Antibiotic resistance in patients suffering from nosocomial infections in Besat Hospital

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Abstract

This study was performed to determine the trend of antibiotic resistance of the causative organisms among the patients suffering from nosocomial infections in Besat Hospital since 2013 to 2015. In this observational study that was performed as a retrospective cohort, 935 consecutive patients with nosocomial infection were enrolled in Besat Hospital since 2013 to 2015. The trend of antibiotic resistance of the causative organisms among them was determined and contributing factors were assessed. The finding of this study revealed that type of microorganisms had significant variation ($p = 0.024$): while the gram-negative bacilli have shown an increased level of resistance, the gram positive cocci had less resistance. The antibiotic resistance was increased for ampicillin/sulbactam, piperacillin/tazoactam, ceftriaxone, ceftazidime, cefepime, meropenem, gentamicin, amikacin, ciprofloxacine, levofloxacine, nitrofurantoin, and ampicilline. However, it was decreased for colistin. In conclusion, antibiotic resistance has an increasing trend and strategic measures of prevention are needed to reduce nosocomial infections.

Key Words: Antibiotic resistance, trend, nosocomial infection, health care

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Hospital infections and antibiotic resistance are problems that have been reported for many years around the world, causing the monetary burden and prolonged treatment. An epidemiological study on the incidence of hospital infections in the United States showed that, the risk of infectious diseases has increased steadily. A total of 2 million people are affected by a hospital infection, where it is being imposed on the health system at a cost of $ 4.5 to $ 11 billion. In addition, 80,000 deaths annually occur due to hospital infections.[1] Hospital infections are caused by hospitalization 48 hours after the patient admission or 30 days after being discharged from the hospital. Nosocomial infections are one of the most common types of infections.[2] These infections are mainly caused by bacterial agents, such as Staphylococcus, Pseudomonas and *Escherichia coli*, and are more often observed as pneumonia and urinary tract infections (UTI), in 22 patients per 1,000 people.[2] However, the main cause of infection is not detected in 17% of patients.[2] It is worth noting that *Staphylococcus aureus* is the most common form of pneumonia and *Escherichia coli* in cases of UTI.[3] Of course, the rates and types of hospital infections are different in various hospitals, where the rates of UTI, pneumonia, and bacteremia are the most common types in some hospitals.[4] Therefore, their therapeutic pattern is different in treatment centers where is dominated by predominant microorganisms and resistant types. Antibiotic resistance can be initial or acquired. Resistant agents are generally bacteria that have high virulence, such as *Staphylococcus aureus*. Also, antibiotic resistance is related to their history of use. The most important steps in preventing hospital infections are identifying the factors that affect these infections and taking precautionary measures based on the use of appropriate strategies.[5] In this regard, In this regard, the establishment of surveillance systems is important to track the trend of hospital infections [6]. The importance and necessity of this is especially more for antibiotic resistance because, according to available reports, this

Table 1. *Frequency distribution of the agent type in studied years*

			Germ Type			
			Gram - Bacillus	G + Cocci	Yeast	Total
Year	**2013**	Count	255	36	0	291
		% within Year	87.6%	12.4%	.0%	100.0%
	2014	Count	302	38	3	343
		% within Year	88.0%	11.1%	.9%	100.0%
	2015	Count	281	20	0	301
		% within Year	93.4%	6.6%	.0%	100.0%
Total		Count	838	94	3	935
		% within Year	89.6%	10.1%	.3%	100.0%

issue is rising. By identifying the pattern of antibiotic resistance changes, it is possible to provide suggestions on how antibiotics are administered, and how to change their course, as well as empirical treatment. Therefore, the present study was aimed to investigate the change in the pattern of antibiotic resistance in the microorganisms causing nosocomial infections during the years 2013 to 2015 in Besat Hospital.

