# The pattern of antibiotic resistance of common bacteria causing nosocomial infections

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# Abstract

Background: Nosocomial infection is one of the most important health problems across the world. Nosocomial infection causes 99,000 deaths and patients spend over 30 million dollars per year in America. The current study aimed to determine the pattern of antibiotic resistance of common bacteria causing nosocomial infections in Besat Hospital, Hamedan, Iran.

Methods: This cross sectional prospective study was conducted in Besat hospital for four months. Each of the non-pediatric patients in different wards of the hospital with various types of nosocomial infections in accordance with CDC guidelines were enrolled, and cultured chip samples, urine, blood and wound specimens for culture and susceptibility were sent to a laboratory. All micro-organisms isolated from cultures were considered in antimicrobial resistance patterns. Antimicrobial resistance pattern (Kirby-Bauer method) of bacterial isolates was determined according to the report/ test table of CLSI M100-S23 instructions. **Results:** Of 10,332 hospitalized patients we reported 266 (2.6%) with nosocomial infections and the VAP was the most common nosocomial infection. Among 266 bacterial isolates, the highest prevalent bacterium belonged to the E. coli with prevalence 61(22.9%) followed by Klebsiella, Acinetobacter and S. aureus with prevalence of 42(15.8%), 36(13.5%) and 26(9.8%), respectively.

In Gram-negative bacteria maximum resistance to ciprofloxacin and minimum resistance to Colistin and Imipenem was observed. The prevalence of MRSA in VAP, CLA-BSI and SSI was 3.3, 22.2 and 54.5 %. Resistance to Vancomycin in Staphylococci was not observed, but in Enterococci resistance to Vancomycin was 42.9%.

Conclusion: The main problem in this hospital is MDR Gram-negative infections rather than Staphylococ-cus aureus.

Knowing the pattern of antimicrobial resistance can prevent prescribing inappropriate antibiotics and effective steps can be taken towards reducing microbial resistance.

Key words: antibiotic resistance, nosocomial, infection, drug Resistance.

#### Background

Nosocomial infection is one of the most important health problems of health across the world. Based on estimation, in 2002 only 7.1 million Nosocomial infection occurred ed in America. HAI causes 99,000 deaths and patients spend over 30 million dollars per year in America(1). Also in other continents of the world there is a high prevalence of these infections(2). In America, more than 30% of hospital infections are caused by Gram-negative bacilli in intensive care units (ICU), and 70% of hospital infections are caused by these microbes. Between Gram-negative bacilli that cause hospital infections, Enterobacteriaceae are the most common family. Unfortunately, resistant Gram-negative bacilli, including Pseudomonas aeruginosa, Acinetobacter baumannii and Enterobacteriaceae producing betalactamase (ESBL) or Carbapenemases are growing in all parts of the world (1) and the frequency of ESBLproducing Enterobacteriaceae family can reach up to 60% (3). In addition Gram-negative bacilli, has increased the prevalence of nosocomial infections with resistant gram-positive cocci such as Staphylococcus aureus and Enterococcus with a rate of about 50-60%(4) for Staphylococcus aureus and 30% for Enterococcus. Since, proper knowledge of the patterns of microbial resistance and its trend in every hospital is needed, so describing antibiotic treatment empirically to finalize the culture results and antibiotic sensitivity tests(5), can be effective in reducing the mortality rate and operative measures should be taken to prevent the development of microbial resistance in different wards of hospitals. Therefore, this study aimed to determine the pattern of antibiotic resistance of common bacteria causing nosocomial infections in the hospital.

## Methods

This cross sectional prospective study was conducted in Besat hospital, Hamedan, Iran in 2016. The hospitalized non-pediatric patients in different wards of hospital with various types of nosocomial infections such as; Ventilator Associated Pneumonia (VAP), Catheter Acquired Urinary Tract Infection (CA-UTI), Surgical Wound Infection (SC) and Central Line Associated-Blood Stream Infection (CLA-BSI) were involved in the study. At first, the necessary coordination with hospital microbiology laboratory was done for use of proper differentiation media and antibiotics disks (Mast Company). In order to unify the definitions of the four mentioned nosocomial infections we used definitions of the Center for Disease Control and Prevention (CDC). Tracheal, urine, blood, surgical wound samples were sent to the laboratory for culture and antibiotic susceptibility test. The identification of bacteria, especially Gram-negative bacilli was used for the same set of diagnostic tests. Antimicrobial resistance pattern (Kirby-Bauer method) of bacterial isolates was determined according to the report/ test table of CLSI M100-S23 instructions(6). For patients resistant to meropenem, vancomycin and colistin, E-test was used. Finally, data were analyzed by SPSS (Version 15) software.

