Journal of evidence-based medical research

Antibacterial Prevalence of Multidrug Resistant Pseudomonas Aeruginosa from Critically Ill Patients

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Abstract

Background: *Pseudomonas aeruginosa*, an adaptive pathogen leads to broad-spectrum infection in human. The treatment of infection is difficult as *Pseudomonas aeruginosa* is innately imperious to numerous antibiotics.
Objective: Therefore, the aim of this study is to investigate multiple drug resistance (MDR) pattern of *Pseudomonas aeruginosa*.
Methods: For this purpose, laboratory based positive samples from different sources including blood, urine, peritoneal fluid and tracheal swabs were selected and then processed for the isolation of MDR *Pseudomonas aeruginosa*. Bacterial spp. was isolated and purified by using standard microbiological practices. Purified cultures were processed for the bacterial identification by using different staining techniques, morphological, physiological and biochemical analysis. Final characterizations was performed, on the basis of 16S rRNA analysis. For this purpose, genomic DNA was extracted and 16S rRNA primers designed. Gene amplification of 16S rRNA was performed with the help of 16S rRNA primers in TaqMan polymerase chain reaction. Attribute of *MDR* was assessed by performing antibiotic drug sensitivity reaction.
Results: Antibiotic reveled the resistance of *Pseudomonas aeruginosa* against multiple drugs. For instance, 47% *Pseudomonas aeruginosa* were resistant to carbimipenem, 46% were resistant to meropenem, 37% were resistant to tazobactam, 56% were resistant to ciprofloxacin, 49% were resistant to gentamycin, 44% were resistant to cetazidmine and 53% were resistant to levofloxacin. Results showed lowest resistance towards tazobactam and highest to ciprofloxacin. The attribute of highest resistance against ciprofloxacin was further evaluated by gene amplification of ciprofloxacin resistant *Pseudomonas. Aeruginosa*. Gene amplification revealed the 90% ciprofloxacin resistant strains contained the *ParC gene.*
Conclusions: In this study, we concluded that selected *Pseudomonas aeruginosa* showed high resistant pattern against ciprofolxacine and carbapanam, which indicated *Pseudomonas aeruginosa* as life threatening pathogen for human.
Keywords: Pseudomonas aeruginosa, Antibacterial, Drug Resistance

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Introduction

Pseudomonas aeruginosa is a ubiquitous pathogen and Gram-negative bacteria. *(1)*. *P. aeruginosa* is a familiar microorganism *(2)*. *P. aeruginosa* was first identified in 1894, and it is one of the most important spp *(3)*. It is found in plant, sediments fungi, water, soil, sea and rhizosphere plant *(4)*.Approximately 11-13.8% nosocomial infection are due to *P. aeruginosa*. *P. aeruginosa* are responsible for a lots of hospital acquired disease in ICU, approximately 13.2-22.6% nosocomial pneumonia in pediatric ICU is also mostly caused by *P. aeruginosa*. *P. aeruginosa* was associated with being liable for about 6% of all cases *(5)*.In 2003 as per NNIS information, *P. aeruginosa* isolates in ICU about fluoroquinolones 29.5%, Imipenem 21.1%, and third-age cephalosporins 31.9% and between 1998 and 2002 all were greater than mean antimicrobial resistant rates. *(6)*. Phenotypically, *P. aeruginosa* isolated from severe infections are extensively different from those isolated from prolonged infections.*(7)*.Three domains's lipopolysaccharide of .*P. aeruginosa* makes a polysaccharide core region, a membrane-anchored lipid A, and an extremely changeable O-specific polysaccharide (O-antigen or O-polysaccharide)*(8)*.Due to continued outbreak of antimicrobial resistant strains, therapeutic options are becoming increasingly limited; so the morbidity and mortality due to *Pseudomonas aeruginosa* has been increased *(9)*.

