Antimicrobial Resistance Pattern of Nosocomial Infections at a Referral Teaching Hospital

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A B S T R A C T

Background: The choice of appropriate antibiotics to treat nosocomial infections requires knowledge of antibiotic resistance pattern in the hospitals. The aim of this study was to determine antimicrobial resistance patterns of common pathogens of nosocomial infections (pneumonia, UTI, bloodstream infection, wound infection) in a referral teaching hospital.

Methods: This cross-sectional study was conducted over a 6-month period. The pathogens isolated from biological samples of hospitalized patients with nosocomial pneumonia, UTI, bloodstream infection, or wound infection underwent antibiotic susceptibility testing by Kirby-Bauer method (disk diffusion test).

Results: Over the study period, 442 cases of infection were recorded. Pneumonia (n = 204, 46.2%) and UTI (n = 118, 26.7%) showed the most frequency followed by BSI (n = 71, 16.1%) and wound infection (n = 49, 11%). *Acinetobacter baumannii* was the most common pathogen of nosocomial pneumonia infection that showed the most susceptibility to colistin (100%). *Escherichia coli*, the most common pathogen of urinary tract infections, showed the highest sensitivity to colistin (100%). *Staphylococcus epidermidis* was the most common bloodstream infection pathogen that showed the most sensitivity to vancomycin (100%). *Enterococcus spp.*, the most common pathogens of wound infection, had the most susceptibility to linezolid (100%).

Conclusion: Nosocomial infections in our hospital have high rate of resistance to antibiotics shows the importance of improvement in antibiotic use and infection control.

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Introduction

Nosocomial infections (NIs) are defined as infections occurring after 48 hours of hospital admission. NIs, also known as hospital-acquired infections, are global health problem affecting both developed and developing countries (1). The patient in the hospital has the risk of nosocomial infections as a result of impaired defense mechanisms, applying invasive methods, exposure to broad-spectrum antibiotics, and the colonization with resistant microorganisms (1, 2). The prevalence of NIs is various between 1.5% and 26.1%

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among different countries (3). The prevalence in Iranian hospitals has been reported between 1.3% and 10% (3). The increasing rate of NIs causes more antibiotic usage leading to high economic burden and increasing rates of morbidity and mortality (3, 4).

Antibiotic resistance is a natural biological outcome of excessive antibiotic use. This usually occurs when a microorganism acquires a gene which allows it to inactivate the antibiotic or nullify its antimicrobial activity (5). The rapid development of antimicrobial resistance as well as its dissemination and burden becomes a serious public health problem worldwide, as world health organization (WHO) emphasized its importance in World Health Day 2011 (6). According to the Centers for Disease Control and Prevention (CDC) reports, more than 70% of the bacteria causing NIs are resistant to at least one of the medications used to treat them (7). These resistant infections have been more deadly than those caused by antibiotic-susceptible strains of the same species (8). In response to these concerns, improving antibiotic prescription as well as monitoring of antimicrobial susceptibility pattern is part of the strategy to reduce antibiotic resistance (7, 9). These strategies have not been implemented in most developing countries favoring the emergence of resistant bacteria. In Iran, there is no efficient surveillance system for monitoring of antimicrobial resistance. Furthermore, limited published data is available regarding antimicrobial resistance pattern of pathogens originating from hospitals, while knowledge about this pattern is essential for appropriate empirical treatment of the infections. So, in the present study, we evaluated the antibiotic resistance pattern of four prevalent NIs at a referral teaching hospital in Isfahan, Iran.

Methods

This was a prospective cross-sectional study performed during a 6-month period from March to September 2017 at Al-Zahra hospital of Isfahan affiliated to Isfahan University of Medical Sciences. The study was approved by ethical committee of Isfahan University of Medical Sciences. All hospitalized adult patients (>18 years-old) with any nosocomial infections of pneumonia, urinary tract infection, wound infection, and bloodstream infection were eligible for the study. Over the study period, clinical specimens including blood, urine, wound pus, and respiratory specimens (sputum or broncho-alveolar lavage [BAL] fluid) were collected aseptically from patients with > 48 hours of hospitalization in any ward with clinical signs and symptoms of bloodstream infection (BSI), urinary tract infection (UTI), wound infection, or pneumonia, respectively, and were immediately transported to the hospital microbiology lab. All specimens underwent microbial culture and if growth occurred, differential cultures and tests were performed to identify bacterial strains. All patients with positive culture were evaluated for nosocomial infection using definitions of Center for Disease Control and Prevention/National Healthcare Safety Network (CDC/NHSN) (10). Demographic data (age and sex), medical ward, infection type, and the causative pathogen and its resistance pattern were recorded for all included patients. The first three variables were extracted from the patient's medical profile, while the last two ones were recorded from the report of microbiology lab.