Materials and Methods

This observational study was conducted as a retrospective cohort study. A total of 935 patients with nosocomial infections during the years 92 to 94 were selected and examined in Besat Hospital. Also, antibiotic resistance patterns were studied in microorganisms based on antibiogram and their relationship with other variables was evaluated. Data were analyzed using SPSS software version 13. Mean and standard deviation were determined for quantitative variables while absolute and relative frequency was recorded for qualitative variables. Chi-Square, Fisher, T-independent and ANOVA test were used to evaluate the variables. A p value < 0.05 was considered significant.

Results and Discussion

In the present study, a total of 935 patients with nosocomial infections were evaluated, from of which 514 cases (55%) were male and 421 (45%) were female. Sex distribution was not statistically significant in the studied years (p > 0.05).The mean age of patients in studied years was 63.9 ± 36.18 to 66.38 ± 29.18 years. The frequency of age distribution of patients did not show a significant difference (p > 0.05). Regarding to the type of cultivation, 631 cases belonged to sputum culture (67.5%), followed by 49 blood cultures (5.2%), 187 urine culture (20%), 68 ulcer culture (7.3%). The distribution of the type of patient sample did not show a significant difference (p > 0.05). Regarding the frequency of disease type, 363 cases were related to Acinetobacter (38.8%), followed by *E .coli* (207 cases; 22.1%), *Staphylococcus aeruginosa* (140; 15%), *Staphylococcus aureus* (50; 5.3%), and other agents including coagulase-negative *Staphylococci*, *Enterobacter*, *Klebsiella*, and *Candida*. The type of agent in the studied years was found to be significantly different (p = 0.001), so that pseudomonas decreased and *Acinetobacter* showed an increased incidence. Regarding the frequency of resistance to vancomycin, 5 cases (93.7%) were susceptible to vancomycin and 7 cases (6.3%) were resistant. Frequency of vancomycin resistance in patients was not significantly different in studied years (p > 0.05). Regarding the frequency of oxacillin resistance, 30 cases (42.7%) were susceptible to oxacillin and 40 were resistant. There was no significant difference in the frequency of oxacillin resistance in patients during the studied years (p > 0.05). Resistance to ampicilin / sulbactam was seen in 152 cases (39%), while 238 cases (61%) were susceptible. Distribution of ampicillin / sulbactam resistance in patients in studied years was demonstrated to be significant, where had U pattern (p = 0.014). Moreover, the resistance of piperacillin / tazobactam was seen in 272 cases (56%), while 214 (44%) were susceptible. It is worth noting that resistance to piperacillin / tazobactam in patients showed a significant level where it showed an incremental pattern (p = 0.037). Furthermore, 32 cases (43.2%) revealed resistance to cefazolin, while 42 (56.8%) were susceptible. The frequency of resistance to cefazolin did not show significant difference among patients in studied years (p > 0.05). In addition, frequency of cefoxitin resistance was found in 25 cases (43.9%), however, 32 cases (56.1%) were susceptible to this antibiotic. There was no significant difference in frequency distribution of

***Table 2**. Pattern of antibiotic resistance based on age of patients*

Year	Antibiotic resistance
2013	Age was not associated with any antibiotic resistance (p > 0.05).
2014	Senior age had a significant correlation with Clindamycin resistance (p = 0.044).
2015	The higher age group had a significant association with resistance to gentamicin (p = 0.018) and the age was significantly correlated with clindamycin resistance (p = 0.034).

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***Table 3.** Change in the pattern of antibiotic resistance based on gender of patients*

Year	Antibiotic resistance
2013	Female gender was associated with antimicrobial resistance to amikacin (P = 0.049).
2014	Male sex was associated with antimicrobial resistance to levofloxacin (P = 0.012).
2015	Gender was not associated with any antibiotic resistance (P> 0.05).

