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Original Article

Epidemiological surveillance of endogenous and exogenous nosocomial infections

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Abstract

Aim: Nosocomial infections (NIs) represent a major public health problem in developed, and even more in developing countries. Based on the origin of the pathogen, NIs are divided into endogenous caused by microorganisms of the patient's microflora, and exogenous caused by pathogens from the patient's environment or by the same microorganism isolated elsewhere from patient's body. The main aim of this research was to determine the frequency, etiology and types of NIs at the Clinic for Surgery of the University Clinical Center Tuzla.

Material and Methods: 5.039 patients were prospectively followed for the development of endogenous and exogenous NIs (January-December 2015). The definition of NI was performed using standardized the National Healthcare Safety Network (NHSN) criteria.

Results: Based on continuous epidemiological surveillance, the incidence of NI was 3.51%; with a total of 177 registered infections, 24 endogenous and 153 exogenous. The most common NIs were urinary tract infections (UTIs) (14.29% endogenous and 85.71% exogenous) and surgical site infections (SSIs) (16.67% endogenous and 83.33% exogenous), p<0.001. Gram-negative bacteria were predominant (76.84%) over Gram-positive bacteria (23.16%). Gram-positive bacteria mainly caused bacteremia, while Gram-negative bacteria were most commonly isolated from UTIs and SSIs. The most common Gram-negative bacteria were *Klebsiella pneumoniae* (24.86%) and *Pseudomonas aeruginosa* (22.6%), and among Gram-positive, *Staphylococcus aureus* (10.73%) and coagulase-negative staphylococci (7.91%).

Conclusion: Epidemiological surveillance is considered a key link in the program for the prevention and control of NIs. The most important, and the ultimate goal and purpose of conducting epidemiological surveillance are to reduce and eliminate the risk factors, which can lead to a reduction in NI incidence rate. Determining the endemic rates of NIs provides an objective understanding of the overall NI status in an institution as well as existing risk factors for the occurrence of these infections.

Keywords: Bacterial infection; epidemiology; nosocomial infections;surveillance

INTRODUCTION

Nosocomial infection (NI) is any clinically pronounced disease that occurs as a result of admission of patients to a healthcare facility or therapeutic, diagnostic or other procedures applied in the treatment of underlying disease. It may occur after the discharge of patients from a healthcare facility or in the consultative polyclinic and outpatient care, and among hospital staff.

NI for epidemiological surveillance is defined as; a local or systemic disease (condition) caused by an infectious agent (one or more) or toxin that is not present or incubating at the time of admission to a hospital or any other healthcare facility.

An infection is considered nosocomial if it occurs within 48 hours (the typical incubation period for most bacterial nosocomial infections) after admission, or later, and also if found to be associated with surgery, and manifested within 30 days after surgery if an implant was not installed, or within one year if installed (1,2).

Based on the origin of microorganisms, nosocomial infections are divided into endogenous caused by microorganisms of the patient's microflora and exogenous caused by microorganisms from the environment or by the same microorganism isolated elsewhere from patient's body (2).

The significance of the problem with NIs is reflected through several implications associated with them.

Medical implications

Nosocomial infections represent a significant cause of additional morbidity and mortality, as well as a

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contributing factor to prolonged hospital treatment. At the individual level, for each patient, they are the cause of a new compromise of health status (3).

Legal implications

Legislation in the majority of countries defines the obligations of healthcare institutions to health protection, especially in fields with additional exposure to risks and dangers (4).

Economic implications

The economic implications of nosocomial infections can be viewed in two ways: disease cost and disease prevention cost. The cost of the disease can be viewed through both direct and indirect costs. The direct costs are specific and are reflected through treatment costs, additional diagnostics and prolonged hospitalizations. Indirect costs are lower and less specific. They relate to the additional suffering and anxiety of the patient.

The cost of prevention implies the relationship between the cost of infection prevention programs and the benefits derived from those programs. Studies published so far indicate that, ultimately, the benefits of a prevention program outweigh the cost of the disease (5-8).

Ethical implications

The fundamental reason for the existence of a healthcare system and the provision of medical services is to achieve positive changes in the health of patients and to minimize all risks that may arise during their provision. Current knowledge suggests that it is impossible to create a hospital without risk and that it is virtually impossible to talk about the elimination of nosocomial infections (9).