#### Results

Of 10,332 hospitalized patients we reported 266 (2.6%) of nosocomial infections and the VAP was the most common nosocomial infection with a prevalence of 110 (41.6%) cases. Among 266 bacterial isolates, the highest prevalent bacterium belonged to the E. coli with prevalence 61(22.9%) followed by Klebsiella, Acinetobacter and S. aureus with prevalence of 42(15.8%), 36(13.5%) and 26(9.8%), respectively (Table 1). 60.9% of Staphylococcus aureus isolated were resistant to cefoxitin (MRSA) but none of them were resistant to vancomycin. Acinetobacter had the highest resistance to ciprofloxacin (74.3%) and the lowest resistance to colistin (8.3 %). For Pseudomonas, Klebsiella and E. coli, the most effective and the most resistant was to colistin and ciprofloxacin, respectively. In patients who suffered from VAP, only 4 out of 110 cases were related to the S. aureus which among those 3 cases were reported MRSA, so MRSA prevalence in the VAP was 3.3%. As well, MRSA prevalence in SSI was 54.4% and CLA-BSI accounted for 22.2%. In the Enterococcus isolates, the resistance to ampicillin and vancomycin were 57.1% and 42.9%, respectively. The resistance rate to colistin in the Acinetobacter was 8.3%, followed by imipenem with prevalence 42.9%. Also in Pseudomonas and Klebsiella, after colistin the minimum of the resistance was observed to imipenem, but regarding E. coli, followed by colistin, the least resistance was seen to aminoglycoside (Table 2). As shown in Table 3 pattern of resistance in the E. coli isolated of urinary tract infection (UPEC), all were susceptible to the carbapenems and only 25% were resistant to the ciprofloxacin. In VAP caused by 101 gram negative isolates, antibacterial resistance pattern showed that the least resistance was related to colistin (19.8%) and the highest was linked to t ciprofloxacin(56.9%),( Table 4). Of 20 cases which were resistant to colistin in VAP, 17, 2 and 1 of those respectively were associated with Proteus, Acinetobacter and E.coli. Pattern of bacterial resistance in Gram negative organisms caused Central line associated blood stream infection (CLA-BSI) and showed that the highest and lowest resistance was attributed to the Ceftriaxone and Colistin with frequency 77.8% and 11.5%, respectively (Table 5). In CLA-BSI, after colistin, the lowest resistance was observed to imipenem (38.5%), but in SSI, after colistin, the minimum of resistance was reported to piperacillin-tazobactam. Among 3 isolates of Gram negative organisms caused Central line associated blood stream infection (CLA-BSI) which were resistant to colistin, 1, 1 and 1 cases of those belonged to the Proteus, Acinetobacter and Serratia, respectively. Also as shown in Table 6 among 3 isolates of Gram negative organisms causing surgical site infection (SSI) which were resistant to colistin, 2 and 1 cases of those belonged to the Proteus, Serratia, respectively.

#### Table 1: Types of clinical samples and common bacteria in nosocomial infections

Samples types	Frequency (%)	Bacterial types	Frequency (%)
BC	46(17.6%)	E.coli	61(22.9%)
UC	23(8.8%)	Klebsiella	42(15.8%)
SC	82(31.4%)	Acinetobacter	36(13.5%)
Tc	110(41.6%)	Staphylococcus aureus	26(9.8%)

Note: BC; Blood culture, UC; Urine culture, SC; Surgical wound culture, TC; Tracheal culture (*Table 2: Pattern of resistance in isolated bacteria - is on the next page*)

#### Table 3. Pattern of resistance in the E. coli isolated of urinary tract infection (UPEC)

Antibiotics types	Susceptibility (%)	Resistance (%)
Ciprofloxacin	75	25
Imipenem	100	0
Meropenem	100	0
Aminoglycoside	50	50

Table 4. Pattern of bacterial resistance in Gram negative organisms caused Ventilator associated pneumonia (VAP)

Antibiotics types	Susceptibility (%)	Resistance (%)
Cefipime	45.9	54.1
Aminoglycoside	67.6	32.4
Ciprofloxacin	43.1	56.9
Tazocin	68.6	31.4
Imipenem	79.4	20.6
Meropenem	63.7	36.3
Colistin	80.2	19.8
Ampisulbactam	64	36

Table 5. Pattern of bacterial resistance in Gram negative organisms caused by Central line associated blood stream infection (CLA-BSI)

Antibiotic	Susceptibility (%)	Resistance (%)
Cefipime	37	63
Aminoglycoside	44.4	55.6
Ciprofloxacin	29.1	70.9
Tazocin	51.9	48.1
Imipenem	61.5	38.5
Meropenem	57.7	42.3
Colistin	88.5	11.5
Ampicilin/sulbactam	44.4	55.6
Ceftriaxone	22.2	77.8

