



# Surveillance of Nosocomial Infections in a Bulgarian Neonatal Intensive Care Unit

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## Abstract

**Introduction:** Nosocomial infections (NI) are frequent complications in neonatal intensive care units (NICU) which result in high morbidity and mortality.

**Aim:** To determine and analyze the incidence, risk factors and etiologic agents of NI in newborns admitted in the NICU to help planning future surveillance and prevention strategies.

**Materials and methods:** A prospective cohort study was carried out at the NICU of St George University Hospital, Plovdiv, Bulgaria from January 1, 2017 to June 31, 2018. The number of neonates included in the study was 507. Descriptive statistics such as count, percent, mean and standard deviation was used. Chi-square test was performed to prove associations. Odds ratios, with 95% confidence intervals, were computed from the results of the binominal logistic regression analyses.

**Results:** Of the 507 hospitalized newborns in NICU, 48 presented with 54 NI. The incidence and the density incidence rates were 9.5% and 7.67 per 1,000 patient-days, respectively. Nosocomial infections were detected in neonates from all birth weight (BW) classes, but it was low BW and premature neonates that were at major risk to acquire them. The most common infection sites were ventilator-associated pneumonia (VAP) (67.27%), bloodstream infection (23.64%) and conjunctivitis (9.09%). Major pathogens were Gram-negative such as *Klebsiella pneumoniae*, *E. coli*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. In the multivariate logistic regression analysis NIs were strongly associated with intubation, presence of a venous catheter, the duration of antibiotic treatment and increased CRP > 10 mg/l.

**Conclusions:** This report highlights the burden of NIs, identifies the major focus for future NI control and prevention programs.

## Keywords

aetiology, incidence, newborn, nosocomial infection, risk factors

## INTRODUCTION

Improvements in the neonatal intensive care have increased the survival of critically ill newborns.<sup>1</sup> At birth, newborns, especially premature and low birth weight neonates, are

devoid of efficient structural barriers of a protective endogenous microbial flora and of a mature immune system.<sup>2,3</sup> Furthermore, this population of vulnerable patients is often dependent on invasive procedures that are associated with a higher risk for infections. Nosocomial infections (NI) have become a major problem in many neonatal intensive

care units (NICUs) that complicate the hospitalization of patients and result in considerable morbidity and mortality, increased length of stay and increased health care costs.<sup>4,5</sup>

The most frequent infections in NICUs are bloodstream infections, pneumonia, and necrotizing enterocolitis (NEC); less frequent complications are infections of the eyes, mouth or skin.<sup>6,7</sup> In developed countries, the incidence rate of nosocomial infections ranges from 6 to 9 infections per 1000 patient-days, with 3- to 20-fold higher rates in developing countries.<sup>8,9</sup> 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.<sup>10,11</sup>

Effective surveillance is important to evaluate the epidemiology, the associated risk factors, and the causative microorganisms.

There are numerous risk factors for nosocomial infection among the newborns hospitalized for intensive care. The major risk factors can be categorized into intrinsic and extrinsic factors. The intrinsic factors include characteristics such as gestational age, birth weight, severity of the disease, immunologic maturity. The extrinsic factors include hospital stay, use of invasive devices, medications, exposure to hospital environment and hospital staff, hygiene and hospital infection control practices. Understanding the risk factors associated with nosocomial infections is a prerequisite for the development of prevention strategies.

## AIM

The aims of this study were to determine and analyze the incidence, risk factors and etiology of nosocomial infections in newborns admitted to neonatal intensive care unit (NICU) in order to help planning future surveillance and prevention strategies.

## MATERIALS AND METHODS

A prospective cohort study was carried out at the NICU of St George University Hospital in Plovdiv, Bulgaria between January 1, 2017 and June 31, 2018.

**Inclusion criteria:** patients admitted to the intensive care unit during the study period with medical pathology for observation, diagnosis or treatment and hospitalized for more than 48 hours.

**Exclusion criteria:** those patients whose stay in the NICU was less than 48 hours, and patients hospitalized before the beginning of the study.

The inclusion criteria were met by 507 neonates and they were included in the study.

To detect any risk factor of infection either maternal, natal or postnatal, a chart for epidemiologic surveillance was developed.

The information collected for the mothers was as follows: complete obstetric history of the mother, age, previ-

ous pregnancy, pathology before or during the pregnancy, change in the amniotic fluid, premature rupture of membranes (PROM) >18 h, maternal fever >38°C, maternal urinary tract infection (UTI), bacterial vaginosis, isolation of pathogens from vaginal secretions.