P. aeruginosa caused hospital-acquired infection, ventilator-associated pneumonia and caused hospitalized patient's respiratory tract contamination. *(10)*. The intrinsic pattern of resistance of microorganism found integrated *(11)*.The hydrophilic nature and natural phenomenon of chromosomal mediated β- lactamase, Amp C and efflux pump found in the membrane of *P. aeruginosa*, all contribute to intrinsic resistance. The outer membrane is semipermeable that prevents the small hydrophilic molecules like β-lactam antibiotics from entering into the membrane's porin protein channels *(12)*.*P.* aeruginosa's external layer is estimated to be 10-100 times less permeable than that of *E. coli*, with less amount of huge passage porins (developed via (*OprF*) furthermore a numerous quantity of tiny passage porins (developedzz via proteins like *OprD* and *OprB*) *(13)*. There are six RND efflux pumps in the (RND) resistance–nodulation–division family *(14)*.It is found on objects like toilets, hospital room sinks, showers, and patient care equipment, especially respiratory ventilators because it is non-picky and need only few nutrients *(15)*.

It is also found in GIT rather than not a major part of human normal flora *(16)*. Nosocomial or hospital-acquired infections are referred to as healthcare-associated infections (HAI) *(17)*.The abundant worldwide spread of multiple drug resistant *P. aeruginosa*. has become a public health problem *(18)*. Both inherent and learnt mechanisms, antibiotic resistance have been discovered in *P. aeruginosa (16)*.Carbapenems are used as a first-line treatment for *P. aeruginosa(19)*.*Pseudomonas aeruginosa*, and *Acinetobacter baumannii*, posing a critical threat to global public health. The fatality rate of MDR Gram-negative infections are higher than other gram-negative infections *(20)*

Gram-negative infections are developing more common and difficult to treat *(21)*.The stock of antibiotics available for resistant gram-negative infections has become fewer in number due to the introduction and spread of carbapenem-resistant bacteria *(21)*. This study aims to sum up the novel data on the epidemiology of carbapanam and ciprofloxacin resistance in Pakistan for non-fermenting *Gram-negative rods*, resistance mechanisms, including molecular epidemiology and prevalence in both endemic and outbreak situations.

Material and Methods

This cross sectional study conducted at. Microbiology Department, Chugtai lab Lahore from January 2012 to January 2013. Clinical samples (urine, pus, wound swabs, ascitic and bronchial fluid, blood) were collected. Materials used was Culture bottles**,** Purification Media(Nutrient Agar (Oxoid)**,**L- Agar MacConkey Agar (Oxoid) and Blood Agar was used. Biochemical test used was Gram Staining and Oxidase Test.

Identification

Clinical isolates were identified by standard methods. They were inoculated on Blood agar (Oxoid), Mac Conkeys agar (Oxoid) and Cystine lactose electrolyte deficient agar (Oxoid). Isolates were identified on the basis of colony morphology, Gram staining and biochemical tests including Oxidase, Triple sugar iron test, Catalase test,SIM Motility Test Citrate test.

Antimicrobial Testing

Antimicrobial activity were accomplished on Muller Hinton Agar utilizing anti-infection circle by utilizing plate dispersion strategy. The plate fashioned anti-infection dealers utilized are cefepime (FEP-30µg),ceftazidimie(CAZ-30µg),imipenem(IPM-10µg),meropenem(MEM-10µg),amikacin(AK-30µg),gentamicin(CN-10µg), tobramycin(TOB-10µg), ciprofloxacine(CIP-5µg), levofloxacine(LEV-5µg) and pipracillin/tazobactam(TZP-110µg). Kirby-bauer plate dissemination strategy, typical microbiology procedure for challenging development of microorganisms. From new subculture detach, inoculum were picked and swabbed it on the outside of Mueller Hinton agar. Anti-toxin circle were permeated on the outside of vaccinated agar dish and later instant brooding dated finished, the region of hindrance noticed and estimated.

DNA Extraction

There are 3 basic steps involved in DNA extraction, that is, lysis, precipitation and purification. In lysis, the nucleus and the cell are broken open, thus releasing DNA. This process involves mechanical disruption and uses enzymes and detergents like Proteinase K to dissolve the cellular proteins and free DNA.The other step, which is known as precipitation, separates the freed DNA from the cellular debris. It involves use of sodium (Na+) ions to neutralize any negative charge in DNA molecules, making them less water soluble and more stable. Alcohol (e.g isopropanol or ethanol) is then added, causes precipitation of DNA from the aqueous solution since it does not dissolve in alcohol.After separation of DNA from aqueous solution, it is then rinsed with alcohol, a process known as purification. Purification removes all the remaining cellular debris and unwanted material. Once the DNA is completely purified, it is usually dissolved in water again for convenient storage and handling.

