Prevalence Of Bacterial Resistance To Colistin, Meropenem, Piperacillin-Tazobactam, Ceftazidime, Vancomycin And Amikacin Antibiotics Based On Culture And Sensitivity In The Indonesian And Shifa Hospitals In Palestine: A Retrospective Study

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Purpose:

Antibiotic (AB) drugs save life millions since their evolution. Irrational use of the AB is associated with the emergence of resistant strains of bacteria and increased treatment burden. This study aims to evaluate bacterial resistance to meropenem, piperacillin-tazobactam, ceftazidime, colistin, vancomycin, and amikacin in Indonesian & Shifa Hospitals.

Methods:

We conducted a retrospective study in state hospitals with 640 beds. The data was extracted from the microbiology lab database between May 2019 and November 2022. The specimens were cultured on different media including blood agar, MacConkey agar, and other media. Isolates were identified by standard microbiological techniques colonial morphology, Gram stain, coagulase, oxidase, and the use of several biochemical tests.

Result:

A total of 13338 cultures were obtained of whom 4514 were positive (34,3%). Of the total specimen, 2106 (46.6%) were males and 2408 (53.4%) were females. E. coli is the most common organism at 38.3%, Klebsiella at 25%, Pseudomonas aeruginosa 14.9%, S.aureus 16.2% and acinetobacter 5.6%. The resistance to the mentioned antibiotics shows that there is high resistance to meropenem 78.4% for Acinetobacter and piperacillin/tazobactam 72.9% for the same organism, colistin has the lowest resistance around 10%, vancomycin 29% for S.aureus, and amikacin up to 32%. Pseudomonas aeruginosa resistance to ceftazidime was 40%.

Conclusion:

These results showed increased bacterial resistance among colistin, meropenem, piperacillin-tazobactam, vancomycin, and 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

Declaration of interest: None

Keywords:

Antibiotic, culture, bacteria, resistant, meropenem, colistin

Introduction

Antibiotics (AB) drugs are the most popularly prescribed globally and in our country with the absence of antibiotic stewardship to control these medications[1,2]. Irrational use of the AB is associated with the emergence of resistant strains of bacteria, adverse effects, and an increased treatment burden[3-5]. Proper use of antibiotic with improving policies result in a better outcome with fewer side effects and cost effectiveness[6,7]. Globally there is an increase in antibiotic consumption resulting in increased morbidity and mortality but it helps develop an antimicrobial stewardship program and increase awareness of resistance, adverse drug reactions, and drug interaction of antibacterial drugs[8,9]. The emergence of resistant bacteria, endangering the efficacy of antibiotics which saved millions of lives, and bacterial infections have again become a

threat[10-13]. Antibiotic resistance is attributed to the overuse and misuse of these medications, as well as a lack of new drug development for new generations of these drugs[14-16]. Globally there increasing emergent strains of, Staphylococcus aureus (MRSA), multidrug-resistant (MDR), and extended-spectrum beta-lactamase (ESBLs)-producing bacteria have become a major global healthcare problem[17,18]. Multidisciplinary approaches across healthcare sectors in addition to developing novel strategies to fight these pathogens such as probiotics, vaccines, and antibiotic stewardship help solve this problem[18,19]. Unfortunately due to the rapid increase in infections caused by multidrug-resistant strains of the colistin is now increasingly used, and its use is increasing and there is the increasing emergence of resistant enterobacterial strains and acquired colistin resistance to opportunistic pathogens, like Escherichia coli and Klebsiella pneumonia[20-22]. Based on the surveillance findings in Israel U.S.A and other European countries there is an increasing emergence of carbapenem resistance strains of Klebsiella pneumonia, Escherichia coli Pseudomonas aeruginosa Acinetobacter baumannii [23-26]. In developed countries, hematological malignancies (HM) account for 8 to 10% of cancers diagnosed annually and one-third die from their carbapenem-resistant (CR) pathogens and infectious complications[27]. Currently, antibiotic options for the treatment of carbapenem-resistant Enterobacteriaceae (CRE) are very limited, with polymyxins, tigecycline, fosfomycin, and plazomicin[28]. For these reasons, the emergence and rapid spread of carbapenem, piperacillin-tazobactam, and colistin resistance, mainly among Gram-negative bacteria, constitutes a global public-healthcare problem of major importance.