One of the main activities in the modern strategy of combating NIs is the implementation of surveillance. Epidemiological surveillance is defined as the continuous collection (detection and registration), processing, comparison, interpretation and submission of data on NI. The primary goal of NI surveillance is the prevention and control of nosocomial infections. One of the most important roles in organizing surveillance has the hospital epidemiologist, who coordinates the work of medical technicians or nurses trained in surveillance. Their joint activity provides the necessary data to detect infected patients, determine the incidence and prevalence of infections, determine the factors that cause infections, and monitor the effectiveness of measures to prevent and control them (10).

The aim of this study was to establish active epidemiological surveillance of nosocomial infections at the Clinic for Surgery of the University Clinical Center Tuzla (UKC) and to determine: frequency of nosocomial infections, distribution of endogenous and exogenous NIs by anatomical site, distribution of NIs by patients' age and gender, etiology of NIs and distribution of bacterial agents by type of NI.

MATERIAL and METHODS

This was a prospective study, performed between January 1 and December 31, 2015, on a sample of 5,039 patients admitted at the Clinic for Surgery, University Clinical Center Tuzla (a tertiary care hospital, serving a population of over 500,000 people). Only those patients hospitalized for at least 48 hours were included in the study. The NI definition and classification criteria were based on the internationally recognized definitions established by the CDC/NHSN Surveillance Definition of Healthcare-Associated Infection and Criteria for Specific Types of Infections in Acute Care Setting.

Infections of endogenous origin, caused by microorganisms from the patient's skin, gastrointestinal or upper respiratory tract, include:

-Endogenous bacteremia established without a recognizable origin of infection by the same microorganism found at another anatomical site at the time of positive hemoculture.

-Endogenous respiratory infections caused by aspiration of endogenous bacteria from the oropharynx and upper gastrointestinal tract into the tracheobronchial tree.

-Endogenous urinary infections caused by microorganisms from the patient's body.

-Endogenous infections of the surgical site as a result of the spread of endogenous microorganisms to previously uncontaminated zones.

Infections of exogenous origin, caused by microorganisms from the patient's environment or by the same microorganism isolated from another body site, include:

-Exogenous bacteremia resulting from documented infection by the same microorganism elsewhere on the body or penetration of the microorganism into the bloodstream via the external surface of the catheter and other medical devices.

-Exogenous respiratory infections resulting from documented infection by the same microorganism elsewhere on the body or the penetration of microorganisms into the respiratory tract by intubation, mechanical ventilation and the use of other invasive devices.

-Exogenous urinary infections caused by the penetration of exogenous bacteria into the bladder due to catheterization.

-Exogenous infections of the surgical site resulting from documented infection by the same microorganism elsewhere on the body or penetration of the microorganisms during surgery and other therapeutic manipulations (2).

The study used multiple tests, conducted through several surveys, which had features of a research instrument and were adapted to this type of testing. Each recorded nosocomial infection case had a separate research protocol, which included the following data: registration of a patient with the nosocomial infection, analysis of medical records, continuous microbiological assessment of the infected patient, information on testing for staff carriers, data on contamination of hospital environment and equipment, information on admission and transfer of the patient in the period of possible infection contraction, possible contacts between infected patients.

Statistical analysis

Standard methods of descriptive statistics were used in the statistical process of analyzing the results. The test that was used to determine the significance of the differences between the samples was the Chi-squared test. Values of p <0.05 were considered as statistically significant

RESULTS

In 2015, a total of 177 nosocomial infections (NIs) were registered at the Clinic for Surgery, 24 endogenous and 153 exogenous (Table 1). The NI incidence rate was 3.51%, with the highest incidence rates observed in August (5.08%), April (4.85%) and September (4.76%) and the lowest in January (1.32%) and February (2.02%). A total of 5,039 patients were treated at the Clinic for Surgery in 2015. The average monthly number of patients treated in 2015 was 419.917 patients, $\overline{X}$ = 419.917 with standard deviation (S.D.)=27.62 and standard error (S.E.)=7.97. The highest number of treated patients was in May (461), and the lowest in December (377).

