

Research Paper

Investigating the Variation in Antibiotic Resistance Pattern in Bacteria Isolated from Patients with Nosocomial Infection in Allameh Bohlool Gonabadi Hospital from 2017-2020



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ABSTRACT



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**Key words:**  
Antibiotic resistance pattern, Multidrug resistance, Nosocomial infections

**Aims** Nosocomial infections have always been a serious threat to hospitalized patients, and in recent years, the emergence of antibiotic-resistant isolates has aggravated the severity of this problem. The type and rate of bacteria causing nosocomial infection can vary across different geographical areas; therefore, it is of utmost importance to periodically check the type of infection and variations in the antibiotic resistance pattern of bacteria. Therefore, this study aimed to assess the variation in antimicrobial resistance patterns in bacteria isolated from patients with nosocomial infection hospitalized in Allameh Bohlool Gonabadi Hospital from 2017-2020.

**Materials & Methods** The present cross-sectional descriptive study was conducted on 392 patients with nosocomial infection admitted to Allameh Bohlool Gonabadi Hospital from 2017-2020. The age and gender of the patients, the hospital department, the type of hospital infection, the cause of the infection, and the pattern of antibiotic resistance were extracted from the patient's files. Finally, all the data were analyzed in SPSS software (version 21) using descriptive statistical tests, and the variation in antimicrobial resistance pattern in bacteria isolated from patients with nosocomial infection was investigated.

**Findings** Out of 44,204 examined patients, 392 cases had nosocomial infections. The rate of nosocomial infection was 0.88%. Ventilator-related pneumonia (32.14%), urinary infection (27.55%), and surgical site infection (20.15%) were the most common nosocomial infections. The highest rate of nosocomial infections was related to the intensive care unit. *E. coli* (17.6%), *Klebsiella* (12.2%), and *Acinetobacter* (10.9%) were the dominant pathogens causing nosocomial infections. The results regarding the variation in antibiotic resistance pattern demonstrated that the rate of antibiotic resistance and the frequency of isolates with multidrug resistance increased over four years. All the isolates showed 100% resistance to ampicillin. Gentamicin and amikacin were the most effective antibiotics used for gram-negative bacilli.

**Conclusion** As evidenced by the obtained results, there was a significant increasing trend in the resistance of isolates to all studied antibiotics during these four years; moreover, the frequency of multidrug-resistant strains was also increasing. Furthermore, the marked increase in antibiotic resistance among isolates causing nosocomial infections in recent years is a serious risk. Therefore, a thorough knowledge of antibiotic resistance patterns can be of great help to physicians in selecting more appropriate antibiotics for treatment and preventing the development of antibiotic resistance.

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مقاله پژوهشی

## بررسی تغییر الگوی مقاومت آنتی بیوتیکی در باکتری‌های جدا شده از بیماران با عفونت بیمارستانی در بیمارستان علامه بهلول گنابادی طی سال‌های ۱۳۹۶-۱۳۹۹


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### چکیده

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**هدف** عفونت‌های بیمارستانی همواره تهدیدی جدی برای بیماران بستری در بیمارستان به شمار می‌روند و در سال‌های اخیر ظهور ایزوله‌های مقاوم به آنتی بیوتیک نیز بر شدت این معضل افزوده است. نوع و میزان شیوع باکتری‌های مولد عفونت بیمارستانی می‌تواند در مناطق جغرافیایی مختلف متفاوت باشد بنابراین بررسی دوره‌ای نوع عفونت و نیز تغییر الگوی مقاومت آنتی بیوتیکی باکتری‌ها بسیار حائز اهمیت می‌باشد. از اینرو این مطالعه با هدف بررسی تغییر الگوی مقاومت میکروبی در باکتری‌های جدا شده از بیماران مبتلا به عفونت بیمارستانی بستری در بیمارستان علامه بهلول گنابادی در طی سال‌های ۱۳۹۶ تا ۱۳۹۹ انجام شد.

**مواد و روش‌ها** بررسی مقطعی- توصیفی حاضر بر روی پرونده ۳۹۲ بیمار با عفونت بیمارستانی بستری در بیمارستان علامه بهلول گنابادی در طی سال‌های ۱۳۹۶ تا ۱۳۹۹ انجام شد. سن و جنسیت بیماران، بخش بستری، نوع عفونت بیمارستانی، علت عفونت و الگوی مقاومت آنتی بیوتیکی از پرونده بیماران استخراج و در نهایت تمامی داده‌ها وارد نرم افزار SPSS نسخه ۲۱ شده و توسط تست‌های آماری توصیفی، تجزیه و تحلیل گردید و تغییر الگوی مقاومت میکروبی در باکتری‌های جدا شده از بیماران مبتلا به عفونت بیمارستانی مورد بررسی قرار گرفت.