After identification of grown bacterial strain, antibiotic susceptibility test was performed by Kirby-Bauer (disk diffusion) method in accordance with the instructions of the Clinical and Laboratory Standards Institute (CLSI) (11). The antibiotic disks (Padtan Teb, Iran) used for susceptibility testing were selected based on the type of pathogen according to CLSI instructions (11).

The primary outcome measures were antimicrobial resistance pattern of the four mentioned nosocomial infections and their causative nosocomial pathogens. The secondary outcome measures were the frequency of each evaluated nosocomial infection and the related pathogens.

SPSS software version 20 (SPSS Inc., USA) was used for data analysis. The results of qualitative variables (sex, medical ward, infection type, pathogen type, and resistance pattern) were reported as frequencies and percentages, while the only quantitative variable (age) was reported as mean ± SD.

Results

During the study period, 442 patients with nosocomial infections were recognized, of whom 266 (60.2%) were male and 176 (39.8%) were female. The mean ± SD of patients age was 50.32 ± 21.30.

Pneumonia (n=204, 46.2%) and UTI (n=118, 26.7%) showed the most frequency followed by BSI (n=71, 16.1%) and wound infection (n=49, 11%).

Most NIs were observed in intensive care units (ICU; 57.7%) followed by the wards internal (general) diseases

(n=27,6.1%), infectious diseases and rheumatology/ nephrology (n=22, 5% each), neurology and cardiology/ dermatology (n=20, 4.5% each), organ transplantation (n=14, 3.2%), neurosurgery (n=10, 2.3%), gastrointestinal diseases (n=9, 2%), neurosurgical ICU (n=8, 1.8%), orthopedic and laparoscopy (n=6, 1.4% each), and cardiac/coronary care unit (CCU) and thoracic surgery (n=5, 1.1% each).

Table 1 presents the frequency of each pathogen as the causative agent of every evaluated NI. As shown, *Acinetobacter baumannii* (n=139; 31.4%) and *Klebsiella pneumoniae* (n=93; 21%) were the most frequently isolated nosocomial pathogens. Furthermore, *A. baumannii, E. coli, S. epidermidis,* and *Enterococcus spp.* were the most frequent pathogens causing pneumonia, UTI, BSI, and wound infection, respectively.

Table 1. Frequency of isolated pathogens from each nosocomial infection.

Pathogen	n	Nosocomial Infection n (%)			
		UTI	BSI	Wound infection	Pneumonia
Acinetobacter baumannii	139	14 (11.9%)	19 (26.8%)	5 (10%)	101 (49.5%)
Klebsiella pneumoniae	93	29 (24.6%)	6 (8.5%)	10 (20%)	48 (23.5%)
Escherichia coli	44	34 (28.8%)	2 (2.8%)	6 (12%)	2 (1%)
Pseudomonas aeruginosae	41	13 (11%)	8 (11.3%)	2 (4%)	18 (8.8%)
Enterococcus spp.	40	16 (13.6%)	5 (7%)	14 (28%)	5 (2.5%)
Staphylococcus aureus	30	1 (0.8%)	2 (2.8%)	10 (20%)	17 (8.3%)
Staphylococcus epidermidis	23	1 (0.8%)	21 (29.6%)	1 (2%)	0
Proteus mirabilis	19	6 (5.1%)	1 (1.4%)	0	12 (5.9%)
Enterobacter spp.	9	4 (3.4%)	5 (7%)	0	0
Streptocossus Group D	3	0	0	2 (4%)	1 (0.5%)
Citrobacter frundii	1	0	1 (1.4%)	0	0
Streptococcus viridans	1	0	1 (1.4%)	0	0
Total	442	118 (100%)	71 (100%)	49 (100%)	204 (100%)

n, number; UTI, urinary tract infection; BSI, bloodstream infection.