Aim

This study aims to focus attention on Acinetobacter, E. coli, P, aeruginosa, K.pneumonia and S.aureus resistance to antibiotics based on bacterial culture and sensitivity with focus attention to colistin, meropenem, piperacillin-tazobactam, ceftazidime, and amikacin.

Methods

The study was a retrospective conducted in the Indonesian and Shifa Hospitals Gaza Strip- Palestine with nearly 640 beds. Urine, pus, blood, body fluids, sputum, cerebrospinal fluid (C.S.F), semen ear, and nose samples obtained by the microbiology department as part of routine care for hospitalized infected patients. Data concerning antibiotic culture and sensitivity in the hospital were collected between the 1st of May 2019 and the 1st of November 2022 with approval from the local Ethical Committee. Data collection was done from the electronic database by a clinical pharmacist. All cultures were recorded including bacteria and anti-biotic sensitivity based on the culture. No additional clinical specimens were obtained for research purposes; therefore, informed consent was not required.

Sample collection

The specimens were cultured on different media including blood agar MacConkey agar and other media. Isolates were identified by standard microbiological techniques colonial morphology, Gram stain, coagulase, oxidase, and several other biochemical tests. A total of 13138 cultures were obtained of whom 4514 were positive (34,3%) and the rest is negative. Bacterial isolates including K. pneumonia and E. coli strains Pseudomonas aeruginosa, Staphylococcus aureus and Acinetobacter were recovered see (Table 3). 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. Susceptibility to colistin was evaluated by agar dilution method based on clinical breakpoints defined by the European Committee on Antimicrobial Susceptibility Testing. Minimum inhibitory concentrations for colistin were also measured by broth micro-dilution according to the standards. Detection of carbapenem, vancomycin, and colistin resistance isolates was considered serious as it is the most dangerous isolates

Statistical Analysis

All categorized variables were analyzed using percentages using SPSS version 20. We calculate the percentage of each specimen, for each type of bacterial isolate, and the bacterial sensitivity to the antibiotic. The antibiotics are categorized as sensitive denoted(S), intermediate denoted (I) and resistant denoted (R) based on the ability to inhibit bacterial growth (see results below). The study was approved by the HELSINKI committee PHRC/HC/1205/22.

Results

The study was conducted in the Indonesian and Shifa hospitals-Gaza. Data concerning antibiotic use in the hospital were collected from the 1st of May 2019 to November 2022 by a clinical pharmacist. The total number of specimens is 13138 of which 4514(34,3%) are positive for the antibiotics and bacteria mentioned above and the rest was excluded. Of the total specimen (46.6%) were males and (53.4%) were females (Table 1). The positive cultures were (71% urine, 15.7% pus, 6.8% blood, 3,9% body fluids, and 1.2% sputum (Table 2). The distribution of microorganisms shows that E. coli is the most common organism at 38.3%, Klebsiella at 25%, S.aureus 16.2, Pseudomonas aerugiosa at 14.9, and Acinetobacter at 5.6%(Table 3). Table (4) show that the resistance of S. aureus to vancomycin is high at 29%. The results of (Table 5) clarify that bacterial resistance to amikacin was (83.3 Acinetobacter, 26.1 E.coli, 32.2, K. pneumonia, and 24.6 Pseudomonas). The incidence of Acinetobacter and K.pneumonia resistance to meropenem is high at 78.4% and 21.2% respectively, also

piperacillin/tazobactam resistance to Acinetobacter is high at 72.9% while it is low for other species (6.6% E.coli, 6.2 Kleibsella and 6.8% for pseudomonas) as seen in (table 6&7). There is high resistance against ceftazidime, 84.4% for Acinetobacter, 51.2% for E. coli, 63.8% for K. pneumonia, and 41% for Pseudomonas(Table 8). The most effective antibiotic based on the results of this study for gram-negative bacteria is colistin with a sensitivity of 89.3% for acinetobacter and more than 90% for the other species(table 9).

