DOI: https://doi.org/10.54393/pbmj.v5i7.667

PAKISTAN BIOMEDICAL JOURNAL

https://www.pakistanbmj.com/journal/index.php/pbmj/index

Volume 5, Issue 7 (July 2022)

Original Article

Multi Drug Resistance *Pseudomonas aeruginosa* Frequency and Antibiogram in a Tertiary Teaching Care Hospital in Pakistan

Syed Hasnain Ali Shah[1], Wajid Ali[2*], Furqan Ali Shah[3], Shaikh Fahad Falah[4], Erum Rehman[5], Amna Umar[5], Yumna Hidayat[6], Saira Afreen[6], Aayesha Riaz[7], Irfan Ullah[6]

[1]Department of Pharmacology, Kabir Medical College, Peshawar, Pakistan
[2]Department of Pharmacology, Ayub medical College, Abbottabad, Pakistan
[3]Department of Pharmacology, Pak International Medical College, Peshawar, Pakistan
[4]Department of Pharmacology, Khyber Girls Medical College, Peshawar, Pakistan
[5]Department of Pharmacology, Peshawar Medical and Dental College, Peshawar, Pakistan
[6]Department of Life Sciences, School of Science, University of Management and Technology, Lahore, Pakistan
[7]Department of Parasitology and Microbiology, Faculty of Veterinary and Animal Sciences PMAS Arid Agriculture University Rawalpindi

ARTICLE INFO

Key Words:
Multi Drug Resistance, Pseudomonas aeruginosa, Antibiotics, Susceptibility, Resistance

How to Cite:
Ali Shah, S. H., Ali, W. ., Ali Shah, F. ., Fahad Falah, S. ., Rehman, E. ., Umar, A. ., Hidayat, Y. ., Afreen, S. ., Riaz, A. ., & Ullah, I. . (2022). Multi Drug Resistance Pseudomonas Aeruginosa Frequency and Antibiogram in A Tertiary Teaching Care Hospital in Pakistan: Frequency and Antibiogram of Pseudomonas aeruginosa . Pakistan BioMedical Journal, 5(7). https://doi.org/10.54393/pbmj.v5i7.667

***Corresponding Author:**
Wajid Ali
Department of Pharmacology, Ayub Medical College, Abbottabad, Pakistan
dr.wajidali161@gmail.com

Received Date: 7th July, 2022
Acceptance Date: 14th July, 2022
Published Date: 31st July, 2022

ABSTRACT

Antibiotic usage and misuse increases the risk of developing bacteria that are resistant to treatment. A Gram-negative, aerobic bacillus called Pseudomonas aeruginosa is mostly responsible for nosocomial opportunistic infections. **Objectives:** To assess pathogen load and drug susceptibility profiles of Peshawar clinical specimens collected with MDR *Pseudomonas aeruginosa* isolates. **Methods:** Isolates were gathered from a variety of specimens, including pus, tracheal aspirate, swabs containing wound samples, fluids such as urine or blood, from department of microbiology hospital of Khyber teaching Peshawar. Clinical in-vitro study which were carried out at the Pharmacology Department, University of Peshawar. Kirby Bauer Disc diffusion method was used to identify the pattern of antibiotic susceptibility. Requirements of Clinical and Laboratory Standards Institute (2018) were followed for processing samples. **Results:** *P. aeruginosa* was found to be multidrug-resistant in about 56 percent of cases. The majority of the isolates (36.5%) were found in people between the ages of "60-80". Pus included the greatest percentage of MDR *P. aeruginosa* (34.2%), followed by tracheal aspiration (21.7 percent). Colistin had the highest sensitivity (100%) and was followed by ceftolozane/tazobactam (61 percent). With imipenem, the least sensitivity was noticed (20 percent). However, all anti-pseudomonal medications showed an increase in resistance. **Conclusion:** In our system, MDR *P. aeruginosa* infections are becoming more frequent. This threat can be avoided by prescribing antibiotics carefully. For the community to receive appropriate healthcare, regular lab identification and surveillance of this resistant pathogen is necessary.