The incidence of endogenous urinary tract infections (UTIs) was 14.29% and exogenous 85.71% (Table 2). Endogenous surgical site infections (SSIs) were represented by 16.67%, and exogenous ones by 83.33%, while endogenous respiratory tract infections (RTIs) were represented by 26.09% and endogenous by 73.91%. The prevalence of endogenous bacteremia was 17.65% and exogenous 82.35%. Other infections (OIs) were 11.11% endogenous and 88.89% exogenous. There was a statistical difference between the number of endogenous and exogenous UTIs, SSIs and OIs, $\chi2$= 14.78, p<0.001;

Table 1. Incidence rates of NIs at the Clinic for Surgery, UKC Tuzla in 2015

Year: 2015	No. of NI			No. of treated patients	NI rates (%)
	endogenous	exogenous	Total		
January	1	4	5	379	1.32
February	1	7	8	396	2.02
March	2	11	13	436	2.98
April	3	19	22	454	4.85
May	2	16	18	461	3.90
June	3	15	18	444	4.05
July	2	15	17	427	3.98
August	4	18	22	433	5.08
September	3	17	20	420	4.76
October	1	12	13	408	3.19
November	1	10	11	404	2.72
December	1	9	10	377	2.65
Total	24	153	177	5039	3.51

Abbr: NI: nosocomial infection; UKC: University Clinical Center

Table 2. Distribution of endogenous and exogenous NIs by anatomical site at the Clinic for Surgery

Year: 2015	NI by anatomical site				
	UTI (n=56)	SSI (n=54)	RTI (n=23)	Bacteremia (n=17)	OI (n=27)
	% (n)	% (n)	% (n)	% (n)	% (n)
endogenous	14.29 (8)	16.67 (9)	26.09 (6)	17.65 (3)	11.11 (3)
exogenous	85.71 (48)	83.33 (45)	73.91 (17)	82.35 (14)	88.89 (24)

Abbr: UTI: urinary tract infection; SSI: surgical site infection; RTI: respiratory tract infection; OI: other infection; NI: nosocomial infection χ2= 12.04, p<0.001; and χ2=7.75, p<0.01, respectively. There was no statistical difference between the number of endogenous and exogenous RTIs and bacteremia, χ2=1.92, p>0.05 and χ2=2.56, p>0.05, respectively.

UTIs were most common in patients older than 65 years (42.85%), while patients in the age range from 46 to 65 years had UTIs in 32.14% of cases, and patients between 19 to 45 years of age in 19.64% of cases (Table 3). Surgical site infections were most commonly reported in patients aged 46-65 years (38.89%), while patients older than 65 years had SSIs in 27.77% of cases, and patients aged 19-45 years in 25.93% of cases. Respiratory tract infections were mainly reported in patients older than 65 years (52.17%), followed by patients aged 46-65 years (26.09%), while patients aged 19-45 had RTIs in 17.39% of cases. Bacteremia was most prevalent in patients older than 65 years in 41.18% of cases, followed by patients aged 46-65 years in 23.53% of cases, as well as 19-45 years of age (23.53 %). Other infections were equally present in patients older than 65 years and those in the range from 45 to 65 years of age with 29.63% each, while in patients aged 19 to 45 years, they occurred in 25.93 % of cases.

UTIs were more common in men (82.14%), as were SSIs (61.11%), followed by RTIs (65.22%) and OIs (51.85%). Only bacteremia was more common in women, in 52.94% of cases.

Table 3. Distribution of NIs by patients' age and gender at the Clinic for Surgery, UKC Tuzla

	NI by anatomical site				
Year: 2015	UTI (n=56)	SSI (n=54)	RTI (n=23)	Bacteremia (n=17)	OI (n=27)
	% (n)	% (n)	% (n)	% (n)	% (n)
Age (years)					
<18	5.35 (3)	7.41 (4)	4.35 (1)	11.76 (2)	14.81 (4)
19-45	19.64 (11)	25.93 (14)	17.39 (4)	23.53 (4)	25.93 (7)
46-65	32.14 (18)	38.89 (21)	26.09 (6)	23.53 (4)	29.63 (8)
>65	42.85 (24)	27.77 (15)	52.17 (12)	41.18 (7)	29.63 (8)
Gender					
Male	82.14 (46)	61.11 (33)	65.22 (15)	47.06 (8)	51.85 (14)
Female	17.86 (10)	38.89 (21)	34.78 (8)	52.94 (9)	48.15 (13)

