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Research Article

PSEUDOMONAS AERUGINOSA ISOLATES FROM URINARY TRACT INFECTION AND THEIR ANTIMICROBIAL SUSCEPTIBILITY PATTERN WITH SPECIAL REFERENCE TO CARBAPENEMS

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A B S T R A C T

Background: Urinary tract infections (UTIs) are one of the most common bacterial infections affecting humans. Incidence of UTIs in women in the age group of 20-40 years is found to be around 25 to 30%. Incidence in older women above 60 years of age is from 4 to 43%. Catheterization of urinary tract is one of the most common independent risk factor for UTI. Despite advances in antimicrobial therapy, the mortality and morbidity associated with *P. aeruginosa* induced UTIs remain significantly high. The aim of this study is to determine the antimicrobial susceptibility pattern of *P. aeruginosa* isolated from urinary tract infection with special reference to Carbapenem resistance and to guide clinicians for appropriate antimicrobial therapy for reduction of morbidity & mortality in hospitalized patients.

Materials and Methods: This is a retrospective analysis from January 2016 to December 2017. Urine samples collected in appropriate sterile manner were screened for polymorphonuclear leucocytes and bacteria by routine microscopic examination. Isolated *Pseudomonas aeruginosa* strains in significant count which are oxidase positive, non-lactose fermenters from MacConkey's agar were identified with Matrix assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF MS). Antibiotic susceptibility was performed by VitekCompact™ 2 (Biomeuriux, France) as per CLSI standards establishing MIC (Minimum Inhibitory Concentration).

Results: During the study period we have received 17011 urine samples for routine microscopy and aerobic culture and antimicrobial susceptibility. Of 17011 urine samples, 5407 samples were from male patients and 11604 were from female patients. Of 5407 urine samples from male, 422(7.8%) patients grew *P. aeruginosa*. Of 11604 urine samples from female, 265(2.2%) patients grew *P. aeruginosa*. Overall positivity rate for *P. aeruginosa* from 17011 urine samples was 4.03%. Of the 687 isolates of *P. aeruginosa,* 407(59.24%) isolates were sensitive to Doripenem, 15 were intermediate and 265(38.57%) were resistant.Of the 687 isolates of*,* 405(58.95%) isolates were sensitive, 12 were intermediate and 270 (39.30%) were resistant with Imipenem. Of the 687 isolates*,* 437(63.60%) isolates were sensitive to Meropenem, 19 were intermediate and 231(33.62%) were resistant. The average susceptibility of *P. aeruginosa* with carbapenems was 60.59% and resistance was 37.16%. Among three carbapenems, meropenem is found to have better susceptibility in-vitro as compared to imipenem and doripenem but in-vivo studies are needed further to establish the comparison and efficacy.

Discussion: *P. aeruginosa* infections are increasing both in hospital and in general community. It has been reported as one of the leadingnosocomial pathogen. *P. aeruginosa* is the third leading causeof hospital-acquired urinary tract infections (UTIs), accounting for about 12 % of all hospital acquired infections. Extensive use ofantimicrobial agents as empirical therapy without evidence of culture susceptibility pattern and local antibiogram has resulted in development of drug resistance including multidrug resistant (MDR) and extensively drug resistant (XDR) organisms.Infectionscaused by *P. aeruginosa* are difficult to treat andoften require combination of drugs to prevent emergence of drug resistance. High rates ofresistance to antibiotics are associated with nosocomial *P. aeruginosa* strains.

Conclusion: *P. aeruginosa* remains one of the most important and difficult to treat nosocomial pathogen. MDR strains are increasingly being reported and, in these cases, the choice of therapy often becomes very limited. While the medical community awaits the development of new drugs, MDR *P. aeruginosa* strains are likely to represent an increasing threat, and every effort should be made to preserve as long as possible, or to restore, the efficacy of currently available agents.

INTRODUCTION

A urinary tract infections (UTIs) is an infection in any part of your urinary system-kidneys, ureters, bladder and urethra.