Table 2 shows the resistance pattern of isolated nosocomial pathogens. As shown, colistin was the most effective antibiotics against gram-negative pathogens (susceptibility of 100%). Regarding gram-positive microorganisms, vancomycin and linezolid were the most effective antibiotics against isolated *Staphylococci* and *Enterococci*, respectively. Furthermore, high rate of resistance was observed in *A. bumannii, P. aeruginosae*, and *K. pneumonia* strains to meropenem (96.6%, 74.3%, and 77.1%, respectively).

Table 2. Resistance pattern of isolated pathogens to evaluated antibiotics.

Pathogen	Antibiotic	Frequency		Resistance n (%)		
		S	I	R		
A. baumannii	Ciprofloxacin	142	12 (8.5)	-		130 (91.5)
	Levofloxacin	142	12 (8.5)	-		130 (91.5)
	Amikacin	142	34 (23.9)	1 (0.7)		107 (75.3)
	Meropenem	146	5 (3.4)	-		141 (96.6)
	Cefepime	124	3 (2.5)	-		121 (97.5)
	Ceftazidime	124	4 (3.2)	3 (2.4)		117 (94.4)
	Doxycycline	100	60 (60)	-		40 (40)
	Colistin	136	136 (100)	-		-
	Ampicillin/sulbactam	142	31 (21.8)			111 (78.2)
P. aeruginosa	Ciprofloxacin	27	5 (18.5)	-		22 (81.5)
	Levofloxacin	33	10 (30.3)	-		23 (69.7)
	Amikacin	40	21 (52.5)	1 (2.5)		18 (45)
	Meropenem	39	9 (23)	1 (2.5)		29 (74.3)
	Cefepime	38	8 (21)	-		30 (79)
	Ceftazidime	39	12 (30.7)	-		27 (69.3)
	Colistin	33	33 (100)	-		-
S. epidermidis	Ciprofloxacin	19	3 (15.7)	-		16 (84.3)
	Gentamicin	21	6 (28.6)	1 (4.7)		14 (66.7)
	Oxacillin	18	8 (44.4)	-		10 (55.6)
	Co-trimoxasole	22	3 (13.6)	-		19 (86.4)
	Erythromycin	22	1 (4.5)	-		21 (95.5)
	Vancomycin	22	22 (100)	-		-
	Clindamycin	20	-	-		20 (100)
Enterococcus spp.	Ciprofloxacin	22	2 (9.1)	-		20 (90.9)
	Levofloxacin	19	1 (5.3)	-		18 (94.7)
	Penicillin	30	15 (50)	-		15 (50)
	Linezolid	30	30 (100)	-		-
	Ampicillin	30	16 (53.3)	-		14 (46.7)
	Vancomycin	30	18 (60)	-		12 (40)
	Tetracycline	26	6 (23)	-		20 (77)

Table 2. Continued.

		n	S (%)	I (%)	R (%)
S. aureus	Ciprofloxacin	23	13 (56.5)	-	10 (43.5)
	Erythromycin	24	9 (37.5)	-	15 (62.5)
	Clindamycin	20	10 (50)	-	10 (50)
	Gentamycin	26	13 (50)	-	13 (50)
	Oxacillin	23	11 (47.8)	-	12 (52.2)
	Co-trimoxazole	26	21 (80.7)	-	5 (19.3)
	Vancomycin	27	27 (100)	-	-
K. pneumoniae	Ciprofloxacin	86	17 (19.7)	1 (1.2)	68 (79.1)
	Levofloxacin	72	20 (27.7)	1 (1.3)	51 (70.8)
	Amikacin	89	45 (50.5)	1 (1.1)	43 948.3)
	Colistin	89	89 (100)	-	-
	Nitrofurantoin	86	11 (12.8)	7 (8.1)	68 (79.1)
	Ceftriaxone	89	11 (12.5)	-	78 (87.6)
	Meropenem	87	2 (22.9)	-	67 (77.1)
	Cefepime	83	25 (30.1)	1 (1.2)	57 (68.7)
	Ceftazidime	85	24 (28.2)	2 (1.1)	60 (58%)
Enterobacter spp.	Ciprofloxacin	8	6 (75)	-	2 (25)
	Levofloxacin	8	7 (87.5)	-	1 (12.5)
	Amikacin	9	8 (88.9)	-	1 (11.1)
	Meropenem	9	8 (88.9)	-	1 (11.1)
	Ceftazidime	9	3 (33.3)	-	6 (66.7)
	Ceftriaxone	9	1 (11.1)	-	8 (88.8)
P. mirabilis	Ciprofloxacin	19	2 (10.5)	2 (10.5)	15 (79)
	Levofloxacin	17	2 (11.7)	2 (11.7)	13 (17.6)
	Amikacin	19	2 (10.5)	1 (5.2)	16 (84.3)
	Meropenem	19	9 (47.3)	1 (5.2)	9 (47.3)
	Cefepime	19	2 (10.5)	-	17 (89.5)
	Ceftazidime	19	2 (10.5)	-	17 (89.5)
E. coli	Ciprofloxacin	43	20 (46.5)	-	23 (53.5)
	Levofloxacin	43	42 (95.4)	1 (2.3)	1 (2.3)
	Amikacin	44	2 (10.5)	1 (5.2)	16 (84.3)
	Meropenem	44	43 (97.7)	-	1 (2.3)
	Cefepime	41	25 (61)	3 (7.3)	13 (31.7)
	Ceftazidime	41	18 (44)	-	23 (56)
	Co-trimoxazole	45	18 (41)	1 (2)	26 (57)
	Nitrofurantoin	30	23 (76.7)	1 (3.3)	6 (20)

