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RESEARCH ARTICLE

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

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ABSTRACT
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.
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. 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*. In addition, 94.3% (115/122) of *Escherichia coli* isolates were meropenem sensitive. However, the *Klebsiella species* had higher meropenem resistance than other pathogens (30/112; 26.8%). Moreover, 89.7% (26/29) of *Acinetobacter* species isolates were meropenem resistant. 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**.** 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.

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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 *Escherichia coli* was observed in 27.5% of sample isolates, the next type of bacteria was *Pseudomonas aeruginosa* (19.6%). 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). Also the study findings reported that 36.4% of total meropenem sensitive isolates (71.3%) were *Escherichia coli*, followed by *Pseudomonas aeruginosa* (17.7%). However, the *Klebsiella Spp.* was the higher resistant type of bacteria (26.8%).

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. 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.

Our 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). However, 58% (65/112) of sputum samples isolates were meropenem resistance**.**

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 our study and in most of the studies analysed. The reason for this could be respiratory infection, being the most common hospital-acquired infection.

In our 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. The use of carbapenem for the treatment of infection should be reserved for situations where the infection is polymicrobial or for isolates resistant to other antibiotics. Antibiotic resistance is increasing at an alarming rate, leading to increased morbidity, mortality and treatment costs. A key factor in the development of antibiotic resistance is the inappropriate use of antibiotics. 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.

CONCLUSION

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 *Pseudomonas aureginosa*. Despite efforts

to control carbapenem resistance, a definite solution to the problem is still far from achievement.

CONFLICT OF INTEREST

No conflict of interest is associated with this work.

REFERENCES

1. Francis S Codjoe, Eric S Donkor. Carbapenem Resistance: A Review. Med Sci. 2018; 6: 1.
2. Klynveld Peat Marwick Goerdeler (KPMG) LLP. The Global Economic Impact of Anti-Microbial Resistance; KPMG LLP: London, UK, 2014.
3. Knapp KM, English BK. Carbapenems. Semin. Pediatr. Infect. Dis. 2001; 12, 175–185.
4. Lee CR, Lee JH, Park KS, Kim YB, Jeong BC, Lee SH. Global dissemination of Carbapenemase-producing Klebsiella pneumoniae: epidemiology, genetic context, treatment options, and detection methods. Front Microbiol. 2016; 7: 895.
5. Lister PD, Wolter DJ, Hanson ND. Antibacterial-resistant *Pseudomonas aeruginosa*: clinical impact and complex regulation of chromosomally encoded resistance mechanisms. Clin Microbiol Rev. 2009; 22(4):582-610.
6. Moazami-Goudarzi S, Eftekhar F. Assessment of carbapenem susceptibility and multidrug resistance in *pseudomonas aeruginosa* burn isolates in Tehran. Jundishapur J Microbiol. 2013; 6(2):162-165.
7. Mulla S, Charan J, Panvala T. Antibiotic sensitivity of Enterobacteriaceae at a tertiary care center in India. Chron Young Sci. 2011; 2:214-18.
8. Mahajan G, Sheemar S, Chopra S, Kaur J, Chowdhary D. Carbapenem resistance and phenotypic detection of carbapenemases in clinical isolates of *Acinetobacter baumanni*. Indian J Med Sci. 2011; 65: 18-25.
9. Shivesh P. Carbapenem sensitivity profile amongst bacterial isolates from clinical specimens in Kanpur city. Indian J Crit Care Med. 2006; 10(4):250-53.
10. Shashikala, Kanungo R, Srinivasan S, Devi S. Emerging resistance to carbapenems in hospital acquired Pseudomonas infection: A cause for concern. Indian J Pharmacol. 2006; 38:287-88.
11. Sachinkumar W, Vivek I, Ghadge P, Bhore AV. Hospital based infections of Gram- negative organisms. Indian J Basic Appl Med Res. 2013; 2(7):797-800.
12. Bijayini B, Anupam D, Purva M, Arti K. High prevalence of carbapenem resistant *Pseudomonas aeruginosa* at a tertiary care centre of north India. Are we under-reporting? Indian J Med Res. 2008; 128:324-25.
13. Basher RM. Phenotypic Detection of New Delhi Metallo-Beta-Lactamase Producing Gram Negative Bacilli causing Pyogenic infections in Khartoum State. African J Med Sci. 2016; 1:2.
14. Abdulateef K, Abodi F, Ali S. Detection of Metallo B-Lactamase Enzyme In some Gram Negative Bacteria Isolated from Burn Patients in Sulamani city, Iraq. Eur Scientific J. 2014; 10: 485-496.
15. Noyal MG, Menezes GA, Harish BN, Sujatha S, Parija SC. Simple screening tests for detection of carbapenemases in clinical isolates of non fermentative Gram-negative bacteria. Indian J Med Res. 2009; 129: 707-712.
16. Nagaraj S, Chandran SP, Shamanna P, Macaden R. Carbapenem resistance among *Escherichia coli* and *Klebsiella pneumoniae* in a tertiary care hospital in South India. IJMM. 2012; 30(1):93-5.
17. Yusuf I, Yusha'u M, Sharif AA, Getso MI, Yahaya H, *et al.* Detection of Metalo-Beta-Lactamases Among Gram Negative Bacterial Isolates from Murtala Muhammed Specialist Hospital, Kano and Almadina Hospital, Nigeria. Bayero J Pure Applied Sci. 2012; 5: 84-88.
18. Noyal MG, Menezes GA, Harish BN, Sujatha S, Parija SC. Simple screening tests for detection of carbapenemases in clinical isolates of nonfermentative Gram-negative bacteria. Indian J Med Res. 2009; 129: 707-712.

Table 1: Distribution of Study variables

Variable	Level of variable	Frequency	Percent
Culture Result	S	316	71.3
	I	15	3.4
	R	112	25.3
	Total	443	100.0
Sex	M	298	67.3
	F	145	32.7
	Total	443	100.0
Age order	Less 20	66	14.9
	21-40	95	21.4
	41-60	174	39.3
	Up to60	108	24.4
	Total	443	100.0
Type of bacteria	*Escherichia coli*	122	27.5
	Proteus Spp	5	1.1
	Pseudomonas aeruginosa	87	19.6
	Coagulase negative Staphylococci	55	12.4
	Staphylococcus aureus	23	5.2
	Klebsiella Spp	42	9.5
	Acinetobacter species	29	6.5
	Klebsiella pneumoniae	51	11.5
	Streptococcus spp.	10	2.3
	Enterobacter Spp	9	2.0
	Serratia Spp	1	0.2

Cont…

	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 sample	Urine Culture	32	7.2
	Blood Culture	138	31.2
	Wound Swab For Culture	41	9.3
	Pus For Culture and 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 and 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

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

Variable		Culture results				P- value
		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	
	Pseudomonas 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			Total	P-value
		S	I	R		
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	