

Nosocomial infections in the pediatric intensive care units in Lithuania

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Key words: nosocomial infection; pediatric intensive care; incidence rate; risk factors.

Summary. *Objective.* The aim of the study was to collect the data on incidence rates, pathogens of nosocomial infections, and antimicrobials for treatment of nosocomial infections.

Material and methods. Data were collected between March 2003 and December 2005 in five pediatric intensive care units using a modified patient-based HELICS protocol. Nosocomial infection was identified using the Centers for Disease Control definitions. All patients aged between 1 month and 18 years that stayed in the units for more than 48 hours were eligible for inclusion in this study.

Results. A total of 1239 patient admissions and 7601 patient-days were evaluated. In 169 children (13.6%), 186 nosocomial infections occurred. The incidence density was 24.5 per 1000 patient-days, the incidence rate – 15.0 per 100 admissions. The highest incidence density was observed in the 6–12-year age group (31.2 per 1000 bed-days). Nosocomial infection rates per 1000 device-days were 28.8 for ventilator-associated pneumonia, 7.7 – for bloodstream infection, and 3.4 – for urinary tract infection. The most common site of infection was respiratory tract (58.8%). Secondary bacteremia developed in 18 (10.6%) patients. *Haemophilus influenzae* (20.1%), *Acinetobacter spp.* (14.2%), and *Staphylococcus aureus* (17.6%) were the most frequently isolated microorganisms. The most common antimicrobials used were first- and second-generation cephalosporins 74 (31.0%) and broad-spectrum penicillins 70 (29.3%).

Conclusions. In Lithuanian pediatric intensive care units, the incidence rates of nosocomial infections were comparable to the available data from other countries, except for the ventilator-associated pneumonia rate, which was relatively high. *H. influenzae*, *Acinetobacter spp.*, and *S. aureus* were the most prevalent pathogens. The first- and second-generation cephalosporins and broad-spectrum penicillins were the most common antimicrobials in the treatment of nosocomial infections.

Introduction

Nosocomial infections (NIs) are a worldwide healthcare and public health problem, which places a substantial burden on individual patients and on the health care system and result in major complications of serious illnesses (1–4). NIs are a common cause of higher morbidity, mortality, and longer stays in the hospital (4–9). Children, hospitalized in intensive care units (ICUs), are unique population in regard to specific risk factors for NIs. Small children have enhanced susceptibility to many infections because of immaturity of their immune system. Children's exposure to environmental contamination (toys, diaper, hugging) is increased, they are treated using multidisciplinary medical and surgical approach; however, children have fewer chronic or degenerative disorders (5, 10, 11). The overall reported incidence of

NIs ranges from 6.1% to 29.6% in the pediatric intensive care units (PICUs) (5, 6, 8, 9, 11–16). However, to our knowledge, there are no published data about the incidence rates of NIs in PICUs of Eastern European countries.

Here we report the data on incidence rates, pathogens of nosocomial infections, and antimicrobials prescribed for the treatment of nosocomial infections. In addition, we compare the length of stay and mortality rate in the group of patients with NIs vs. without NIs.

Material and methods

Patients and setting. Data were collected between March 2003 and December 2005 from five PICUs in Lithuania: three in the University Hospitals and two in the regional central hospitals as subunits of general

ICUs. All five units, which participated in the study voluntarily, represent about 60% of all PICUs. The surveillance of NIs was carried out with permission of Lithuanian Bioethics Committee, issued in 2002.

All patients aged between 1 month and 18 years were eligible for inclusion in this analysis. All patients that stayed in the units for more than 48 hours were included.

Surveillance procedures and definitions. This report presents data from national NI surveillance system launched in 2003 in Lithuania. Participation of ICUs is voluntary, but requirement of minimum 6-month surveillance time per year and not shorter than 2-month continuous data collection should be followed. A patient-based NI surveillance protocol adopted from HELICS protocol was established (17, 18). Patients in departments were examined by physicians on duty, and standard data collection form was filled out where firstly general patient data (gender, age, referral place), clinical profile (medical, surgical, trauma), and patient status on admission (presence of infection, antibiotics at the time of admission, surgical operation within 1 month before admission) were indicated, and then risk factors during stay in a PICU, infection diagnosed during hospital stay, its treatment and outcome (discharge or death) were recorded daily.

