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In Vitro activity of Imipenem against Clinical Isolates from Jordanian Children

Dr. Al-Shara Mohammad

Dept. of Pharmacology, Faculty of Nursing, Irbid National University, Irbid, Jordan

ABSTRACT

Over the past decade, carbapenem-resistant have been recognized in health-care settings as a cause of difficult-to-treat infections associated with increased morbidity, mortality and healthcare costs. To evaluate the in-vitro activity of imipenem against clinical isolates from children. A total of 2083 bacterial pathogens were isolated and identified from various clinical specimens. These included 293 (14.1%) *Escherichia coli,* 433 (20.8%) *Klebsiella spp*, 18 (0.80%) *Proteus spp*, 48 (2.3%) *Pseudomonas aeruginosa*, 1077 (51.7%) *S. Aurous*, 144 (6.9%) *Strepto coccus* and 70 (3.4%) *Enterobacter***.** over all the study period, the highest susceptibility rate to imipenem was 72.3% for *E. coli* isolates, whereas the lowest susceptibility rate of 42.9% was recorded for *S. Aurous*. The entire organisms showed low susceptibility to imipenem. The activity of imipenem against all the isolates of organisms fell far above the acceptable levels indicating wide spread and inappropriate use of imipenem in pediatric infections. So it is the time to think, plan and formulate a strong antibiotic policy to address this present scenario

Keywords: Imipenem, *Escherichia coli*, *Klebsiella pneumoniae*, antimicrobial susceptibility, empiric therapy

Corresponding author

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INTRODUCTION

Antimicrobial resistance is a major public health problem worldwide, and several reports suggest that it is an increasing problem of phenomenal proportions, affecting both developed and developing countries. [1] Infections caused by resistant bacteria have been shown to be more frequently associated with increased morbidity and mortality than those caused by susceptible pathogens. [2,3] In areas of concentrated use, such as hospitals, this had led to lengthened hospital stays, increased health care costs and in extreme cases, to untreatable infections.

The past several decades have seen the spread of pathogenic isolates with resistance to broad-spectrum antimicrobials. Therefore, clinicians have relied on the carbapenem antimicrobial class (imipenem and meropenem,) to treat infections caused by these resistant organisms. Carbapenem-resistant isolates were relatively uncommon in the United States before 2000 [4]. Carbapenem resistance is complex; it can occur in different pathogenic isolates and be mediated by several mechanisms spread widely around the world which is different from resistance in methicillin-resistant *Staphylococcus aureus* (MRSA), which is one bacterial species and is mediated by a single mechanism.[5] Carbapenem-resistant isolates can spread in health-care settings and cause infections with mortality rates of 40% to 50%.[6-8]

However, there is little information on imipenem resistance pattern in Jordan. Therefore, this retrospective study was conducted to determine the rate of resistance to imipenem by pathogens isolated from cultures of clinical specimens received from children inpatient and outpatients at Princess Rahmah Hospital during a period of 5 years (2005-2009).

MATERIALS AND METHODS

This study was carried out in the diagnostic Medical Microbiology Laboratory of Princess Rahmah Hospital located in Irbid, Jordan, between 2005-2009. A total of 2083 bacteria isolates were identified from different clinical specimens using standard bacteriological methods. These clinical specimens included blood, urine, ear swabs and conjunctival swabs. Microbiological and antibacterial susceptibility data of this study obtained from records of diagnostic Medical Microbiology Laboratory of Princess Rahmah Hospital. These data were filled in a prepared data sheet.

The antimicrobial susceptibility patterns of these isolates to antibiotics were determined using the Kirby-Bauer method of disc diffusion test.[9] Study protocol was approved by the Ethics Committee of the ministry of health in Jordan (MOH, REC, 08, 0057).

Statistical Analysis:

Data were analyzed using SPSS (version15 for Windows) to calculate the frequencies and cross tabulation.

