene standards and other measures²⁹⁻³⁵.

Our survey showed that the rates of NIs vary considerably within different centers. This variation may be due to differences in clinical practices and work overload. An alternative study design to recognize the contributing factors may help to practice change and to decrease the NIs in the centers with higher rates.

Participating centers (in alphabetical order) and corresponding physicians (in parentheses) Akdeniz University Faculty of Medicine (Nihal Oygür), Bakirkoy Maternity and Children Teaching Hospital (Sultan Kavuncuoğlu, Sibel Özbek), Celal Bayar University Faculty of Medicine (Nermin Tansuğ), Cerrahpasa Medical Faculty, Istanbul University (Yıldız Perk, Barbaros Ilikan), Çukurova University Faculty of Medicine (Mehmet Satar, Hacer Yapıcıoğlu Yıldıztaş), Dokuz Eylül University Faculty of Medicine (Nuray Duman, Abdullah Kumral), Dr. Sami Ulus Maternity and Children's Hospital (Ayşegül Zenciroğlu, Gönül Tanır), Ege University Faculty of Medicine (Nilgün Kültürsay, Özge Altun Köröğlu), Eskişehir Osmangazi University Faculty of Medicine (Arif Akşit, Neslihan Tekin), Hacettepe University Faculty of Medicine (Şule Yiğit, Ayşe Korkmaz), Kocaeli University Faculty of Medicine (Ayşe Sevim Gökalp, Ayşe Engin Arısoy), Marmara University Faculty of Medicine (Eren Özek, Hülya Bilgen), Mersin University Faculty of Medicine (Aytuğ Atıcı, Ali Haydar Turhan), Süleyman Demirel University Faculty of Medicine (Hasan Çetin), Trakya University Faculty of Medicine (Betül Acunaş, Ülfet Vatanserver), Zeynep Kamil Maternity and Children's Hospital (Aysu Say, Feray Güven).

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