Most infections involve the lower urinary tract- the bladder and the urethra. Urinary tract infections are one of the most common bacterial infections affecting human being throughout their life[1, 2]. Urinary tract infections are common in women, and many women experience more than one infection during their lifetimes. Incidence of UTIs in women in the age group of 20-40 years is found to be around 25 to 30%. Incidence in older women above 60 years of age isfrom 4 to 43%[3, 4, 5].UTIs

can be classified as complicated or uncomplicated[6, 7] based on underlying medical or surgical conditions (physiological or pathological). The predisposing factors in complicated UTIs are congenital anatomical defects, vesicouretic reflux (VUR), obstruction due to calculus or traumatic obstruction, urogenital surgeries, metabolic diseases like diabetes mellitus and generalized immunosuppression especially in patients of organ transplantation[8, 9, 10]. Catheterization of urinary tract is one of the most common independent risk factor which predisposes the host to develop complicated UTIs[11, 12, 13]. Catheterization of urinary tractmay lead to damage of mucosal layer, which disrupts the natural mucosal barrier and allows bacterial colonization[14]. Organisms can gain entry via extra luminal routeby moving across the outer lumen of catheter or by intraluminal route by directly entering the interior of catheter[15,16]. The organisms most commonly responsible for catheter-associated UTIs are *Escherichia coli*, *Proteusmirabilis*, *Pseudomonas aeruginosa*, *Klebsiellapneumoniae* and E*nterococcus faecalis*[17,18]. However, there is paucity of literature in relationto pathogenesis of UTIs caused by *P. aeruginosa*. Despite advances in antimicrobial therapy, the mortality and morbidity associated with *P. aeruginosa* induced UTIs remain significantly high. This unfavourable outcome is due to our inability to develop therapeutic strategies to prevent the disease which in turn is due to incomplete understanding aboutthe pathogenesis of the disease. The aim of this study is to determine the antimicrobial susceptibility pattern of *Pseudomonas aeruginosa* isolated from urinary tract infection with special reference to Carbapenem resistance and to guide clinicians for appropriate antimicrobial therapy for reduction of morbidity & mortality in hospitalized patients.

MATERIALS AND METHODS

Urine (midstream, catheterized and suprapubic aspiration) specimens collected from patients with suspected UTI were processed in the Department of Microbiology, Metropolis healthcare limited, Mumbai, India. During the study period (January 2016to December 2017), Gram negative, oxidase positive, non-lactose fermenting colonies isolated in significant counts ($>1\times10^5$cfu/ml) in pure culture were included in the study. UTI was defined as the presence of any one of the following symptoms: fever, burning, urgency, frequency of micturition, supra pubic tenderness and growth of$>=1\times10^5$cfu/ml of *Pseudomonas aeruginosa* from un-centrifuged urine specimen. Patients undergone suprapubic aspiration, evenlesser colony count ($<1\times10^5$cfu/ml) with presence of polymorphonuclear leucocytes was considered significant and included in the study. The objective of this study was to determine the antibiotic susceptibility pattern of the isolated strains of *Pseudomonas aeruginosa* with special reference to carbapenem resistance and to guide clinicians for appropriate antimicrobial therapy for reduction of morbidity & mortality in hospitalized patients. This study was performed with patients admitted in a tertiary care hospital, developing symptoms of UTI at least after 48 hours of admission. Few patients from community acquired infection with symptoms of UTI have also been included in the study. Cases of urinary tract infection with established nonbacterial aetiology (fungal UTI) excluded from the study. Urine samples collected in appropriate sterile precautions were screened for pus cells and bacteria by routine microscopic examination. This was followed by plating on MacConkey's agar and Blood agar by T streaking method with an inoculating loop of 4 mm diameter (10 µl of un-centrifuged urine specimen). Inoculated plates were incubated overnight at 37^{o}c. Isolated colonies of *Pseudomonas aeruginosa* which are oxidase positive and non-lactose fermenters from MacConkey's agar were identified with Matrix assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF MS). Antimicrobial susceptibility was performed by VitekCompact^{TM} 2 (Biomeuriux, France) as per CLSI guidelines establishing MIC (Minimum Inhibitory Concentration) of the tested antimicrobials.