Results

Isolation of Gram Negative Bacterial Species

Collected different samples of blood, urine, pus and sputum were performed under Gram staining procedure showed characteristics feature of Gram negative bacillus bacteria i.e. pink colored rode shaped colonies, estimated 0.5 to 0.8 µm by 1.5 to 3.0 µm. Almost all strains are motile via a single polar flagellum.

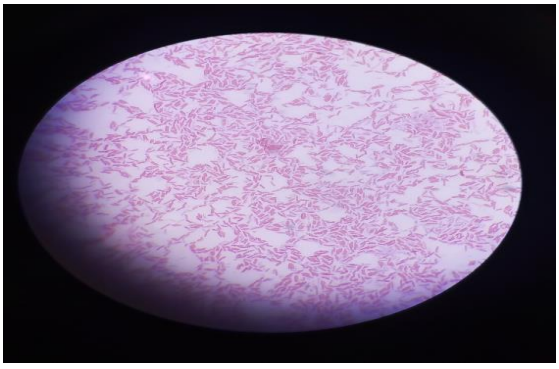

Figure 1: Slide for Gram Negative Rode Bacteria

Isolation of bacterial species

From collected samples of blood, urine, pus and sputum 57 positive bacterial strains of *Psudomonase. aeruginosa* were cultured on blood MacConkey Cystein Lactose electrolyte deficient (CLED).

1: Culture colonies of Psudomonase aeruginosa on Blood agar

P. aeruginosa strains derived different forms. One form has a seared egg shape, which is huge, smooth, by equal boundaries and an elevated form. One more type, acquired from respiratory and urinary passage secretions, has a mucoid form. For *P.aeroginosa*, large flat spreaded colonies were obtained with β-hemolysis pattern and the colonies obtained were grayish in color with fruity odor.

Figure 2: Hemolytic Flat Colonies on Sheep Blood Agar

2: Culture colonies of psudomonase aeruginosa on macConkey agar & CLED

On macConkey agar nonlactose fermenting, pale colored colonies were obtained, while on CLED agar green colored colonies of *P. aeroginosa* were obtained. Total number of sample was 100 .out of these 57-show positive blood culture on *macConkey* agar and *CLED*

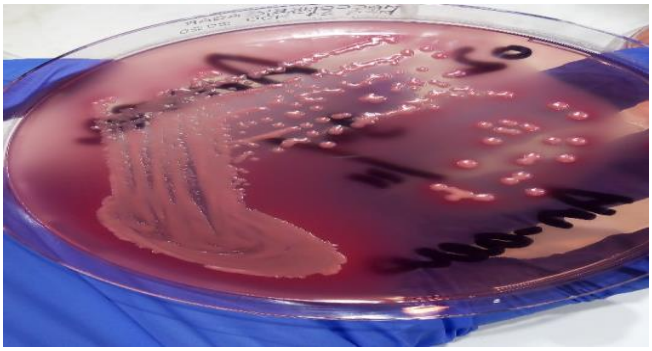

Figure 3: Pale Flat Colonies on MacConkey Agar

Biochemical characterization of psudomonase aeroginosa

Colonies obtained from culture plates were then subjected to biochemical characterization.

1. Oxidase test:

P. Aeruginosa containing oxidase enzyme, oxidized the phenylendiamine present in reagent and gave purple color. Organism changes its tone from dry (colorless) to dim purple shade inside 5-10 seconds and showed oxidase positive outcome. Total number of sample was 100.Out of these 57-show positive oxidase test.

