Original Article

Nosocomial Infections Caused by Drug-Resistant Bacteria in a Referral University Hospital, Tehran, Iran

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Abstract

Background: The emergence of antimicrobial-resistant pathogens associated with hospital-acquired infections (HAIs) is a major public health problem worldwide. Although being drug resistance is common in some countries and rare in others, the extent of this condition is not precisely known in most parts of Iran.

Materials and Methods: Clinical specimens from patients who had been in the hospital for at least 48 hours were included in this study. The pattern of antibiotic resistance was determined by disk diffusion method as recommended by the Clinical Laboratory and Standards Institute (CLSI).

Results: Of 11164 patients that were investigated, 369 (3.3%) had nosocomial infections. The most frequently isolated organisms from all sites of infections were *Acinetobacter species* (14.2%), *Escherichia coli* (13.7%) and *Pseudomonas aeruginosa* (9.9%). Among the Gram-negative bacilli, *Acinetobacter spp* was mostly resistant to ciprofloxacin, ceftriaxon, co-trimoxazole and centamicin, while *P. aeruginosa* was frequently resistant to ampicillin/sulbactam (87%). Imipenem and piperacillin/tazobactam were the most active antimicrobials against gram-negative microorganisms whereas vancomycin was the antimicrobial agent most consistently active against the Gram-positive *cocci*.

Conclusions: This study highlights the importance of antimicrobial-resistant pathogens associated with nosocomial infection in Tehran, Iran. Using proper diagnostic criteria as well as administering more effective treatment may limit the frequency of drug-resistant bacteria associated with HAIs.

Keywords: Hospital-acquired infections, Antimicrobial-resistant bacteria, Iran

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Introduction

Hospital-acquired infections (HAIs) are a major public health problem in Iran and an obstacle to nosocomial infection control programs. According to the latest report that has been released by Ministry of Health and Medical Education in Iran, the nosocomial infection rate increased from 0.6% in 2007 to 1.1% in 2010[1]. Moreover, based on the several local studies, antimicrobial-resistant bacteria were responsible for a significant proportion of nosocomial infections in adults and children[2]. These microorganisms are even showing rising rates of resistance to new expensive antibiotics subsequently

considered the treatment of choice. This is due to the widespread use of broad-spectrum antibiotics in health care settings for empiric treatment of infections. The production of β- lactamase enzymes, decreasing permeability and increasing active efflux of the antibiotic are among the most common mechanisms of resistance in these pathogens[3]. Infections due to these antimicrobial-resistant bacteria are mostly associated with increased treatment failure, higher mortality, longer hospital stays, and higher health care costs[4]. Cases of antimicrobial-resistant bacteria are reported mainly from developed countries, where proper nosocomial infection surveillance programs have been established for the identification of HAIs and associated bacteria. However, the occurrence of these pathogens associated with nosocomial infections in many low- and middle-income settings like Iran is rarely addressed in literatures. In this regards, this study was designed: (1) to determine the prevalence of antimicrobial-resistant pathogens associated with nosocomial infections and (2) to summarize rates of antimicrobial resistance in the most common isolated pathogens.

Methods

Setting and study populations: This retrospective study was performed in one of the referral university hospitals in Tehran, Iran. The classical information for each patient that was referred to medical and surgical wards with intensive care units was analyzed. The information recorded for each patient included; age, gender, department, date of admission, date of surgical operations, predisposing conditions (blood pressure, renal failure, diabetes, malignancies, immunodeficiency), and factors related to health care, including surgery procedures, mechanical ventilation, intravascular catheter and urinary catheter. According to the Center for Disease Control and Prevention (CDC) definitions, all patients hospitalized for >48 h were included [5]. The CDC criteria were used to identify nosocomial infections[5]. Clinical specimens, including blood, urine, wound/tissue, cerebrospinal fluid and respiratory specimens were collected from patients in different wards of the hospital.

Bacterial isolation: All specimens were collected at the bed site, transferred to the laboratory immediately and were inoculated on proper culture media within two hours. Only one isolate per patient was included. Methods used for confirmation of identification-included examination of colonial morphology, haemolytic characteristics on appropriate agar media, Gram stain and rapid identification tests (catalase, oxidase, coagulase, bile solubility and spot indole).

