Original article

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Healthcare-Associated Infections and microbiological analysis at Clinic for anesthesia and intensive therapy in a tertiary health institution during a one-year period

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The term Healthcare Associate Infections (HAI) or Nosocomial Infections (NI) refers to infections that occur in patients during their stay and treatment in medical conditions, but were not present at the time of admission and they should manifest at least 48h after hospital admission. HAIs are more frequent in developing countries (5.7-19.1%) than in developed ones (3.5-12%). Antimicrobial resistance is one of the global and burden health problems and it is inevitable consequence of using antimicrobial drugs. Unjustified use of antibiotics has lead to antimicrobial resistance and changes in the causative pathogens responsible for HAIs. These types of infections prolong the length of hospital stay, lead to long-term disability, increase morbidity and mortality. The most common types of HAIs are: Ventilator Associated Pneumonia (VAP), Central Line Associated Bloodstream Infections (CLABSI), Catheter-Associated Urinary Tract Infections (CAUT) and Surgical Site Infections (SSI).

The aim of this study was to determine the most common bacteria causes of HAIs as well as the distribution according to the type of isolated bacteria from different types of samples.

The retrospective study was conducted at the Clinic for anesthesia and intensive therapy, University Clinical Center Nis, during the period from beginning of 2024 until the end of the same year. The patient samples were obtained, namely: blood, groin swab, oral cavity swab, wound swab, rectum swab, armpit swab, urine, aspirate from the endotrachal tube, nose swab, drain content, abdominal cavity content, tip of the central venous catheter, tip of the drain and aspirate from bronchia. The material was sent to the local microbiological laboratory with the aim of obtaining biogram and antibiogram.

Our results showed that total number of samples was 1464. Of them, 232 (15.85%) were blood samples, 179 groin swabs (12.23%), 166 oral cavity swabs (11.34%), 132 wound swabs (9.02%), 122 rectal swabs (8.33%) 108 armpit swabs (7.38%), 106 urine samples (7.24%), 94 endotracheal aspirate samples (6.42%), 63 nose swabs (4.30%), 56 aspirates (3.83%), 43 drain contents (2.94%), 15 abdominal cavity contents (1.02%), 15 tips of the central venous catheter (1.02%), 11 tips of the drain (0.75%), 10 aspirates from bronchia (0.68%) and 112 (7.65%) the other samples.

Depending of the type of bacteria, the distribution was: Klebsiella sp. 20.15%, Enterooccus Faecalis 19.26%, Acinetobacter sp. 14.41%, Pseudomonas aeruginosa 7.9%, Escherichia coli 7.17%, Staphylococcus epidermidis 4.99%, Proteus mirabilis 3.96%, Enterococcus Faecium 2.94%, Enetrobacter sp.2.94% and Staphylococcus sp.2.19%. Klebsiella sp. was the dominant bacteria isolated from oral cavity swab (3.28%), Enterococcus Faecium from groin swab (5.60%), Acinetobacter sp. from endotracheal aspirate (1.91%), Pseudomonas aeruginosa from wound swab (2.25%) and Escherichia coli from rectal swab (1.84%)

Healthcare Associated Infections have a lot negative impact on hospitalized patients. They lead to permanent disability, prolong patients' length of stay and increased mortality as well as expenditure and waste of medical resources. The predominance of microorganisms depends both on the hospital conditions, as well as on the patients and antibiotics prescribed by physicians. It is recommended to establish a precise schedule for antibiotic use in each region based on the most common pathogens and antibiotic resistance pattern and a surveillance programs as important tools which would be helpful to the clinicians to choose the most appropriate antimicrobial therapy for hospitalized patients.

