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Original Article

The epidemiology of pathogen microorganisms in hospital acquired infections

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Abstract: This study aimed to determine the prevalence and type of hospital acquired infections (HAIs), distribution of predominant pathogens and antimicrobial susceptibilities of nosocomial isolates. Diagnosis of HAIs was made subcategorized as bloodstream infection (BSI), surgical site infection (SSI), urinary tract infection (UTI), respiratory tract infection (RTI). The identification and antibiotic susceptibility of pathogen microorganisms of HAIs was detected with the use of the automatic identification and antibiogram system. Coagulase negative Staphylococcus (CNS) has been identified as the pathogen microorganism in BSIs and SSIs significantly higher than the UTIs and RTIs (P<0.001). *Acinetobacter baumanii ve Acinetobacter spp.* were significantly higher in RTIs (P<0.001). *Klebsiella pneumoniae* was identified as the significantly higher pathogen microorganism in SSIs than BSIs (P=0.035). *Escherichia coli* was most significantly higher in UTIs, and then in SSIs (P<0.001). *Candida spp. ve Enterococcus spp.* were significantly higher in UTIs (P<0.001). *Pseudomonas spp*. was significantly higher in RTIs than BSIs (P=0.011). Extended spectrum beta lactamase (ESBL) resistance of *E. coli* ve *Klebsiella* isolates in HAIs was detected to be 44.6%. Carbapenem resistance of non-fermantative microorganisms were established as 69%. Methicilline resistance of staphylococci in HAIs was detected as 81.5%. Methicilline and carbapenem resistance were the most frequently detected in BSIs (67.4%, 40.2%), ESBL resistance was the most frequently detected in SSIs (36%). The increasing detection rates of multiresistant microorganisms in HAIs limits antimicrobial prophylaxis and treatment of infections. More epidemiological datas are needed to compare different treatment approachments.

Keywords: Hospital acquired infection, pathogen, extended spectrum beta lactamase, carbapenem, methicillin

Introduction

Hospital acquired infection (HAI) is an important complication bringing along some problems like prolongation of hospitalization, increase in mortality and morbidity rate and prolongation of the treatment period [1, 2]. In HAIs drug-resistant pathogens has generally been ascribed to the widespread use of antimicrobial agents [3]. Changes in the types of pathogens isolated in serious infections might also affect resistance patterns because different bacterial species inherently have differing antimicrobial susceptibilities [4]. Several studies have reported that infection with an antibiotic resistant strain of an organism is associated with greater mortality and costs and longer intensive care unit (ICU) lengths of stay than infection with the non-resistant strain [5-9]. In the face of emerging multiresistant organisms, antimicrobial prophylaxis and treatment have become increasingly difficult, and timely and accurate epidemiological information is needed for guiding appropriate empirical therapy [10]. This study aimed to determine the prevalence and type of HAIs, distribution of predominant pathogens and antimicrobial susceptibilities of nosocomial isolates in hospitalized Cardiology and Cardiovascular surgery patients at Bursa YuksekIhtisas Training and Research Hospital during a 57 month period (January 2011-2015 October).

Materials and methods

A retrospective observational cohort study was conducted at Bursa YuksekIhtisas Training and Research Hospital, Turkey which is a tertiary care hospital located in the South Marmara Region. Cardiology and Cardiovascular surgery patients diagnosed with HAI between January 2011-October 2015 at the clinical departments

Table 1. Comparisons of the presentation rates of the microorganisms in infection groups