Drug Susceptibility Testing: The isolated bacteria were inoculated on Mueller Hinton agar (Mast group Ltd, Merseyside, UK) and antimicrobial susceptibility testing was performed using disk diffusion method as recommended by Clinical and Laboratory Standard Institute (CLSI No: M2-A9).

The antibiotic disks were provided from Mast diagnostic group Ltd. The antibiotic panels for each group of isolates were selected according to CLSI guidelines (No: M100-S16). Quality control was assured by concurrent testing with the American Type Culture Collection (ATCC) strains including *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853 and *Staphylococcus aureus* ATCC 25923.

The following antibiotics; ciprofloxacin, ofloxacin, erythromycin, oxacillin, gentamicin, co-trimoxazole, chloramphenicol, vancomycin, rifampin, imipenem, ceftazidime, cefotaxime, ceftriaxon, piperacillin/tazobactam, ampicillin/sulbactam and amikacin, were used for antimicrobial susceptibility testing.

Statistical Analysis: Statistical analysis was carried out using SPSS version 20 (SPSS Inc., Chicago, IL, USA).

Results

Table 1: Characteristics of patient and hospital-acquired infections (HAIs) Prevalence.

Wards	Patients		HAIs	
	No.	%	No.	%
Women's Surgery, Gynecology & Oncology	1753	15.7	35	2
Neonatal care	1499	13.4	11	0.7
Ear, nose, throat	1398	12.5	11	0.7
Plastic surgery	1115	9.9	26	2.3
Obstetric	950	8.5	9	0.9
Endocrinology and Rheumatology	854	7.6	16	1.8
Pediatrics	819	7.3	7	0.8
General surgery	742	6.6	27	3.6
Intensive care	726	6.5	57	7.8
Thoracic surgery	651	5.8	11	1.6
Hematology	345	3	104	30
Neonatal intensive care	270	2.4	37	13.7
Bone Marrow Transplant	42	0.3	18	42.8
Total	11164	100	369	3.3

Prevalence of HAI: During the study period, 11164 patients (45.4% male and 54.6% female) were investigated, of whom 369 (3.3%) had nosocomial infections. The high rates of HAIs were observed among patients admitted in Bone Marrow Transplant units, followed by haematology unit, neonatal intensive care units, ICU and general surgery unit. The lowest prevalence of HAIs occurred in Neonatal care ward (Table 1). Bloodstream infection (BSI) was the most common infection (50.4%) among reported cases, followed by surgical sites infection (SSI, 20.3%), urinary tract infections (UTI, 16.2%) and lower respiratory tract infection (LRI, 13 %). LRI was the most common nosocomial infection in intensive care units, whereas in surgical wards the most prevalent HAI type was SSI. In hematology ward, the HAI was more heterogeneous but was mainly BSI.

Microbiology data: Microbiological reports were available for 343 (93%) of patients with HAIs. The most prevalent microorganisms from all sites of infection was *Acinetobacter species* (14.2%), followed by *E. coli* (13.7%), *P. aeruginosa* (9.9%), *Staphylococcus aureus* (9.0%), *Klebsiella* spp. (6.1%), *Enterobacter* spp. (5.8%), *Enterococcus* spp. (4.3%), *Staphylococcus epidermidis* (4.0%), *Candida* spp. (3.4%) and coagulase-negative Staphylococci (1.7%) (Table 2). Depending on the site of infection, the most frequently isolated pathogens were *Acinetobacter species* for LRI and BSI, *E. coli* for UTI and *S. aureus* for SSI.

Drug susceptibility patterns: *Acinetobacter spp*. and *P. aeruginosa* was the most antibiotic-resistant pathogens. According to the susceptibility results, imipenem and piperacillin/tazobactam were the most active antimicrobials against gram-negative bacilli whereas vancomycin was the antimicrobial agent most consistently active in vitro against the Gram-positive *cocci* (Table3 and Table4).

Risk factors associated with HAIs: The prevalence of HAIs was higher among females than males (3.3% and 3.3%). It increased with age from 1.8% in those less than 30 years to 8.3% among patients 70 years old or older (Table 5). Patients hospitalized for more than 20 days had a higher prevalence (16.8%) than those with shorter hospital stays. Patients with malignancies had a higher prevalence than those without. Prevalence was also higher among patients with surgical

operations. Patients hospitalized in ICUs had higher prevalence of HAIs than those on other wards. Patient characteristics like immunodeficiency, mechanical ventilation, intravascular catheter and urinary catheter did not associate with HAI.