INTRODUCTION

The primary therapeutic method utilized in medicine to treat a variety of bacterial illnesses is antimicrobial medication. One of the most significant developments in contemporary science is the production of antibiotics. Millions of lives have been saved by antibiotics. One of the biggest challenges in the world is the emergence of antibiotic resistance [1]. Increased use and occasionally abuse of antibiotics leads to the development of germs that no longer respond to treatment [2]. Pseudomonas aeruginosa is an aerobic, non-fermenting Gram-negative bacillus that predominately causes nosocomial opportunistic infections [3]. P. aeruginosa with therapeutic medicine also have the capacity for acquiring and expressing the number of mechanisms of resistance

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via the "loss of the OprD porins, overexpression of efflux pumps, modifications in the target site, and production of specific b-lactamases and carbapenemases enzymes"[4]. Fluoroquinolones (ofloxacin, ciprofloxacin), antipseudomonal penicillins (ticarcillin, piperacillin), cephalosporins (ceftazidime, cefepime), aminoglycosides (amikacin, gentamicin), and carbapenems are now the most effective medications against P. aeruginosa [5]. As defined by Center for Disease Control and Prevention, MDR P. aeruginosa has developed resistance to at least one agent in three or more groups of antibiotics [6]. Global superbug MDR P. aeruginosa has been related to adverse outcome measures, such as increased morbidity and mortality [7]. About 10,000 individuals are admitted to hospitals each year due to infections caused by P. aeruginosa MDR, and in extreme instances, fatality rates of up to 20 percent have been reported [8]. P. aeruginosa is determined to be a highly common cause of nosocomial pneumonia and a variety of infections of the eye, ear, and urinary tract [9]. Drug-resistant bacteria appeared to be the result of concurrent "overuse and illogical use of antibiotics" as well as the de-novo production of certain resistant germs [10]. Because of this, P. aeruginosa is almost resistant to the use of several antibiotics in the treatment of life-threatening illnesses [11]. It is necessary to analyze a recent in-depth investigation via resistance of antimicrobial pattern by MDR P. aeruginosa in order to gauge this organism's susceptibility to routinely prescribed antibiotics. The medical professionals might then employ this knowledge to optimize the range of effective treatment options available. The goal of the current study was to assess the prevalence and trends in antibiotic susceptibility of MDR P. aeruginosa isolated from various clinical samples at the Peshawar hospital.

METHODS

An in-vitro clinical trial was conducted at the Pharmacology Department, Peshawar University. In the Kyber Teaching Hospital's Microbiology Lab, 1800 samples from pus, swabs having wound sample, fluids like blood and urine, and endotracheal secretion was proceeded in October 2021 for the sensitivity and culturing according to established guidelines starting. Specimens were inoculated on MacConkey and Blood Agar and the petri dishes were incubated for 24 hours at 37°C. All of the catalase, as well as gram-negative and positive oxidase colonies, were determined beforehand toward the species levels employing a standard microbiological procedure. The Kirby-Bauer disc diffusion method was used to assess antibiotic susceptibility. In this method a lawn of bacterial inoculum was made on 150 mm Mueller Hinton Agar plate (Oxoid UK). Antibiotic disc of Piperacillin/ tazobactam (100/10ug), Imipenem (10 µgm), Aztreonam (30 µgm), Ceftazidime (30 µgm), Amikacin (30 µgm), Gentamicin (10 µgm), Ciprofloxacin (5 µgm), Colistin (10 µgm), Ceftolozane/tazobactam (30/10µgm) were placed on agar plates which were then incubated at 35°C for 16–24 hours prior to results being determined. According to CLSI recommendations(2018), inhibition zone of growth in every disc of antibiotic was assessed and classified either as sensitive or resistant. SPSS (Version 21.0) was used to analyze the data. Descriptive analyses were given as mean with Standard Deviation for the numerical variables. For categorical variables, frequency and percentage were determined. The relationship between antibiotic susceptibility and resistance patterns were evaluated using the chi-square test. P values lower than 0.05 were considered significant.