Key words: Healthcare associated infection, nosocomial, bacteria, antibiotic

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Intrahospitalne infekcije i mikrobiološka analiza na Klinici za anesteziologiju i intenzivnu terapiju tercijarne zdravstvene ustanove tokom jednogodišnjeg perioda

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Naziv intrahospitalne infekcije ili nozokomijalne infekcije podrazumeva one infekcije koje se javljaju kod pacijenata u zdravstvenim ustanovama, a koje nisu bile prisutne u vreme prijema u zdravstvenu ustanovu i manifestuju se u prvih 48 sati. Češće su u zemljama u razvoju (5.7-19.1%) nego u razvijenim zemljama (3.5-12%). Antimikrobna rezistenca predstavlja globalni problem koji nastaje kao posledica upotrebe antimikrobnih lekova. Neopravdana upotreba antibiotika dovodi do razvoja bakterijske rezistence i promene uzročnika infekcije odgovornih za intrahospitalne infekcije. Ove vrste infekcija produžavaju dužinu bolničkog lečenja, dovode do invaliditeta, povećavaju morbiditet i mortalitet. Najčešći tipovi intrahospitalnih infekcija su: pneumonija povezana sa upotrebom respiratora, centralnim venskim katetrom uzrokovane infekcije krvi, kateterom uzrokovane urinarne infekcije i infekcije hirurških rana.

Cilj ove studije je bio odrediti najčešće bakterijske uzročnike intrahospitalnih infekcija, kao distribuciju uzročnika prema vrsti biološkog materijala.

Ova retrospektivna studija je sprovedena na Klinci za anesteziologiju i intenzivnu terapiju, Univerzitetskog Kliničkog Centra u Nišu, u vremenskom periodu od početka do kraja 2024.godine. Uziman je biološki material od pacijenata i to: krv, bris prepona, bris usne duplje, bris rane, bris pazuha, bris čmara, urin, endotrahealni aspirat, bris nosa, obični aspirat, sadržaj drena, saržaj trbušne duplje, vrh centralnog venskog katetra, vrh drena, bronhoaspirat i ostalo. Sav biološki materijal poslat je u mikrobiološku laboratoriju radi dobijanja biograma i antibiograma.

Naši rezultati su pokazali da je ukupan broj materijala bio 1464. Među njima 232 (15,85%) je bilo uzoraka krvi, 179 (12,23%) briseva prepona, 166 briseva usne duplje (11,34%), 132 briseva rane (9,02%), 122 (8,33%) briseva čmara, 108 (7,38%) briseva pazuha, 106 (7,24%) uzoraka urina, 94 (6.42%) endotrahealnih aspirata, 63 (4,30%) briseva nosa, 56 (3.83%) aspirata, 43 (2,94%) sadržaja drenova, 15 (1,02%) sadržaja trbušne duplje, 15 (1,02%) vrhova centralnih venskih katetera, 11 (0,75%) vrhova drena, 10 (0,68%) aspirata iz bronhija i 112 (7,65%) ostalih uzoraka

U zavisnosti od vrste bakterija, distrbucija je bila sledeća: Klebsiella sp. 2015%, Enterooccus Faecalis 19,26%, Acinetobacter sp. 14,41%, Pseudomonas aeruginosa 7,9%, Escherichia coli 7,17%, Staphylococcus epidermidis 4,99%, Proteus mirabilis 3,96%, Enterococcus Faecium 2,94%, Enetrobacter sp.2,94% i Staphylococcus sp.2,19%.Klebsiella sp. je bila dominantno prisutna u brisu usne duplje (3,28%), Enterococcus Faecium u brisu prepona(5,60%), Acinetobacter sp. u endotrahealnom aspiratu(1,91%), Pseudomonas aeruginosa u brisu rane(2.,25%) i Escherchia coli u brisu čmara(1,84%).

Intrahospitalne infekcije imaju ogroman negativni uticaj na hospitalizovane pacijente. Dovode do dugotrajne invalidnosti, produženog boravka i lečenja, povećanja smrtnosti, potrošnje medicinskih resursa i troškova lečenja. Uzročnici ovih infekcija zavise kako od bolničkih uslova, tako i od samih pacijenata i antibiotika koje prepisuju lekari. Preporučljivo je da postoje smernice za davanje antibiotika u svakom regionu u zavisnosti od najčešćih uzročnika i same antibiotske rezistencije, što će biti od pomoći zdravstvenim radnicima u odabiru najadekvatnije antimikrobne terapije za hospitalizovane pacijente.