n, number; S, sensitive; I, intermediate; R, resistant; *A. baumannii, Acinetobacter baumannii*; *P. aeruginosa, Pseudomonas aeruginosa*; *S. epidermidis, Staphylococcus epidermidis*; *S. aureus, Staphylococcus aureus.*

Table 3 shows the susceptibility pattern of nosocomial infections to evaluated antibiotics. As presented, UTI showed the most sensitivity to colistin followed by amikacin and meropenem. (83%).

BSI and wound infection had the most susceptibility to colistin and linezolid, respectively. Furthermore, pneumonia showed the most sensitivity to colistin (100%) and co-trimoxazole

Table 3. Susceptibility pattern of each nosocomial infection to evaluated antibiotics.

| Antibiotic | Susceptibility | Nosocomial Infection Susceptibility, n (%) | | | |
		Urinary tract infection	Bloodstream infection	Wound infection	Pneumonia
Ciprofloxacin	S	30 (28.8)	20 (36.4)	10 (30.3)	16 (11.2)
	I	1 (1)	0	0	3 (2.1)
	R	73 (70.2)	35 (63.6)	23 (69.7)	124 (86.7)
Levofloxacin	S	31 (32.2)	22 (61)	6 (28.5)	13 (10)
	I	1 (1)	0	0	2 (1.6)
	R	64 (66.7)	14 (39)	15 (71.5)	113 (88.4)
Amikacin	S	56 (58.3)	20 (48.7)	14 (48.3)	61 (34.5)
	I	1 (1)	0	0	4 (2.3)
	R	39 (40.7)	21 (51.3)	15 (51.7)	112 (63.2)
Gentamicin	S	1 (25)	6 (22.2)	8 (47)	10 (14.4)
	I	0	0	1 (6)	0
	R	3 (75)	21 (77.8)	8 (47)	59 (85.6)
Meropenem	S	52 (53.1)	16 (41)	8 (29.6)	18 (10)
	I	0	0	0	2 (1.1)
	R	46 (46.9)	23 (59)	19 (70.4)	160 (88.9)
Cefepime	S	35 (37.6)	4 (10)	5 (20.8)	9 (6)
	I	2 (2.2)	0	0	1 (0.7)
	R	56 (60.2)	36 (90)	19 (79.2)	139 (93.3)
Ceftazidime	S	31 (33.4)	6 (15)	3 (15)	9 (7)
	I	1 (1)	2 (5)	0	0
	R	61 (65.6)	32 (80)	17 (85)	120 (93)
Colistin	S	47 (100)	21 (100)	18 (100)	170 (100)
	I	0	0	0	0
	R	0	0	0	0
Nitrofurantoin	S	31 (44.3)	-	-	-
	I	3 (4.3)	-	-	-
	R	36 (51.4)	-	-	-

Table 3. Continued.