The main risk factors for nosocomial infections were recorded, e.g. mechanical ventilation, arterial/central line, urinary catheter, peripheral venous catheter, intracranial pressure device, bronchoscopy, tracheostomy), and Standard Centers for Disease Control and Prevention definitions of infections were used (19). An infection was defined as NI if it occurred 48 hours after admission to the unit or within 48 hours after discharge. In addition to site of infection, its causative pathogen was determined; secondary bacteremia, if present, and antimicrobial therapy, if prescribed, were specified.

Statistical analysis. The data from the data collection forms were checked twice, entered into a database (EpiData, version 2.1), and analyzed with EpiInfo (version 6.04d) and Statistica (version 6.0) software. The size of the sample was appropriate for statistical analysis.

NI incidence (number of NI divided by number of patients admitted), NI incidence density (number of NI divided by number of patient-days), device-associated rate (number of NI divided by number of device-days), and device utilization ratio (number of device-days divided by patient-days) were calculated.

The patients for analysis were divided into four

age groups: infants (aged 1 month to <1 year), preschool children (1–5 years), children (6–12 years), and adolescents (>12 years). Types of NIs, incidence rates (NI incidence, NI incidence density, and device-associated rate), and device utilization ratios were compared among the age groups.

In addition, the sample was divided into two groups (with NIs and without NIs), and the groups were compared by age, gender, length of stay, and the mortality rate.

Categorical variables were evaluated using the chi-square (χ^2) test. Continuous variables were evaluated using Kolmogorov-Smirnov, Mann-Whitney *U*, and *t* test as appropriate. The significance level was $P < 0.05$.

Results

General data

A total number of 1239 children admitted to PICUs were analyzed: 740 (59.7%) boys and 499 (40.3%) girls. Mean age of boys was 6.6 years (SD, 6.1), girls – 6.2 years (SD, 5.9). The greatest proportion of the patients was in 1–5-year age group (37.2%, $n=461$). The mean length of stay in PICU was 6.1 bed-days (SD, 6.6; median, 4; minimum, 3; maximum, 136). Mean number of days from admission to PICU to onset of NI was 6 days (SD, 5.2; median, 4; minimum, 2; maximum, 36). Fifty-six (33.5%) patients have acquired NIs before the fourth day, 78 (46.7%) – during the fourth–seventh day, 33 (19.8%) – after the seventh day of their stay at PICUs.

The half of the patients ($n=625$, 50.7%) was admitted from home, 393 (31.9%) – from other ICUs, 215 (17.4%) – from other wards or hospitals. The greatest proportion of patients had surgical pathology ($n=598$, 48.4%). There were 503 (40.7%) medical and 118 (9.6%) trauma patients.

A total number of 562 (45.4%) patients had an infection, 352 (28.4%) patients were treated with antibiotics at the time of admission to PICUs, and 157 (12.7%) were operated on within one month before the admission.

The overall mortality rate was 3.4% ($n=42$). Distribution of the dead patients by the referral place was as follows: at home – 18 (42.9%), at other wards or hospitals – 14 (33.3%), at other ICUs – 10 (23.8%).

Almost all patients had at least one risk factor during their stay in PICU: 31.7% of the patients were mechanically ventilated (mean duration, 5.5 days), 26.2% had a central line catheter (mean duration, 6.4 days), and 56.0% of the patients had a urinary catheter (mean duration, 4.7 days). Device utilization ratios

Table 1. Incidence rates of nosocomial infections (NIs) by types in the age groups and device utilization ratio by types in the age groups

Age groups	Nosocomial infections				Device utilization ratio ⁴
	Number of NIs (n)	Incidence ¹	Incidence density ²	Device associated rate ³	
Pneumonia					Mechanical ventilator
1 month – <1 year	5	2.4	3.1	11.5	0.25
1–5 years	20	4.3	7.6	30.2	0.24
6–12 years	18	6.8	13.1	42.4	0.29
>12 years	21	7.0	10.6	30.9	0.35
All	64	5.2	8.4	28.8	0.28
Bloodstream infection					Central line
1 month – <1 year	2	0.9	1.2	4.9	0.26
1–5 years	9	2.0	3.4	12.9	0.26
6–12 years	4	1.5	2.9	10.6	0.27
>12 years	1	0.3	0.5	1.7	0.29
All	16	1.3	2.1	7.7	0.27
Urinary tract infection					Urinary catheter
1 month – <1 year	3	1.4	1.9	6.3	0.30
1–5 years	5	1.1	1.9	3.1	0.70
6–12 years	1	0.4	0.7	1.3	0.55
>12 years	4	1.3	2.0	2.9	0.53
All	13	1.0	1.7	3.4	0.43