RESULTS

One thousand eight hundred and seventy-seven P. aeruginosa strains were isolated from the 1800 samples on the basis of identification techniques. 80 (46%) of these were P. aeruginosa with non-MDR and 98 (56%) were P. aeruginosa MDR. According to the Table 1, prevalence of MDR P. aeruginosa was much more common in females (55 percent) as compared to males, who made up 47 percent of the population.

TOTAL SAMPLES	MDR	NON-MDR
1800	98 (56%)	80 (46%)
Male 86	46 (47%)	41 (51.7 %)
Female 90	53 (55%)	38 (47 .9%)

Table 1: Total number of P. aeruginosa samples

According to the data represented in Table 2, the majority of the isolates were collected from pus (35 percent), followed by tracheal aspiration (21.7 percent), urine (19.7 percent), and the least amount was obtained from ear swabs (3.2 percent). The statistically significant P value was less than 0.05. Compared to the outpatient department, where the percentages of isolates were 60 and 42 percent respectively, the indoor patient department have seen a higher percentage of the organism.

SOURCE	MDR	NON-MDR	P-value
	98 (56 %)	80 (46 %)	
Pus	34 (35.1%)	13 (16.2%)	
Tracheal asp	21 (21.7%)	18 (22.6%)	
Urine	19 (19.7%)	25 (31.5%)	0.035
Sputum	15 (15.5%)	15 (18.8%)	
Blood	11 (11.2%)	9 (11.2%)	
Ear swab	3 (3.2%)	5 (6.2%)	

Table 2: P. aeruginosa MDR prevalence in specimens

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As demonstrated in Table 3, surgical ward had the highest percentage of MDR P. aeruginosa isolates 27(28.2 percent), while gynecology ward had the lowest percentage 4 (5.2 percent). Increased resistance to practically all anti-pseudomonal medications was seen in MDR P. aeruginosa. The most pronounced resistance was seen with imipenem (82.7 percent). The percentage of people showing resistance to Ciprofloxacin were 81.5%, Ceftazidime (79%), Gentamycin (75.3%), Amikacin (67%), Piperacillin/tazobactam (63%) and Ceftolozane/tazobactam (41%), respectively. According to Figure 1, all samples of MDR P. aeruginosa were completely susceptible to colistin.

DEPARTMENTS	MDR	NON-MDR
Ward of Gynecology	4 (5.2%)	1 (1%)
ICU	17 (17.6%)	18 (22.6%)
Surgical ward	27 (28.2%)	31 (39.1%)
Medicine ward	12 (12.4%)	9 (11.2%)

Table 3: The proportion isolates of the MDR found on behalf of various department