Table 1 Minimum inhibitory concentrations (MIC) of antimicrobials used for *Pseudomonas aeruginosa*

Antimicrobial	MIC µg/ml			Comments
	S	I	R	
Doripenem	<=2	4	>=8	Breakpoints for doripenem are based on a dosage regimen of 500 mg every 8 h.
Imipenem	<=2	4	>=8	Breakpoints for imipenem are based on a dosage regimen of 1 g every 8 h or 500 mg every 6 h.
Meropenem	<=2	4	>=8	Breakpoints for meropenem are based on a dosage regimen of 1 g every 8 hour.
Colistin	<=2	-	>=4	Colistin should generally be given with a loading dose and at maximum recommended doses, and used in combination with other agents. (The only approved MIC method for testing is broth micro dilution. Disk diffusion and gradient diffusion should not be performed-2018 CLSI).
Polymyxin B	<=2	4	>=8	-
Gentamicin	<=4	8	>=16	-
Amikacin	<=16	32	>=64	
Piperacillin-tazobactam	<=16/4	32/4-64/4	>=128/4	Breakpoints for piperacillin (alone or withtazobactam) are based on a piperacillin dosage regimen of at least 3 g every 6 h.
Ceftazidime	<=8	16	>=32	Breakpoints are based on a dosageregimen of 1 g every 6 h or 2 g every 8 h.
Cefepime	<=8	16	>=32	
Ciprofloxacin	<=1	2	>=4	-
Levofloxacin	<=2	4	>=8	
Norfloxacin	<=4	8	>=16	For testing and reporting of urinarytract isolates only.

Adapted from CLSI. Performance Standards for Antimicrobial Susceptibility Testing. 27th ed. CLSI supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2017.
S= Susceptible; I= Intermediate; R= Resistant.*P. aeruginosa* may develop resistance during prolonged therapy with all antimicrobial agents. Therefore, isolates that are initially susceptible may become resistant within 3 to 4 days after initiation of therapy. Testing of repeat isolates may be warranted.

RESULTS

Table 2 Susceptibility pattern of *Pseudomonas aeruginosa* isolates from urinary tract infection

Organism (N=687) / Antibiotic	*Pseudomonas aeruginosa* (N=687)		
	S	I	R
Doripenem	407	15	265
Imipenem	405	12	270
Meropenem	437	19	231
Colistin	681	-	6
Polymyxin B	681	0	6
Gentamicin	404	28	255
Amikacin	427	10	250
Piperacillin-tazobactam	590	15	82
Ceftazidime	418	24	245
Cefepime	412	30	245
Ciprofloxacin	334	29	324
Levofloxacin	354	19	314
Norfloxacin	358	15	314

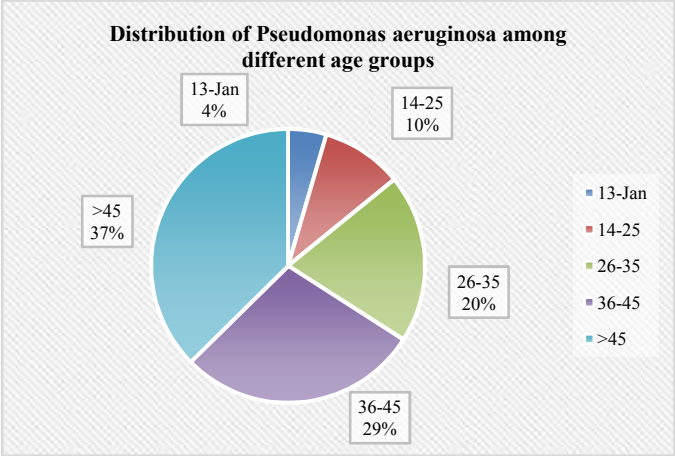
S= Susceptible; I= Intermediate; R= Resistant

Of the 687 strains of *Pseudomonas aeruginosa*, 6 isolates were resistant to colistin and polymyxin B with MIC more than 4 µg/ml and 8 µg/ml respectively.