Ključne reči: Intrahospitalne infekcije, nozokomijalne, bakterije, antibiotic

Introduction

The term Healthcare Associated infections (HAI) or Nosocomial Infections (NI) refers to infections that occur in patients during their stay and treatment in medical conditions, but were not present at the time of admission and they should manifest at least 48h after hospital admission. (1-3) Under the term HAIs are not only the hospital infections, but also infections acquired in any healthcare facilities, public and private (nursing homes, ambulatory, rehabilitation centers) which provide healthcare or diagnostic service to the patients. According to WHO data, about 5 -15% of hospitalized patients develop HAIs (4) and the results of EPIC II study showed that HAIs can be expected in even 51% of patients in ICUs. (5) The lack of data results in an inadequate and insufficiently developed system of supervision and control.

HAIs are more frequent in developing countries (5.7-19.1%) than in developed ones (3.5-12%) (6). Among newborns the occurrence of ICU related infections are 3-20 times higher. Two third of operated patients develop HAI in developing countries, which s nine times higher than in developed regions (7). By reviewing the literature it is estimated that 10-70% of HAIs are preventable with appropriate infection control. (8)

The most common risk factors for HAIs are: mechanical ventilation, critical care units, wound and burn units, dialysis unit, operation theatres, delivery rooms, neonates, prolonged hospital stay, utilization of invasive life-prolonging procedures including venous and arterial catheterization, urinary catheterization, invasive intracranial pressure monitoring, prior and prolonged antibiotic therapy, colonized neighboring patients and health care personnel, poor immune system of the patient, chronic and debilitating disease and diabetes. (9) In addition to host's susceptibility, it is important what are the biological characteristics of the infectious agent. (10)

The aim

The aim of this study was to determine the most common bacteria causes of HAIs as well as the distribution according to the type of isolated bacteria from different types of samples.

Materials and methods

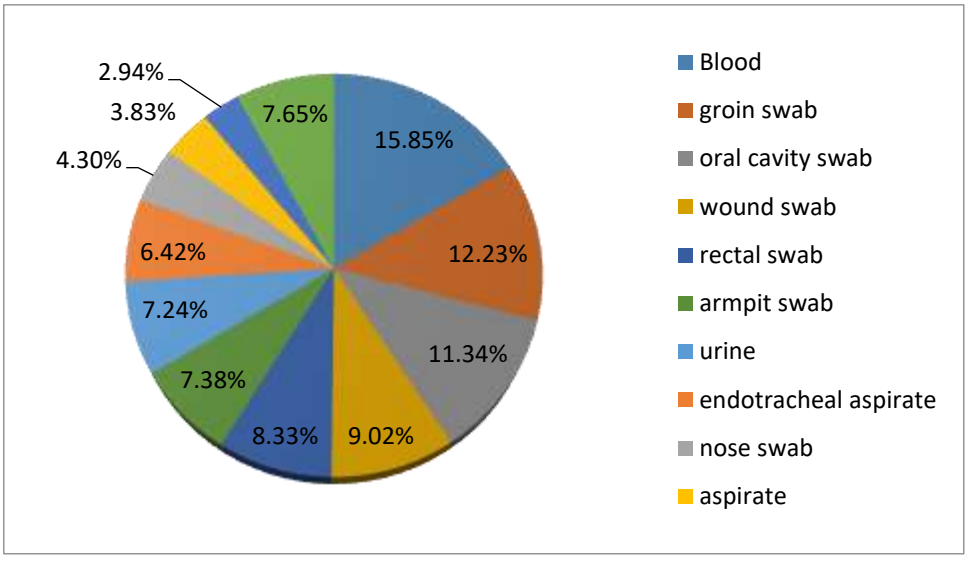
The retrospective study was conducted at the Clinic for anesthesia and intensive therapy, Clinical Center Nis, Serbia, during the period from beginning of 2024 until the end of the same year. The patient samples were obtained, namely: blood, groin swab, oral cavity swab, wound swab, rectum swab, armpit swab, urine, aspirate from the endotrachal tube, nose swab, drain content, abdominal cavity content, tip of the central venous catheter, tip of the drain and aspirate from bronchia. The material was sent to the local microbiological laboratory.

The data are presented as absolute numbers and percentages, which are then compared with data from literature.

Results

The total number of samples was 1464. Of them, 232 were blood samples, 179 groin swabs, 166 oral cavity swabs, 132 wound swabs, 122 rectal swabs, 108 armpit swabs, 106 urine samples, 94 endotracheal aspirate samples, 63 nose swabs, 56 aspirates, 43 drain contents, 15 abdominal cavity contents, 15 tips of the central venous catheters, 11 tips of the drains, 10 aspirates from bronchia and 112 the other samples, (unclassified). (Figure 1.)