The variables for newborns were: admission date and time, gestational age, birth weight, sex, height, head circumference, mode of conceiving, mode of delivery, congenital malformations, information for intrauterine retardation, 1-minute and 5-minute Apgar scores. In addition, information about the duration of hospital stay, use of invasive devices (endotracheal tube/mechanical ventilation (MV), central/umbilical/peripheral venous catheter (CVC/UVC/PVC), parenteral feeding, continuous positive airway pressure (CPAP)), administration of antibiotics and duration of antibiotic treatment, laboratory findings were collected.

The definition of NI was based on a definition of the Centers for Disease Control and Prevention (CDC) which defines it as an infection not present or incubating at the time of NICU admission.<sup>12</sup> Additionally, we used the criteria of the German National Reference for Surveillance of Nosocomial Infections NEO-KISS.<sup>13</sup>

Bloodstream infection was defined as the isolation of pathogens from blood culture with the presence of at least 2 or more clinical and laboratory signs and symptoms. The clinical symptoms included elevated temperature > 37.8°C, hypothermia, frequent apnea, bradycardia <80 b/m, lethargy, feeding intolerance. The laboratory findings included C-reactive protein (CRP) > 10 mg/l, abnormal white blood cell count > 48 h after birth (Leu > 22 000/mcg or Leu < 5000/mcg), thrombocytopenia (Thr < 150 000/uL)

Pneumonia was defined as clinically unstable respiratory conditions with at least 2 or more clinical and laboratory signs, chest X-ray findings showing new or progressive infiltrate and isolation of a pathogen from endotracheal aspirate. The clinical signs included elevated temperature > 37.8°C, hypothermia, frequent apnea/bradypnea/tachypnea, bradycardia <80 b/m, change in tracheal secretions - color, quantity. Laboratory findings CRP > 10 mg/l, abnormal white blood cell count (Leu > 30 000/mcg or Leu < 5000/mcg), thrombocytopenia (Thr < 150 000/uL).

## Microbiological analysis

The Laboratory of Microbiology in St George University Hospital in Plovdiv using automated methods for identification (Becton Dickson Diagnostic Instrument Systems and VITEK, bioMerieux), processed all microbiological cultures. Antimicrobial susceptibility testing is determined using the disk diffusion method of Bauer-Kirby. Standard antibiogram discs were used (Bul Bio, NCIPD Ltd, Bulgaria).

## Statistical analysis

Numeric variables were presented as mean ± standard deviation (mean ± SD) or median (25th percentile; 75th per-

centile), if not normally distributed. Categorical variables were presented as percentages and counts (n,%). Chi-square test was performed for the association between potential risk factors and NI. The variables with  $p < 0.10$  in the univariate analyses were included in binomial logistic regression model in order to identify independent risk factors for NI. Odds ratios, with 95% confidence intervals, were computed from the results of the logistic regression analyses. A  $p$ -value  $< 0.05$  was considered statistically significant for all tests. For statistical analysis of the data we used SPSS Statistics v. 25 Package for Social Sciences (Armonk, NY: IBM Corp.).

## RESULTS

A total of 507 hospitalized newborns and 481 mothers entered the study. 48 neonates were diagnosed with 54 nosocomial infections giving an overall nosocomial infection rate of 9.5 per 100 hospitalized patients and a nosocomial infection incidence rate of 7.67 infections per 1000 patient-days.

The median age of the mothers of the studied neonates was 27.8 years; 25th percentile – 23.00 yrs., 75th percentile – 32.00 yrs (Table 1). Physician had tracked the pregnancy of 89.6% of all mothers. In almost one-fifth (18.5%) of the mothers, a pathologic condition prior to pregnancy was recorded and notably higher was the proportion of pregnant women with a pathologic pregnancy (36.2%). Among the mothers of infected neonates, the percentage of pathologic pregnancies was even higher - 51.06%. We found an association between pathologic pregnancy and NI ( $\chi^2=5.001$ ,  $p=0.025$ ).

Higher proportion of the studied neonates were delivered through cesarean section (63.5%, 322/507) and we found

an association between the method of delivery and NI ( $\chi^2=17.035$ ,  $p=0.000$ ). Infection was more common in males (60.42%, 29/48) compared to females (39.58%, 19/48). Most of them were premature neonates (68.75%, 33/48) and low birth weight (66.67%, 32/48) (Table 2). There is a statistically significant difference between the mean birth weight and gestational age of infected and non-infected neonates.