Ceftriaxone	S	6 (28.6)	0	2 (28.6)	1 (2.6)
	I	0	0	0	0
	R	15 (71.4)	11 (100)	5 (71.4)	38 (97.4)
Ampicillin/sulbactam	S	-	-	-	2 (22.2)
	I	-	-	-	0
	R	-	-	-	7 (77.8)
Ampicillin	S	4 (50)	1 (11.1)	2 (22.2)	1 (25)
	I	0	0	0	0
	R	4 (50)	8 (88.9)	7 (77.8)	3 (75)
Co-trimoxazole	S	0	7 (24.2)	9 (64.3)	29 (82.8)
	I	0	0	0	0
	R	15 (100)	22 (75.9)	5 (35.7)	6 (17.2)
Vancomycin	S	15 (83.4)	15 (80.2)	6 (46.2)	16 (76.2)
	I	0	0	0	0
	R	3 (16.6)	2 (11.8)	7 (53.8)	5 (23.8)
Penicillin	S	4 (40)	2 (33.3)	3 (30)	2 (50)
	I	0	0	0	0
	R	6 (60)	4 (66.7)	7 (70)	2 (50)
Oxacillin	S	-	3 (17.6)	5 (50)	6 (42.8)
	I	-	0	0	0
	R	-	14 (82.4)	5 (50)	8 (57.2)
Clindamycin	S	-	1 (4.5)	4 (50)	3 (30)
	I	-	0	0	0
	R	-	21 (95.5)	4 (50)	7 (70)
Erythromycin	S	-	2 (7.6)	4 (36.4)	5 (27.8)
	I	-	0	0	0
	R	-	24 (92.4)	7 (63.6)	13 (72.2)
Doxycycline	S	0	1 (14.3)	1 (12.5)	6 (10.9)
	I	0	0	0	0
	R	3 (100)	6 (85.7)	7 (87.5)	49 (89.1)
Linezolid	S	6 (100)	5 (100)	14 (100)	5 (100)
	I	0	0	0	0
	R	0	0	0	0

n, number.

Discussion

In the present research, the studied pathogens, in order of decreasing frequency, were *Acinetobacter baumannii, E. coli, Staphylococcus aureus, Klebsiella pneumoniae, Entrobacter spp.*, and *Enterococcus spp.*

Our study shows a high prevalence of nosocomial infections in our hospital and high rate of antimicrobial resistance among the causative pathogens complicating antibiotic treatment and its outcomes. Nosocomial infections become prominent in surgical wards because of surgical interventions and operative procedures and furthermore hospitals particularly acute care units, surgical and medical units are important breeding ground for the development and spread of antibiotic-resistant bacteria. This necessitates strict infection control. Among the four types of nosocomial infections examined in Al-Zahra hospital, pneumonia was the most common infection. Similarly, other studies have reported pneumonia and UTI as the most frequent infections (13, 14). *Acinetobacter baumannii* was the most frequently isolated pathogen in our study followed by *Klebsiella pneumoniae* and *E. coli*. Conversely, another previous study conducted in a referral teaching hospital, *S. aureus* was the most frequently isolated pathogen. This is consistent with the reports of several studies that reported *S. aureus as* the most common bacteria recovered from BSI and pneumonia (18-21). Similar to our results, in the study of Zamani et al., gram-negative bacteria were the most frequent causes of nosocomial infections (15). Also, in the study of Rajabi et al., *Acinetobacter baumannii* and *Klebsiella* were the most common pathogens (16).

Our results showed *E. coli* and *K. pneumoniae* as the most frequent pathogens causing nosocomial UTIs. Similarly, in a study on nosocomial UTI in a refferal teaching hospital in Tehran, *E. coli* was the most frequently isolated bacteria followed by *K. pneumoniae*, *P. aeruginosae* and *A. baumannii* (22). These results were also shown in other similar studies in Iran (23, 24) and other countries (25-27). High rate of resistance of this type of infection to antibiotics including meropenem, ciprofloxacin, and levofloxacin, observed in our study, shows the necessity of implementing new strategies in the hospital for more rational use of antimicrobial agents.

Although several reports from United States and Europe have shown S. aureus as a frequent Bloodstream pathogen (28-30), in our study, the first rank of the most common BSI pathogens belonged to *S. epidermidis* that showed the most sensitivity to vancomycin (100%) and highest resistance to Clindamycin (100%) and Erythromycin (95.5%). However, gram-negative pathogens, especially *A. baumannii*, had also a major role in this type of infection in our hospital. Therefore, both gram-positive and gram-negative bacteria should be considered for empiric treatment of BSI.