$$^1 \frac{\text{Number of NIs}}{\text{Number of patients admitted}} \times 100$$

$$^2 \frac{\text{Number of NIs}}{\text{Number of patient-days}} \times 1000$$

$$^3 \frac{\text{Number of device-associated NIs}}{\text{Number of device-days}} \times 1000$$

$$^4 \frac{\text{Number of device-days}}{\text{Number of patient-days}}$$

were similar among the age groups for ventilator ($\chi^2=0.40$, $df=3$, $P>0.05$), central line ($\chi^2=0.00$, $df=3$, $P>0.05$), and for urinary catheter ($\chi^2=1.60$, $df=3$, $P>0.05$) (Table 1).

Incidence and types of nosocomial infections

One hundred sixty-nine children (13.6%) had a total of 186 nosocomial infections (NIs), 155 children (91.7%) had only one episode of NI, and 14 children (8.3%) had two or more episodes.

The incidence of nosocomial infections was 24.5 per 1000 patient-days, and the rate of NIs per 100 admissions was 15.0. No significant differences in the incidence of nosocomial infections was observed among the age groups ($\chi^2=3.32$, $df=3$, $P>0.05$), but the highest incidence density was in the 6–12-year age group ($\chi^2=11.09$, $df=3$, $P=0.01$) (Table 2). There was no significant difference in NI incidence observed

between genders as well (15.5% of boys vs. 14.2% of girls, $P>0.05$).

The highest device-associated rate for pneumonia (PNE) (42.4 per 1000 ventilation-days) was found among 6–12-year-old children ($\chi^2=17.95$, $df=3$, $P<0.0001$). The highest device-associated rate for bloodstream infection (BSI) (12.9 per 1000 catheter-days) was found in children aged 1–5 years ($\chi^2=10.24$, $df=3$, $P=0.02$). However, the age groups were homogenous by the device-associated rate for urinary tract infection (UTI) ($\chi^2=3.94$, $df=3$, $P>0.05$) (Table 1).

The most common site of NIs was respiratory tract (58.8%). There was a statistically significant domination of other lower respiratory tract infections (LRTIs) in the two age groups: 6–12 years and >12 years. However, the distribution of NIs by site in the age groups was similar (Table 3).

Secondary bacteremia developed in 18 (10.6%)

Table 2. Nosocomial infections (NIs) incidence rates by age

Age groups	Number of patients (n)	Nosocomial infections		
		Number (n)	Incidence ¹	Incidence density ²
1 month – <1 year	212	28	13.2	17.4
1–5 year	461	62	13.4	23.6
6–12 year	265	43	16.2	31.2
>12 year	301	53	17.6	26.7
Total	1239	186	15.0	24.5

$$^1 \frac{\text{Number of NIs}}{\text{Number of patients admitted}} \times 100$$

$$^2 \frac{\text{Number of NIs}}{\text{Number of patient-days}} \times 1000$$

patients with NIs. The most common NIs, which led to secondary bacteremia, were as follows: surgical site infection (SSI) (n=4, 22.2%), PNE (n=3, 16.7%), UTI (n=3, 16.7%), LRTI (n=2, 11.1%), and central nervous system (CNS) infection (n=2, 11.1%).

Pathogens of nosocomial infections

The total number of 157 (84.4%) NI cases were tested microbiologically. There was a growth of pathogens in 134 (85.4%) cases, no growth – in 8 (5.1%); the answer was missing in 15 cases (9.5%).

The most common pathogens of NIs were *Haemophilus influenzae* (20.1%), *Staphylococcus aureus* (17.6%), and *Acinetobacter* spp. (14.2%) (Fig.). Two cases of methicillin-resistant *S. aureus* (MRSA) were recorded (5.5% of all *S. aureus*). *H. influenzae* (29.8%) and *S. aureus* (19.0%) were the most common pathogens of PNE, *H. influenzae* (25.4%) and *Acinetobacter* spp. (22.0%) – of LRTI, *E. coli* (53.8%) and *Enterococcus* spp. (23.1%) – of

UTI, and *P. aeruginosa* (22.2%) – of SSI.

