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Trends in Antimicrobial Resistance in Gaza Strip, 2020–2022: Retrospective Study

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Abstract

Objectives: In this study, we analyzed the data on antimicrobial resistance in the bloodstream**.** This study aims to evaluate the bacterial resistance in the Gaza Strip and compare with that in other countries.

Methods: This study was conducted retrospectively in the Indonesian and Shifa hospitals in the Gaza Strip of Palestine. The isolates were collected from 2020 to 2022 and compared with those from other countries. Chi square test to compare between means. P- value less than 0.05 was considered statistically significant.

Results: The incidences of bloodstream infections as well as the resistance against most antibiotics increased. The exceptions were a decreased incidence of P. aeruginosa infection and a decrease in resistance against ceftazidime. Overall, the incidence and resistance of antimicrobials were higher than other countries.

Conclusion: These results showed increased trends to bacterial resistance except for ceftazidime. A specialist in clinical microbiology should take an active role in prescribing antibiotics in hospitals based on laboratory and epidemiological data besides clinical experience. Also, antibiotic stewardship should be constructed and activated in our country to, as this will decrease the emergence of resistant strains and decrease the burden

Keywords: Antibiotics, Gaza Strip, Blood stream infection, Carbapenem, colistin

Key Message: The trend of bacterial resistance in the Gaza strip were unknown. The results of this study reveals increased incidence of bacterial infection by the mentioned bacteria and increased resistance to the mentioned drugs in this study. The importance of this study increase awareness to bacterial resistance and construction of antibiotic stewardship.

Abbreviations

WHO: world health organization. MDR: multi drug resistance. AMR: anti-microbial resistance. MRSA: methicillin resistant staph aureus. EUCAST: European Committee on Antimicrobial Susceptibility Testing's. IC: infection control. ESBL: extended-spectrum beta-lactamase. CLSI : Clinical and Laboratory Standards Institute. R: resistant. I: intermediate. S: sensitive.

Introduction

The emergence of antimicrobial-resistant strains is increasing worldwide [1]. It results from the overuse of these agents among humans and animals [2]. Antibiotic resistance occurs when infectious bacterial strains survive

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Mansour HM, et al. J Pharm Pharmacol Res 2023
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after exposure to inappropriate antibiotics [3]. According to World Health Organization (WHO) predictions, if antibiotic resistance continues to increase, infectious diseases will become the most common cause of death worldwide [4]. In hospital care, the Germany review has discovered that the proportion of MRSA isolates showed a declining pattern, while the indicator of ESBL in E. coli shows an increasing trend. In addition, K. pneumoniae infections were found to be more frequent. [5]. In another review, there was increased resistance to carbapenems and aminoglycosides among some hospitals in Germany [6]. Based on the data from southern and eastern Europe, the carbapenem-resistant Acinetobacter spp. is high. [7]. In Saudi Arabia, the prevalence of MDR A. baumannii resistance to colistin and tigecycline has been reported to be high in many hospitals [8, 9].

Based on a systematic analysis, E. coli, followed by S. aureus, K. pneumoniae, S. pneumoniae, A. baumannii, and P. aeruginosa, are the leading pathogens for deaths associated with resistance [10]. In Thailand, the 30-day mortality rate caused by multidrug-resistant bacteremia was elevated and was high [11]. Regarding some bacteria, antimicrobial resistance remains unchanged or decreases in many countries, while other countries show an increase [12]. Based on the available data, some reports suggest that by 2050, nearly 10 million people will die annually due to antimicrobial-resistant strains. [13]. The results from this effort will contribute to the assessment of the burden of anti-microbial resistance (AMR) and provide essential health intelligence to guide interventions and policies for measuring the impact of interventions on future burdens [14]. Multidisciplinary approaches across healthcare sectors, in addition to developing novel strategies to fight these pathogens such as probiotics, vaccines, and antibiotic stewardship, will help to solve this problem [15, 16]. Several studies conducted in the Gaza Strip revealed increased multidrug bacterial resistance, even against carbapenems and colistin [17, 18].

This study aims to evaluate the bacterial resistance in the Gaza Strip and compare with that in other countries.

Methods

This study was conducted retrospectively in the Indonesian and Shifa hospitals in the Gaza Strip of Palestine. The data were collected from the electronic database by a clinical pharmacist. All cultures were recorded, including bacteria and antibiotic sensitivity based on the culture's results. No additional clinical specimens were obtained for research purposes; therefore, informed consent was not required. Data concerning antibiotic culture and sensitivity in the hospital were collected between January 2020 and November 2022. The study was approved by the Helsinki Committee (PHRC/HC/1205/22).