**یافته‌ها** از مجموع ۴۴۲۰۴ بیمار مورد بررسی، ۳۹۲ بیمار عفونت بیمارستانی داشتند. در این مطالعه شیوع عفونت بیمارستانی ۰/۸۸ درصد بود. پنومونی وابسته به ونتیلیاتور (۳۲/۱۴٪)، عفونت ادراری (۲۷/۵۵٪) و عفونت محل جراحی (۲۰/۱۵٪) شایع‌ترین شکل عفونت بیمارستانی بودند. بیشترین میزان عفونت بیمارستانی مربوط به بخش مراقبت‌های ویژه بود. باکتری *E. coli* (۱۷/۶٪)، کلبسیلا (۱۲/۲٪) و آسینتوباکتر (۱۰/۹٪) پاتوژن‌های غالب مولد عفونت‌های بیمارستانی بودند. نتایج مربوط به بررسی تغییر الگوی مقاومت آنتی بیوتیکی نشان داد که میزان مقاومت آنتی بیوتیکی و فراوانی ایزوله‌های با مقاومت چند دارویی در طی ۴ سال روند افزایشی داشت. تمام ایزوله‌ها به آمپی سیلین مقاومت ۱۰۰٪ نشان دادند. جنتامایسین و آمیکاسین موثرترین آنتی بیوتیک مورد استفاده برای باسیل‌های گرم منفی بود.

**نتیجه‌گیری** با توجه به نتایج این مطالعه، الگوی مقاومت آنتی بیوتیکی در طی این ۴ سال روند افزایشی داشته است و فراوانی سویه‌های با مقاومت چند دارویی نیز رو به افزایش بوده است. از طرفی افزایش قابل توجه مقاومت آنتی بیوتیکی در بین ایزوله‌های عامل عفونت بیمارستانی در سال‌های اخیر یک خطر جدی است. بنابراین شناخت الگوی مقاومت آنتی بیوتیکی می‌تواند به پزشک در انتخاب آنتی بیوتیک مناسب برای درمان بیماران کمک کننده باشد.

**کلیدواژه‌ها:**  
 الگوی مقاومت آنتی بیوتیکی  
 عفونت بیمارستانی  
 مقاومت چند دارویی

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## Introduction

Nosocomial infections are recognized as one of the most daunting challenges posed to healthcare centers due to their great contribution to increased mortality, disability, length of hospitalization, and treatment costs. According to the World Health Organization (WHO), nosocomial infections refer to those occurring within 48 hours of hospital admission, 3 days of discharge, or 30 days of an operation [1]. According to the WHO report, one out of every 20 hospitalized patients suffers from nosocomial infection. These infections cause or contribute to 99,000 deaths each year, imposing a high cost of 26-32 million dollars on society [2, 3]. Various factors are involved in increasing the risk of nosocomial infections, including underlying disease, disease severity, length of hospitalization, and invasive devices, such as ventilators and urinary catheters [2].

Surveys by the WHO in different regions of the world demonstrated that 5%-25% of patients admitted to hospitals suffer from nosocomial infections. This rate has been reported as 25% in the intensive care unit (ICU) in developed countries and up to 50% in developing countries. Therefore, the risk of nosocomial infections in patients hospitalized in the ICU is 5-7 times higher than that in general wards [4]. Furthermore, according to the studies conducted, the overall prevalence of these infections in Iran is reported to be 4.6% [5]. Nosocomial infections are mainly caused by pathogenic bacteria, such as *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Proteus* [6].

The amount and type of nosocomial infection vary across different hospitals and medical centers; nonetheless, urinary infections, surgical site infections, respiratory infections, and infections of the circulatory system account for more than 80% of nosocomial infections [7]. Antimicrobial resistance is the ability of microorganisms to survive in the presence of antimicrobial substances at concentrations usually sufficient to inhibit or kill them. Currently, available antibiotics are less effective on microorganisms, and the development of new strategies is essential for their management [8]. Bacterial resistance exhibits different mechanisms, such as modifying the antibiotic's target by the bacteria, inactivating bacterial enzymes, reducing drug permeability, and expelling the antibiotic from inside the cell [9, 10].