Antimicrobial therapy of nosocomial infections

Antimicrobials were prescribed to 155 (91.7%) patients with NIs. Monotherapy was the most commonly practiced (99 patients, 63.9%), while two antimicrobials were prescribed to 48 (31.0%) patients, three – to 5 (3.2%) patients, and 3 (1.9%) were given four antimicrobials. The antimicrobials used for treatment of NIs were first- and second-generation cephalosporins (n=74, 31.0%), broad-spectrum penicillins (n=70, 29.3%), aminoglycosides (n=28, 11.7%), third- and fourth-generation cephalosporins (n=26, 10.9%), narrow-spectrum penicillins (n=21, 8.8%), and glycopeptides (n=12, 5.0%).

Length of stay and the mortality rate

The groups of patients with NIs and without NIs were homogenous by age and gender ($P>0.05$).

The length of stay for patients with NIs was more

Table 3. Distribution of nosocomial infections by site of infection in the age groups

Nosocomial infection	Age groups				Chi-square (df)	P value	All N (%)
	1 month – <1 year N (%)	1–5 years N (%)	6–12 years N (%)	>12 years N (%)			
Pneumonia	5 (17.9)	20 (32.3)	18 (41.9)	21 (39.6)	7.5 (3)	>0.05	64 (34.1)
Other lower respiratory tract infection	5 (17.9)	10 (16.1)	15 (34.9)	16 (30.2)	9.13 (3)	0.03	46 (24.7)
Bloodstream infection	2 (7.1)	9 (14.5)	4 (9.3)	1 (1.9)	4.05 (3)	>0.05	16 (8.6)
Surgical site infection	6 (21.4)	3 (4.8)	2 (4.7)	3 (5.7)	6.81 (3)	>0.05	14 (7.5)
Urinary tract infection	3 (10.7)	5 (8.1)	1 (2.3)	4 (7.5)	1.66 (3)	>0.05	13 (7.0)
Gastrointestinal infection	2 (7.1)	2 (3.2)	1 (2.3)	0	2.78 (3)	>0.05	5 (2.7)
Skin/soft tissue infection	1 (3.6)	1 (1.6)	1 (2.3)	0	1.41 (3)	>0.05	3 (1.6)
Systemic infection	0	6 (9.7)	0	3 (5.7)	5.91 (3)	>0.05	9 (4.8)
Other infections	4 (14.3)	5 (8.1)	1 (2.3)	4 (7.5)	2.55 (3)	>0.05	14 (7.5)
Total	28 (100.0)	62 (100.0)	43 (100.0)	53 (100.0)	3.39 (3)	>0.05	186 (100.0)

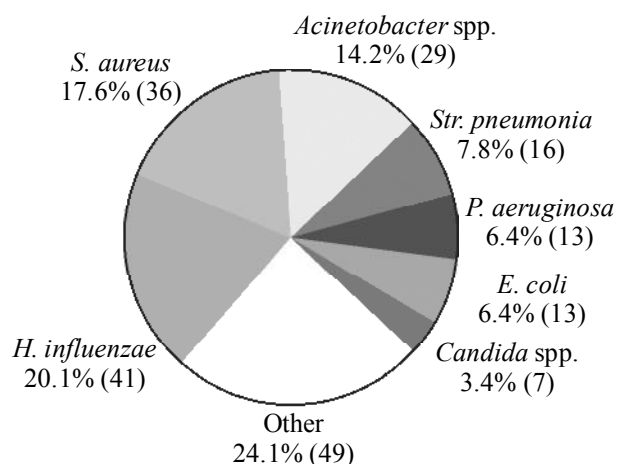


Fig. Etiology of nosocomial infections (n=204)

than twice longer as compared with the patients without NIs (11.7 days vs. 5.2 days, $P < 0.0001$). The mortality rate was almost three times higher in patients with NIs as compared to patients without NIs (7.7% vs. 2.7%, $P < 0.001$) (Table 4).

Discussion

Prevention of NIs is the key procedure in quality of healthcare. Accurate data on NI rates are essential for evaluation of current infection prevention activities and for planning further interventions in hospital as well as at national level (20).

This is the first report on NI rates in pediatric ICUs in the Baltic region. National compulsory NI reporting system existing in Lithuania for more than 20 years was missing data on NIs in ICUs. Therefore, data from new active surveillance system were very needful. It was very important to evaluate newly obtained data by comparing with data from other studies and NI surveillance systems even if it is complicated as the criteria of NIs and data collection methods might vary. Comparison of data is quite profound in one study or surveillance system due to obvious differences

between PICUs: severity of pathology, organization of work, etc. (5–7, 9, 14, 15, 21–24). Therefore, comparison of the data obtained from large databases or multicenter prospective incidence studies is more rational. Despite some limitations (hospitals are required to submit only 1 month of data, case finding methods are not specified, units are very different, etc.), the database of National Nosocomial Infections Surveillance System (NNIS) contains large amount of data from over 50 PICUs in the United States (11, 25). A similar database in European Union has not been completed yet, and data from PICUs are not available (17, 18).