Ventilator-associated pneumonia (VAP) was the most common NI (67.27%,  $n=36$ ), followed by bloodstream infection (23.64%,  $n=13$ ) and conjunctivitis (9.09%  $n=5$ ). The median time to NI diagnose was 8.5 days. During the study period 4 neonates with NI died which resulted in lethality rate of 8.33%.

Gram-negative bacteria (74.16%) were the most prevalent pathogenic cause of nosocomial infection in our research. Four microorganisms (*Klebsiella pneumoniae*, *E. coli*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*) from the Gram-negative flora were most commonly isolated. From the Gram-positive bacteria, the leading pathogens were *Coagulase-negative Staphylococcus* (CoNS) (13.49%) and *Enterococcus faecalis* (7.87%). The distribution of pathogens is demonstrated in Table 3.

For the period of the study, 7175 patient-days were registered, the median hospital stay for the neonates being 10 days: 25th percentile - 7.00 days, 75th percentile - 17.00 days. Infected patients had a significantly longer median hospital stay (26.50 days: 25th percentile - 18.25 days, 75th percentile - 44.75 days) than non-infected patients (10.00 days: 25th percentile - 7 days, 75th percentile - 14 days) ( $t=7.22$ ,  $p < 0.0001$ ). The use of invasive devices in patients with NI was statistically significantly longer than in patients without NI (Table 2).

Birth weight and the medical reason for admission were directly associated with the length of hospital stay. In the

**Table 1.** Characteristics of the mothers of neonates with or without nosocomial infection

Variables	Mothers of neonates with NI (n=47)	Mothers of neonates without NI (n=434)	p-value
Mother's age, mean±SD	28.57±6.43	27.75±6.67	0.418
Antenatal care (visits), n (%)			
Yes	44 (93.7)	387 (89.17)	0.343
No	3 (6.3)	47 (10.83)	
Maternal disease before pregnancy, n (%)			
Yes	9 (19.15)	80 (18.43)	0.90
No	38 (80.85)	354 (81.57)	
Maternal disease during pregnancy, n (%)			
Yes	24 (51.06)	150 (34.56)	0.025
No	23 (48.94)	284 (65.44)	
PROM >18 h, n (%)			
Yes	5 (10.6)	32 (7.37)	0.425
No	42 (89.4)	402 (92.63)	

**Table 2.** Characteristics of the neonates with or without infection

Characteristics	Nosocomial infection		p-value
	Yes (n=48)	No (n=459)	
Mode of delivery, n (%)			
Vaginal	20 (41.67)	165 (35.95)	0.000
Cesarean	28 (58.33)	294 (64.05)	
Sex, n (%)			
Male n (%)	29 (60.42)	260 (56.64)	0.62
Female n (%)	19(39.58)	199(43.36)	
Gestational age, wk, n (%)			
≤28	14 (29.17)	16 (3.49)	
28-32	10 (20.83)	23 (5.01)	0.000
32-36.6	9 (18.75)	169 (36.82)	
≥37	15 (31.25)	251 (54.68)	
Birth weight, gr n (%)			
≤999	11 (22.92)	15 (3.27)	
1000-1499	12 (25)	24 (5.23)	0.000
1500-2499	9 (18.75)	154 (33.55)	
≥2500	16 (33.33)	266 (57.95)	
1 minute APGAR score	5.3±2.7	7.2±2	0.000
5 minute APGAR score	8.4±2.1	9.2±1	0.000
Hospital stay, days	33.63±20.42	12.12±9.16	0.000
Duration of CVC/UVC use, days	7.83±6.8	2.5±1.9	0.000
Duration of PVC use, days	32.5±20.25	11.04±8.75	0.000
Length of mechanical ventilation, days	14.65±11.75	3.68±4	0.000
Duration of antibiotic treatment, days	29.27±18.71	10.34±7.42	0.000

**Table 3.** Pathogens isolated in patients with NI (n=89)

Microorganism	Microorganisms in patients with NI n (%)
Gram positive	
Coag. (-) Staphylococcus	12 (13.49)
MRSA	1 (1.12)
Enterococcus faecalis	7 (7.86)
Enterococcus faecium	3 (3.37)
Overall Gram-positive	23 (25.84)
Gram-negative	
Klebsiella pneumoniae	19 (21.35)
Klebsiella oxytoca ESBL+	4 (4.49)
E. coli	10 (11.24)
Enterobacter spp.	4 (4.49)
Pseudomonas aeruginosa	9 (10.12)
Acinetobacter baumannii	9 (10.12)
Acinetobacter lwoffii	2 (2.25)
Stenotrophomonas maltophilia	4 (4.49)
Chryseobacterium spp.	3 (3.37)
Achromobacter spp	2 (2.25)
Overall Gram-negative	66 (74.16)

group of neonates weighing 2499-1500 g, the proportion of patients without NI was higher, whereas in the groups of very low (<1499 g) and extremely low birth weight neonates (<999 g) the proportion of patients with NI increased significantly. Another factor that can contribute to the longer hospital stay is the reason for intensive care admission (pre-existent morbidity). Among the infected neonates, the leading pathologic conditions that resulted in hospital admission were birth asphyxia, congenital pneumonia, and bronchopulmonary dysplasia.