Pathogen microorganism	BSI n=273	UTI n=51	RTI n=122	SSI n=158	*p*-value
CNS	66 (19.50%)[a*]	0[b*]	0[b*]	31 (19.60%)[a*]	<0.001
S. aureus	49 (17.90%)[a*]	0[b*]	7 (5.70%)[b*,c*]	20 (12.70%)[a*,c*]	<0.001
Acinetobacter baumanii	33 (12.10%)[a*]	0[a*]	36 (29.50%)[b*]	18 (11.40%)[a*]	<0.001
Acinetobacter spp.	23 (8.40%)[a*]	2 (3.90%)[a*]	24 (19.70%)[b*]	8 (5.10%)[a*]	<0.001
Enterococcus faecalis	20 (7.30%)[a*]	2 (3.90%)[a*,b*]	0[b*]	5 (3.20%)[a*,b*]	0.009
Klebsiella pneumoniae	11 (4%)[a*]	3 (5.90%)[a*,b*]	10 (8.20%)[a*,b*]	8 (13.80%)[b*]	0.035
Pseudomonas aureginosa	10 (3.70%)	3 (5.90%)	9 (7.40%)	6 (3.80%)	0.378
E. coli	9 (3.30%)[a*]	20 (39.20%)[b*]	8 (6.60%)[a*]	27 (17.10%)[c*]	<0.001
Candida spp.	9 (3.30%)[a*]	10 (19.60%)[b*]	0[a*]	0[a]	<0.001
Enterococcus faecium	8 (2.90%)	1 (2%)	0	3 (1.90%)	0.235
Candida albicans	8 (2.90%)	1 (2%)	0	1 (0.60%)	0.124
Serratia marcendens	6 (2.20%)	0	2 (1.60%)	3 (1.90%)	0.967
Enterococcus spp.	5 (1.80%)[a*]	6 (11.80%)[b*]	0[a*]	3 (1.90%)[a*]	0.001
Enterobacter cloacae	3 (1.10%)	0	1 (0.80%)	6 (3.80%)	0.161
Klebsiella spp	2 (0.70%)	1 (2%)	5 (4.10%)	6 (3.80%)	0.051
Enterobacter aerogenes	2 (0.70%)	0	4 (3.30%)	2 (1.30%)	0.232
Citrobacter spp.	2 (0.70%)	1 (2%)	1 (0.80%)	1 (0.60%)	0.688
Enterobacter spp.	2 (0.70%)	0	1 (0.80%)	1 (0.60%)	1.000
Bacillus spp.	2 (0.70%)	0	0	1 (0.60%)	1.000
Pseudomonas spp.	1 (0.40%)[a*]	0[a*,b*]	6 (4.90%)[b*]	3 (1.90%)[a*,b*]	0.011
Stenotrophomonas maltophilia	1 (0.40%)	0	3 (2.50%)	0	0.115
Streptococcus spp.	1	0	0	0	-
Proteus mirabilis	0	1 (2%)	1 (0.80%)	3 (1.90%)	0.152
Streptococcus pneumoniae	0	0	2	0	-
Morganella morgagni	0	0	1 (0.80%)	1 (0.60%)	0.376
Acinetobacter lwoffii	0	0	0	1	-
Klebsiella oxycota	0	0	1	0	-

*In the table, if the percent values related to the groups and the letters (a, b, c) presented with them are the same, this corresponds to similarity of the related groups. If different, it means discrepancy. **Skin and soft tissue infections are not included in the comparisons as the number of data were not enough.

and intensive care units of Cardiology and Cardiovascular surgery were included in the study.

The registry of detected infections used the classification of infections into the following clinical forms of infections: bloodstream infection (BSI), surgical site infection (SSI), urinary tract infection (UTI), respiratory tract infection (RTI), skin and soft tissue infection (SSTI). Diagnosis of HAIs was made based on Centers for Diseases Control criteria.

Microbiological analysis

Microbiological tests were conducted on patients with suspected HAI. The following clinical material was collected for the microbiological tests: blood, urine, swab from the wound, sputum, tracheal aspirate, the tips of vascular catheters and others. Positive blood cultures were identified by the clinical microbiology laboratory (BACTEC 9240 Blood Culture System; Becton Dickinson Biosciences). For nosocomial bacteremia, the originating source is then identified and subcategorized. The identification and antibiotic susceptibility of staphylococci, bacilli from the Enterobacteriaceae family, nonfermenting bacilluswas detected with the use of the automatic identification and antibiogramsystem (Microscan Walkaway). The identification of *Candida spp*. was made with the use of API c AUX (bioMe'rieux, France).

Statistical analysis

Datas are expressed by frequency and by related percent values. Comparisons between gr-

Table 2A. ESBL resistance ratios of gram-negative pathogen microorganisms in HAIs

Pathogen microorganism	ESBL (+)	ESBL (-)
E. coli	27 (54%)	38 (61.3%)
Klebsiella pneumoniae	17 (34%)	15 (24.2%)
Klebsiella spp.	5 (10%)	9 (14.5%)
Klebsiella oxycota	1 (2%)	0

Table 2B. Carbapenem resistance rates of gram negative pathogen microorganisms in HAIs

Pathogen microorganism	Carbapenem resistant	Carbapenem sensitive	Colistin resistant
Acinetobacter baumanii	79 (62.2%)	8 (14.0%)	0
Acinetobacter spp.	40 (31.5%)	17 (29.8%)	0
Acinetobacter lwoffii	0	1 (%1.8)	0
Pseudomonas aureginosa	6 (4.7%)	23 (40.4%)	0
Pseudomonas spp.	2 (1.6%)	8 (14.0%)	0

Table 3. Resistance rates of staphylococci in HAIs

Pathogen microorganism	Methicilline resistant	Methicilline sensitive
S. aureus	51 (36.2%)	25 (78.1%)
CNS	90 (63.8%)	7 (21.9%)