Discussion

and associated bacteria[8-10]. However, the prevalence of HAIs and related bacteria in many low- and middle-income settings like Iran is rarely addressed in literatures. Some important reasons for their under-reporting in this country include the lack of communication between physicians and microbiologists, lack of standardized or accepted

Table 2: Isolated micro-organisms according to different types of nosocomial infections

Microorganisms	UTI No. (%)	SSI No. (%)	BSI No. (%)	LRI No. (%)	Other No. (%)	Total No. No. (%)
Acinetobacter species	4 (7.0)	8 (11.4)	18(11.4)	19(43.1)	0	49(14.2)
Escherichia coli	20 (35.0)	14 (20.0)	9 (5.7)	3 (6.8)	1 (6.6)	47 (13.7)
Pseudomonas aeruginosa	8 (14.0)	9 (12.8)	12 (7.6)	3 (6.8)	2 (13.3)	34 (9.9)
Staphylococcus aureus	0 (0.0)	22 (31.4)	6 (3.8)	3 (6.8)	0 (0.0)	31 (9.0)
Klebsiella species	6 (10.5)	1 (1.4)	8 (5.0)	4 (9.0)	2 (13.3)	21 (6.1)
Enterobacter species	10 (17.5)	1 (1.4)	6 (3.8)	2 (4.5)	1 (6.6)	20 (5.8)
Enterococcus species	4 (7.0)	3 (4.2)	5 (3.1)	0 (0.0)	3 (20.0)	15 (4.3)
Staphylococcus epidermidis	1 (1.7)	2 (2.8)	11 (7.0)	0 (0.0)	0 (0.0)	14 (4.0)
Candida species	2 (3.5)	2 (2.8)	4 (2.5)	1 (2.2)	3 (20.0)	12 (3.4)
coagulase-negative Staphylococci	0 (0.0)	0 (0.0)	6 (3.8)	0 (0.0)	0 (0.0)	6 (1.7)
Other organisms	2 (3.5)	8 (11.4)	71 (45.2)	9 (20.4)	4 (26.6)	9 4(27.9)
Total	57 (100.0)	70 (100.0)	157 (100.0)	44 (100.0)	15 (100.0)	343 (100.0)

The infections due to antimicrobial-resistant pathogens associated with nosocomial infections are becoming an increasing problem in many countries in the world. Exposure to these bacteria has different microbiological and clinical implications, as they are capable of colonizing or infecting both immunocompetent and immunocompromised individual patients in hospital settings[6,7]. Cases of nosocomial pathogens are reported mainly from developed countries, where proper nosocomial infection surveillance program has been established for the identification of HAIs criteria to determine HAIs and associated pathogens, limited laboratory facilities and overburden of other community diseases. The absence of information regarding the distributions of HAIs and antimicrobial-resistant pathogens poses significant challenges for hospital infection control strategies.

According to present study, the prevalence of HAI in our hospital was 3.3%. This rate of HAIs was relatively higher from those of previous studies. During 2009–2010, Assar and others reported that 3.1% of admitted patients at a teaching hospital had nosocomial infection[11]. Moreover, the HAI prevalence

Table 3: Resistance rates (%) for the most common gram-positive microorganisms associated with HAIs.

Organism	No. isolates	CIP*	ERT	OXA	GEN	COT	CHL	VAN	RIF
S. aureus	31	40	56	56	30	37	43	17	45
S. epidermidis	14	28	54	73	41	50	10	0	0
***Enterococcus* spp**	15	37	83	66	0	66	47	22	0

*Ciprofloxacin, Erythromycin, Oxacillin, Gentamicin, Co-Trimoxazole, Chloramphenicol, Vancomycin, Rifampin.

Table 4: Resistance rates (%) for the most common Gram-negative microorganisms associated with HAIs.