Abbr: NI: nosocomial infection; UTI: urinary tract infection; SSI: surgical site infection; RTI: respiratory tract infection; OI: other infection; UKC: University Clinical Center

Table 4 shows that as a cause of NI at the Clinic for Surgery in 2015, Gram-positive bacteria were isolated and identified 41 times, namely: 19 *Staphylococcus aureus* (*S. aureus*), 14 coagulase-negative staphylococci (CoNS) and 8 *Streptococcus species* (*Streptococcus* spp.). Gram-negative bacteria were isolated and identified 136 times: 44 *Klebsiella pneumoniae* (*K. pneumoniae*), 40 *Pseudomonas aeruginosa* (*P. aeruginosa*), 17 *Escherichia coli (E. coli)*, 16 *Proteus mirabilis (P. mirabilis)*, 10 *Citrobacter* species (*Citrobacter* spp.) and 9 *Acinetobacter species* (*Acinetobacter spp*.). There was no statistically significant difference between the type of isolated Gram-positive bacteria, χ2=2.30; p>0.05. There was a high statistical difference between the type of isolated Gram-negative bacteria, χ2 =43.10; p<0.001.

Table 4. Bacterial agents isolated from patients with NI at the Clinic for Surgery in 2015

Gram-positive bacteria	23.16 (41)
Staphylococcus aureus	10.73 (19)
CoNS	7.91 (14)
Streptococcus species	4.52 (8)
Gram-negative bacteria	76.84 (136)
Klebsiella pneumoniae	24.86 (44)
Acinetobacter species	5.08 (9)
Pseudomonas aeruginosa	22.60 (40)
Escherichia coli	9.60 (17)
Proteus mirabilis	9.04 (16)
Citrobacter species	5.65 (10)
Total	100 (177)

Abbr: NI: nosocomial infection; coagulase-negative staphylococci: CoNS

UTIs were most commonly caused by *P. aeruginosa* (33.93%), followed by *K. pneumoniae* (28.57%), then *P. mirabilis* (12.50%), *E.coli* (10.71%), *Citrobacter* spp. (5.36%), as well as *S. aureus* and *Streptococcus* spp. with 3.57% each, and finally *Acinetobacter* spp. with a frequency of 1.79% (Table 5).

Surgical site infections were mostly caused by *K. pneumoniae* (20.37%), followed by *P. aeruginosa* (18.52%) and *P. mirabilis*

(14.81%). *S. aureus* was the cause of SSIs in 12.96% and *E. coli* in 9.26% of cases, while *Acinetobacter* spp., *Citrobacter* spp. and CoNS caused 7.41% of SSIs, each. *Streptococcus* spp. were causative agents in 1.86% of SSI cases.

Respiratory tract infections were mainly caused by Gram-negative bacteria, namely *P. aeruginosa* (21.74%), *K. pneumoniae* (26.09%), while *Acinetobacter* spp. caused RTIs in 8.70% and *E. coli* in 13.04% of cases. *S. aureus* was the causative agent of RTIs in 13.04% of cases, and *Streptococcus* spp. were reported in 4.35% of RTI cases, while CoNS and *Acinetobacter* spp. were found in 8.70% of cases, each. *P. mirabilis* was registered as the causative agent in 4.35% of RTI cases.

Bacteremia was mostly caused by Gram-positive cocci: *S. aureus* (29.41%), followed by CoNS (11.76%), and *Streptococcus spp.* (5.88%). Of the Gram-negative bacteria the most frequent were *K. pneumoniae* (25.53%), followed by *P. aeruginosa* and *E. coli* with 11.76% of cases each. *Acinetobacter* spp. were detected in 5.88% of bacteremia cases.