Table 3 Distribution of *Pseudomonas aeruginosa* isolates among males and females

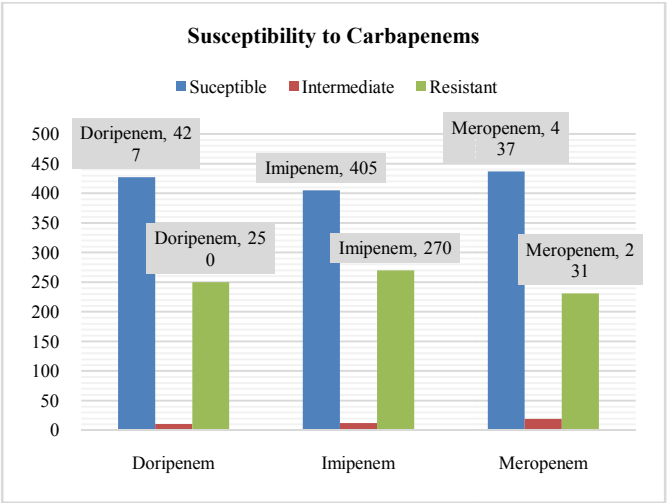
Sex	Total no of Samples Tested by Culture	No of Positives for *P. aeruginosa* (%)	No of Negatives for *P. aeruginosa* (%)
Male	5407(31.78%)	422(7.8%)	4985(92.19%)
Female	11604(68.21%)	265(2.2%)	11339(97.71%)
Total	17011	687	16324

During the study period (January 2016to December 2017) we have received 17011 urine samples for routine microscopy and aerobic culture and antimicrobial susceptibility. Of 17011 urine samples, 5407 samples were from male patients and 11604 were from female patients. Of 5407 urine samples from male, 422(7.8%) patients grew *P. aeruginosa.* Of 11604 urine samples from female, 265(2.2%) patients grew *P. aeruginosa.* Overall positivity rate for *P. aeruginosa*from 17011 urine samples was 4.03%.

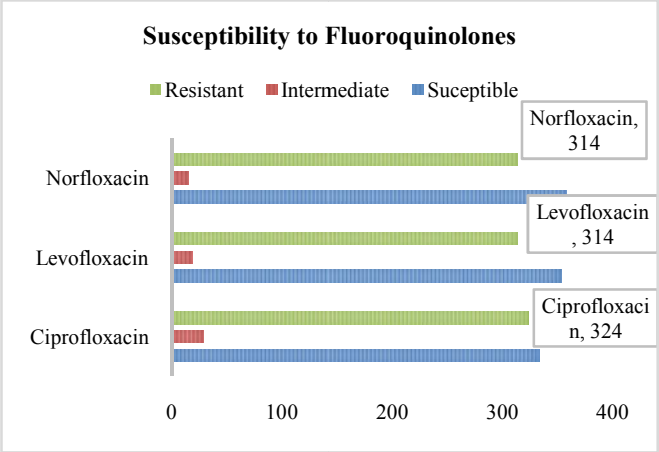


Graph 1 Distribution of *Pseudomonas aeruginosa* among different age groups

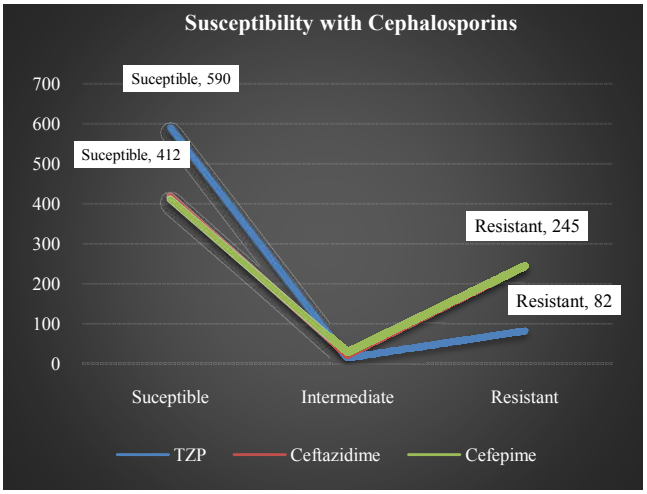
Of the total 687 strains of *P. aeruginosa*, maximum patients 257(37.40%) were in more than 45 years of age group followed by 36-45 years of age group with isolation rate of 28.52%. Only 31 samples grew *P. aeruginosa* in the age group of 1-13 years.