Studies conducted around the world indicate that nosocomial infections are mainly caused by antibiotic-resistant organisms. Antimicrobial resistance is a naturally occurring process. Nonetheless, factors, such as inappropriate and excessive use of antibiotics, indiscriminate access to antibiotics, and a failure to monitor their use are among the most important reasons for the

marked increase in drug-resistant bacteria [5]. Today, the emergence of new mechanisms of microbial resistance has turned into one of the most serious challenges that threaten human health in the modern era. Moreover, the ongoing spread of multidrug-resistant bacteria has raised a global concern, which has led to an increase in mortality rates and healthcare costs. Moreover, the spread of multidrug-resistant strains has restricted the treatment methods effective for infectious diseases [11].

Antimicrobial resistance aggravates nosocomial infections, reduces the effectiveness of antibiotics, and increases healthcare costs, treatment duration, and mortality [12, 13]. Nosocomial infections are one of the serious health and treatment problems presented to every country, contributing to the death of numerous hospitalized patients every year; moreover, antibiotic resistance is increasing among patients with nosocomial infections. Therefore, assessing the epidemiology of nosocomial infections and their antibiotic resistance patterns is a practical step in controlling these infections in the hospital and reducing mortality and treatment costs. To the best of our knowledge, no study has been conducted in this regard in Gonabad; therefore, the present study aimed to assess the variation in the antibiotic resistance pattern of bacteria isolated from patients with nosocomial infection in Allameh Bohlool Gonabadi Hospital from 2017-2020.

## Materials and Methods

In this descriptive cross-sectional study, the medical files of 392 patients with nosocomial infections hospitalized in Allameh Bohlool Gonabadi Hospital from 2016-2019 were examined. Based on the study by Akbari et al. [14] and considering the significance level of 95% and the acceptable error of 0.05, the required sample size was calculated at 380 cases using the following formula:

This research was approved by the Regional Research Ethics Committees of Gonabad University of Medical Sciences (IR.GMU.REC.1399.074). Patients with nosocomial infections (patients who develop infections 48-72 hours after hospitalization, three days after discharge, or 30 days after surgery) who had a complete medical file were recruited in this study, and patients with incomplete file information were excluded from the study. The required information was extracted from the patient's medical files and recorded on relevant checklists. This information included age, gender, hospital ward, length of hospitalization, bacterial species, type of infection, used instrument, and antibiotic resistance pattern (using disk diffusion method and based on CLSI standard) of bacteria isolated from the medical records of patients with nosocomial infection from 2016-2019. Patients with incomplete clinical information were excluded from the study. Subsequently, all data were

analyzed in SPSS software (version 21) using mean and standard deviation for quantitative variables with a normal distribution, median and range for quantitative variables with a non-normal distribution, and number and percentage for describing qualitative variables.

## Results

In this study, a total of 392 patients with nosocomial infection were included, out of whom 173 (44.13%) cases were male and 219 (55.87%) subjects were female. Most patients (52.80%) were seniors (those 65 and older), and the prevalence of nosocomial infections was 0.88%. In this study, the ICU had the highest rate of nosocomial infection among other hospital units, and 183 (46.68%) patients were hospitalized in the ICU.

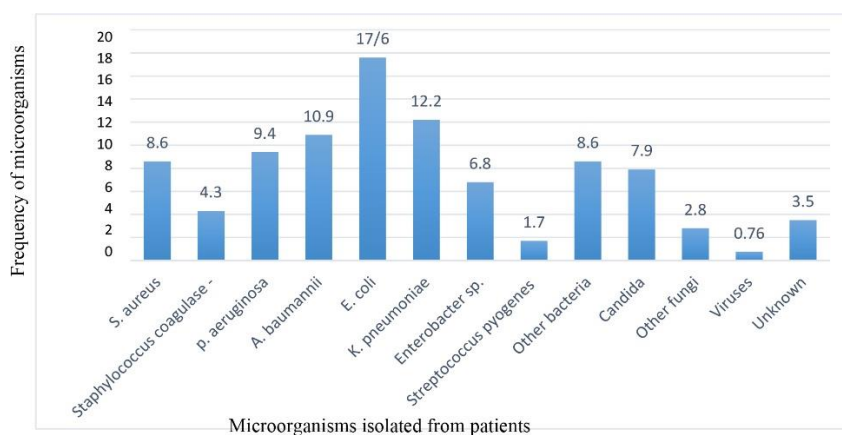
During the study years, ventilator-associated pneumonia (32.14%) was the most common form of nosocomial infection, followed by urinary tract infection (27.55%) and surgical site infection (20.15%). In this study, the mean length of hospitalization (admission to discharge) was 26.4 days (Table 1).