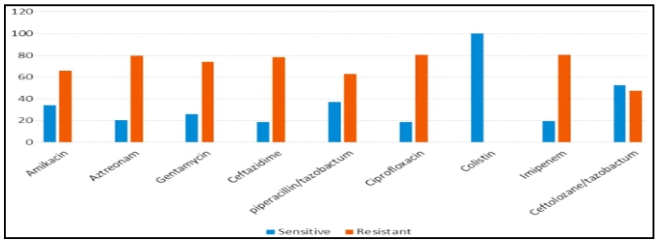

Figure 1: The pattern of resistance and sensitivity from MDR P. aeruginosat

DISCUSSION

A well-known Gram negative bacillus called P. aeruginosa has been related to a wide range of diseases, particularly in immunocompromised people, including pneumonia, bacteremia, and also the infections of the urinary system, skin, and soft tissues [12]. P. aeruginosa clinical isolates have the potential to be resistant to numerous classes of antibiotics, leaving clinicians with a limited selection of therapeutic antibacterial medications or regimen options for the treatment of infectious illnesses. In this study, MDR P. aeruginosa was found to be 56.2 percent common, compared to 57.8 percent and was comparable to the study reported by Zahoor et al., [13]. Studies conducted in the Punjab, Lahore and Rawalpindi produced the mentioned findings: 22.7 percent, 20 percent, and the 21 percent. A study carried out in an Indian tertiary care facility found an 85 percent frequency worldwide [14]. In 2017, 47 percent frequency was noted in Africa. Meanwhile, Egypt also reported a greater frequency (56%) in 2015. From 235 different strains of pseudomonas, 14% of MDR isolates were found. Given the substantial literature review that has been done above, it can be said that P. aeruginosa resistance has been steadily rising over time in Pakistan and throughout the rest of the world. The unusual structure of the P. aeruginosa, with a genomic size (bp = 6.3M) is consider the largest sequence of all the bacteria and thus may be the cause of the rise in resistance. This sequence's flexibility results in resistances that are inherent to antibiotics, including regulatory genes in the greatest number, which are also responsible for mutational modifications in the efflux pump or the porin structure [15]. In this study, females (55%) were more likely than males (47 percent) to have MDR P. aeruginosa. A study conducted in Nepal revealed the following findings, with nearly identical results for both genders (55.1%) and men (44.9 percent) [16]. A study conducted in Pakistan in 2017 produced conflicting findings, showing P. aeruginosa (MDR) that were much prevalent in the males (56 percent) than in females (46 percent). Study carried out in the Iraq and also in India have produced conflicting findings. In those investigations, P. aeruginosa (MDR) prevalence in males were higher as compared to females, at 55% and 56%, respectively [17]. The gender prevalence may vary with regional variation and study era could help to explain this. In our investigation, the majority isolates of P. aeruginosa (34.2%) was detected in pus, following tracheal aspiration (21.7%) and urine (19.7 percent). Our findings are somewhat consistent with past research in which pus samples were the most frequent source [18]. A proportion of patients with surgical injury issues were found to have damaged areas that were easy targets for nosocomial infections. This explains why isolates exist in the largest amount in the pus. Other potential contributing factors to the development of the resistant strains include the use of antiseptics without proper protocols and inadequate ward cleanliness. In our analysis, the surgical ward contributed the majority of MDR strains (27.9%), followed by the intensive care unit (17.6%), the medicine ward (12.4%), and the gynecological ward (5.2 percent). According to a 2018 study by Saeed et al., the ICU is a substantial source of MDR isolates [10]. The depleting effects of a protracted hospital stay and the usage of medical equipment like airways, cannula and catheters etc. make intensive care unit patients particularly conducive to infection [19]. Currently available drugs against MDR P. aeruginosa include Fluoroquinolones (ofloxacin, ciprofloxacin) and antipseudomonal penicillins (ticarcalin, piperacllin), cephalosporins (ceftazidime, cefepime), aminoglycosides (amikacin, gentamicin) and carbapenems (imipenem, meropenum). Yet, strains of P. aeruginosa have ultimately outplayed our most effective curative measures. Our research, like other studies, has shown resistance very high to each of -lactam antibiotic. The antibiotics, imipenem (81.6%), ciprofloxacin (81.5%), ceftazidime (79%), and gentamycin (75.3%) were shown to have the highest

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resistance to MDR strains, whereas Colistin (100%) and C/T showed the maximum susceptibility in these bacteria (41 percent). MDR P. aeruginosa has the highest resistance to imipenem (100 percent), followed by the gentamycin (98 percent), amikacin (77.8 percent) and the piperacillin/Tazobactam (68.1 percent). It is clear that prevalence of Pseudomonas MDR strain is rising in Pakistan. The widespread use of these medications in secondary care hospitals is to blame for the rise in resistance in our community. According to a widely accepted idea, the usage of antibiotics and the emergence of resistance are related causally. Ceftazidime was 100 percent resistant to P. aeruginosa, whereas imipenem was 95% sensitive, according to an Iraqi investigation [20]. The gram-negative bacteria are treated with the polymyxin B antibiotic colistin. Although the clinical use of this medication as well as empirical treatments are limited because of its confined index of therapeutic as well as its significant side effects, colistin is a sensitive medication both in our environment and throughout the world [17].

CONCLUSION

Over the past few decades, resistance of P. aeruginosa has increased. The results of the current study indicated that MDR strains were highly resistant to common treatment drugs. The medication that demonstrated the excellent activity against Pseudomonas was ceftolozane/tazobactum. For the community to receive appropriate healthcare, there must be regular lab identification and surveillance of this resistant infection.

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