In some studies, *P. aeruginosae* was reported as the most common infective pathogen in wound infections (31-33). However, in the present study, we found *Entrococci, S. aureus*, and *K. pneumoniae* as the most common pathogens of nosocomial wound infection. Therefore, empiric treatment of nosocomial wound infections should provide appropriate coverage, including either linezolid or vancomycin with colistin, for these pathogens pending culture results.

In conclusion, nosocomial infections in our hospital have high rate of resistance to antibiotics representing the importance of improvement in antibiotic use and infection control. The most common pathogens causing nosocomial pneumonia, UTI, BSI, and wound infection include *Acinetobacter baumannii, E. coli, Staphylococcus epidermidis,* and *Enterococcus spp.*, respectively. Colistin is the most effective antibiotic against *Acinetobacter baumannii* and *E. coli*, while vancomycin and linezolid *were* the most effective antibiotics against *Staphylococcus epidermidis*, and *Enterococcus spp.*, respectively.

References

1. Georgia A. National Nosocomial infectious surveillance (NNIS) system Reports, data summary from January 1992 through June 2004, issued October 2004. Am J Infect Control 2004;32(8):470-85.

2. Revelas A. Healthcare - associated infections: A public health problem. Niger Med J 2012;53(2):59-64.

3. Gastmeier P, Geffers C, Schwab F, Fitzner J, Oblanden M. Development of surveillance system for nosocomial infections, the component for neonatal intensive care units in Germany. J Hosp Infect 2004;57(2):126-31.

4. Phu VD, Wertheim HF, Larsson M, et al. Burden of Hospital Acquired Infections and Antimicrobial Use in Vietnamese Adult Intensive Care Units. PLoS One 2016;11(1):e0147544

5. Fanders SA. Collard HR. Saint S. Nosocomial pneumonia: state of the science. Am J Infect Control 2006;34(2):84-93.

6. Kaoutar B, Joly C, Heriteau FL, Barbut F, et al. Noscoomial infections and hospital mortality: a multicenter epidemiological study. J Hosp Infect 2004;58(4):268-75.

7. Sahu MK, Siddharth B, Choudhury A, et al. Incidence, microbiological profile of nosocomial infections, and their antibiotic resistance patterns in a high volume Cardiac Surgical Intensive Care Unit. Ann Card Anaesth 2016;19(2):281-7.

8. Klevens RM, Edwards JR, Richards CL, et al. Estimation healthcare associated infections and deaths in U.S. hospitals 2002. Public Health Rep 2007;122(2):160-6.

9. Jeong SH, Bae IK, Kwon SB. Investigation of a nosocomial outbreak in ICU. J Hosp Infect 2005:59(3):242-8.

10. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control 2008;36(5):309-32.

11. Clinical and Laboratory Standards Institute. M100: Performance standards for antimicrobial susceptibility testing, 27th edition [pamphlet]. Wayne, Pennsylvania: Clinical and Laboratory Standards Institute; 1998.

12. Mohammadimehr M, Feizabadi MM, Bahadori O, Khosravi M. Study of prevalence of gram-negative bacteria caused nosocomial infections in ICU in Besat hospital in Tehran and detection of their antibiotic resistance pattern-year 2007. Iranian Journal of Medical Microbiology 2009;3(2):47-54.

13. Cook PP1, Catrou PG, Christie JD, Young PD, Polk RE. Reduction in broad spectrum antimicrobial use associalted with no improvementin hospital antibiogram. J Antimicrob Chemother 2004;53(5):853-9.

14. Fish DN, Ohlinger MJ. Antimicrobial resistance: factors and outcomes. Crit Care Clin 2006;22(2):291-311.

15. Yates RR. New intervention strategies for reducing antibiotic resistance. Chest 1999;115(3 Suppl):24S-27S.

16. File TM Jr. Overview of resistance in the 1990s. Chest 1999;115(3 Suppl):3S-8S.

17. Zamani S, Nasiri MJ, Khoshgnab BN, Ashrafi A, Abdollahi A. Evaluation of antimicrobial resistance pattern of nosocomial and community bacterial pathogens at a teaching hospital in Tehran, Iran. Acta Med Iranica 2014;52(3):182-6.

18. Rajabi M, Esmaeili M, Rafiei H, Aflatoonia MR, Esmaeili R. Nosocomial Infections and Epidemiology of Antibiotic Resistance in Teaching Hospitals in South East of Iran. Glob J Health Sci 2016;8(2):190-197.