Organism	No. isolates	IPM*	CIP	CAZ	CEF	COT	TZP	A/S	AMK	GEN
Escherichia coli	47	0	38	50	73	76	4	57	13	25
Pseudomonas aeruginosa	34	20	52	50	81	85	27	87	23	28
Klebsiella pneumonia	21	0	23	0	45	65	0	63	7	16
Enterobacter spp	20	0	21	0	81	24	30	78	10	0
Acinetobacter spp	49	12	68	15	89	80	24	14	20	70

*Imipenem, Ciprofloxacin, Ceftazidime, Ceftriaxon, Co-trimoxazole, Piperacillin/Tazobactam Ampicillin/Sulbactam, Amikacin, Gentamicin

of 3.3% in our study was also higher than what was reported by Iranian Nosocomial Infection Department[1]. Many studies and prevention programs in Iran focus on the impact of HAIs in the ICU[12]. However, our data clearly indicate the importance of HAIs in other types of hospital wards i.e. Bone Marrow Transplant units and Haematology unit. Therefore, one of the policy recommendations resulting from this study was to extend the of HAI prevention strategies to non-ICU wards. Moreover, individual hospitals should use their own observation and then use the result in order to decide which control measures to select.

In all wards, BSI was the principal type of infection found in this study and accounted for the majority of hospital-acquired infections. According to the literatures, use of central catheters in hospitalized patients has been suggested as important risk factors for development of BSI[13]. In this regard, hand-washing before catheters insertion, use maximal barriers during catheter insertion, provide an effective antisepsis, choose an appropriate insertion site, avoid routine central venous catheters replacement and staff training are strongly recommended to avoid further occurrence of BSI in hospital settings[14].

As shown in the Table 2, Gram-negative bacilli were the most isolated pathogens from all clinical specimens in different parts of the hospital. Over the last decade, *Acinetobacter* spp. has been known as an important nosocomial pathogen that is often multidrug resistant and cause life-threatening infections[15]. It represents that the first causal agent of nosocomial infection in the present study and is the most frequent pathogen isolated from the LRI and BSI. Moreover, in the current study, *Acinetobacter spp*. and *P. aeruginosa* were the most antibiotic-resistant microorganisms (Table 4). The increased prevalence of antimicrobial-resistant pathogens associated with nosocomial infections may have several negative impacts on hospital and health issues; for example, patients infected with these pathogens require

prolonged and expensive chemotherapy, which has considerable implications for the individual patient and for the health care settings. Furthermore, resistance to antimicrobial agents is frequently associated with increased risk of treatment failures and acquiring new drug resistance. Therefore, active infection control committee and appropriate antimicrobial therapy will prevent or lower the emergence of antimicrobial-resistant pathogens.

Conclusion

In conclusions this study highlights the importance of antimicrobial-resistant pathogens associated with nosocomial infection in Tehran, Iran. Using proper diagnostic criteria as well as administering more effective treatment may limit the frequency of drug-resistant bacteria associated with HAIs.

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Table 5: Patient characteristics and exposure to extrinsic risk factors.

General characteristics	No. of patients	%	No. of infections	%
Sex				
Male	5062	45.4	164	3.2
Female	6102	54.6	205	3.3
Total	11164	100.0	369	6.5
Age				
<30	3662	32.8	66	1.8
30-70	5834	52.2	164	2.8
>70	1668	15.0	139	8.3
Total	11164	100.0	369	12.9
Length of stay				
<7	4238	38.0	16	0.3
7-20	5632	50.5	135	2.3
>20	1294	11.5	218	16.8
Total	11164	100.0	369	19.4
Malignancy				
Yes	83	0.8	4	4.8
No	11081	99.2	365	3.2
Total	11164	100.0	369	8.0
Immune deficiency				
Yes	51	0.5	1	1.9
No	11113	99.5	368	3.3
Total	11164	100.0	369	5.2
Intravascular catheter				
Yes	1615	14.5	33	2.0
No	9549	85.5	336	3.5
Total	11164	100.0	369	5.5
Urinary catheter				
Yes	2108	18.9	25	1.1
No	9056	81.1	344	3.7
Total	11164	100.0	369	
Mechanical ventilation				
Yes	871	7.8	5	0.5
No	10293	92.2	364	3.5
Total	11164	100.0	369	4.0
Surgical operations				
Yes	696	6.2	34	4.8
No	10468	93.8	335	3.2
Total	11164	100.0	369	8.0
Specialty				
Paediatrics	819	7.3	7	0.8
Surgery	742	6.6	27	3.6
Intensive Care Unit	726	6.5	57	7.8

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