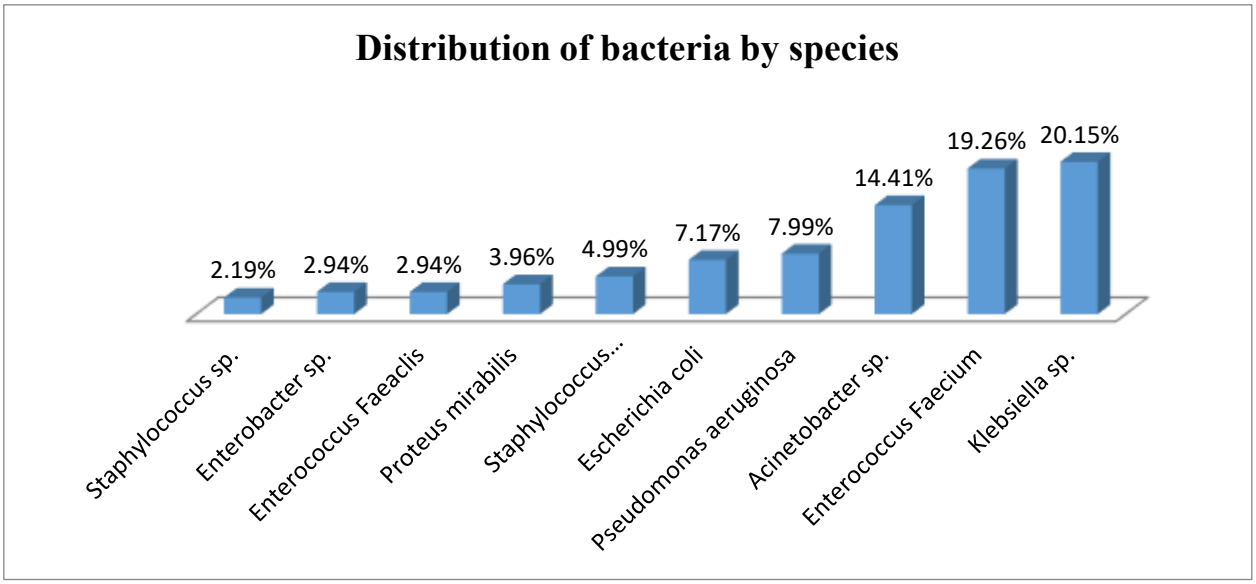
Figure 1. Distribution according to sample type



Depending of the type of bacteria, the distribution was: *Klebsiella sp*. 20.15%, *Enterooccus Faecalis* 19.26%, *Acinetobacter sp*. 14.41%, *Pseudomonas aeruginosa* 7.9%, *Escherichia coli* 7.17%,

Staphylococcus epidermidis 4.99%, *Proteus mirabilis* 3.96%, *Enterococcus Faecium* 2.94%, Enetrobacter sp.2.94% and *Staphylococcus sp.*2.19%. (Figure 2.)

Figure 2. Distribution of bacteria by species



Klebsiella sp. was the dominant bacteria isolated from oral cavity swab (3.28%), *Enterococcus Faecium* from groin swab (5.60%), *Acinetobacter sp*. from endotracheal aspirate (1.91%), *Pseudomonas aeruginosa* from wound swab (2.25%) and *Escherichia coli* from rectal swab (1.84%). (Table 1.)