In this study, gram-negative bacilli were the most common causative agents of hospital infection, among which *Escherichia coli* (17.60%), *Klebsiella* (12.20%), and *Acinetobacter* (10.90%) were the most dominant pathogens. *Staphylococcus aureus* (8.60%) was the most abundant gram-positive cocci isolated from nosocomial infections. In 90.7% of patients, *Candida*, and in 2.80% of patients, other fungi were identified as the causative agents of nosocomial infection (Figure 1).

**Table 1.** Demographic characteristics of patients

Year	2017 n (%)	2018 n (%)	2019 n (%)	2020 n (%)	2017-2020 n (%)
Gender					
Male	(34.03) 33	(47.50) 38	(51.49) 52	(43.86) 50	(44.13) 173
Female	(65.97) 64	(52.50) 42	(48.51) 49	(56.14) 64	(55.87) 219
Age groups					
0-4 years	(3.90) 3	(5.00) 4	(5.94) 6	(1.75) 2	(3.83) 15
5-14 years (child)	(5.15) 5	(2.50) 2	(1.98) 2	(1.75) 2	(2.80) 11
15-24 years old (teenager)	(15.46) 15	(5.00) 4	(5.94) 6	(6.14) 7	(8.17) 32
25-44 years old (young)	(11.34) 11	(17.50) 14	(15.84) 16	(15.79) 18	(15.05) 59
45-64 years old (middle-aged)	(19.59) 19	(12.50) 10	(16.84) 17	(19.03) 22	(17.35) 68
65≥ (elderly)	(45.37) 44	(57.50) 46	(53.46) 54	(55.26) 63	(52.80) 207
Department					
CCU	(1.03) 1	(0) 0	(4.95) 5	(3.50) 4	(2.56) 10
ICU	(51.54) 50	(51.25) 41	(29.70) 30	(54.39) 62	(46.69) 183
NICU	(4.12) 4	(5.00) 4	(2.97) 3	(0.87) 1	(3.06) 12
Pediatric	(0) 0	(0) 0	(0.99) 1	(1.75) 2	(0.76) 3
Surgery	(24.75) 24	(17.50) 14	(25.75) 26	(10.55) 12	(19.38) 76
Internal medicine	(18.55) 18	(25.99) 20	(34.63) 35	(22.80) 26	(25.26) 99
Gynecology	(0) 0	(1.25) 1	(0.99) 1	(6.14) 7	(2.29) 9
Type of infection					
ventilator-associated pneumonia	(29.89) 29	(37.50) 30	(22.77) 23	(38.59) 44	(32.14) 126
Pneumonia	(16.49) 16	(6.25) 5	(19.80) 20	(9.65) 11	(13.27) 52
Urinary tract infection	(26.80) 26	(32.50) 26	(24.75) 25	(27.20) 31	(27.56) 108
Bloodstream infections	(1.03) 1	(2.50) 2	(2.97) 3	(1.75) 2	(2.04) 8
Surgical site infection	(22.69) 22	(13.75) 11	(23.76) 24	(19.30) 22	(20.16) 79
Others	(3.09) 3	(7.50) 6	(5.94) 6	(3.50) 4	(4.84) 19
Total	97	80	101	114	392

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**Figure 1.** Frequency of microorganisms isolated from patients

The results of this study demonstrated that during the study years, antibiotic resistance displayed an increasing trend among all bacterial isolates, and the highest antibiotic resistance was observed in *Acinetobacter*, which was resistant to Cotrimoxazole, Ciprofloxacin, ampicillin, meropenem, cefepime, ceftazidime, nitrofurantoin, and norfloxacin in 100% of cases. The lowest antibiotic resistance was related to *Staphylococcus aureus* isolates, 100% of which were sensitive to imipenem, meropenem, and nitrofurantoin.