Although the NI incidence was not the highest in PICUs of Lithuania (15.0% or 24.5/1000 patient-days) as compared with other reports from PICUs (22.2–29.7%) (6–9, 14, 15, 21) and adult ICUs by EPIC study (20.6%) (24), it was higher than reported by NNIS (6.1% or 14.1/1000 patient-days) (25) and some other studies (6.1–10.2%) (5, 22, 23).

As in most studies from PICUs (6, 8, 14, 23) and adult ICUs (24), PNE and LRTI were most prevalent NIs and accounted for 58.8% of all NIs with minor variations in the age groups. However, there are reports from PICUs where BSI (5, 7, 21, 22) and UTI (15) are the main sites of NIs, but in Lithuania these infections were recorded relatively rare.

The overall ventilator-associated pneumonia (VAP) incidence rate was very high when compared to data from other studies (28.8 vs. 8.9–18.7) (6, 7, 15, 26, 27). VAP rate in the age groups from >1 to ≤ 12 years (30.2–42.6) considerably exceeded the 90th percentile as compared to NNIS data (25). This points out the need to re-evaluate the current respiratory care practices, hygienic regulations, as the ventilator utilization ratio is not high when compared to NNIS data – it corresponds to the 25th percentile in the age group from 1 month to ≤ 12 years and to the 50th percentile in the age group of >12 years (25).

Table 4. Patients with vs. without nosocomial infections (NIs)

Characteristic	Patients with NIs (n=169)	Patients without NIs (n=1070)	P value
Age, years, mean (SD)	7.1 (6.2)	6.3 (6.0)	>0.05
Gender, N (%)			>0.05
boys	102 (60.4)	638 (59.6)	
girls	67 (39.6)	432 (40.4)	
Length of stay, days, mean (SD)	11.7 (8.7)	5.2 (5.7)	<0.0001
Mortality rate, %	7.7	2.7	<0.001

The central line-associated BSI rate (7.7) was lower as compared to the data from the majority of reported studies (6, 7, 9, 11, 13, 28) but higher than it is described in the European study (8). Similarly to VAP, the central line-associated BSI rate in the age group from >1 to ≤12 years (10.6–12.9) exceeded 90th NNIS percentile (25).

The urinary catheter-associated UTI rate (3.4) in general was not high as compared with reported data, which are very different across the world (1.8–25.5) (6–9, 11, 13). Only the infant group diverged with UTI rate (6.3) exceeding the 75th NNIS percentile (25). This may indicate a problem of excessive use of urinary catheters increasing the risk of UTI, whereas urinary catheter utilization ratio corresponded to the 50th percentile in the infant group and exceeded the 90th percentile in the age group of >1 year when compared to NNIS data (25). It is evident that the main risk factor for UTI is urinary catheter placement itself and its duration (29, 30). It is worth noting that the low rate may reflect a problem of undiagnosed infections. Most of UTIs are not severe and self-limiting, and microbiological investigations in such cases are not performed routinely in Lithuania.

We determined rather different pathogens in our study, where *H. influenzae*, *S. aureus*, and *Acinetobacter* spp. were prevailing. It differs from the reported data (6, 8, 22, 23), and it could be explained by the early onset of NIs (before the fourth day) in one-third of the patients. The other reason is the fact that the lower respiratory tract is a highly predominant site of infection. The prevalence of *Candida* was low (n=7, 3.4%), and it was not obtained from blood. In addition, the prevalence of MRSA was low (n=2, 5.5%).

The use of antimicrobials seems to be quite favorable. The use of penicillins and first- second generation cephalosporins accounted for 69.1% of all the cases.

Length of stay at PICUs was longer for patients with NI vs. without NI as it is reported in most studies (6–9). The same applies to mortality rate. This issue is always very sensitive in clinical practice. In some reports, NI is claimed to be responsible for a higher mortality rates in PICUs (5–7, 15, 27), in some not (26, 28, 31). In our study, the two groups (with NIs and without NIs) were homogenous by age and by gender, but unfortunately, the severity of underlying condition was not recorded. Higher mortality rate for patients with NIs could be influenced partly by underlying pathology as well as by NIs. The pediatric index of mortality (PIM) scoring would be helpful and suitable in this case. Unfortunately, it was impossible to introduce this index from the beginning of surveillance as only one PICU was using it routinely (32, 33).