Significant risk factors in the univariate analysis associated with NIs are presented in **Table 4**. We performed a binary logistic regression to ascertain the effects of the significant variables on the likelihood that participants have NIs. The logistic regression model was statistically significant ( $\chi^2(4)=100.27, p<0.0005$ ). The model explained 40.0% (Nagelkerke  $R^2$ ) of the variance in NIs and correctly classified 90.1% of cases. The independent risk factors in the multivariate analysis were intubation, increased CRP, duration of antibiotic therapy (>7 days), and PVC indwelling time (>14 days) (**Table 5**).

**Table 4.** Univariate analysis of the risk factors associated with nosocomial infections

Variables	Cases with NI (n=48)	Cases without NI (n=459)	OR <sup>a</sup>	95%CI <sup>b</sup>	p-value <sup>c</sup>
Birthweight (<2000 g)	26	85	5.2	2.8-9.6	<0.0001
Gestational age (<37 weeks)	31	193	2.5	1.3-4.6	0.003
Gender (male/female)	29	260	1.2	0.6-2.1	0.617
Mode of delivery (vaginal/cesarean)	28	294	0.8	0.4-1.4	0.434
Reanimation	38	176	6.1	2.9-12.6	<0.0001
Intubation	30	68	9.6	5.1-18.1	<0.0001
Pathologic conditions during pregnancy or at delivery	24	150	1.9	1.1-3.6	0.027
CVC/UVC	46	353	6.9	1.6-28.9	0.002
CVC/UVC indwelling time (>14 days)	2	6	26.4	5.2-135.2	<0.0001 <sup>d</sup>
PVC indwelling time (> 14 days)	38	90	15.6	7.5-32.5	<0.0001
Duration of MV (> 7 days)	28	10	22.9	8.9-58.4	<0.0001
Patient days (>14 days)	40	108	16.2	7.4-35.8	<0.0001
Duration of antibiotic therapy (>7 days)	47	236	40.0	5.5-292.7	<0.0001
Duration of antibiotic therapy (>14 days)	37	70	17.6	8.6-36.2	<0.0001
Increased CRP>10 mg/l	22	55	6.3	3.3-11.9	<0.0001

<sup>a</sup>: odds ratio; <sup>b</sup>: 95% confidence interval; <sup>c</sup>: Pearson  $\chi^2$ ; <sup>d</sup>: Fisher exact probability test

**Table 5.** Risk factors for nosocomial infections in the binary logistic regression analysis

Variables	OR <sup>a</sup>	95% CI <sup>b</sup>	p-value
Intubation	4.7	2.3-9.7	0.000
Increased CRP>10 mg/l	2.4	1.2-5.2	0.016
Duration of antibiotic therapy (>7 days)	11.4	1.4-90.8	0.022
PVC indwelling time (>14 days)	4.0	1.8-9.1	0.001

<sup>a</sup>: odds ratio; <sup>b</sup>: 95% confidence interval

## DISCUSSION

Nosocomial infections in the NICU are a relevant, major medical problem. As much as 9.5% (7.67/1000 patient-days) of the patients in our NICU were diagnosed with NI, with 47.92% of infections occurring in very low birth weight infants (<1499 g). Previous study in the same NICU in 2012 revealed a median incidence rate of NI of 12.2 per 100 hospitalized patients<sup>14</sup> which shows a non-significant decline in the incidence rate. In our country there are a limited number of studies considering neonatal nosocomial infections. Gladilova and Ribarova<sup>15</sup> for the period 2010-2011 discovered that 2% of all hospitalized neonates were diagnosed with a nosocomial infection. A research paper from 2014 of the National Center of Infectious and Parasitic Diseases (NCIPD) identifies 1062 NIs for the whole country and an incidence rate of 1.93%.<sup>16</sup> In this report, the information from physiological nurseries and NICUs is not separated. The incidence rates from our study are higher compared with the few published papers in the

country. This can be explained by the prospective monitoring and the active registration of the cases of NI. On the other hand, the cited studies from Bulgaria are based on official data from the system for passive surveillance of NI. Another problem present in our country is that a lot of the cases of NI are not proven microbiologically.<sup>17</sup>

The incidence rates of NI reported by research from other countries vary widely: 6–50 per 100 hospitalized patients and 5–62 per 1000 patient-days<sup>18-20</sup>, which is consistent with our results. Apart from that, it is very difficult to compare data from different studies because of the differences in study methodology, populations included, infection detection methods, and definitions used for NI.