The antibiotic resistance of *E.coli* isolates to meropenem gradually increased during the study years. In total, within four years, 100% of *E.coli* isolates showed resistance to ampicillin, ceftazidime, tetracycline, and

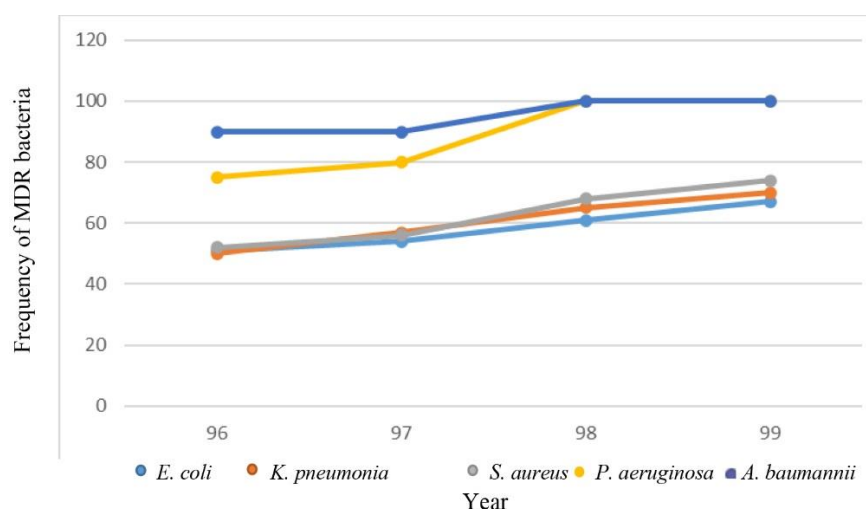
erythromycin. *Klebsiella* clinical isolates exhibited maximum resistance (100%) to ampicillin, ceftazidime, norfloxacin, erythromycin, and penicillin, followed by ceftriaxone (91.66%) and imipenem (76.83%). *Pseudomonas aeruginosa* had the highest resistance (100%) to ceftriaxone, ceftazidime, and ampicillin, and antibiotic resistance increased in isolates of this bacterium over four years (Table 2).

The frequency of multidrug-resistant isolates by year is illustrated in Figure 2. In total, the most and least abundant multidrug-resistant isolates were *Acinetobacter* strains and *E.coli* isolates, respectively. The frequency of multidrug-resistant isolates displayed an increased trend during four years (Figure 2).

**Table 2.** Antibiotic resistance of bacteria isolated during 1997-2020

Bacterium Antibiotics (%)	<i>Escherichia coli</i>	<i>Klebsiella pneumoniae</i>	<i>Acinetobacter baumannii</i>	<i>Staphylococcus aureus</i>	<i>Pseudomonas aeruginosa</i>
Cotrimoxazole	73.81	75	100	25	83.3
Ciprofloxacin	71.15	51.2	100	16.66	63.6
Ceftriaxone	66.44	91.66	88.88	100	100
Gentamicin	69.85	48.41	66.66	50	45.5
Amikacin	58.5	47	83.33	100	60.5
Trimethoprim	66.66	50	85	100	100
Meropenem	62.77	50	100	0	75
Imipenem	70.73	76.83	91.66	0	33.3
Tetracycline	100	-	100	-	-
Norfloxacin	75	100	100	100	100
Nitrofurantoin	38.63	66.66	100	-	57.1
Clindamycin	-	-	-	50	-
Cefazolin	100	100	100	75	100
Ampicillin	100	100	100	100	100
Ceftazidime	50	50	100	40	66.6
Cefepime	66.66	67	100	-	80
Erythromycin	100	100	-	80	-
Penicillin	-	100	-	100	-

## Internal Medicine Today



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**Figure 2.** Comparing the frequency of multidrug-resistant bacteria by year

## Discussion

The present study aimed to assess the variation in antibiotic resistance patterns in pathogens isolated from

patients with nosocomial infections admitted to Allameh Bohlool Gonabadi Hospital from 2017-2020. According to the obtained results, the prevalence of nosocomial infections was 0.88%, which is relatively low. In a meta-

analysis study by Mosadegh Rad, the prevalence of nosocomial infection in Iranian hospitals was reported between 0.32% and 9.1% [15]. In this regard, the rate of nosocomial infection was estimated at 2.7% in Amir Al-Momenin Hospital in Tehran, 1.7% in a military hospital in Tehran, and 3.06% in Kamkar Hospital in Qom [18-16]. The low rate obtained in our study can be attributed to the failure to identify some people with nosocomial infections or some patients acquiring these infections after being discharged from the hospital.