Table 4. Distribution of resistance patterns rates in HAIs

HAI	ESBL (+)	Carbapenem resistant	Methicilli-neresistant
BSI	11 (22%)	51 (40.2%)	95 (67.4%)
RTI	10 (20%)	49 (38.5%)	4 (2.8%)
UTI	11 (22%)	2 (1.6%)	0
SSI	18 (36%)	25 (19.7%)	42 (29.8%)

oups are done with Fisher's exact chi-square test, Pearson chi-square test and Fisher-Freeman-Halton tests. When the number of the group is more than two, analysis of the subgroups included the calculation of corrected Bonferroni *p* values. Analysis are done in SPSS programme (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) and P<0.05 is accepted as statistically significant.

Results

In our study, we have retrospectively identified HAIs in 585 (2.09%) of 27.886 patients who have been hospitalized in Cardiology and Cardiovascular Surgery clinical departments and ICUs of our hospital between January 2011-October 2015. 64.1% of the patients were followed in ICU and 35.9% of then were followed in the clinical department. HAIs in our hospital were identified with the following frequency: BSIs were the most common with 36.5% of the cases, SSIs 29.4%, RTIs 24.8%, UTIs 8.7% and SSTIs 3.4%.

606 pathogen microorganisms were isolated in HAIs and those were distributes as: BSIs 45,3%, SSIs 26%, RTIs 20.1%, UTIs 8.4%, SSTIs 0.3%. Distribution of the microorganisms in HAIs is shown in **Table 1**. The most frequent microorganism was identified as CNS 16% and then comes *Acinetobacter baumanii* 14.3%, *S. aureus* 12.5%, *E. coli* 10.8%, *Acinetobacter spp*. 9.4%, *Klebsiella pneumoniae* 5.3%, *Pseudomonas spp.* 4.8%, *E. faecalis* 4.5%, *Candida spp.* 3.2%.

CNS has been identified as the pathogen microorganism in BSIs and SSIs significantly higher than the UTIs and RTIs (P<0.001) (**Table 1**). *Acinetobacter baumanii ve Acinetobacter spp.* were significantly higher in RTIs (P<0.001) (**Table 1**). *Klebsiella pneumoniae* was identified as the significantly higher pathogen microorganism in SSIs than BSIs (P=0.035) (**Table 1**). *E. coli* was most significantly higher in UTIs, and then in SSIs (P<0.001) (**Table 1**). *Candida spp. ve Enterococcus spp.* were significantly higher in UTIs (P<0.001) (**Table 1**). *Pseudomonas spp*. was significantly higher in RTIs than BSIs (P=0.011) (**Table 1**).

In BSIs 55.5% gram-positive microorganisms, 38.3% gram-negative microorganisms, 6.2% fungi was found. The most frequently determined five microorganisms were CNS (19.50%), *S. aureus* (17.90%), *Acinetobacter baumanii* (12.10%), *Acinetobacter spp.* (8.40%), *E. faecalis* (7.30%) (P<0.001).

The most common microorganisms in SSIs were CNS (19.62%), *E. coli* (17.09%), *S. aureus* (12.66%), *Acinetobacter baumanii* (11.39%), *Acinetobacter spp.* (5.06%) (P=0.004).

The most common microorganisms in RTIs were *Acinetobacter baumanii* (29.51%), *Acinetobacter spp.* (19.67%), *Klebsiella pneumoniae* (8.20%), *Pseudomonas aeruginosa* (7.38%), *E. coli* (6.56%) (P<0.001).

The most common five microorganisms in UTIs were *E. coli* (39.22%), *Candida spp*. (19.61%), *Enterococcus spp*. (11.76%), *Klebsiella pneumoniae* (5.88%), *Pseudomonas aeruginosa* (5.88%) (P=0.006).

E. coli (50%) and *Pseudomonas aeruginosa* (50%) were isolated from SSTIs (n=2).

ESBL resistance of *E. coli* ve *Klebsiella* isolates in HAIs was detected to be 44.6%. Among HAIs, ESBL resistance was 54% in *E. coli,* 34% in *K. pneumoniae* (**Table 2A**).

Carbapenem resistance of non-fermantative microorganisms were established as 69%. *Acinetobacter* species showed resistance to carbapenem 82% and *Pseudomonas* species showed carbapenem resistance 20.5% (**Table 2B**). The highest resistance tocarbapenem was detected in *Acinetobacter baumanii* (62.2%). There were no gram negative bacteria resistant to colistin (**Table 2B**).