cefoxitin resistance in patients during the studied years (p > 0.05). Our findings demonstrated that 63 cases (11.9%) were susceptible to ceftriaxone and 466 (88.1%) were resistant to ceftriaxone. The frequency of resistance to ceftriaxone showed significant changes, indicating an incremental pattern (p = 0.010). With regard to the frequency of resistance to ceftazidime, 49 cases (9.9%) revealed susceptibility to this antibiotic, while 445 (90.1%) confirmed antibiotic resistance. As a result, significant changes were found in the frequency of resistance to ceftazidime in patients, where an incremental pattern was achieved (p = 0.001). Regarding resistance to cefepime, 103 cases (20.2%) showed sensitivity and 406 (79.8%) were resistant. The frequency of resistance to imipenem among patients was significantly higher in studied years and had an incremental pattern (p = 0.001). In the studied years, 132 cases (24.8%) were sensitive to imipenem and 400 cases (75.2%) showed resistance. The frequency of imipenem resistance in patients in studied years did not reveal a significant difference (p > 0.05). Moreover, Resistance to meropenem was also found in 353 cases (67.5%), but the sensitivity of this biotype was found in 170 (32.5%) patients. The frequency of resistance to meropenem in patients demonstrated a significant change in studied years and had a reverse U pattern (p = 0.002). With regard to the frequency of resistance to gentamicin, 88 cases (23.1%) were found to be susceptible while 293 cases (66.9%) were identified to be resistant. The frequency of resistance to gentamicin in patients revealed significant changes over the years and was U-shaped pattern (p = 0.002). In this study, other antibiotics such as amikacin, ciprofloxacin, levofloxacin, nitrofurantoin, clostin, and ampicillin have been evaluated. Frequency of resistance in patients in studied years revealed significant changes where u-shaped patterns were observed regarding amikacin, ciprofloxacin, levofloxacin.It should be noted that in the case of clostine, a decreasing resistance pattern was demonstrated and an incremental resistance pattern was determined for ampicillin. It is worth noting that there were no significant differences in resistance to antibiotics such as clindamycin, rifampicin, clotrimazole, linezolid and nalidixic acid in studied years. On the other hand, diversity of antibiotic resistance patterns based on age, gender type of sample and type of agent in the subjects are listed listed in Tables 2 to 5. The findings of this study revealed that the frequency distribution of the agent type had significant changes (P = 0.024): gram negative bacilli increased notably, while gram positive cocci decreased (Table 1). The trends in antibiotic resistance pattern of bacterial agents based on the age of the subjects was significant in few cases (p <0.05) that are shown in table 2. The change in antibiotic resistance pattern based on gender was also significant in few cases (Table 3; p <0.05). The trend of changing the patterns of antibiotic resistance based on the type of sample was significant in some cases (p <0.05), that are shown in Table 4. In addition, there was a significant relationship between the trend of antibiotic resistance pattern and type of agent in most cases (Table 5; p <0.05).

Establishing surveillance systems for tracking the trend of infectious diseases is of particular importance.[6] This is especially true for antibiotic resistance because it is increasing among patients. By identifying the pattern of antibiotic resistance, suggestions can be made on how antibiotics are administered, so the study was designed to assess the changes in antibiotic resistance pattern among microorganisms involved in nosocomial infections. Microorganisms had significant variation (p = 0.024). The gram-negative bacilli have shown an

Table 4. *Antibiotic resistance pattern based on sample type*

Year	Antibiotic resistance
2013	The blood sample was associated with antibiotic resistance to vancomycin (p = 0.001), oxacillin (p = 0.021), ceftriaxone (p = 0.002), cefipime (p = 0.013), linzolide (p = 0.003) and clindamycin (p = 0.015). A sample of phlegm was associated with antibiotic resistance to piperacillin / tazobactam (p = 0.001), meropenem (p = 0.001), amikacin (p = 0.001) while the urine sample was related to antibiotic resistance to nalidixic acid (p = 0.001).
2014	Blood samples were correlated with antibiotic resistance to ceftriaxone (p = 0.001), Cefepime (p = 0.001), *meropenem* (p = 0.001), amikacin (p = 0.001), and colistin (p = 0.040). The association of sputum samples with antibiotic resistance was detected in a number of bacteria including piperacillin / tazobactam (p = 0.001), ceftazidime (p = 0.043), imipenem (p = 0.001), gentamicin (p = 0.001), and ciprofloxacin (p = 0.001).
2015	The association of blood samples with antibiotic resistance was observed only in ceftriaxone (p = 0.001) and cefepime (p = 0.001). Furthermore, the sputum samples had a significant relationship with antibiotics in terms of drug resistance including piperacillin / tazobactam (p = 0.001), imipenem (p = 0.001), moropenem (p = 0.001) and amikacin (p = 0.001) ciprofloxacin (pp = 0.027) and levofloxacin (p = 0.016). While urine specimens were associated with antibiotic resistance to co-trimoxazole (p = 0.005)

