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Original Article

The Comparative Efficacy of Imipenem and Meropenem On Different Bacterial Strains Obtained from Clinical Samples

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ABSTRACT

The most serious threat to patient's and the public's health is the resistance of clinically relevant microorganisms to antimicrobials. **Objective:** This study's primary objective was to compare the susceptibility profiles of imipenem and meropenem on various bacterial strains. **Methods:** 101 distinct patients' positive samples of blood and pus were collected and sent to a pathology lab in Lahore (Mughal Diagnostic and Research laboratory Lahore). On Macconkey, CLED, and Blood Agar media, five bacterial strains; *E. coli*, *P. aeruginosa*, *Enterococcus species*, *Klebsiella* species and *S. typhi* were isolated and resurrected. Following microscopical (gram staining) and biochemical tests to identify these bacterial strains, the antibiotic sensitivity of these bacterial strains was assessed. **Results:** The findings of this investigation clearly demonstrated that imipenem is more sensitive than meropenem. Imipenem demonstrated improved sensitivity to all of the bacterial strains included in the study, especially *E. coli*, *P. aeruginosa*, various *Enterococcus*, *Klebsiella*, and *S. typhi*, imipenem showed a sensitivity of 84.15%, while meropenem showed a sensitivity of 40.59%. **Conclusions:** The current investigation came to the conclusion that antibiotics (imipenem and meropenem) are becoming more resistant to bacteria as a result of their growing and frequent use. Physicians started to worry about the developing antibiotic resistance due to the indiscriminate use of these treatments after more than a decade of increased antibiotic consumption in the era.

INTRODUCTION

One of the primary methods of contemporary medicine for treating infections is antibiotic treatment. Many antibiotics were developed during the "golden era" of antibiotics, which lasted from the 1930s to the 1960s [1]. Antimicrobial resistance (AMR) is a growing global threat to human, animal, and environmental health. This is a result of multidrug-resistant (MDR) bacteria, also known as "superbugs," emerging, spreading, and remaining persistent [2]. The effectiveness of an antimicrobial agent is severely compromised by the possibility of tolerance or resistance developing from the first time this compound is used. This is true for antimicrobial agents used to treat infections caused by bacteria, viruses, fungi, and parasites. Several physiological and biochemical mechanisms may influence the development of this resistance. Various institutes and agencies around the world have recognized this serious global public health issue. Many recommendations and resolutions have been proposed, as well as several reports, but little progress has been made thus far. Unfortunately, the rise in antibiotic resistance is a continuing problem [3]. Drug-resistant infections affect one-third of ICU patients globally, which significantly raises patient mortality and medical expenses [4-6]. In >70% of non-complex cases, both outpatients and inpatients, UTI is caused by Escherichia coli bookkeeping [7]. Other Gram negative microbes include Klebsiella spp., Enterobacter spp., Pseudomonas aeruginosa, and Proteus spp. Gram positive microscopic organisms include Enterococcus spp., Staphylococci, and Streptococci [8]. Uropathogenic E. coli has been linked to 70-95% of urinary

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tract infections (UTI) worldwide. This bacterium is capable of developing resistance to nearly every antibacterial therapy that has been discovered. Unfortunately, antibiotic resistance is significantly higher among UTI patients with UPEC infections [9]. Carbapenems are critical components of our antibiotic arsenal. Carbapenems have the broadest spectrum of activity and the greatest potency against Gram-positive and Gram-negative bacteria of any of the hundreds of different -lactams. As a result, when patients with infections become critically ill or are suspected of harbouring resistant bacteria, they are frequently used as "last-line agents" or "antibiotics of last resort" [10]. The peculiar structure of carbapenems, which is defined by a carbapenem attached to a -lactam ring, gives protection against the majority of -lactamases, including metallo—lactamase (MBL) and extended spectrum -lactamases. Carbapenems exhibit broad spectrum antibacterial action [11]. Along with imipenem, meropenem is a broad-spectrum antibacterial drug that belongs to the carbapenem family. It is typically used to treat patients who are moderately to seriously unwell and have polymicrobial or nosocomial infections [12]. Meropenem is recommended for use as empirical therapy in both adults and children with a wide range of dangerous illnesses before the identification of the causative organisms or for sickness caused by one or more susceptible bacteria [13].

METHODS

Isolation of Bacterial Strains:

101 distinct patients' positive samples of blood and pus were collected and sent to a pathology lab in Lahore (Mughal Diagnostic and Research laboratory Lahore). On Macconkey, CLED, and Blood Agar media, five bacterial strains; *E. coli*, *P. aeruginosa*, *Enterococcus species*, *Klebsiella* species and *S. typhi* were isolated and resurrected. Following microscopical (gram staining) and biochemical tests to identify these bacterial strains, the antibiotic sensitivity of these bacterial strains was assessed.

Antibiotic Assay (Kirby–Bauer method)

The prepared Muller-Hinton Agar medium was individually inoculated with each recovered bacterial strain. We used Oxoid Company's commercially available antibiotic discs (imipenem and meropenem). Using a sterile disc dispenser, the antibiotic discs were evenly distributed across the surface of the agar plate. To ensure that these had a direct connection with agar, discs were only lightly pressed. The plates were then kept at 37°C for a further 24 hours. After incubation, the data were interpreted as being sensitive, resistant, or intermediate [14].