Graph 2 Of the 687 isolates of *P. aeruginosa,* 407(59.24%) isolates were sensitive to Doripenem, 15 were intermediate and 265(38.57%) were resistant.Of the 687 isolates of *P. aeruginosa,* 405(58.95%) isolates were sensitive, 12 were intermediate and 270 (39.30%) were resistant with Imipenem.Of the 687 isolates of *P. aeruginosa,* 437(63.60%) isolates were sensitive to Meropenem, 19 were intermediate and 231(33.62%) were resistant. The average susceptibility of *P. aeruginosa* with carbapenems was 60.59% and resistance was 37.16%. Among these three carbapenems, meropenem is found to have better susceptibility in-vitro as compared to imipenem and doripenem but in-vivo studies are needed further to establish the comparison and efficacy.



Graph 3 Graph 1: Of the 687 isolates of *P. aeruginosa,* 334(48.61%) isolates were sensitive to Ciprofloxacin, 29 were intermediate and 324(47.16%) were resistant. Of the 687 isolates of *P. aeruginosa,* 354(51.52%) isolates were sensitive, 19 were intermediate and 314(45.70%) were resistant with Levofloxacin. Of the 687 isolates of *P. aeruginosa,* 358(52.11%) isolates were sensitive to Norfloxacin, 15 were intermediate and 314(45.70%) were resistant. The average susceptibility of *P. aeruginosa* with Fluoroquinolones was 50.74% and resistance was 46.18%. Norfloxacin is used for testing and reporting of urinary tract isolates only.



Graph 4 Of the 687 isolates of *P. aeruginosa,* 590(85.88%) isolates were sensitive to Piperacillin-tazobactam (TZP), 15 were intermediate and 82(11.93%) were resistant. Of the 687 isolates of *P. aeruginosa,* 418(60.84%) isolates were sensitive, 24 were intermediate and 245(35.66%) were resistant with Ceftazidime. Of the 687 isolates of *P. aeruginosa,* 412(59.97%) isolates were sensitive to Cefepime, 30 were intermediate and 245(35.66%) were resistant. Piperacillin-tazobactam (TZP), which has got good anti-pseudomonal activity is found more sensitive (85.88%) as compared to other cephalosporins.

DISCUSSION

Pseudomonas *aeruginosa* infections are increasing both in hospital and in general community. It has been reported as one of the leading nosocomial pathogen, particularly among immune compromised patients admitted in intensive care units. It is also a predominant pathogen isolated in burn infections. *Pseudomonas aeruginosa* is the third leading cause of hospital-acquired urinary tract infections (UTIs), accounting for about 12 % of all hospital acquired infections. Instrumentation of urinary tract leads to breach in anatomical barrier that causes invasion of the organism into blood stream causing bacteraemia and septicaemia. This has been shown to be the source of nearly 40 % of *Pseudomonas* bacteraemia. *P. aeruginosa* has been identified as the fourth most common causing catheter associated urinary tract infections. Urinary tract infection caused by *P. aeruginosa* are usually hospital-acquired and related to urinary tract catheterization, instrumentation of urinary tractor surgery and prolonged hospitalisation with intensive antimicrobial chemotherapy[19]. *P.aeruginosa* was the second most common cause ofpneumonia, the fourth most common cause of urinary tract infection, and the sixth most common blood stream isolate inintensive care units (ICUs). Potential reservoirs of *Pseudomonas* infection have been identified in hospital environment, including respiratory equipment, cleaning solutions, disinfectants, sinks, vegetables, flowers, endoscopes, andphysiotherapy pools[20].