Bacterial isolates, including K. pneumonia, E. coli strains, Pseudomonas aeruginosa, Staphylococcus aureus, and Acinetobacter, were considered seriously. Susceptibility testing, detection of bacterial culture and sensitivity, including ESBL, and determination of minimum inhibitory concentrations were done on amikacin, vancomycin, colistin, piperacillin/tazobactam, meropenem, and ceftazidime for the previously mentioned bacteria. Data on colistin resistance for 2017 were not reported by the European Committee on Antimicrobial Susceptibility Testing's (EUCAST) warning concerning the results of susceptibility testing [19]. Data on population size was taken from the World Bank [20].

Statistical Analysis

All categorized variables were analyzed using percentages using SPSS v. 23. We calculate the percentage of each specimen, for each type of bacterial isolate, and the bacterial sensitivity to the antibiotic. We tested for significant changes over time in bloodstream infection (BSI) incidence using the Chi square test to compare between means. P- value less than 0.05 was considered statistically significant. The antibiotics are categorized as sensitive (S), intermediate (I), and resistant (R) based on their ability to inhibit bacterial growth. Here we focused on the resistant strains, so they were only mentioned in our surveillance.

Results

Data on the incidence of bloodstream infection (BSI) and the proportion of resistant isolates are presented in the tables above. The following trends were observed:

- An increase in the incidence of all Acinetobacter baumannii infections (8.7 to 16.5 per 100,000 populations, $p < 0.001$) and the incidence of carbapenem-resistant A. baumannii (decreased 4%, $p = 0.4$, not significant), while the proportion of A. baumannii isolates resistant to carbapenems remained stable at70–80%.
- An increase in the incidence of all Escherichia coli BSI (65.6 to 81.7 per 100,000 populations, $p < 0.04$) and amikacine-resistant E. coli BSI (13.7% to 32.4%, $p < 0.001$). The proportion of E. coli isolates with resistance to ceftazidime decreased by 1.5% ($p = 0.07$), fluoroquinolones and carbapenem increased to 28% and 63%, respectively($p<0.001$).
- There is a decrease in the incidence of all Klebsiella pneumoniae BSI (55.6 to 51.9 per 100,000 populations, $p = 0.05$), while carbapenem-resistant K. pneumoniae BSI increased (22.2% to 25.5% $p = 0.001$). The proportion of K. pneumoniae isolates with resistance to ceftazidime decreased from 62 to 57.1%($p=0.06$).
- The incidence of Pseudomonas aeruginosa BSI increased from 26.7 to 28.6 per 100,000 populations, $p < 0.23$,

Mansour HM, et al. J Pharm Pharmacol Res 2023
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while the incidence of carbapenem-resistant P. aeruginosa increased from 12.5 to 19.6. The observed increase in carbapenem-resistant isolates did not achieve statistical significance (p = 0.07).

- The incidence of all Staphylococcus aureus BSI increased, from 29.7 to 38.1 per 100,000 populations ($p < 0.001$). The incidence of BSI caused by methicillin-resistant S. aureus (MRSA) increased from 15% to 23% (p = 0.001).
- There is a significant increase in the incidence of bacterial resistance to all the mentioned antibiotics ($p < 0.05$) except for ceftazidime; there is no significant decrease (p = 0.07), see Table 2.

Discussion

Between 2020 and 2022, the incidence of BSI caused by most antibiotic-resistant organisms significantly increased in Gaza-Strip except for ceftazidime, which decreased. The underlying cause is unknown but may be due to decreased use of this antibiotic in the last two years. It is worth mentioning that resistance proportions were higher than those observed in neighboring countries, southern Europe, and the

Table 1: Incidence per 100000 population and percent resistant to each anti biotic.

Bacterial isolares	No. of isolates	Incidence per 100000 population	Amikacin	Ceftazidime	Ciprofloxacin	Colistin	Meropenem	Piperacillin -tazobactam	Vancomycin
Year 2020									
A. baumannii	112	8.7	57.5	80.5	84.5	5.1	75	75.1	
E. coli	842	65.6	13.7	58	46.4	9.5	11.2	19	NA
K. pneumonia	713	55.6	18.9	62	53.9	7.1	22.2	34	NA
P. aeruginosa	343	26.7	16.3	63.8	44.2	10.5	12.5	25	NA
S. aureus	382	29.7	20.4	63.7	43.9	5.2	11.8	20.4	15
Average resistance			**25.4**	**65.6**	**54.6**	**7.5**	**26.5**	**32.2**	**15**
Year 2022									
A. baumannii	212	16.5	62.3	82.3	87.1	8.2	71.4	78.3	NA
E. coli	1049	81.7	32.4	57.1	59.8	9.7	18.3	34.3	NA
K. pneumonia	666	51.9	31.3	57.1	55.8	11	25.5	36.3	NA
P. aeruginosa	367	28.6	23.2	53.4	39.9	8.7	19.6	32.7	NA
S. aureus	489	38.1	27.8	50	47.8	11.4	20.6	33.8	23.9
Average resistance			**35**	**60**	**58.1**	**9.8**	**31.1**	**37.4**	**23.9**