Other infections were mainly caused by Gram-positive bacteria, namely *S. aureus* (7.41%), *Streptococcus* spp. (11.11%) and CoNS (22.22%), while the most common Gram-negative bacteria was *K. pneumoniae* (25.93%), followed by *P. aeruginosa* (14.81%) and *Citrobacter* spp. (11.11%). *E. coli* and *Acinetobacter* spp. were recorded as causative agents of OIs in 3.70% of cases.

Table 5. Distribution of bacterial agents of NI by anatomical site at the Clinic for Surgery

Causative agents of NIs	NI by anatomical site				
	UTI (n=56)	SSI (n=54)	RTI (n=23)	Bacteremia (n=17)	OI (n=27)
	% (n)	% (n)	% (n)	% (n)	% (n)
Staphylococcus aureus	3.57 (2)	12.96 (7)	13.04 (3)	29.41 (5)	7.41 (2)
CoNS	0 (0)	7.41 (4)	8.70 (2)	11.76 (2)	22.22 (6)
Streptococcus species	3.57 (2)	1.85 (1)	4.35 (1)	5.88 (1)	11.11 (3)
Klebsiella pneumoniae	28.57 (16)	20.37 (11)	26.09 (6)	23.53 (4)	25.93 (7)
Acinetobacter species	1.79 (1)	7.41 (4)	8.70 (2)	5.88 (1)	3.70 (1)
Pseudomonas aeruginosa	33.93 (19)	18.52 (10)	21.74 (5)	11.76 (2)	14.81 (4)
Escherichia coli	10.71 (6)	9.26 (5)	13.04 (3)	11.76 (2)	3.70 (1)
Proteus mirabilis	12.50 (7)	14.81 (8)	4.35 (1)	0 (0)	0 (0)
Citrobacter species	5.36 (3)	7.41 (4)	0 (0)	0 (0)	11.11 (3)

Abbr: NI: nosocomial infection; UTI: urinary tract infection; SSI: surgical site infection; RTI: respiratory tract infection; OI: other infection; coagulase-negative staphylococci: CoNS

DISCUSSION

Nosocomial infection is often an unavoidable risk associated with medical treatment. Due to advances in treatments of serious illnesses, there are more and more patients with reduced immunity to infection. At the same time, the use of intravenous and urinary catheters, respirators, complicated surgeries and other factors that reduce the defense mechanisms, make patients susceptible to infections. Epidemiological surveillance of nosocomial infections is a cornerstone of prevention and control.

Incidence studies allow for continuous monitoring of patients to detect the emergence of NIs of all types in all wards over a given period of time. The advantage is that these studies provide insight into the global situation as well as identify potential NI clusters. Based on continuous epidemiological surveillance of NI at the Clinic for Surgery of the UKC Tuzla in 2015, NI incidence rate of 3.51% was recorded, with a total of 177 registered infections, of which 24 were endogenous and 153 exogenous.

A prevalence survey conducted by the World Health Organization (WHO) in 55 hospitals of 14 countries located in Europe, Eastern Mediterranean, South-East Asia, and Western Pacific, reported an average NI rate of 8.7%. The most frequent nosocomial infections were SSIs, UTIs, and RTIs. The highest prevalence of nosocomial infections occurred in intensive care units and acute surgical and orthopedic wards. Infection rates were higher among patients with increased susceptibility, due to old age, underlying disease, or chemotherapy (11).

In 2001, a one-day trial was conducted in 19 Clinics for Surgery in Slovenia to determine the prevalence of NI and to identify predominant microorganisms and risk factors. A total of 6,695 patients had a prevalence of NI of 4.6%, which is approximately the same as the results of our study (12). Similar research has been done by Gikas et al in Greece with patients in surgical wards. Their results showed that in two research years (1999 and 2000) the NI rate in surgical patients was 14.3% and 10.1%, respectively (13).

In our study, the distribution of NI at the Clinic for Surgery in 2015 showed that the most common were UTIs with a total of 56 (31.63%) infections, or 14.29% of endogenous and 85.71% of exogenous UTIs (p <0.001), followed by SSIs with a total of 54 (30.5%) infections, 16.67% endogenous and 83.33% exogenous (p <0.001). According to the literature data, the urinary tract and surgical site infections account for more than half of reported nosocomial infections, with up to 35-40% of UTIs, usually caused by Gram-negative organisms, and 25-30% of SSIs (14-16). Narong et al at the University Hospital of Thailand found a NI rate of 8.35%, while the distribution of NI by anatomical site was 37.9% for SSIs, 26.3% for UTIs, 24.3% for RTIs, bacteremia 7.1% and OIs 4.4% (17).