Extensive use of antimicrobial agents as empirical therapy without evidence of culture susceptibility pattern and local antibiogram has resulted in development of drug resistance. The novel evolutionary antimicrobial resistance mechanisms of bacteria have also resulted in the emergence of drug resistant bacteria including multidrug resistant (MDR) and extensively drug resistant (XDR) organisms. The in-vivo efficiency ofmany antimicrobial agents used for treatment of infections has becomequite limited due to the development of resistance. There is a severe threat from antimicrobial resistant organisms that is accumulatingand accelerating day by day[21]. The increasing prevalence of health-care associated infections (HAIs) produced by multidrug-resistant (MDR) *P. aeruginosa* strains severely compromises theselection of appropriate antimicrobial therapy. Therefore these HAIs are associated with significant morbidity and mortality and additional health care cost[22]. For *P. aeruginosa*, antibiotic resistance is an increasing problem and is known to be resistant to all the available antimicrobials including carbapenems, older agents like polymyxin B and colistin, aminoglycosides, fluoroquinolones and anti-pseudomonal antibiotics like piperacillin-tazobactam and cefeperazone-salbactam. A varying degree of resistance to all known anti-pseudomonal antibiotics have been reported in different areas of theworld by different authors[23, 24].

The current increase in incidence of MDR isolates of *P. aeruginosa* raises serious concerns. Multidrug-resistance in *P. aeruginosa* is defined as the resistance to ≥3 of the following classes of antibiotics: penicillin's/cephalosporins/monobactams, carbapenems, amino glycosides, and fluoroquinolones[25]. The increasing prevalence of MDR *P. aeruginosa* from 36 to 52 % were reported in one of the Egyptian study from clinical and environmental samples. These environmental sources act as a reservoir for dissemination of organisms into health care settings[26]. Antimicrobial susceptibility and ESBL prevalence studies with *P. aeruginosa* from burn patients conducted in Pakistan and Iran have reported, 29 and 30 % MDR phenotype respectively[27]. *P. aeruginosa* is notorious to develop drug resistance during prolonged therapy with all antimicrobial agents. Therefore, isolates that are initially susceptible may become resistant within 3 to 4 days after initiation of therapy. Testing of repeat isolates may be warranted. Infections caused by *P. aeruginosa* are difficult to treat andoften require combination of drugs to prevent emergence of drug resistance[28]. High rates ofresistance to antibiotics are associated with nosocomial *P. aeruginosa* strains. It has been associated with sporadicor clustered cases of infection generally confinedto single hospitalization units[29].During the study period (January 2016to December 2017) we have received 17011 urine samples for routine microscopy and aerobic culture and antimicrobial susceptibility. Of 17011 urine samples, 5407 samples were from male patients and 11604 were from female patients. Of 5407 urine samples from male, 422(7.8%) patients grew *P. aeruginosa.* Of 11604 urine samples from female, 265(2.2%) patients grew *P. aeruginosa.* Overall positivity rate for *P. Aeruginosa* from 17011 urine samples was 4.03%. In the present study higher proportion of males (7.8%) were detected positive for *P. aeruginosa* than their female (2.2%) counterparts. These results are in concordance with other studies which have reported higher prevalence of *P. aeruginosa* in males than in females[30, 31].In one of the study from North Nigeria, where females found to be more commonly infected by this pathogen as compared with males[32]. Another important factor in this study is age group of the patients. The isolation rate was higher among old age greater than 45 years. Of the total 687 strains of *P. aeruginosa*, maximum patients 257(37.40%) were in more than 45 years of age group followed by 36-45 years of age with isolation rate of 28.52%. Only 31 samples grew *P. aeruginosa* in the age group of 1-13 years. In view of this study advancing age might be one of the predisposing factor. There are studies from North Nigeria that reported similar observation with higher incidence in older population. Thus it is wise to give due attention to UTI when catheterizing older patients. Increasing resistance to different antipseudomonal drugs particularly among hospital strains has been reported world-wide. This is a serious therapeutic problem in the management. In our study we have tested susceptibility profiles of *P.aeruginosa* to commonly used antimicrobial agents in the area. Of the 687 isolates of *P. aeruginosa,* 334(48.61%) isolates were sensitive to Ciprofloxacin, 29 were intermediate and 324(47.16%) were resistant. 354(51.52%) isolates were sensitive, 19 were intermediate and 314(45.70%) were resistant with Levofloxacin. With norfloxacin of the 687 isolates of *P. aeruginosa,* 358(52.11%) isolates were sensitive, and 314(45.70%) were resistant. In general average susceptibility of *P. aeruginosa* with Fluoroquinolones was 50.74% and resistance was 46.18%. Norfloxacin is used for testing and reporting of urinary tract isolates only.The Susceptibility of the isolates to Ciprofloxacin is very important for local consumption compared to other studies, whereby 40.5%[33], 50%[34] and 72.41 %[35] susceptibility were observed, ciprofloxacin and norfloxacinshould be given due attention and should be used when necessary as an alternative therapeutic agent for resistant isolates.

