RESEARCH ARTICLE

STUDY OF RESISTANCE FOR RECENTLY MARKETED CARBAPENEM DRUG AMONG HOSPITALISED PATIENTS IN SANA'A, YEMEN

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Abstract

Objective: Carbapenem resistance is a major and a future public health problem globally. It occurs mainly among Gram-negative bacteria. Meropenem is the recently marketed carbapenem drug in Yemen. However, recent emergence of carbapenem-resistant isolates has become a major healthcare concern. The current study was designed to estimate the prevalence of meropenem resistance among hospitalised patients in Sana'a, Yemen.

Methods: The study was performed at a local hospital in Sana'a, Yemen. The records of Meropenem susceptibility were taken for hospitalised patients. A total of 443 Meropenem susceptibility samples were collected from August, 2017 to July, 2018. The meropenem susceptibility was studied against several isolated pathogens.

Results: Out of 443 study sample, 316 (71.3%) were meropenem sensitive isolates and 25.3% of samples were resistant. The *Escherichia coli isolates* were observed in 27.5% of sample, followed by *Pseudomonas aeruginosa* (19.6%). 36.4% of total meropenem sensitive isolates (115/316) were *Escherichia coli*. 82.4% (42/51) of *Klebsiella pneumonia* isolates were meropenem sensitive and 32.2% (28/87) of *Pseudomonas aeruginosa* were meropenem resistance. In the present study, 34.5% (109/316) of meropenem sensitive isolates were from blood cultures, followed by sputum cultures (23.7%; 75/316). However, 58% (65/112) of sputum culture isolates were meropenem resistance.

Conclusion: This study concluded that the percentage of resistance to meropenem was high (25.3%) and cannot be neglected. Continued surveillance to closely monitor trends as well as infection control and antibiotic stewardship activities are necessary to preserve treatment options. A more careful monitoring for use of broad-spectrum antibiotics should be instituted.

Keywords: Meropenem, prevalence, resistance.

INTRODUCTION

Carbapenems are the most effective drugs against most bacteria. Bacterial resistance continues to increase, and drug researchers and manufacturing industries are not producing new drugs to replace the existing antimicrobials against which resistance has developed. The economic impact related to antimicrobial resistance was expected to cost over $105 billion annually worldwide[1]. Recently, occurrence of antibiotics resistance is quickly changing. Many deaths have demonstrated as a consequence of this in Europe. About 25,000 of subjects may die each year as a result of infection related to antibiotics resistance[2]. Globally, the resistance reports of bacterial infections are alarming. Carbapenems have a broad spectrum and a unique structure against most β lactamases such as metallo-β-lactamase (MBL) and extended spectrum β-lactamases[3]. The carbapenem resistance has been increasing world-wide over the last years with local differences in prevalence and mechanisms of resistance[4]. The emergence and spread of resistance to these antibiotics constitute a major public health problem[5]. In addition, carbapenems are the effective drugs for treatment of multidrug-resistance (MDR) isolates. However, the carbapenem-resistant among these isolates has recently increasing and become a worldwide alarm concern[6]. Because of MDR, there are few alternatives for treatment of patients with serious infections[5]. Meropenem is the recently marketed

carbapenem drug in Yemen. Carbapenem resistance is a major public health problem and in progress globally. Thus, the aim of current study was to estimate the prevalence of meropenem resistance among hospitalised patients in Sana'a, Yemen.

METHODS

The study was performed at a local hospital in Sana'a, Yemen. The records of Meropenem susceptibility were taken for hospitalised patients. Meropenem susceptibility samples were collected from August, 2017 to July, 2018. The meropenem susceptibility was studied against several isolates. Full ethical clearance was obtained from the qualified authorities who

approved the study design. All data were analyzed using SPSS Statistics 21.

RESULTS

According to the present study, the mean age of study sample (n=443) was 45.8 year (with SD±20.66 year) and ranged between 1 and 92 years. Out of 443 samples, 311 (71.3%) were meropenem sensitive isolates and only one four of samples (25.3%) were resistant. Also (67.3%) of total patients were males and (32.7%) were female. Among 443 of patients, (39.3%) was aged between 41-60 years and 24.4% up to 16 years. The *E. coli* was observed in 27.5% of sample isolates, the next type of bacteria was *P. aeruginosa* (19.6%).