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Table 5. *Change in antibiotic resistance patterns based on the type of agents*

Year	Antibiotic resistance
2013	There was correlation between agents and antibiotic resistance for all antibiotics ($p < 0.05$) other than vancomycin, linezolid and cotrimoxazole
2014	There was a correlation between agents and antibiotic resistance for all antibiotics ($p < 0.05$).
2015	A significant association was found between agents and antibiotic resistance in all antibiotics ($p < 0.05$) with the exception of oxacillin, cefazolin, cefoxitin, nalidixic acid, nitrofurantoin, rifampicin and clindamycin

increased level of resistance, while the gram positive cocci had less resistance. The antibiotic resistance was increased for ampicillin / sulbactam, piperacillin / tazoactam, ceftriaxone, ceftazidime, cefepime, meropenem, gentamicin, amikacin, ciprofloxacine, levofloxacine, nitrofurantoin, and ampicilline. However, it was decreased for colistin. Behzadnia et al. 2014,[7] evaluated the nosocomial infections in children in north of Iran for identifying the antibiotic sensitivity of their causative organisms. They reported that all the gram positive and negative bacterial isolates revealed remarkable resistance to antibiotics. Moreover, multidrug-resistannce of *Acinetobacter spp.* was found by the mentioned study.[6] Pseudomonas spp. (36.84%) and Acinetobacter spp. (28.02%) were mostly found in isolated samples. However, pseudomonas showed a significant decrease in our research, while an increase in the frequency of *Acinetobacter* was reported. Necati Hakyemez et al. in Turkey assessed nosocomial *A. baumannii* antibiotic resistance in patients suffering from nosocomial infections.[8] The most effective antibiotics in isolated strains included imipenem, meropenem, colistin and tigecycline, as reported previously by Necati Hakyemez et al.[8] However, they showed that the antibiotic resistance level against imipenem and meropenem has increased over the years,an observation that our research findings confirm. Another study demonstrated antibiotic-resistant *Acinetobacter Baumannii* infections in another Hospital in Tehran, Iran. As reported by Vahdani et al,[9] the highest resistance belonged to ceftazidime (96%), followed by ceftizoxime (95%), ceftriaxone (93%), ciprofloxacin (85%), co-terimoxazole (85%), gentamicin (68%), amikacin (58%) and imipenem (9%). Report that gram-positive bacteria, in particular Staphylococcus aureus, have a 100-percent resistance to ceftriaxone, cotrimoxazole and cefotaxime, while they have a high sensitivity to vancomycin. There was also a high resistance among gram-negative bacteria to the antibiotics investigated in mentioned study, including ceftriaxone, cefotaxime and cotrimoxazole.[9] Accordingly, the frequency of agents involved in nosocomial infections will vary from region to region.[4,9,10]. In our study, the type of microorganism influence antibiotic resistance. Weinstein et al.[11] in the United States indicated that antibiotic resistance of the causative organisms is increasing among the patients with nosocomial infections, specificlly for *staphylococci*, and enterobacteriaceae (*Pseudomonas aeruginosa*), as we confirm with present findings. We

may concluded that antibiotic resistance is increasing in nosocomial infections in our Hospital. New strategic measures are needed to reduce them by prevention programs. It is recommended that further studies are performed to confirm our results by higher sample size and multicenter approch. Furthermore, investigations are needed on the factors that affect antibiotic resistance.

List of acronyms

UTI - Urinary tract infection

Author's contributions

Authors contributed equally to the manuscript.

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Conflict of Interest

The authors declare no conflicts of interests.

Ethical Publication Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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