Aminoglycosides, especially amikacin and gentamicin is a known frontline antibiotic in the treatment of bacterial infection by gram negative bacteria. However, emerging reports showed increased prevalence of resistance to these drugs. In this study, 36.75 % isolates were observed resistant for aminoglycosides. This resistance with aminoglycosides is lower when compared with studies conducted in North-eastern Nigeria[36] in which all isolates were found resistant. Acquired resistance to aminoglycosides can be due to the production of aminoglycoside-modifying enzymes encoded by horizontally acquired resistance determinants, or by mutations that reduce aminoglycoside accumulation in the bacterial cell[37]. The most prevalent aminoglycoside-modifying enzymes found in P. aeruginosa are the acetyl-transferases AAC(6¢)- II (resistance to gentamicin, tobramycin and netilmicin), AAC(3)-I (resistance to gentamicin), AAC(3)-II (resistance to gentamicin, tobramycin and netilmicin) and AAC(6¢)-I (resistance to tobramycin, netilmicin and amikacin), and the adenylyl-transferase ANT(2¢)-I (resistance to gentamicin and tobramycin)[38, 39]. In-vitro susceptibility data are essential support for the selection of antimicrobial chemotherapy for *P. aeruginosa* infections, because of the frequency and variability of acquired resistance shown by clinical isolates. Susceptibility testing is well standardised for most anti-pseudomonal agents, but there are no recommended breakpoints for susceptibility testing of polymyxin B or colistin[40]. MIC determination is preferable in the case of these drugs because the correlation with disk diffusion testing is relatively poor[41].Of the 687 strains of *Pseudomonas aeruginosa*, 6 isolates were resistant to colistin and polymyxin B with MIC more than 4 µg/ml and 8 µg/ml respectively. Colistin should generally be given with a loading dose and at maximum recommended doses, and used in combination with other agents. The only approved MIC method forcolistin and polymyxin B testing is broth micro dilution. Disk diffusion and gradient diffusion should not be performed as per CLSI 2018 guidelines (CLSI. Performance Standards for Antimicrobial Susceptibility Testing. 28th ed. CLSI supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2018). These strains were not confirmed with broth micro dilution method but they were retested with same automated system which has produced similar results. The rationale for combination chemotherapy is essentially to reduce the chances of selection of resistant mutants during therapy, as well as to exploit the potential synergistic activity of some agents. The preferred combination remains aminoglycosides and b-lactams, as synergism between these drugs has been demonstrated by invitro studies[42, 43, 44] and results of several clinical studies point to the superiority of similar regimens as opposed to monotherapy for the treatment of *P. aeruginosa* bacteraemia, especially in neutropenic patients[45, 46, 47, 48]. Most physicians continue to prefer combination therapy for treatment; combination chemotherapy, although not showing an unequivocally superior effect to monotherapy, has never been shown to be inferior[49, 50].