#### Table 6. Pattern of bacterial resistance in Gram negative organisms caused by SSI

Antibiotic	Susceptibility (%)	Resistance (%)
Cefipime	65.3	34.7
Aminoglycoside	71.4	28.6%
Ciprofloxacin	42.9	57.1%
Tazocin	87.6	18.4%
Imipenem	79.2	20.8%
Meropenem	67.3	32.7%
Colistin	93.9	6.1%
Ampicilin/sulbactam	67.3	32.7%
Ceftriaxone	40.8	59.2%

Gram (-)	Taz	ocin	Amino	glycoside	5	epime	Colist	. <u>5</u>	Ampicill	in/ Sulba	actam	
	s	*	s	œ	S	œ	S	æ	S	╞	æ	
E. coli	69.69	30.4	78.6	21.4	20	20	98.4	1.6	64.3		35.7	
Klebsiella	73.2	26.8	53.7	46.3	53.7	46.3	100	0	56.1		43.9	
Acinetobacter	•	•	42.9	57.1	37.1	25.7	25.7	8.3	38.9		61.1	
Pseudomonas	73.2	26.8	46.3	53.7-	86.6	13.4	100	0	76.5		23.5	
Gram (-)	Ciprofi	loxacin	Imipe	шеш	Merop	enem	ESBL- positive					
	s	8	s	œ	s	æ	3					
E. coli	25	75	76.4	23.6	53.6	46.4	50					
Klebsiella	34.1	6:59	92.6	7.4	80.5	19.5	46.3					
Acinetobacter	25.4	74.3	57.1	42.9	51.4	48.6	•					
Pseudomonas	57.9	42.1	92.7	7.3	80.5	19.5	46.3					
Gram (+)	Cipro	ofloxacin	Co-tr	imoxazol	2	/ancomy	/cin	Cefox	ütine	Ampi	icillin	Penicilli
	s	×	s	æ		s	~	s	В	s	æ	s
S. aureus	60.9	39.1	1 78.3	21.7	7 1(	000	0	60.9	39.1	•		•
Enterococcus	•		•		5	7.1	42.9		0	42.9	57.1	57.1

Table 2: Pattern of resistance in isolated bacteria

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#### Discussion

Based on the reports, around 75% of the burden of nosocomial infections is present in developing countries(7). Since Iran as a part of these developing countries is faced with this problem properly strategies should be developed to deal with it. In the present study the most common organism in nosocomial infection was E.coli, and similarly , Edrinc et al reported the most isolated organism was E.coli (8). But some studies have reported Acinetobacter baumannii as the most prevalent organism (9). Rate of resistance to antibiotics among hospital and community bacteria have augmented significantly during the previous decade(10). Some studies have revealed that antibioticresistant infections are related with increased morbidity and mortality in comparison with antibiotic-susceptible infections(11). In the study conducted by Cucu et al in 2014 in Hungary, resistance to ciprofloxacin was 52.2%; similarly, in our study the resistance rate in E. coli was 75%. In the same study resistance rate to aminoglycoside was 76.1%, but in our study, the resistance to the mentioned antibiotic was about 21%(12). In our study, the resistance rate to third generation cephalosporins was high; this finding is similar to the study carried out by Movahedian et al which indicated that K. pneumoniae showed the highest resistance to routine third generation Cephalosporins(13). Additionally, a study conducted by Mansury et al also showed the most resistance of K. pneumoniae bacteria to third generation Cephalosporins(14). Through the three past decades, ESBLs producing gram-negative Enterobacteriaceae particularly, E. coli and K. pneumoniae have created severe problems both in hospital and community acquired infections worldwide and ESBLs producing bacteria had significantly greater fatality than those with non-ESBL isolates(15). Accordingly the different studies from many part of Iran have stated that the prevalence of ESBL producing clinical isolates of E. coli varied between 45.2 to 67.2%(16), which confirmed our study, because the prevalence of ESBL producing E. coli isolates was 50% and the rate in both pseudomonas and Klebsiella was about 46%. ESBL infections cause heavy burden on patients including; increased hospital costs, length of stay, and rate of mortality(17). Another study conducted in Qazvin showed the high prevalence of ESBL producing E. coli isolates, also. In A. baumannii, the most resistance was observed against ciprofloxacin and the most effective antibiotic was colistin. Colistin is effective against gram-negative bacilli (including P. aeruginosa, E. coli, Klebsiella pneumoniae) and colistin was used as therapy for nosocomial infections caused by multidrug-resistant P. aeruginosa and A. baumannii (18). The notable exception of gram-negative bacilli is the high level inherent resistance of Proteus species to the colistin that often are highly resistant. Providencia species, Serratia, and Moraxella catarrhalis, Burkholderia also have a similar situation. In this study, one of the reasons for higher resistance to Colistin in the VAP, is high prevalence of Proteus species in the VAP.(19). In Pseudomonas, the most effective antibiotic was colistin with susceptibility 100% and the most resistance was observed in ciprofloxacin with prevalence 53.7%. As seen in the results section, the