RESULTS

To evaluate the bacteria associated with wounds their colony morphological features such as color, colony shape and consistency of colonies were observed as shown in table 1.

Sr. No.	Bacterial Isolates	Number of Samples	Morphological Characteristics			
			Colony Shape	Color	Margin	Consistency
1.	E. coli	42	Circular	Pink	Entire	Smooth
2.	P. aeruginosa	19	Circular	Colorless	Irregular	Mucoid
3.	Enterococcus Species	13	Circular	Red	Entire	Smooth
4.	Klebsiella Species	16	Large Circular	Pinkish red	Entire	Mucoid
5.	S. typhi	11	Circular	Colourless	Irregular	Smooth

Table 1: Morphological Characterization of bacterial isolates

13 bacterial isolates were identified as gram negative out of 101 studied samples, while 88 were identified as gram positive as shown in figure 1. These isolates were then put through biochemical and antimicrobial susceptibility tests.

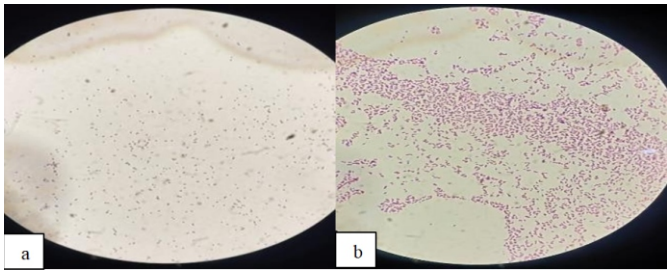

Figure 1: Microscopic identification of bacterial isolates (a) indicating Enterococcus species (b) indicating P. aeruginosa in light microscope.

Biochemical Characterization:

Bacterial isolates were subjected to various biochemical tests, yielding the following results as tabulated in table 2.

Sr. No.	Bacterial Isolates	Number	Biochemical Test				
			SIM Test	Citrate Test	TSI Test	Catalase Test	Urease Test
1.	E. coli	42	Positive	Negative	Positive	Positive	Negative
2.	P. aeruginosa	19	Negative	Positive	Positive	Positive	Negative
3.	Enterococcus Species	13	Negative	Negative	Negative	Negative	Negative
4.	Klebsiella Species	16	Negative	Positive	Negative	Positive	Positive
5.	S. typhi	11	Negative	Negative	Negative	Positive	Negative

Table 2: Biochemical Characterization of Bacterial Isolates

Evaluation of Antibiotic Activity:

The pathogens in the samples were already resistant to other antibiotics when they were treated with imipenem and meropenem antibiotics, which are commonly used to treat severe bacterial infections. Imipenem is more sensitive than meropenem, with 85 sensitive cases, 11 resistant cases, and 5 intermediate cases. Meropenem has 41 sensitive cases, 51 resistant cases, and 9 intermediate cases, represented in figure 2.

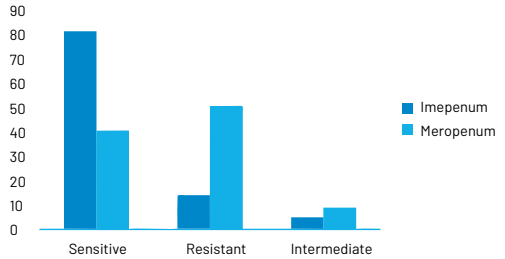

Figure 2: Imipenem and meropenem activity as sensitive,

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resistant, and intermediate in patients with bacterial infections

The observed results clearly show that imipenem is more sensitive than meropenem. Imipenem demonstrated increased sensitivity against all of the bacterial strains, including E. coli, P. aeruginosa, Enterococcus species, Klebsiella species, and S. aureus, S. typhi, imipenem demonstrated 84.15% sensitivity, while meropenem demonstrated 40.59% sensitivity. Following the Kirby-Bauer methodology, we found that Imipenem is 35.7% sensitive in male patients and 48.5% sensitive in female patients. Meropenem, on the other hand, was 17.8% sensitive in males and 22.8% sensitive in females. In terms of resistance patterns, imipenem is less resistant in males (7.9%) and females (2.9%) than meropenem, which is resistant in males 22.8% and females 27.8% against bacterial strains. Comparison of Imipenem and Meropenem Sensitivity against Bacterial Species isolated from clinical samples table 3.

Sr. No.	Specimen	Imipenem		Meropenem
		Sensitive	Resistant	Sensitive
1.	Blood	16 (15.84%)	01 (0.1%)	13 (12.87%)
2.	Urine	40 (39.60%)	05 (4.9%)	12 (11.9%)
3.	Pus Swab	29 (28.71%)	05 (4.9%)	16 (15.84%)

Table 3: Susceptibility patterns of imipenem and meropenem among specimens

Susceptibility pattern of meropenem and imipenem against pathogens table 4.