Table 2: Mean change in the resistance to the mentioned antibiotics

	Mean		% change	p-value
	resistant 2020	resistant 2022		
Amikacin	25.4	35	↑ 37.7	0.005
Ceftazidim	65.6	60	↓ 8.5	0.07
Ciprofloxacine	54.5	58.1	↑ 6.6	0.014
Colistin	7.5	9.8	↑ 30.6	0.0001
Meropenem	26.5	31.1	↑ 17.3	0.0001
Piperacillin/tazobactam	32.2	37.4	16.1	0.028
Vancomycin	15	23.9	59.3	0.0001

Mansour HM, et al. J Pharm Pharmacol Res 2023
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United States of America. Despite the outbreak of third-generation cephalosporin and ciprofloxacin-resistant strains in the Gaza Strip, no national intervention was implemented to combat this problem. The absence of intervention will result in increased bacterial resistance, even to carbapenems and other wide-spectrum antibiotics, as mentioned above. This failure should catalyze the construction of a national-wide infection control (IC) program that should perform annual surveillance of antimicrobial susceptibility. It should include the establishment of a central reference laboratory, the creation of a national antibiotic stewardship program, and the enhancement of IC programs within healthcare centers and universities to increase awareness and overcome this problem. These actions will enhance the trends toward decreasing the emergence of antibiotic-resistant organisms reported here.

Our report has a number of limitations. Firstly, it was conducted in two hospitals, which means that the data cover nearly 70% of the Gaza Strip. In addition, we did not differentiate between community-acquired and hospital-acquired infections. Thus, it is predicted that the resistance to hospital-acquired infections may be higher than the one reported here. Moreover, we faced a lack of a national standard for reporting antimicrobial susceptibility. Although most microbiology laboratories in the Gaza Strip employ Clinical and Laboratory Standards Institute (CLSI) breakpoints, it is possible that for certain antibiotic categories, CLSI breakpoints are higher than those issued by the European Committee on Antimicrobial Susceptibility Testing (EUCAST). Levels of antimicrobial resistance, as we reported, are lower than they would be utilizing EUCAST criteria.

As noted above, the absence of interventions against bacterial resistance resulted in an increase in the proportion of carbapenem-resistant K. pneumoniae infections from 22.2% in 2020 to 25.3% two years later, explaining the difference in the proportion of carbapenem-resistant K. pneumoniae infections between Gaza and other southern countries. Our data and previous university studies in Gaza indicate an increase in the incidence of bloodstream infections due to colistin and extended-spectrum beta-lactamase (ESBL)-producing bacteria. The use of targeted control efforts against ESBL has been cited as one factor explaining the limited spread of ESBL in other countries, like Europe, as compared with ESBL-producing bacteria.

An important difference in the epidemiology of ESBL-producing and carbapenem-resistant Gram-negative bacteria is the role of asymptomatic carriers in the community. Carbapenem resistance is primarily hospital acquired (nosocomial), with little to no transmission in the community. These carriers serve as a major reservoir for infections with ESBL-producing bacteria in hospitals, implying that interventions limit the success of controlling the spread of these organisms. In Gaza, due to the absence of planned intervention, the combined incidence of BSI with typically hospital-acquired antibiotic-resistant organisms increased at the same time that the incidence of ESBL-producing E. coli BSI rose. Ongoing efforts are necessary to further inhibit the spread of resistant organisms, including the development of interventions aimed at community settings. Our study is strong because it contains real-world data from a large number of specimens. Also, it is the first study conducted in the Gaza Strip that compares antibiotic resistance between two periods.

Conclusion

These results showed increased trends to bacterial resistance except for ceftazidime. A specialist in clinical microbiology should take an active role in prescribing antibiotics in hospitals based on laboratory and epidemiological data besides clinical experience. Also, antibiotic stewardship should be constructed and activated in our country to control AB use even in the outpatient clinic, as this will decrease the emergence of resistant strains and decrease the burden.

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Availability of data and materials

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Authors' contributions

Hashem: Main author, the conception and design of the study, writing and final approval of the version to be submitted. Khalil: proofreading, Analysis and interpretation of data. Rana and Ahmed: Data collection and drafting the article for important intellectual content.

All authors read and approved the final manuscript.

Ethics approval and consent to participate

Publication was approved by the Palestine Ministry of Health. As per MoH policy, the article, which reports national aggregated data, publically available on the MoH, was not subject to ethics committee approval.

Consent for publication

Not applicable.

Mansour HM, et al. J Pharm Pharmacol Res 2023
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Competing interests

The authors declare that they have no competing interests.

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