resistance to colistin in Pseudomonas was 0%, but in A. baumannii was 8.3%. Similar to our study no resistance was observed to Pseudomonas in Denmark and UK(20). A notable point in this study was the high resistance of gram-negative bacteria to ciprofloxacin, possibly because of excess prescription of antibiotics in outpatients and inpatients. While the antibiotic resistance of S. aureus to the same antibiotic and cefoxitin was 39.1%. In this study, gram-negative susceptibility to imipenem was more than meropenem which was indicative of lack of crossresistance between the two antibiotics and likely because of the high consumption of meropenem in this hospital. According to a study of European countries. ICUs pneumonia was the highest nosocomial infection(21). In hospitalized patients, nosocomial pneumonia is the leading cause of morbidity and mortality. The important risk factor for the development of nosocomial pneumonia is the use of ventilator(19). Obtaining VAP might be not only be via ventilator. Health workers especially nurses have an important role in inhibiting colonization of bacteria by mechanical ventilation(22). In the present study, 3 out of 4 S. aurous isolates were Methicillin-resistant S. aureus (MRSA). Methicillin-resistant S. aureus isolates are seen in hospital/community acquired infections(20). Interestingly, the prevalence of MRSA in SSI was 54.6%, in fact it is a high rate. Generally, aerobic gram-positive cocci including Staphylococcus are predominant, and resistant organisms such as methicillin-resistant S aureus (MRSA) indicates a growing percentage of these infections(23). Several studies reported S. aureus as the most prevalent organism (24) followed by Pseudomonas aeruginosa, E. coli, and K. pneumoniae(25) which results are in contrast with our results. The susceptibility pattern of SSI strains is varying owing to the increasing emergence of antibacterial resistant bacteria isolates such as MRSA causing difficulties in selecting the empirical treatment(26). In selecting the empirical regimens of VAP two points should be considered : First, the overall prevalence of MRSA in VAP related to this hospital was 3.3%, so, according to the IDSA guidelines, given that the prevalence of MRSA is less than 10 to 20 %, it is not needed to describe vancomycin or linezolid in the empirical regime, unless the patient has the risk of antimicrobial resistance(21). Secondly, to cover gram negatives, two antibiotics with anti-pseudomonas in the empirical regime for VAP should be considered. For this reason, in regard to the acquired resistance pattern, the best regime includes imipenem and colistin or aminoglycosides, and for those critically ill with VAP diagnosis, colistin should be a part of the empirical regime until determining time of antimicrobial pattern, however, in regard to the high resistance of gram negative organisms to ciprofloxacin in the VAP, in the empirical regime its use is not recommended. In the SSI, the empirical regime can include pipracilin-tazobactam for covering gram negative bacteria, although regarding the MRSA prevalence in SSI which is about 54.5%, depending on the culture and antibiogram, vancomycin should be a part of empirical regime. However, regarding S. aureus, no case of vancomycin resistance was seen in this study, but 42.9% of Enterococcus cases were resistant to vancomycin and 57.1% were resistant to Ampicillin.

So, use of linezolid appears necessary in Enterococcus resistant to vancomycin. Although antimicrobial resistance to imipenem and meropenem in E. coli were 23.6% and 46.4%, respectively, in E. coli isolated of CA-UTI, no case of resistance to carbapenem was observed and resistance to ciprofloxacin in E. coli was not isolated; CA-UTI was reported at 75% contrary to the E. coli isolated of CA-UTI with prevalence of 25%. Therefore, the use of carbapenems in sepsis caused by CA-UTI is effective.

# Conclusion

According to the results, the main problem in this hospital is MDR Gram-negative infections rather than the staphylococcus aureus. Knowing the pattern of antimicrobial resistance from prescribing inappropriate antibiotics can be prevented and an effective step taken towards reducing microbial resistance. Also prescribing appropriate empirical antibiotics until finalized culture results and antibiotic sensitivity test, to reduce mortality and hospital infections caused by the nosocomial infections should be undertaken. In future studies, the pattern of antimicrobial resistance of nosocomial infection surveillance system to reform the health care system and surveillance on hospital infections is essential.

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