It is worthy of note that 51.06% of the women in the study had some pathological condition during pregnancy (Table 1). An association was discovered between pathology during pregnancy and NI ( $\chi^2=5.001$ ,  $p=0.025$ ). We believe that it is a factor related to the mother that might increase the risk of NI in neonates, although in the binary logistic regression it showed to be non-significant ( $p>0.05$ ).

The premature rupture of membranes >18 h is a factor discussed in the literature that might increase the risk of sepsis in newborns.<sup>21</sup> According to WHO<sup>22</sup>, in 8% of pregnant women PROM >18 h is being registered annually, although in some countries, such as China<sup>23</sup> the rates can be even 19%. In our study PROM was registered in 7.7% of all pregnant women and the proportion of the mothers of infected neonates with PROM was even higher - 10.42%, but we were unable to find an association with NI.

Most of the neonates included in the study were born by cesarean section (63.5%). In a similar study in Greece, the authors observed even higher proportion of cesarean section (71.7%).<sup>24</sup> According to recent guidelines, cesarean births shouldn't exceed 19 of 100 neonates.<sup>25</sup> We found an association between the mode of delivery and NI and other researchers have also found a similar relation between NI and cesarean section.<sup>26</sup>

Babazono et al.<sup>27</sup> have analyzed risk factors for NI in NICU and showed that the infection incidence was significantly higher in boys (OR 1.28; 95% CI 0.43-3.75). Our study also suggests higher susceptibility of male babies to NI (OR 1.2; 95% 0.6-2.1). In this study we also observed the highest incidence of NI in patients weighing less than 1499 g (**Table 1**). Birth weight is an important factor that can increase the risk of infection. A 3% increase in the rate of NI for every 500 g decrement in birth weight has been previously reported.<sup>28</sup>

The risk of infection in our study was also inversely related to the gestational age. We found the highest incidence of NI in the group of neonates age 32 weeks or less (**Table 1**) and an association was observed between premature birth and NI ( $\chi^2=51.542$ ,  $p=0.000$ ). According to Glenn Mayhall<sup>29</sup> gestational age is one of the key determinants for defining the risk of NI.

Pneumonia was the most frequent NI (67.27%), followed by bloodstream infection (23.64%) and conjunctivitis (9.09%). This distribution is in agreement with other studies.<sup>18,24,30</sup> It is difficult to compare the results with studies from our country because there is no separate information for NICU. Gladilova and Ribarova<sup>15</sup> in their research paper identified infections of the sensory organs as the most frequent infections in neonatology units, followed by respiratory, enteric and bloodstream infections. According to the literature, the bloodstream infections in the developed countries are the leading NI in NICU followed by pneumonia.<sup>7,31,32</sup> These differences in distribution might be explained by the methodologies used for diagnosis, but the consistent variations between studies from developed and developing countries does suggest that the diversity in infection control standards and in clinical practices are probably also important.<sup>33</sup>

The median time to NI diagnosis was 8.5 days in our study. Other authors have observed median time to diagnosis of 15-19 days.<sup>18,34</sup> The lethality among patients with NI in our study was 8.33% and this correlates with results of other researchers.<sup>35,36</sup> It is very difficult to differentiate what is the role of the NI over this unfavourable outcome,

but in our opinion the infection has aggravated the severe pathology diagnosed in the infected neonates and has contributed to the outcome.

The risk for NI is directly associated with the length of the hospital stay. There was a statistically significant difference in the duration of hospital stay between infected and non-infected neonates. The patients with NI had almost 3-fold longer hospital stay (**Table 2**). We think this might be explained by the severe pathology diagnosed in the infected neonates at the time of admission and the lower birth weight of those neonates on the other side compared to the group of non-infected neonates. These factors suggest a need for a longer duration of the hospital stay. Although we found a statistically significant difference between the two groups, the logistic regression analysis didn't outline the hospital stay as a risk factor ( $p>0.05$ ).