Table 1. Distribution according to the type of the sample and isolated bacteria

			Klebsiella sp.		E.Faecium		Acinetobacter sp.		Pseudomonas aeruginosa		Escherichia coli	
Sample type	Number of samples	% of samples	No.	%	No.	%	No.	%	No.	%	No.	%
Blood	232	15.85%	3	0.20%	13	0.89 %	6	0.41%	6	0.41%	9	0.61 %
Groin swab	179	12.23%	30	2.05%	82	5.60 %	18	1.23%	9	0.61%	18	1.23 %
Oral cavity swab	166	11.34%	48	3.28%	51	3.48 %	22	1.50%	13	0.89%	17	1.16 %
Wound swab	132	9.02%	24	1.64%	7	0.48 %	25	0.71%	33	2.25%	5	0.34 %
Rectal swab	122	8.33%	16	1.09%	52	3.55 %	7	0.48%	4	0.27%	27	1.84 %
Armpit swab	108	7.38%	19	1.30%	48	3.28 %	20	1.37%	4	0.27%	3	0.20 %
Urine	106	7.24%	43	2.94%	2	0.14 %	13	0.89%	3	0.20%	13	0.89 %
Endotracheal aspirate	94	6.42%	25	1.71%	1	0.07 %	28	1.91%	11	0.75%	2	0.14 %
Nose swab	63	4.30%	12	0.82%	14	0.96 %	17	1.16%	5	0.34%	3	0.20 %
Aspirate	56	3.83%	12	0.82%			22	1.50%	8	0.55%	2	0.14 %
Drain content	43	2.94%	18	1.23%	3	0.20 %	2	0.14%	1	0.07%		
Abdominal cavity content	15	1.02%	2	0.14%					2	0.14%	3	0.20 %
Central venous catheter tip	15	1.02%	6	0.41%	3	0.20 %	2	0.14%	1	0.07%		
Drain tip	11	0.75%	2	0.14%			2	0.14%	1	0.07%	1	0.07 %
Bronchial aspirate	10	0.68%	5	0.14%			2	0.14%				
Other	112	7.65%	39	0.25%	6	0.41 %	22	1.50%	13	0.89%	1	0.07 %
Total	1464	100%	**295**	**20.15 %**	**282**	**19.26%**	**211**	**14.41%**	**117**	**7.99%**	**105**	**7.17 %**

Discussion

Antimicrobial resistance is one of the global and burden health problems and it is inevitable consequence of using antimicrobial drugs. Unjustified use of antibiotics has lead to antimicrobial resistance and changes in the causative pathogens responsible for HAIs. These types of infections prolong the length of hospital stay, lead to long-term disability, increased morbidity and mortality. All this has a negative impact on healthcare costs and annual costs are estimated to be about 7 billion euros in Europe and 6.5 billion dollar in United States. (11) Some of examples are methicillin-resistant *Staphylococcus aureus* (MRSA) which is still an important challenge for many countries. In addition

to MRSA, multidrug-resistant *Escherichia coli*, vancomycin resistant enterococci (VRE), and carbapenem resistant Enterobacteriaceae are becoming a problem of public health importance. (10)

Antibiotic resistance is responsible for the death of a child every five minutes in the Southeast Asian region. Medicines that were used to treat deadly diseases are now losing their potential, precisely because of the development of resistance. (12) Self-medication, inadequate dosage, prolonged use, lack of standards among healthcare institutions are the main reasons. Resistance threatens effective control against bacteria caused by urinary tract infections, pneumonia and blood stream infections. The most common among them are MRSA and multiresistant G- bacteria. (13) In the region of Southeast Asia are strains of *E.coli* and *Klebsiella pneumonia* resistant to third generation cephalosporines ad more than a quarter of infections caused by *S. auerus* are resistant to methicillin. (14)

The sources of HAIs infections are: 1) endogenous-the patient's microflora and most frequently 2) exogenous. Bacteria are the most common causes of HAIs (90%). Some of them are part of the patient's normal flora and lead to infection only when patient's immune system declines. About 5% of HAIs are caused by viruses. (15) Among them, the most common are influenza, HIV, rotavirus, herpes simplex virus and hepatitis. Among the fungi, the most commom causative agents are *Aspergillus sp*. and *Candida albicans.* (16) The main routes of transmission include contact (direct and indirect), airborne, common vehicle (by contaminated items like food, water, medications, equipment) and vector borne (mosquitoes, flies, rats). (17)

Nowadays, according to WHO the most common causes of HAI are *Pseudmonas aeruginosa, Acinetobacter baumanii, Klebsiella pneumonia, Clostrdum difficile, E.coli* and *Staphylococcus aureus*. (18) These bacteria developed additional mechanisms against currently available antibiotics. (19) That is why the development and introduction of new antibiotics into the clinical practice is urgently necessary.