The results obtained on the type of causative agent of NI and their presence at the Clinic for Surgery of UKC Tuzla in 2015 showed that Gram-negative bacteria were predominant (76.84%) over Gram-positive (23.16%). Literature data also indicate that Gram-negative bacteria are more common agents of NI (18-22). Thus, the results from our study were very comparable to the studies conducted by de Oliveira et al and Ak et al, with the reported rate of nosocomial infections caused by Gram-negative bacteria of 77% and 68.8%, respectively (19,21).

During the hospital stay, patients are in contact with a large number of different microorganisms, which puts them at a significant risk of developing NI (1,2,15,16). The characteristics of the microorganisms may influence the onset and outcome of certain types of infections. Bacteria are the most common causative agents of NI and two categories of bacterial pathogens of NI should be distinguished. In the first category are bacteria of the normal flora of healthy people, so-called commensals, which in normal circumstances prevent host colonization by pathogenic bacteria. However, in people with weakened natural defense mechanisms, commensals can cause infection. For example, infections associated with an intravascular catheter induced by CoNS from the skin or a urinary infection caused by *E. coli* originating from the gastrointestinal tract.

The second category includes pathogenic bacteria that have pronounced virulence factors and cause infection in the host, either sporadically or epidemically, regardless of the natural defense mechanisms. These are Gram-positive bacteria (*S. aureus*, ß-hemolytic streptococci), Gram-negative bacteria from the Enterobacteriaceae family (*E. coli*, *Proteus* spp., *Klebsiella* spp.), and Gram-negative non-fermentative bacilli (*Pseudomonas* spp., *Acinetobacter* spp.).

In our study, both types of infections of endogenous and exogenous origin were detected. Overall, the most common bacteria isolated were exogenous Gram-negative bacteria: *K. pneumoniae* and *P. aeruginosa* in 24.86% and 22.6% of cases, respectively. However, S. aureus was responsible for the greatest percentage of SSIs (29.41%), while CoNS was the second most common cause of OIs (22.22%).

The predominance of certain microorganisms causing nosocomial infections somewhat vary from one country to another, but similar to our study, it was previously reported that most of NIs are associated with *S. aureus*, CoNS, *Streptococcus pneumoniae*, *E. coli*, *P. aeruginosa*, *K. pneumoniae*, *Acinetobacter* and Enterococci (15, 23). Agaba et al showed that among the patients admitted to the intensive care unit the commonest Gram-negative organisms were *K. pneumoniae* (28.8%), *Acinetobacter* (21.2%) and *P. aeruginosa* (11.5%), while *S. aureus* was the most common Gram-positive pathogen (13.5%) (14). In a different study from Turkey, microorganisms responsible for most NIs included: *P.aeruginosa* (25%), *S.aureus* (21.4%), *E. coli* (18.7%), and A. *baumannii* (16.9%) (21). Also, consistent with our results, the major pathogen causing bloodstream infections in this study was *S. aureus.*

CONCLUSION

The significance of this research is reflected in the fact that nosocomial infections are a current and ongoing problem of modern medicine, with increasingly fascinating incidence, complications, prolonged hospital treatments and non-negligible material costs. Continuous surveillance may provide insight into the global situation of nosocomial infections in healthcare facilities, and also epidemiological surveillance is considered a key link in the nosocomial infection prevention and control program. The most important, and the ultimate goal and purpose of conducting epidemiological surveillance are to reduce or eliminate the risks, leading to a reduction in the incidence of NI. Determining the endemic rates of nosocomial infections provides an objective understanding of the overall NI status of the institution as well as of existing risk factors for the occurrence of these infections. Finally, in addition to evaluating the effectiveness of infection control measures, continuous efforts are needed to encourage hospital staff to implement these measures, which ultimately leads to legal compliance.

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