Conclusions

The observed incidence density was 24.5 per 1000 patient-days, incidence rate was 15.0 nosocomial infections per 100 admissions, and it was comparable to the available data from the pediatric intensive care units of other countries. The bloodstream infection rate was 7.7 per 1000 central venous catheter-days; urinary tract infection rate was 3.4 per 1000 urinary catheter-days. The ventilator-associated pneumonia rate of 28.8 per 1000 ventilation-days was relatively too high. *Haemophilus influenzae*, *Acinetobacter* spp., and *Staphylococcus aureus* were the most prevalent pathogens, but the prevalence of methicillin-resistant *Staphylococcus aureus* was low. The first- and second-generation cephalosporins and broad-spectrum penicillins were the most common antimicrobials used in treatment of nosocomial infections. The length of stay and the mortality rate were higher in patients with nosocomial infections if compare to patients without nosocomial infections.

Hospitalinės infekcijos Lietuvos vaikų intensyvosios terapijos skyriuose

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Raktažodžiai: hospitalinė infekcija, vaikų intensyvioji terapija, sergamumo dažnis, rizikos veiksniai.

Santrauka. Tikslas. Nustatyti sergamumą hospitalinėmis infekcijomis, dažniausius sukėlėjus ir hospitalinių infekcijų gydymui skiriamus antibiotikus.

Metodai. Duomenys tyrimui rinkti 2003 m. kovo – 2005 m. gruodžio mėn. penkiuose Lietuvos vaikų intensyvosios terapijos skyriuose naudojant modifikuotą HELICS projekto protokolą. Hospitalinės infekcijos

diagnozuotos taikant JAV Ligų kontrolės centro apibrėžimus. Į tyrimą įtraukti visi 1 mėn. – 18 metų vaikai, kurie gydyti vaikų intensyvosios terapijos skyriuose ilgiau kaip 48 val.

Rezultatai. Tyrime dalyvavo 1239 pacientai, kurių gydymo trukmė – 7601 lovadienis. Užregistruoti 186 hospitalinės infekcijos atvejai, pasireiškę 169 (13,6 proc.) vaikams. Sergamumas hospitalinėmis infekcijomis sudarė 15 atvejų 100 ligonių (15,0 proc.) arba 24,5 atvejų 1000 lovadienių. Didžiausias sergamumas nustatytas 6–12 metų amžiaus grupėje (31,2 1000 lovadienių). Nustatytas sergamumas pagrindinėmis hospitalinėmis infekcijomis: 28,8 pneumonijos atvejo 1000 dirbtinės plaučių ventiliacijos dienų, 7,7 kraujo infekcijos atvejo 1000 centrinės venos kateterizacijos dienų ir 3,4 šlapimo organų infekcijos atvejo 1000 šlapimo pūslės kateterizacijos dienų. Dažniausiai registruotos apatinių kvėpavimo takų infekcijos (58,8 proc.). Antrinė bakteriemija užregistruota 18 (10,6 proc.) ligonių, sirgusių hospitaline infekcija. Dažniausi hospitalinių infekcijų sukėlėjai buvo *H. influenzae* (20,1 proc.), *Acinetobacter* spp. (14,2 proc) ir *S. aureus* (17,6 proc.). Gydymui dažniausiai skirti pirmos ir antros kartos cefalosporinai – 74 (31,0 proc.) bei plataus veikimo penicilinai – 70 (29,3 proc.).

Išvados. Sergamumas hospitalinėmis infekcijomis vaikų intensyvosios terapijos skyriuose Lietuvoje buvo panašus kaip kitose šalyse, išskyrus sergamumą ventiliacine pneumonija, kuris buvo didesnis; dažniausi sukėlėjai buvo *H. influenzae*, *Acinetobacter* spp. ir *S. aureus*, dažniausiai hospitalinės infekcijos gydymui skirta pirmos ir antros kartos cefalosporinų bei plataus veikimo penicilinų.

Adresas susirašinėti: V. Gurskis, KMUK Vaikų ligų klinikos Vaikų intensyvosios terapijos skyrius, Eivenių 2, 50009 Kaunas. El. paštas: vaidasg@freemail.lt

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