The invasive devices are part of the advances in intensive care that improve the survival of premature newborns, but on the other hand they increase the risk for NI.<sup>19</sup> The venous cannulation is one of the most frequent procedure done in NICUs because it supports the provision of fluids and medications during the hospital stay. Alongside with the importance of venous catheterization for the intensive care, the venous catheters have proved as significant risk factor for NI.<sup>32,37</sup> In the binary logistic regression, we observed peripheral venous catheter dwelling time > 14 days as an independent significant risk factor for NI. Other studies have also outlined IV cannulation as a significant factor.<sup>26,38</sup>

Intubation in our study showed to be a significant risk factor in the binary regression analysis (OR 4.7; 95% CI 2.3-9.7). Mohammed et al.<sup>26</sup> have also found that endotracheal intubation increases the risk for NI (OR 5.43; 95% CI 3.46-8.5).

The duration of antibiotic treatment longer than 7 days was a significant risk factor in our study (OR 11.4; 95% CI 1.4 - 90.8). Kuppala et al.<sup>39</sup> has also showed that antibiotic therapy > 5 days increases the risk for NI (2.66; 95% CI 1.12-6.30).

The prevalence of Gram-negative microorganisms was statistically significant compared to Gram-positive microorganisms (74.16% and 25.84%, respectively). We found that *Klebsiella spp.* were the most frequently isolated microorganism in patients with NI (25.84%) followed by CoNS (13.49%), *E. coli* (11.24%) and *Enterococcus spp.* (11.24%). For our country, a study in 2014 outlined *Klebsiella pneumoniae* and *Coagulase negative Staphylococcus* as the leading pathogens in the neonatal units.<sup>16</sup> Authors from Brazil<sup>32</sup>, Italy<sup>40</sup>, and Egypt<sup>26</sup> have also observed *Klebsiella spp.* in the highest proportions among patients with NI. Gram-negative bacteria (*Klebsiella spp.*, *E. coli*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*) were the most common agents causing the leading NI-VAP. Although a shift has been noted in developed countries in the last years towards Gram-positive bacteria as agents causing pneumonia Gram-negative bacteria still remain the leading pathogens in less developed countries.<sup>30,40</sup>

## CONCLUSIONS

The study outlines the major characteristics of NI in one of the largest neonatal intensive care units in the country. The most frequent pathogens causing nosocomial infections belonged to the Gram-negative flora: *Klebsiella pneumoniae*, *E. coli*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*. Significant risk factors for NI were intubation, PVC indwelling time more than 14 days, duration of antibiotic treatment longer than 7 days and increased CRP > 10 mg/dl. Future interventions should focus on developing training programs and applying bundles for prevention of ventilator-associated pneumonia.