Table 1: Distribution of Study variables.

Variable	Level of variable	Frequency	Percentage
Culture	S	316	71.3
Result	I	15	3.4
	R	112	25.3
	Total	443	100.0
	M	298	67.3
Sex	F	145	32.7
	Total	443	100.0
	Less 20	66	14.9
Age	21-40	95	21.4
order	41-60	174	39.3
	Up to 60	108	24.4
	Total	443	100.0
	Escherichia coli	122	27.5
	Proteus Spp	5	1.1
	P. aeruginosa	87	19.6
	Coagulase negative *Staphylococci*	55	12.4
	Staphylococcus aureus	23	5.2
	Klebsiella Spp	42	9.5
Type of	*Acinetobacter species*	29	6.5
bacteria	*Klebsiella pneumoniae*	51	11.5
	Streptococcus spp.	10	2.3
	Enterobacter Spp	9	2.0
	Serratia Spp	1	0.2
	Enterococcus Spp	4	0.9
	Proteus vulgaris	2	0.5
	Haemophilus Spp	2	0.5
	Alpha Hemolytic *Streptococcus*	1	0.2
	Total	443	100.0
Type of	Urine Culture	32	7.2
sample	Blood Culture	138	31.2
	Wound Swab For Culture	41	9.3
	Pus For Culture & Sensitivity	52	11.7
	Sputum Culture	143	32.3
	Aspirated Fluid Culture	12	2.7
	General swab for Culture	12	2.7
	Cerepro Spinal Fluid (CSF) C/S	7	1.6
	Pleural Fluid For Culture & Sensitivity	4	0.9
	High Vaginal Swab (HVS) C/S	1	0.2
	Ascitic fluid C/S and sensitivity	1	0.2
	Total	443	100.0

From the study findings, 32.3% of sample was isolated from sputum cultures and 31.2% from blood cultures (Table 1). There was not statistically significant difference between culture results with both sex and age group (*p*-value=0.1 and 0.2 respectively).

However, 40.2% of females had meropenem resistant and 48.2% of samples resistant were aged 41-60 years (Table 2). Results in Table 3 indicated that the relationship between bacteria type and culture results was statistically significant (*p*-value=0.001). The

relationship between culture results and sample type was analyzed in the Table 4. Results in this table showed that there was high significantly relationship (*p*-value=0.001). Also 34.49% of meropenem sensitive isolates were from blood cultures, followed by sputum cultures (23.7%). However, 58% of isolates from sputum cultures were meropenem resistant.

DISCUSSION

In this study, the prevalence of meropenem resistance among isolates was 25.3%. It was similar to a study by Mulla S *et al.*, who reported 30% meropenem resistance[7] and to a study by Mahajan G *et al.*, who found 31.81% meropenem resistance[8]. Some studies recorded lower level of carbapenem resistance. Shivesh P *et al.*,[9] reported 15% and Shashikala *et al.*,[10] found

10.9% carbapenem resistance in their respective studies. In a study by Sachin Kumar Wankhede *et al.*,[11] found 19.40% carbapenem resistant.

Table 2: Distribution of age group and sex according to Culture results.

Variable		Culture results				P
		S	I	R	Total	
Sex	M	219	12	67	298	
	F	97	3	45	145	0.1
	Total	316	15	112	443	
Age group	Less 20	51	3	12	66	
	21-40	70	1	24	95	
	41-60	112	8	54	174	0.2
	Up to60	83	3	22	108	
	Total	316	15	112	443	

Table 3: Distribution of bacteria type according to culture results.