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RESULTS

A total of 2083 bacterial pathogens were isolated and identified from various clinical specimens. These included urine 431 (20.7%), blood 1403 (67.4%), ear swabs 201 (9.6%), conjunctival swabs 48 (2.3%) (Table1).

Table 1: Distribution of pathogens isolated from clinical specimens (2005-2009)

Sample	Year					Total
	2005	2006	2007	2008	2009	
Urine	9	88	15	15	304	431
Blood	161	163	197	355	527	1403
Ear	74	92	5	4	26	201
Eye	13	23	0	5	7	48
Total	257	366	217	379	864	2083

Types of isolates were 293 (14.1%) *Escherichia coli,* 433 (20.8%) *Klebsiella* species, 18 (0.08%) *Proteus* species, 48 (2.3%) *Pseudomonas aeruginosa*, 1077 (51.7%) *S. Aurous*, 144 (6.9%) *Strepto coccus* and 70 (3.3%) *Enterobacter* (Table 2).

In vitro activity of imipenem antibiotic against different bacterial isolates is illustrated in Table 2.

Table 2: Imipenem activity to different bacterial pathogen Isolates (2005-2009)

Pathogen	2005	2006	2007	2008	2009	Total	Significance 2005 vs. 2009
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	P-value
E-coli	10 (12.0)	65 (26.1)	8 (12.5)	16 (25.0)	192 (93.7)	293 (72.3)	0.168
Klebsiella	73 (54.7)	55 (38.1)	64 (68.7)	33 (12.1)	208 (93.2)	433 (69.9)	<0.001
Proteus	1 (0.0)	9 (33.3)	0	0	8(62.5)	18 (44.4)	0.292
Pseudo	19 (52.6)	10 (50.0)	3 (0.0)	6 (0)	10 (90.0)	48 (50.0)	0.046
S. Aureus	109 (49.5)	167 (48.5)	118 (33.0)	314 (6.3)	369 (72.8)	1077 (42.9)	<0.001
Strep. spp	36 (66.6)	51 (41.1)	5 (40.0)	9 (33.3)	43 (93.0)	144 (62.5)	0.003
Enterobacter	7 (85.7)	9 (66.6)	19 (26.3)	1 (100.0)	34 (88.2)	70 (68.5)	0.857
All pathogens	257 (56.0)	366 (42.0)	217 (41.9)	379 (8.4)	864 (84.1)	2083 (55.1)	< 0.001

Among all clinical isolates during over all the period of study, the highest susceptibility rate to imipenem was 72.3% for *E. coli* isolates, whereas the lowest susceptibility rate of 42.9% was recorded for *S. Aurous* (Figure 1).

In comparison between the year of 2005 and 2009, the activity of imipenem significantly increased (P<0.001) from 54.75 upto 93.2% and from 49.5% upto 72.8% against *Klebsiella* and *S. Aurous* respectively. However, the activity of imipenem among all clinical isolates was significantly increased (P<0.001) from 56.0% up to 84.1%., (Table 2).