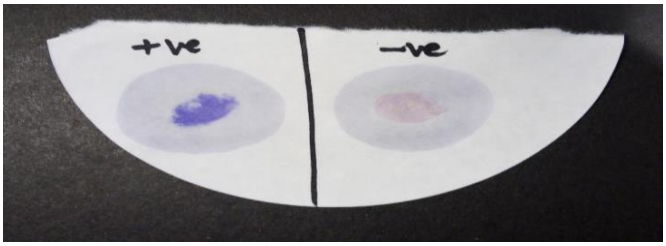

Figure 4: Oxidase Positive for *P. aeruginosa*

2 Triple Sugar Iron Test

The inoculated TSI agar after 37°c for 24 hour for *P. aeruginosa,* Severe aerobes, showed development just on the slant of the cylinder and not the butt and thusly no adjustment of the shade of both slant and butt of the cylinder detected, which indicated that no sucrose, lactose and glucose fermentation happened in *psudomonase aeruginosa,* thus a non-Lactose Fermenter. Total number of sample was 100 .out of these 57-show positive triple sugar iron test.

Figure 5: Triple Sugar Iron Test

3. Catalase test:

Catalase test was performed to identify catalytic property of *Psudomonase aeroginosa*. *P. aeroginosa* released oxygen bubbles when brought into contact of hydrogen peroxide, which indicated the positive catalytic property of *P. aeruginosa*. Total number of sample was 100 .out of these 57-show positive catalase test.

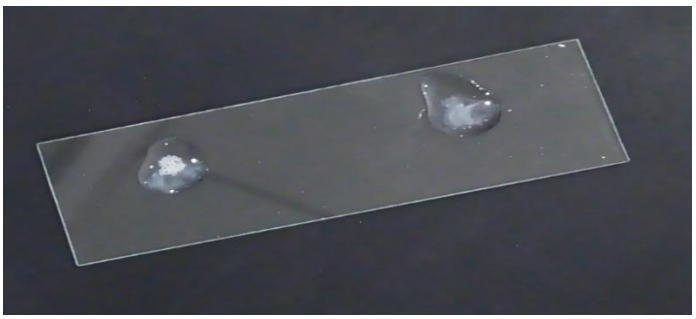

Figure 6: Catalase Test

4. SIM Motility Test (Sulfur Indole Media):

Diffuse, murky developments that spread all through the medium delivering it marginally hazy appearance, which showed the motile behavior of the *pseudomonas aeruginosa*. Total number of sample was 100 .out of this 57-show positive SIM Motility Test.

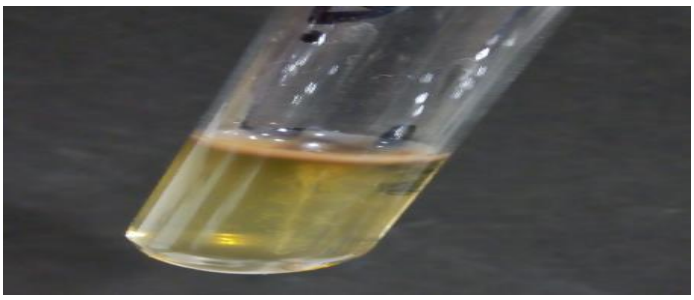

Figure 7: Motility Test

5 Simmons Citrate test:

Simmons citrate test foe *P. aeruginosa* were negative. There was no citrate utilization done by creating a basic response and consequently no adjustment of shade of medium was noticed. Simmons Citrate test.

Figure 8: Simmons Citrate Test

Antibiotioc susptibility:

P. aeruginosa showed wide anti-microbial resistivity design with creation of diffusible shade that changed the color of supplement media from dry to blue color. In this Imipenem (IPM) showed 47% resistivity and 53% sensitivity, Meropenem(MEM) showed 46% resistivity and 54%snsitvity, Tazobactam(TZP) showed 37% resistivity and 63% sensitivity, Ciprofloxacine(CIP) showed 56% resistivity and 44% sesnivity, Gentamicin(CN) showed 49% resistivity and 51% sensitivity, Cetazidimie (CAZ) showed 44% resistivity and 56% sensitivity ,Levofloxacine (LEV) showed 53% resistivity and 47% sensitivity. This indicates that MDR *P. aeruginosa* showed high resistance against ciprofloxacine i.e. 56%.