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## REFERENCES

- Stewart AL, Turcan DM, Rawlings G, et al. Prognosis for infants weighing 1000 grams or less at birth. *Arch Dis Child* 1977; 52:97.
- Brady MT. Health care-associated infections in the neonatal intensive care unit. *Am J Infect Control* 2005; 33:268–75.
- Auriti C, Maccallini A, Di Liso G, et al. Risk factors for nosocomial infections in a neonatal intensive-care unit. *J Hosp Infect* 2003; 53:25–30.
- Weinstein RA. Nosocomial infection update. *Emerg Infect Dis* 1998; 4:416–20.
- Morillo-García Á, Aldana-Espinal JM, Olry de Labry-Lima A, et al. Hospital costs associated with nosocomial infections in a pediatric intensive care unit. *Gac Sanit* 2015; 29(4):282–7.
- Dudeck MA, Weiner LM, Allen-Bridson K, et al. National Healthcare Safety Network (NHSN) report, data summary for 2012, Device-associated module. *J Infect Control* 2013; 41(12):1148–66.
- van der Zwet WC, Kaiser AM, van Elburg RM, et al. Nosocomial infections in a Dutch neonatal intensive care unit: surveillance study with definitions for infection specifically adapted for neonates. *J Hosp Infect* 2005; 61(4):300–11.
- Zingg W, Posfay-Barbe KM, Pittet D. Healthcare-associated infections in neonates. *Curr Opin Infect Dis* 2008; 21(3):228–34.
- Zaidi AK, Huskins WC, Thaver D, et al. Hospital-acquired neonatal infections in developing countries. *Lancet* 2005; 365(9465):1175–88.
- Adams-Chapman I, Stoll BJ. Nosocomial infections in the nursery. In: Tausch HW, Ballard RA, Gleason CA (Eds). *Avery's Diseases of the Newborn*. 8th ed. Philadelphia: Elsevier Saunders; 2005: 578–94.
- Korpela JK, Campbell J, Singh N. Health care associated infections. In: Mhairi MG, Mullett MD, Seshia MM (Eds). *Avery's Neonatology: Pathophysiology and Management of the Newborn*. 6th ed. Philadelphia: Lippincott Williams Wilkins; 2005:1356–83.
- Garner JS, Jarvis WR, Emori TG, et al. CDC definitions for nosocomial infections. *Am J Infect Control* 1988; 16(3):128–40.
- National Reference Center for Surveillance of Nosocomial Infections-NEO-KISS. Available from: <https://www.nrz-hygiene.de/en/surveillance/hospital-infection-surveillance-system/neo-kiss/>
- Kevorkyan A, Krasteva M, Murdjeva M, et al. [Epidemiologic surveillance in neonatology: three different approaches to define the incidence rate of nosocomial infections.] *Nosocomial infections* 2015; 10:71–80 [In Bulgarian].
- Gladilova A, Ribarova N. [Dynamics of distribution and epidemiologic characteristics of nosocomial infections in newborns during the period 2010-2011.] *Bulgarian Medicine Journal* 2012; 6(2):19–25 [In Bulgarian].
- Vladimirova N. [Surveillance of nosocomial infections in Bulgaria in 2014.] 2015. Available from: [https://www.ncipd.org/index.php?option=com\\_docman&view=download&alias=37-analiz-vbi-2014-g&category\\_slug=epidemiologiya-inadzor&Itemid=1127&lang=bg](https://www.ncipd.org/index.php?option=com_docman&view=download&alias=37-analiz-vbi-2014-g&category_slug=epidemiologiya-inadzor&Itemid=1127&lang=bg) [In Bulgarian].
- Ribarova N. [Nosocomial infections in Bulgaria in the period 1990-2002.] *Contemporary Medicine* 2005; 2:17-24 [In Bulgarian].
- Jeong IS, Jeong JS, Choi EO. Nosocomial infection in a newborn intensive care unit (NICU), South Korea. *BMC Infect Dis* 2006; 6:103.
- Urrea M, Iriondo M, Thio M, et al. A prospective incidence study of nosocomial infections in a neonatal care unit. *Am J Infect Control* 2003; 31(8):505–7.
- Tiskumara R, Fakharee SH, Liu CQ, et al. Asia-Pacific Neonatal Infections Study. Neonatal infections in Asia. *Arch Dis Child Fetal Neonatal Ed* 2009; 94(2):F144–8.
- Simonsen KA, Anderson-Berry AL, Delair SF, et al. Early-onset neonatal sepsis. *Clin Microbiol Rev* 2014; 27(1):21–47.
- Flenady V, King J. Antibiotics for prelabour rupture of membranes at or near term. *Cochrane Database Syst Rev* 2002; (3):CD001807.
- Zeng LN, Zhang LL, Shi J, et al. The primary microbial pathogens associated with premature rupture of the membranes in China: a systematic review. *Taiwan J Obstet Gynecol* 2014; 53(4):443–51.
- Nanou C, Paulopoulou I, Liosis G, et al. Risk factor for nosocomial infections in Neonatal intensive care units (NICU). *Health Science Journal* 2015; 9(2):1–6.
- Molina G, Weiser TG, Lipsitz SR, et al. Relationship between cesarean delivery rate and maternal and neonatal mortality. *JAMA* 2015; 314(21):2263–70.
- Mohammed D, El Seifl OS. Bacterial nosocomial infections in neonatal intensive care unit, Zagazig University Hospital, Egypt. *Egyptian Pediatric Association Gazette* 2014; 62(3-4):72–9.
- Babazono A, Kitajima H, Nishimaki S, et al. Risk factors for nosocomial infection in the neonatal intensive care unit by the Japanese Nosocomial Infection Surveillance (JANIS). *Acta Med Okayama* 2008; 62(4):261–8.
- Goldmann DA, Durbin WA Jr, Freeman J. Nosocomial infections in a neonatal intensive care unit. *J Infect Dis* 1981; 144(5):449–59.
- Clen Mayhall C. *Hospital Epidemiology and Infection Control*. 3rd ed. Lippincott Williams & Wilkins. 2005.
- Djordjevic ZM, Markovic-Denic L, Folic MM, et al. Health care-acquired infections in neonatal intensive care units: Risk factors and etiology. *Am J Infect Control* 2015; 43(1):86–8.
- Crivaro V, Bogdanović L, Bagattini M, et al. Surveillance of health-care-associated infections in a neonatal intensive care unit in Italy during 2006–2010. *BMC Infectious Diseases* 2015; 15:152.
- Couto RC, Carvalho EA, Pedrosa TM, et al. A 10-year prospective surveillance of nosocomial infections in neonatal intensive care units. *Am J Infect Control* 2007; 35(3):183–9.