19. Van der Zwet WC, Kaiser AM, van Elburg RM, et al. Nosocomial infections in a Dutch neonatal intensive care unit: surveillance study with definitions for infection specifically adapted for neonates. J Hosp Infect 2005;61:300-11.

20. Soltani R, Khalili H, Abdollahi A, Rasoolinejad M, Dashti-khavidaki S. Nosocomial Gram-positive antimicrobial teaching hospital in Tehran, Iran. Future Microbiol 2012;7(7):903-910.

21. Giacometi A, Cirioni O, Schimizzi AM, et al. Epidemiology and microbiology of surgical wound infections. J Clin Microbiol 2000;38(2):918-22

22. Sader HS, Jones RN, Gales AC, et al. Antimicrobial susceptibility patterns for pathogens isolated from patients in Latin American medical centers with a diagnosis of pneumonia: analysis of results from the SENTRY Antimicrobial Surveillance Program (1997). Diagn Microbiol Infect Dis 1998;32(4):289-301.

23. Pfaller MA, Jones RN, Doern GV, Sader HS, Kugler KC, Beach ML. Survey of bloodstream infections attributable to Gram positive cocci: frequency of occurrence and antimicrobial susceptibility of isolates collected in 1997 in the United States, Canada and Latin America from the SENTRY. Antimicrobial Surveillance Program. Diagn Microbiol Infect Dis 1999;33(4):283-97.

24. Soltani R, Ehsanpoor M, Khorvash F, Shokri D. Antimicrobial susceptibility pattern of extended spectrum β lactamase producing bacteria causing nosocomial urinary tract infections in an Iranian referral teaching hospital. J Res Pharm Pract 2014;3(1):6-11.

25. Talebi Taher M, Golestanpour A. Symptomatic nosocomial urinary tract infection in ICU patients: Identification of antimicrobial resistance pattern. Iranian Journal of Clinical Infectious Diseases 2009;4(1);25 29.

26. Saffar MJ, Enayti AA, Abdolla IA, Razai MS, Saffar H. Antibacterial susceptibility of uropathogens in 3 hospitals, Sari, Islamic Republic of Iran, 2002 2003. East Mediterr Health J 2008;14(3):556-63.

27. Gaynes R, Edwards JR, National Nosocomial Infections Surveillance System. Overview of nosocomial infections caused by gram negative bacilli. Clin Infect Dis 2005;41(6):848-54.

28. Bouza E, San Juan R, Muñoz P, et al. A European perspective on nosocomial urinary tract infections I. Report on the microbiology workload, etiology and antimicrobial susceptibility (ESGNI 003 study). European Study Group on Nosocomial Infections. Clin Microbiol Infect 2001;7(10):523-31.

29. Tankhiwale SS, Jalgaonkar SV, Ahamad S, Hassani U. Evaluation of extended spectrum beta lactamase in urinary isolates. Indian J Med Res 2004;120(6):553-6.

30. Soltani R, Khalili H, Abdollahi A, Rasoolinejad M, Gholami KH. Antimicrobial Susceptibility Pattern of Staphylococcus aureus Strains Isolated from Hospitalized Patients in Tehran, Iran. Iranian Journal of Pharmaceutical Sciences 2010;6(2):125-132.

31. Diekema DJ, Pfaller MA, Jones RN, et al. Survey of bloodstream infections due to gram-negative bacilli: frequency of occurrence and antimicrobial susceptibility of isolates collected in the United States, Canada, and Latin America for the SENTRY antimicrobial surveillance program, 1997. Clin Infect Dis 1999;29(3):595-607.

32. Schmitz FJ, Lindenlauf E, Hofmann B, et al. The prevalence of low- and high-level mupirocin resistance in staphylococci from 19 European hospitals. J Antimicrob Chemother 1998;42(4):489-95.

33. Sabzghabaee A, Abedi D, Fazeli H, et al. Antimicrobial resistance pattern of bacterial isolates from burn wounds in an Iranian university hospital. J Res Pharm Pract 2012;1(1):30-3.

34. Singh NP, Goyal R, Manchanda V, Das S, Kaur I, Talwar V. Changing trends in bacteriology of burns in the burns unit, Delhi, India. Burns 2003;29(2):129-32.

35. Ozumba UC, Jiburum BC. Bacteriology of burn wounds in Enugu, Nigeria. Burns 2000;26(2):178-80.