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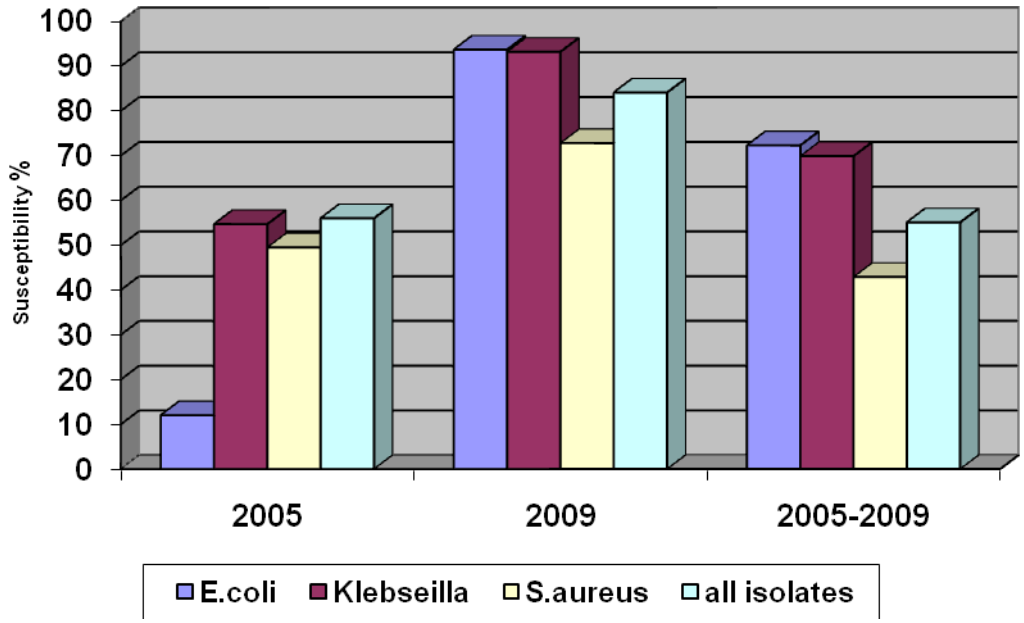
Figure 1: Susceptibility of clinical isolates to imipenem (2005-2009).



DISCUSSION

Results of this study showed that a total of 2083 pathogenic bacteria were isolated during the study period. of isolates were 293(14.1%) *Escherichia coli,* 433 (20.8%) *Klebsiella* species, 18 (0.08%) *Proteus* species, 48 (2.3%) *Pseudomonas aeruginosa*, 1077 (51.7%) *S. Aurous*, 144 (6.9%) *Strepto coccus* and 70 (3.3%) *Enterobacter*. Imipenem is widely used to treat many infections caused by susceptible bacteria, such as urinary tract infections, respiratory tract infections.

Results of this study demonstrate that imipenem had moderate activity against *E .coli* isolates through out the study period which was 72.3%. This results is consistence with results reported in Iran [10,11] and India [12], whereas the imipenem activity was lower than that reported in Croatia [13], Nigeria [14]. However, in comparison of the activity of imipenem against *E. coli* between the year 2005 and 2009 data showed increased in the activity from 12.0% upto 93.7%, but this increment was not significant.

Imipenem had also showed significant increased ($P<0.001$) in its activity against *Klebseilla pneumoniae* with activity rate of 54.7% upto 93.2% in the years of 2005 and 2009 respectively. However, the main rate of activity for the five years of study period was 69.9 % which was lower than that reported elsewhere. [10-13]

In this study, *S. Aureus* showed low susceptibility rate of 42.9% to imipenem which was lower than reported elsewhere.[14,15]

The entire organisms through out of study period showed low susceptibility rate to imipenem (55.1%). In addition, all clinical isolates showed low susceptibility rate to imipenem except *E. coli* which showed moderate susceptibility rate of 72.3%. However, in comparison between the year of 2005 and 2009, most of isolates showed increased in there susceptibility to imipenem and this increment was significant (P<0.001) for *Klebseilla, S. Aureus* and for the entire organisms. This finding is concordance with other findings reported higher resistance of imipenem among pathogenic isolates [12]. The reason for the low activity of imipenem against the tested isolates in this study could be attributed improper use of imipenem in Jordan. However, after the passage of time, different factors are attributable for emergence of resistance. These mainly include; high consumption of antibiotics, irrational use, and incomplete course of therapy, leading to the emergence of resistance and even treatment failures.

CONCLUSION

The present situation is alarming, because it is not long before imipenem, an effective antibiotic would be failed to treat even simple or minor infections. In addition to this, routine antimicrobial susceptibility testing must be timely performed to determine the current status of resistance against antimicrobial agents. Otherwise therapy failures may occur which increase the cost of the therapy as well as recovery time from the underlying disease.

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