Methicilline resistance of staphylococci in HAIs was detected as 81.5%. Methiciline resistance of CNS was 63.8%, and of *S. aureus* was 36.2% (**Table 3**).

Methicilline and carbapenem resistance were the most frequently detected in BSIs (67.4%, 40.2%), ESBL resistance was the most frequently detected inSSIs (36%) (**Table 4**).

Discussion

The rate of HAIs was found as 2.09% in ours study. Davoudi A. et al. [11] found the rate of HAIs was 8.3% in patient underwent open heart surgery, Coskun D et al. [12] reported the incidence of 2.9% HAIs in about of patients that underwent heart surgery. When we compair the the rate of HAIs in our study to the studies examining similar patients, it is found to be low.

HAIs in our hospital revealed those percents: the most frequent was BSIs with 36.5%, SSIs were 29.4%, RTIs were 24.8%, UTIs were 8.7%, SSTIs were 3.4%. Davoudi A. et al. [11] found the rates of SSIs, RTIs UTIs, BSIs as 27.80%, 25.66%, 17.11%, 8.55% respectively. Santo L. et al. [13] found that patients underwent cardiac surgeries showed most commonly RTIs with 51.8%, and then SSIs with 27.7% and BSIs with 20.5%. The rate of HAI type shows difference from study to study.

In our study, the most frequent BSIs was detected to be caused by gram-positive microorganisms with 55.5%, gram negative microorganisms with 38.3% and fungi with 6.2%. The most frequently determined five microorganisms were CNS (19.50%), *S. aureus* (17.90%), *A. baumanii* (12.10%), *Acinetobacter spp.* (8.40%), *E. faecalis* (7.30%) (P<0.001). Wisplinghoff H. et al. [10] found that gram-positive microorganisms caused 65% of BSIs, gram-negative microorganisms caused 25%, fungi caused 9.5% and the most-common organisms causing BSIs were CNS (31%), *S. aureus* (20%), enterococci (9%), and *Candida* species (9%). In several studies, as it has been in our study, it is showed that CNS followed by S. aureus comprised the most prevalent bacteria isolated from BSIs [14-17]. In our study, the most frequent gram negative microorganism in BSIs was found as *A. baumanii* (12.10%) and inRTIs the most frequent pathogens were *A. baumanii* (29.51%), *Acinetobacter spp.* (19.67%) (P<0.001) (**Table 1**). The prevalence rate of *A. baumaniive Acinetobacter spp.* in RTIs was significantly higher than other types of HAIs. (P<0.001) (**Table 1**). Reports of *Acinetobacter spp*. bacteremia are increasing, especially from Asian countries and Iran, Iraq, Kuwait, Afghanistan, India [17-20]. A surveillance study from Iran reported that *Acinetobacter spp*. were the most frequently isolated bacteria in the hospital and community acquired BSIs (32%) [21]. Price LS. et al. [22] reported that the most frequent clinical manifestations of *Acinetobacter* infection are ventilator-associated pneumonia (VAP) and BSIs. Jaggi N. et al. [23] reported that *A. baumannii* contributed to 30.4% VAP, 35.2% catheter associated BSIs, 12.5% SSIs and 2.94% catheter associated UTIs. Overall resistance of *A. baumannii* towards carbapenems was 90% from all hospital isolates. In our study, the rates of *Acinetobacter* infection in RTIs and SSIs were found to be similar with the results of the study by Jaggi N. et al. and even it is the most frequent gram negative microorganism in BSIs, the rate of *A. baumanii* was found as 12.10%. We have determined carbapenem resistance of *Acinetobacter* species with rate of 82% in our study (**Table 2B**). Antibiotic resistance in *A. baumannii* is increasing at an alarming rate leading to increased morbidity, mortality and treatment costs in ICU settings as revealed by surveillance studies from Europe, the Asia Pacific region, Latin America and North America

over the last 3-5 years [24]. The antibiotic susceptibility patterns clearly showed the increasing resistance of *A. baumannii*to various antibiotics as compared to other gram negatives. Colistin (Polymixin E) is one agent which is active against *A. baumannii*. Jaggi N. et al. has been reported colistin resistance as 1.2%. A recent study of clinical isolates from the Western Pacific region showed 3.3% resistance of *A. baumannii*to colistin [23, 25]. We have not detected any resistance of *Acinetobacter* species to colistin in our study.

In our study, the most frequent five microorganisms in SSIs were found to be CNS (19.62%), *E. coli* (17.09%), *S. aureus* (12.66%), *A. baumanii* (11.39%), *Acinetobacter spp.* (5.06%) (P= 0.004). As similar to the results of study, S. Cossin et al. revealed the distribution rate of the microorganisms in SSIs after cardiac surgery as CNS, *S. aureus*, *E. coli* [26].