In general, factors, such as the number of people admitted to the hospital, the type of disease, the size of the hospital, the number of beds, the specialty of the hospital, and the type of services provided in the hospital can affect the prevalence of nosocomial infections [15]. The highest frequency of infections in the present study was observed in the age group over 65 years old (52.8%). Factors, such as a weak immune system, various underlying diseases, and prolonged hospital stay, make this age group more susceptible to nosocomial infections [19].

In the present study, infection caused by a ventilator was the most common form of nosocomial infection, followed by urinary tract infection and surgical site infection (32.4%). In the meta-analysis study by Mosadegh Rad, urinary tract infections, followed by respiratory infections, were reported as the most common type of nosocomial infection in Iranian hospitals [15]. In the study conducted by Darvishpour, surgical site infection, pneumonia, and urinary tract infection were reported as the most common forms of nosocomial infections [20]. Consistent with the results of most studies, In this research, the highest rate of nosocomial infection was related to ICU [21, 22].

Similar to other studies, in this research, *E. coli* was revealed to be the most dominant pathogen [23-27]. In the present study, the rate of variation in antibiotic resistance patterns in common microorganisms was investigated over four years, and it was observed that the microbial resistance and frequency of multidrug-resistant strains had an increasing trend during the study years. These data are in agreement with other reported results regarding the constant increase of antimicrobial resistance, especially among gram-negative bacteria, in different regions across the globe [28, 29].

Based on the results of the present study, *E. coli* demonstrated maximum resistance to ampicillin, cefazolin, and norfloxacin and the lowest resistance to nitrofurantoin and amikacin. In the last year of the study, this bacterium was most sensitive to nitrofurantoin, which is clinically valuable. These findings are in line with the results of other studies [13, 30, 31]. During this four-year study, a significant increase was observed in the antibiotic resistance of *E. coli* strains to meropenem. This finding can be regarded as a warning against

excessive use of this antibiotic.

The results of the present study pinpointed that the maximum antibiotic resistance was observed to ampicillin, cefazolin, and norfloxacin in the clinical isolates of *Klebsiella* as the second dominant pathogen causing nosocomial infections. In addition, consistent with the results of the studies conducted by Samadzadeh and Barak, the lowest antibiotic resistance was related to amikacin and gentamicin [32, 33]. somewhat consistent with some studies, in the present research, *Pseudomonas aeruginosa* isolates had maximum resistance (100%) to norfloxacin, cefazolin, ceftriaxone, and ampicillin [13, 32, 33]. Nonetheless, contrary to the present research, in the study by Shahraki et al. in Zahedan [34], ceftazidime was suggested as the main option in the treatment of *Pseudomonas aeruginosa* infections, while in the present study, 100% of *Pseudomonas aeruginosa* isolates were resistant to ceftazidime.

*Acinetobacter* clinical isolates exhibited high resistance to most antibiotics except gentamicin. These findings are largely similar to those reported in other studies [13, 35, 36]. In accordance with the findings reported by Pooladi, in the present research, multidrug-resistant *Acinetobacter* isolates had a higher frequency than other isolates [36]. Among the notable limitations of this study are the retrospective nature of the study, the insufficient accuracy of information based on records, and the incompleteness of information regarding the culture of some isolates. In brief, the significant increase in antibiotic resistance among isolates causing nosocomial infections in recent years is a dire warning for us. It is suggested to exercise great caution when using resistant antibiotics and periodically check the antibiotic resistance pattern of strains. Moreover, to prevent multidrug resistance, it is recommended to refrain from indiscriminate use and prescription of antibiotics prior to antibiograms.

## Conclusion

As evidenced by the results of this study, there was a significant increasing trend in the resistance of isolates to all studied antibiotics during these four years; moreover, the frequency of multidrug-resistant strains was also increasing. Therefore, a thorough knowledge of antibiotic resistance patterns can be of great help to physicians in selecting more appropriate antibiotics for treatment and preventing the development of antibiotic resistance.

## Ethical Considerations

### Compliance with ethical guidelines

This study was approved by the Regional Research Ethics Committees of Gonabad University of Medical Sciences (IR.GMU.REC.1399.074).

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## Authors' contributions

All authors contributed to this research project.

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## Conflicts of interest

The authors declare that they have no conflict of interest.

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