According to the current guidelines, when the patient is at risk of infection with resistant organisms, it is advisable to use broad-spectrum combination therapy with more than two antibiotics as the initial empirical therapy. (20)

Our results showed that total number of samples was 1464. Of them, 232 (15.85%) were blood samples, 179 groin swabs (12.23%), 166 oral cavity swabs (11.34%), 132 wound swabs (9.02%), 122 rectal swabs (8.33%) 108 armpit swabs (7.38%), 106 urine samples (7.24%), 94 endotracheal aspirate samples (6.42%), 63 nose swabs (4.30%), 56 aspirates (3.83%), 43 drain contents (2.94%), 15 abdominal cavity contents (1.02%), 15 tips of the central venous catheter (1.02%), 11 tips of the drain (0.75%), 10 aspirates from bronchia (0.68%) and 112 (7.65%) the other samples (unclassified).(Figure 1) Depending of the type of bacteria, the distribution was: *Klebsiella sp.* 20.15%, *Enterooccus Faecalis* 19.26%, *Acinetobacter sp.* 14.41%, *Pseudomonas aeruginosa* 7.9%, *Escherichia coli* 7.17%, *Staphylococcus epidermidis* 4.99%, *Proteus mirabilis* 3.96%, *Enterococcus Faecium* 2.94%, Enetrobacter sp.2.94% and *Staphylococcus sp*.2.19%. (Figure 2)

Table 1. shows the distribution of bacteria according to the type of biological material from which they were isolated. *Klebsiella sp.* was the dominant bacteria isolated from oral cavity swab (3.28%), *Enterococcus Faecium* in groin swab (5.60%), *Acinetobacter sp*. in endotracheal aspirate (1.91%), Pseudomonas aeruginosa in wound swab (2.25%) and *Escherichia coli* in rectal swab (1.84%)

The most common types of HAIs are: Ventilator Associated Pneumonia (VAP), Central Line Associated Bloodstream Infections (CLABSI), Catheter-Associated Urinary Tract Infections (CAUT) and Surgical Site Infections (SSI).

Central line associated bloodstream infections (CLABSI) incidence is about 12-25%. (21) Catheters can cause serious and deadly infection, resulting in compromised health and increased in care cost. They are usually caused by gram-positive organisms including Coagulase Negative *Staphylococcus*, *Staphylococcus auerus* and Enterococci. (22)

According to the Liao et al. study (23) of 584 blood samples a total of 267 (45.7%) were caused by fermentative gram-negative organisms, 137 (23.5%) by non-fermentative gram-negative organisms, and 134 (22.9%) by gram-positive organisms. Fungi were isolated in samples (6.8%). The most common bacteria as a cause of blood stream bacteria among gram-negative strains were *Klebsiella spp*. (14%), *E. coli* (14%), *Enterococcus spp.* (11%), *Acinetobacter spp.* (10%), Enterobacter sp. (9%), *S. aureus* (9%) and *Pseudomonas spp.* (8%). In our study, the main cause were gram-positive bacteria, namely *Enerococcus Faecium.*

In 1990 the predominant bacteria causing blood stream infections were gram-positive, namely *Staphylococcus aureus.* Later, in 2000 it was *Acinetobacter baumanii*, and in recent years are gram-negative Enterobactriales (24).

Some of the mortality risk factors according to the above mentioned study are: low body weight, comorbidity with malignancy and liver cirrhosis, high CRP level, high CCI, and internal medicine and hematology/oncology patients.

According to European national prevalence studies the rate of nosocomial urinary tract infections (UTI) are 23-49%. (25) They are manly caused by the patients' microflora, where the catheters serves as a conduit for entry of bacteria and imperfect drainage and retained urine provide the stability to bacterial residence. A common cause of nosocomial urinary tract infection are *E.coli, Pseudomonas aeruginosa, Klebsiella spp*, *Proteus mirabilis, Staphylococcus epidermidis*, Enterococci and *Candida spp.* (26, 27)

Asymptomatic bacteriuria in catheterized patints, according to the most clinicians, should not be treated. As long as the presence of catheter is temporary, this condition is transient end will resolve spontaneously. In justified cases it is recommended to use silver-coated catheters. The most significant preventive measure is to avoid use of the indwelling catheters whenever possible. Study of Jain P et al. (28) showed that in 21% of cases the use of urinary catheters unjustified.