Sr. No.	Pathogens	Imipenem		Meropenem
		Sensitive	Resistant	Sensitive
1.	E. coli	38(37.62%)	04(3.96%)	15(14.85%)
2.	P. aeruginosa	11(10.9%)	06(5.94%)	07(6.93%)
3.	Enterococcus species	13(12.87%)	00(0%)	04(3.96%)
4.	Klebsiella species	12(11.88%)	01(0.1%)	05(4.95%)
5.	S. typhi	11(10.89%)	00(0%)	10(9.90%)

Table 4: Activity of meropenem and imipenem against pathogens

DISCUSSION

Hellinger WC et al., Imipenem and meropenem are carbapenem-class - β-Lactam antibiotics that are among the most widely used antimicrobial drugs available for systematic use in humans. Streptococci, methicillin-sensitive Staphylococci, Neisseria, Haemophilus, anaerobes, and aerobic gram-negative nosocomial pathogens, including Pseudomonas, are all susceptible. Tolerance to imipenem and meropenem can occur during P. aeruginosa treatment, as it has with other -lactam agents; Stenotrophomonas maltophilia is usually resistant to both imipenem and meropenem. Carbapenem is protective against Enterococci, similar to penicillin. In general, it is said that imipenem has stronger in vitro activity against aerobic gram-positive cocci than meropenem, while meropenem has somewhat higher in vitro activity against aerobic gram-negative bacilli [15]. Current study was designed by Ullah F et al., to emphasize on antibiotic adaptability patterns of pathogenic bacteria E. coli, P. aeruginosa, Enterococcus species, Klebsiella species and S. typhi against imipenem and meropenem drugs. Previous research found that E. coli was resistant to imipenem at 3.96% and meropenem at 21.78%. It demonstrates that meropenem is less effective in cases of E. coli. [16] claim that he separated 116 E. coli from patient's urine and used imipenem and meropenem drugs, which showed 98% and 97% susceptibility, respectively. Current research results show that imipenem and meropenem have susceptibility rates of 37.62% and 21.78%, respectively, for the same experiments. P. aeruginosa was more prevalent among the 150 bacteria isolated from surgical sites of patients in a study by Khorvash F et al., [17]. Their resistance to imipenem was 6.4% and to meropenem was 13%, whereas our research work showed the same frequency pattern with results showing an increased resistivity rate against meropenem (11.88%) as compared to resistivity against imipenem [18]. Farhat U et al., studied antimicrobial adaptability patterns and ESBL prevalence in K. pneumoniae from UTI in the North-West of Pakistan, and their findings show that UTI is the most common infection in both male and female patients worldwide. Their findings show that K. pneumoniae (the most common pathogen causing UTIs) has a high susceptibility to antibiotics, particularly imipenem (93.28%) and meropenem (86.96%). Following the same methodology, our current research experiments revealed a sensitivity pattern of 11.88% and 4.95% against Klebsiella spp. respectively for imipenem and meropenem. [19] Mohammed MA et al., demonstrated the prevalence and antimicrobial tolerance pattern of bacterial strains obtained from patients with UTI. He examined 1153 samples, 160 of which were positive. He isolated E. coli as the most common (55.6%) bacteria, followed by P. aeruginosa and Klebsiella at 5.6% and 2.5%, respectively, with increased levels of resistance to imipenem (0.6%) and meropenem (2.5%). Following the methodology described by [19], our results revealed an increase in P. aeruginosa susceptibility patterns to imipenem and meropenem. The observed resistance pattern against imipenem was 5.94% and 11.88% for meropenem, respectively. The changing epidemiology of P. aeruginosa, as well as the impact of carbapenem mechanism, is critical for optimizing antimicrobial therapy in order to prevent and combat infections caused by multidrug resistant P. aeruginosa. Elena Riare and her colleagues studied the carbapenem resistance mechanism in P. aeruginosa and its impact on the activity of imipenem, meropenem, and doripenem in 2011. The study included vy Riera E et al., 175 P. aeruginosa isolates (39%) of the total samples. Only 6.9% of them were less susceptible to imipenem and meropenem. In the current

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study, imipenem showed (9.5%) resistance against P. aeruginosa, which appears to be increasing from the previous study, and meropenem showed slightly more resistance (11.88%). The study raised two points: first, resistance patterns were increasing, and second, imipenem had slightly higher efficacy than meropenem [20].

CONCLUSIONS

Antibiotics (imipenem and meropenem) are becoming more resistant to microbes as they are used more frequently. Because of the increased use of these drugs, imipenem and meropenem are becoming more resistant to E. coli, P. aeruginosa, Enterococcus species, Klebsiella species and S. typhi. Many commonly used antibiotics were ineffective against E. coli. Very little resistance was detected toward imipenem in patients with pneumonia caused by E coli. Patients with typhoid fever brought on by typhi are developing an increased resistance to imipenem and meropenem. Typhi strains that have developed resistance pose a serious threat to the global population, so antibiotics must be prescribed according to the patient's culture and sensitivity. Although meropenem and imipenem are clear, they are equally effective (both bacteriologically and clinically) to treat crucial diseases. Continuous monitoring of susceptibility of clinical pathogenic strains is important.

Conflicts of Interest

The authors declare no conflict of interest.

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