Gender	Number	%
Male	2106	46.6
Female	2408	53.4
Total	4514	100

Table 1: Distribution of samples based on gender.

Specimen	Number	% From All Specimens
Urine	3206	71.0%
Pus	709	15.7%
Blood	308	6.8%
Body Fluids	177	3.9%
Sputum	55	1.2%
C.S.F.	38	0.8%
Semen Fluid	14	0.3%
Ear & nose & Eye swab	9	0.2%
Total	4514	100.0%

Table 2: Specimen distribution and its culture result

Microorganism	No of cultures	%
Escherichia coli	1729	38.3%
Klebsiella	1132	25%
Staphylococcus aureus	738	16.2%
Pseudomonas spp	677	14.9%
Acinetobacter momanii	254	5.6%
Total	4514	100.0

Table 3: Microorganism distribution based on culture result

		I %	R %	S %	Total
BACTERIA	Acinetobacter	0	0	0	254
	Escherichia coli	0	0	0	1729
	Klebsiella pneumonia	0	0	0	1132
	Pseudomonas aerugiosa	0	0	0	677
	S.Aureus	0.4%	29%	71.6%	738
Total					4514

Table 4 : Vancomycin resistance distribution based on culture result

		I %	R %	S %	Total
BACTERIA	Acinetobacter	1.9	83.3	14.8	254
	Escherichia coli	14.1	26.1	59.8	1729
	Klebsiella pneumonia	11.4	32.5	56.1	1132
	Pseudomonas aerugiosa	12.4	24.6	63	677
	S.Aureus	0	17.4	82.6	738
Total					4514

Table 5 : Amikacine resistance distribution based on culture result

		I %	R %	S %	Total
BACTERIA	Acinetobacter	1.1	78.4	20.4	254
	Escherichia coli	1.5	8.7	90.8	1729
	Klebsiella pneumonia	0.8	21.2	78	1132
	Pseudomonas aerugios	0.7	12.9	86.4	677
	S.Aureus	0	0	0	738
Total					4514

Table 6: Meropenem resistance distribution based on culture result

		I %	R %	S %	Total
BACTERIA	Acinetobacter	1.1	72.9	26	254
	Escherichia coli	2.4	15.3	82.3	1729
	Klebsiella pneumonia	2.7	30.3	67	1132
	Pseudomonas aerugios	19.2	18.1	62.7	677
	S.Aureus	0	100	0	738
Total					4514

Table 7 : Piperacillin-Tazobactam resistance distribution based on culture result

		I %	R %	S %	Total
BACTERIA	Acinetobacter	0.5	84.6	14.9	254
	Escherichia coli	5.3	51.2	43.5	1729
	Klebsiella pneumonia	3.9	63.8	32.3	1132
	Pseudomonas aerugios	3.4	41	55.6	677
	S.Aureus	0	0	0	738
Total		138	1755	1264	4514

Table 8: Ceftazidime resistance distribution based on culture result

		I %	R %	S %	Total
BACTERIA	Acinetobacter	1.9	10.7	87.4	254
	Escherichia coli	0.09	6.6	92.5	1729
	Klebsiella pneumonia	0.4	6.2	93.4	1132
	Pseudomonas aerugios	1	8.5	90.5	677
	S.Aureus	0	100	0	738
Total					4514

Table 9: Colistin resistance distribution based on culture result

Discussion

Antibiotics save the life of millions of people since their invention, but their intensive irrational use lead to decreased efficacy and increased bacterial resistance. Their prescription differs between countries and hospitals in the same country. This difference depends on the diseases and epidemiology of the infectious disease in this country. The absence of antibiotic protocols and policies or the absence of antibiotic stewardship can result in the catastrophic emergence of antimicrobial resistance. Sometimes physicians' preferences and differences in educational and health systems participate in this problem. Antimicrobial agents are the most frequently used drugs in Palestine. With the absence of data on the AB consumption rate, the author estimate nearly 90% of our in-hospital patients receive AB.