In our study, the most frequently five microorganisms in RTIs were *A. baumanii* (29.51%), *Acinetobacter spp.* (19.67%), *K. pneumoniae* (8.20%), *P. aeruginosa* (7.38%), *E. coli* (6.56%) (P<0.001). Chung DR. et al. in their multinational study shows that *Acinetobacter spp*., *P. aeruginosa*, *S. aureus*, and *K. pneumoniae* are the most frequent isolated agents from adults with hospital-acquired pneumonia (HAP) and VAP in 10 Asian countries, and these isolated agents are highly resistant to major antimicrobial agents [27]. *Acinetobacter* pneumonia occurs predominantly in intensive care unit (ICU) patients who require mechanical ventilation and tends to be characterized by a late onset. Positive blood cultures and signs of sepsis usually portend a bad prognosis. Additionally, patients with pneumonia due to *Acinetobacter* spend more ventilator days in the ICU before detection of positive cultures than do patients with pneumonia due to other gram-negative bacilli or uninfected patients [28]. The reason of high rate determination of *Acinetobacter* species in our study has been found to be linked to the fact that the ventilator use rate of our hospital was at the average usein Turkey between the years 2011-2015 (ICU data of our hospital was 0.28-UHESA 2014 ICU data was 0.12-0.46) together with our RTI rate which is higher than the Turkey's average. (ICU incidence density of 1000 ventilator days was 7.83 in our hospital-UHESA 2014 ICU datas were 6.5-6.8).

The prevalences of five most frequent microorganisms of UTIs in our study were *E. coli* (39.22%), *Candida spp*. (19.61%), *Enterococcus spp*. (11.76%), *K. pneumoniae* (5.88%), *P. aeruginosa* (5.88%) (P=0.006). *E. coli*was the most common pathogenin UTIs and secondly in SSIs. (P<0.001). *Candida spp. ve Enterococcus spp.* was determined significantly high in UTIs (P<0.001). As similar to the UTI results of our study, multi-center study of Tasbakan M. et al. in Turkey reported that the prevalence of UTIs was 6.77% in ICU with the five leading microorganisms were *E. coli* 45.5%, *Candida spp.* 15.9%, *Klebsiella spp*. 13.3%, *Enterococcus spp.* 10.2% and *Pseudomonas spp.* 10.0% (n=42) [28]. Similar to the results of our study, many studies indicate that at least 10%-15% of hospital acquired UTIs are caused by Candida species. Candiduria is especially common in ICUs and may represent the most frequent UTIs encountered in adult surgical ICUs [29, 30].

In our study, ESBL resistance of *E. coli*ve *Klebsiella* isolates in HAIs was detected to be 44.6%. Among HAIs, ESBL resistance was 54% in *E. coli,* 34% in *K. pneumoniae* (**Table 2A**). ESBL resistance was the most frequently detected in SSIs (36%) (**Table 4**). Blanco MG. et al. reported among nosocomial Enterobacteriacea in Latin America up to 32% of *E. coli* and up to 58% *of K. pneumoniae* isolates are ESBL positive, rates that are higher than in other world regions [31]. The publication of the SMART program medatas of Hawser S. et al. from the Asia-Pacific region in 2007 shows that 42.2% and 35.8% of *Escherichia coli* and *Klebsiella* spp., respectively were ESBL positive; For India for ESBL-positive *E. coli*, *K. pneumoniae* were 79.0%, 69.4%, ESBL-positive *E. coli* rates were also high in China (55.0%) and Thailand (50.8%) [32]. Our study's 44.6% ESBL resistance rate compared with 30%, 17%, 10%, and 8% for Latin America, the Middle East and Africa, the European Union, and North America, respectively [33].

In our study, methicilline resistance of staphylococci in HAIs was detected to be 81.5% respectively (**Table 3**). Methicilline resistance was 63.8% in CNS, 36.2% in *S. aureus*and the most frequently detected in BSIs (67.4%) (**Tables 3**, **4**). Madani N. et al. found that 25.5% of all *S. aureus* HAIs were caused by methicillin-resistant strains and in HAIs 78.3% of CNS were methicillin resistant [34]. In International No-

socomial Infection Control Consortium (INICC) reportglobal study were found resistance of *S. aureus* isolates to methicillin 84.4% vs 56.8% [35].

The increasing detection rates of multiresistant microorganisms in HAIs limits antimicrobial prophylaxis and treatment of infections. More epidemiological datas are needed to compare different treatment approachments.

Disclosure of conflict of interest

None.

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