The study of Nouri et al. (29) showed showed that the most frequent among gram-negative bacteria in urine the most frequent in gram-negative samples were: *E.coli* with 832 (59.6%), *K.pneumoniae* with 139 (9.9%), *P. aeruginosa* 71 (5.09%), Enterobacter sp. 31 (2.2%), *Acinetobacter baumannii* 30 (2.15%) and *Klebsiella oxytoca* 18 (1.2%). The most frequent pathogens from tracheal aspirate were*: K pneumoniae* 164 (27.8%), *Acinetobacter baumannii* 118 (20.06%), *Pseudomonas aeruginosa* 97 (16.4%) and *E. coli* 57 (9.6%). In our study, the most prevalent bacteria was *Klebsiella sp.*

The frequency of Surgical site infections (SSI) is 2-5% surgical patients, mainly caused by endogenous microflora of the patients. Among bacteria, the most often isolated is *Staphylococcus aureus,* commonly found amongst the normal flora of the skin (30, 31) followed by *Candida sp, E. coli, P. aeruginosa and S. epidermidis*. (32)

Nosocomial pneumonia, which develops at least 48 hrs after intubation is defined as Ventilatory associated pneumonia. The prevalence is 10-65% and mortality rate is about 20%. (33, 34). The most common risk factors are elderly men, smokers, coexisting lung diseases and admission because of respiratory problems. (35) The most common pathogens are gram-negative bacteria such as *Acinetobacter sp., Pseudomonas aerugnosa, Klebsiella pneumonia* and gram-positive cocci like *Stalhylococcu aureus*, especially MRSA. (36) In the study George et al. (36, 37) the most common isolate was *Acinetobacter sp.* (37.5%). Our findings are consistent with the above mentioned study

Infection Control Programs and Prevention of HAIs

The standard procedure performed on patients suspected of having infections in ICU implies: 1) Gram staining results, usually available after 24 h; 2) organism identification from the culture, typically returned after 48 h16; 3) the full antibiogram results, which is a susceptibility test for various antimicrobials, available after approximately 72 h. The definitive answer antibiogram will give (38).

Some of the most important preventive measures are: early detection of colonized patient, eradication of the source of reservoir, isolation of infected or colonized patient, emphasis on hand hygiene before and after patient handling, use of disposable gloves, prohibition of unjustified antibiotic prescription/use, establishment and implementation of the surveillance system for antimicrobial resistance, education of hospital staff and community (39).

The Centers for Disease Control and Prevention (CDC) estimates that about 100 million of antibiotics are prescribed annually, of which about 50% are not necessary (40). Patient selection should be based on the patient's tolerance, in addition to the nature of the disease and the pathogen. The goal of antimicrobial therapy is to choose an antibiotic that is selective for the suspected pathogen, has a low probability to cause resistance, and has no adverse reactions (16).

Adequate surveillance of HA involves data collection from various sources: information should include administrative data, demographic risk factors, patient medical history, diagnostic tests and data validation.

Surveillance led by WHO can serve as a guide to help healthcare institutions to introduce their own system of surveillance and control of HA infections. Adequate training of hospital staff is of great

importance in the prevention of HA infections. Also, decontamination f the patient by treating the gut and skin has been proven to effective.

Recently, a strong focus has been placed on the prevention and control of these types of infections, as well as on the non-negligible financial aspect.

In order to reduce the costs it is important: 1) for healthcare facilities to follow strict infection control protocols, 2) to improve surveillance of HAIs, 3) educate the staff to follow the preventive practice, 4) implementation of standard precautions such as hand hygiene practice at bedside. (41)

Conclusion

Healthcare associated infections have a lot negative impact on hospitalized patients. They lead to permanent disability, prolong patients' length of stay and increases mortality and both expenditure and waste of medical resources. The bacteria types as a source of nosocomial infections differ from country to country, even among the institutions in the same region. The predominance of microorganisms depends both on the hospital conditions, as well as on the patients and antibiotics prescribed by physicians. Bacteria find effective defense mechanisms and develop resistance to the most commonly prescribed antibiotics. Thus, temporary cessation in use of certain antibiotics is one of the solutions to reduce resistance, but also giving antibiotics only when needed. Also, it is recommended to establish a precise schedule for antibiotic use in each region based on their antibiotic resistance pattern. Increase in antimicrobial resistance requires a need for surveillance programs as important tools which would be helpful to the clinicians to choose the most appropriate antimicrobial therapy for hospitalized patients.

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