33. Abdel-Wahab F, Ghoneim M, Khashaba M, et al. Nosocomial infection surveillance in an Egyptian neonatal intensive care unit. *J Hosp Infect* 2013; 83(3):196–9.
34. Aziz K, McMillan DD, Andrews W, et al., Canadian Neonatal Network. Variations in rates of nosocomial infection among Canadian neonatal intensive care units may be practice-related. *BMC Pediatr* 2005; 8;5:22.
35. Stoll BJ, Hansen N, Fanaroff AA, et al. Late-onset sepsis in very low birth weight neonates: the experience of the NICHD Neonatal Research Network. *Pediatrics* 2002; 110(2 Pt 1):285–91.
36. Basiri B, Sabzehei MK, Shokouhi M, et al. Evaluating the incidence and risk factors of nosocomial infection in neonates hospitalized in the neonatal intensive care unit of Fatemeh hospital in Hamadan, Iran, 2012 – 2013. *Archives of Pediatric Infectious Diseases* 2015; 3(2):e23327.
37. Umscheid CA, Mitchell MD, Doshi JA, et al. Estimating the proportion of healthcare-associated infections that are reasonably preventable and the related mortality and costs. *Infect Control Hosp Epidemiol* 2011; 2(2):101–14.
38. Távora AC, Castro AB, Militão MA, et al. Risk factors for nosocomial infection in a Brazilian neonatal intensive care unit. *Braz J Infect Dis* 2008; 12(1):75–9.
39. Kuppala VS, Meinzen-Derr J, Morrow AL, et al. Prolonged initial empirical antibiotic treatment is associated with adverse outcomes in premature infants. *J Pediatr* 2011; 159(5):720–5.
40. Orsi GB, d’Ettorre G, Panero A, et al. Hospital acquired infection surveillance in a neonatal intensive care unit. *Am J Infect Control* 2009; 37:201–3.



# Эпидемиологический надзор за нозокомиальными инфекциями в отделении интенсивной терапии новорожденных в Болгарии

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## Резюме

**Введение:** Нозокомиальные инфекции (НКИ) – частые осложнения в отделениях интенсивной терапии новорожденных (ОИТН), которые приводят к заболеваемости и смертности.

**Цель:** Выявить и проанализировать частоту, факторы риска и этиологические агенты НКИ у новорожденных для поддержки будущих стратегий мониторинга и профилактики.

**Материалы и методы:** Проспективное когортное исследование проведено в ОИТН университетской больницы «Св. Георги», Пловдив, Болгария, с 1 января 2017 г. по 31 июня 2018 г. В исследование было включено 507 новорожденных. Использовались такие описательные статистические данные, как количество, процент, среднее значение и стандартная ошибка. Для подтверждения ассоциаций был проведен тест хи-квадрат. Отношение вероятностей с интервальной конфиденциальностью 95% было рассчитано по результатам биномиального логистического регрессионного анализа.

**Результаты:** Из 507 новорожденных, госпитализированных в ОИТН, 48 поступило с 54 НКИ. Процент и частота заболевания составили 9.5% и 7,67 на 1,000 пациенто-дней соответственно. Нозокомиальные инфекции были обнаружены у новорожденных всех весовых категорий (ВК), но именно новорожденные низких ВК и недоношенные дети были подвержены высокому риску заражения. Наиболее частыми инфекциями были вентиляторассоциированная пневмония (ВАП) (67.27%), инфекция кровотока (23.64%) и конъюнктивит (9.09%). Основными возбудителями болезни были грамотрицательные бактерии, такие как *Klebsiella pneumoniae*, *E. coli*, *Pseudomonas aeruginosa* и *Acinetobacter baumannii*. В многомерном логистическом регрессионном анализе НКИ были тесно связаны с интубацией, наличием венозного катетера, продолжительностью лечения антибиотиками и повышенным уровнем С-реактивного белка CRP > 10 mg/l.

**Заключение:** В этом докладе подчёркивается тяжесть НКИ, определяются основные направления будущих программ контроля и профилактики НКИ.

## Ключевые слова

этиология, заболеваемость, новорожденный, нозокомиальная инфекция, факторы риска