Several factors indicate that the emergence and spread of drug-resistant *P. aeruginosa* can be related to the overuse of antimicrobial agents, although the risk appears to differ with different agents. A strong association between use and resistance has been documented for carbapenems. A significant increase in the incidence of imipenem resistant *P. aeruginosa* was observed at a large New York medical centre following an intervention that restricted the use of cephalosporins (in order to control the spread of ceftazidime-resistant Klebsiella pneumoniae) and caused, at the same time, an increased imipenem consumption[51]. A strong association between imipenem use and resistance in *P. aeruginosa* was also observed in a 3-year survey of antimicrobial consumption and resistance carried out in a German hospital[52]. In that study, imipenem consumption was found to be significantly associated with imipenem resistance rates and also with ceftazidime and piperacillin-tazobactam resistance rates from the same month and from the following month. By contrast, no correlation was observed between the consumption of ceftazidime or piperacillin-tazobactam and resistance to the same drugs or to imipenem. Finally, in a cohort study comparing the relative risks for the emergence of resistant P. aeruginosa in patients treated with different anti-pseudomonal agents, imipenem was found to be associated with a significantly higher overall risk of emergence of resistance, and exhibited the highest risk of emergence of resistance to itself. On the other hand, ceftazidime had the lowest overall risk for the emergence of resistance and showed no significant association with the emergence of resistance to itself. Piperacillin and ciprofloxacin showed a low overall risk for emergence of resistance, but were distinctly associated with the emergence of resistance to themselves[53]. In the present study, Of the 687 isolates of *P. aeruginosa,* 407(59.24%) isolates were sensitive to doripenem, 15 were intermediate and 265(38.57%) were resistant. With imipenem, of the 687 isolates*,* 405(58.95%) isolates were sensitive, 12 were intermediate and 270 (39.30%) were resistant. 437(63.60%) isolates were sensitive to meropenem, 19 were intermediate and 231(33.62%) were resistant.Meropenem is found to have overall good susceptibility as compared with other carbapenems in-vitro but further in-vivo clinical evaluation studies are needed to confirm the role of meropenem for treatment of complicated urinary tract infections.

The effect of antimicrobial restriction on *P. aeruginosa* resistance has been investigated in a recently published study carried out in a large teaching hospital[54].In that study, the intervention caused a remarkable reduction in the use of ceftazidime and a consistent reduction in the use of imipenem, and was associated with a significant decrease in the resistance rates to these two drugs. Interestingly, a significant decrease in resistance rates was also observed for piperacillin and aztreonam, notwithstanding minimal changes in the overall use of piperacillin and piperacillin-tazobactam and a consistent increase in the use of aztreonam. In our study, of the 687 isolates of *P. aeruginosa,* 590(85.88%) isolates were sensitive to Piperacillin-tazobactam (TZP), 15 were intermediate and 82(11.93%) were resistant.piperacillin-tazobactam (TZP), which has got good anti-pseudomonal activity is found more sensitive (85.88%) as compared to other cephalosporins. In another prospective study, carried out in a medical ICU in another large teaching hospital, ceftazidime and ciprofloxacin restriction, in combination with an antimicrobial rotation strategy, was shown to be effective in reducing the overall incidence of ventilator-associated pneumonia and the resistance rates of P. aeruginosa to various antimicrobial agents, including extended-spectrum cephalosporins, aminoglycosides and fluoroquinolones[55].

CONCLUSION

P. aeruginosa remains one of the most important and difficult to treat nosocomial pathogens. MDR strains are increasingly being reported and, in these cases, the choice of therapy often becomes very limited, especially when looking for antimicrobial combinations to treat severe infections. An additional matter of concern is represented by the fact that no new antimicrobial agents, active against MDR strains of *P. aeruginosa*, are in advanced stages of development as therapeutic options. While the medical community awaits the development of new drugs, MDR *P. aeruginosa* strains are likely to represent an increasing threat, and every effort should be made to preserve as long as possible, or to restore, the efficacy of currently available agents.

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Conflict of Interest

Author declares no conflicts of interest

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Not applicable

Guarantor

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