Variable		Culture results				*p*-value
		S	I	R	Total	
Bacteria type	*Escherichia coli*	115	3	4	122	
	Proteus Spp	5	0	0	5	
	P. aeruginosa	56	3	28	87	
	Coagulase negative *Staphylococci*	38	5	12	55	0.001
	Staphylococcus aureus	21	0	2	23	
	Klebsiella Spp	12	0	30	42	
	Acinetobacter species	2	1	26	29	
	Klebsiella pneumoniae	42	2	7	51	
	Streptococcus spp.	10	0	0	10	
	Enterobacter Spp	8	0	1	9	
	Serratia Spp	1	0	0	1	
	Enterococcus Spp	1	1	2	4	
	Proteus vulgaris	2	0	0	2	
	Haemophilus Spp	2	0	0	2	
	Alpha Hemolytic *Streptococcus*	1	0	0	1	
	Total	316	15	112	443	

Table 4: Distribution of culture results according to sample type.

Variable		Culture results				*p*-value
		S	I	R	Total	
Sample type	Urine Culture	24	1	7	32	
	Blood Culture	109	7	22	138	
	Wound Swab For Culture	33	1	7	41	
	Pus For Culture and Sensitivity	47	2	3	52	
	Sputum Culture	75	3	65	143	
	Aspirated Fluid Culture	10	1	1	12	
	General swab for Culture	7	0	5	12	
	CSF C/S	7	0	0	7	0.001
	Pleural fluid for culture and sensitivity	3	0	1	4	
	High Vaginal Swab C/S	1	0	0	1	
	Ascitic fluid c/s and sensitivity	0	0	1	1	
	Total	316	15	112	443	

Resistance to carbapenem in this study is low compared to studies from India. In a study in New Delhi by Bijayini Behera *et al.*,[12] carbapenem resistance was found to be 69%, which much on the higher side. Current finding was agreed with the study conducted by Basher *et al.*,[13], in Khartoum state; she found that 25.6% of clinical isolates were resistant to Meropenem antibiotic; also similar to study conducted by Khanda Abdallatif Anwar in Iraq who reported that

22% of the isolates were meropenem resistant[14]. However, less than study conducted by Noyal M *et al.*,[15] which found that 43% of the isolates were meropenem resistant.
In the present study, maximum number of meropenem sensitive isolates was from blood samples 34.5% (109/316) followed by sputum samples 23.7% (75/316). Nagaraj S *et al.*,[16] reported different findings where they observed that the carbapenem-resistant

organisms were isolated mainly from urine samples up to 42%, followed by wound discharge 18% and respiratory secretions 16%. Sputum samples (n=143) and blood samples (n=138) were the most frequent samples received during current study and in most of the studies analysed. The reason for this could be respiratory infection, being the most common hospital-acquired infection. In current study, the resistant of *Pseudomonas* species was in agreement with study findings in Sudan 20%[13]. According to the study findings, 94.3% (115/122) of *Escherichia coli* isolates were meropenem sensitive. This was disagreed with a study done by Sharif A *et al.*,[17] in Nigeria who reported that *E. coli* was the most resistant organism. According to a study conducted by Noyal M *et al.*,[18] *Acinetobacter* was the most resistant organism. Similarly, 89.7% (n=26/29) of *Acinetobacter* species isolates were meropenem resistant in the current study. Carbapenem is the last resort for treatment of life threatening infections in hospital. Judicious use and constant monitoring are essential to check the spread of imipenem/meropenem resistant in hospitals and its subsequent spread in the community. Also attention by the hospital infection control team is essential to implement stringent preventive measures to contain the spread of the infection and promote the judicious use of antimicrobial agents.

CONCLUSIONS

This study concluded that the percentage of resistance to Carbapenem antibiotics was high (25.3%) and cannot be neglected. The most meropenem resistant organisms were *Acinetobacter* species, *Klebsiella* species, and *P. aeruginosa*. Despite efforts to control carbapenem resistance, a definite solution to the problem is still far from achievement.

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AUTHOR'S CONTRIBUTION

Ali A: writing original draft, methodology, investigation. **Ali A:** formal analysis, data curation, conceptualization. **Alnamer R:** writing, review and editing. **Alnosary T:** methodology, formal analysis. All authors revised the article and approved the final version.

CONFLICT OF INTEREST

None to declare.

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