In our study, we focused attention on the incidence of bacterial resistance to different AB with focused attention on colistin, meropenem, piperacillin-tazobactam, ceftazidime, amikacin, and vancomycin. In addition, we focused attention on Acinetobacter, E. coli, K. pneumonia, S. aureus, and P. aeruginosa. After examination of the total samples, we found that urine

and pus samples are the most common respectively. As mentioned above in (table 3) E.coli is the most common followed by Klebsiella then Staph aureus and the least Acinetobacter. In this study, we find the most effective AB for gram-negative strains was colistin with a sensitivity of about 90% for the mentioned above species except Staph aureus by contrast there was increased resistance to piperacillin-tazobactam to the same bacteria. Vancomycin resistance approaches 30% nearly which is higher than other countries in the neighboring country it approaches 12% only based on the last survey. The resistance to amikacin was (E. coli at 26.1, K. pneumonia at 32.5%, P. aeruginosa at 24.6%, and acinetobacter at 83.3%) while it is (E.coli 2.3, K. pneumonia, 6%, P. aerginosa 4%, and acinetobacter 65%) in Israel against amikacin. Meropenem resistance was high (K. pneumonia 21.2%, E.coli 8.7%) compared to other countries the same bacteria were (K. pneumonia 4%, E.coli 0.3%) while it was in the same range for Acinetobacter about 78% and P. aeruginosa about 13%. Compared to our neighboring countries we have a higher rate of resistance to piperacillin-tazobactam (E.coli 15.3% vs 9%, K. pneumonia, 30.3% vs 25%, P. aeruginosa 18% vs 13 %) while for acinetobacter in the same range about 73%. The study shows that there is high resistance for (E. coli 51.25, K. pneumonia 63.8%, P. aeruginosa 41% and acinetobacter 84.6%) while it is (31% E.coli, 50% K. pneumonia, 13%, P. aeruginosa and acinetobacter 83%) in other countries against ceftazidime. The study shows that we have high resistance for (E. coli 6.6, K. pneumonia 6.2%, P. aeruginosa 8.5% and acinetobacter 10.7%) while it is (E.coli 0.2, K. pneumonia, 1.8%, P. aerginosa 0.4, and acinetobacter 0.8%) the neighboring countries against colistin. The increased emergence may be due to extensive irrational use of these ABs or either incorrect dose, duration, or previous incorrect prescription without C/S. The results of our study show can be considered as indicator of the emergence of highly resistant strains of bacteria against these wide-spectrum AB and it is consistent with other neighboring countries, USA Europe, and others worldwide [23-26]. Also, this result is an indicator of the irrational use of AB without controlling agency in our country

Conclusion and recommendation

The results of our study clarify that there is an increased incidence of resistant strains to wide-spectrum antibiotic and reflects the importance of the construction of antibiotic stewardship for controlling these medications based scientifically. There were some limitations of this study as it was conducted in two referred centers. However, the accuracy of data gives strength to the results and makes the study more representative of the patients on antibiotics and makes it a real-world in our region.

Ethics approval and consent to participate: Not Applicable

Consent for publication: Not Applicable

Availability of data and materials: Not Applicable

Competing interests: Not Applicable

Funding: Not Applicable

Authors and contributions:

Dr Hashem : Main author, the conception and design of the study, and final approval of the version to be submitted.data collection and writing.

Dr Khalil and Haytham: Analysis and interpretation of data

Dr Rana and Ahmed : Acquisition of data and drafting the article for important intellectual content

Acknowledgements

We thank the ministry of health which facilitate the process to reach the electronic data file, also we thank those encourage us to complete this work.

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

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