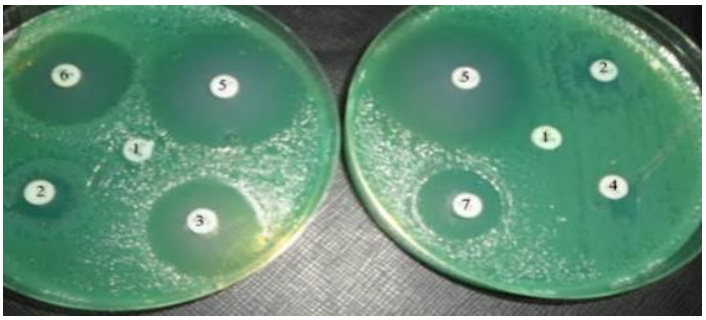

Figure 9: Antibiotic resistivity pattern Psudomonase aeroginsa against 1.Imipenem (IPM),2.Meropenem(MEM),3.Tazobactam(TZP),4.Ciprofloxacine(CIP),5.Gentamicin(CN),6.Cetazidimie (CAZ),7.Levofloxacine (LEV)

Dna Gel Electrophrosis

Collected 57 samples that showed phenotypically resistivity pattern against antibiotics (carbanaem, ciprofloxacine, gentamicine) 20 strains were selected for PCR amplification for genotypic observation that showed positive behavior against *ParC gene*.

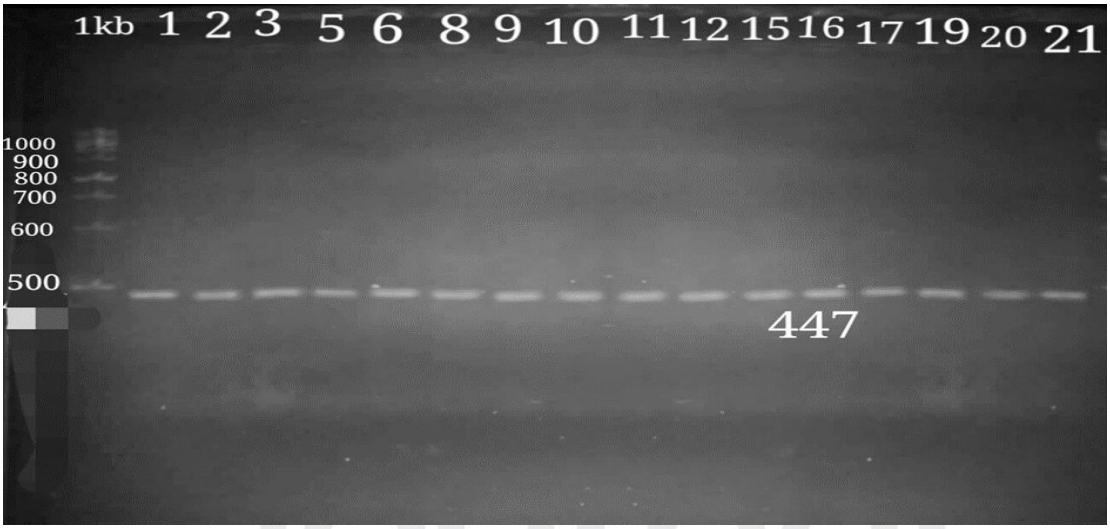

Figure 10: PCR Amplified DNA bands on Gel Electrophoresis

Discussion

Infections of multi drug resistant P. aeruginosa are increasing worldwide. It is an important pathogen frequently involved in various infections especially in severely or terminally ill patients*(5)*.In our study we isolated 57 *pseudomonas spp* out of total 100 samples including blood, urine, pus and sputum. The bacterial strains of *psudomonase aeruginosa* show growth on blood, MacConkey, and Cystein Lactose electrolyte deficient (CLED). The previous study showed a 30% frequency of MDR P. aeruginosa, while study , reported a 22.7% incidence(22).Another study was conducted in Peshawar in 2009 by Farhatullah et al, which reported 29% prevalence of MDR P. aeruginosa. Present study showed that P. aeruginosa was found to be highly resistant against cephalosporin group of antibiotics. Study reported by Wang et al, explained the absolute resistance of Ampicillin, Cephazolin, Cefuroxime and Cefotaxime, which is in accordance with our results.Our study was also supported by Hamza et al, exhibited 100% resistance against Cefixime.While Jombo et al, reported 86% susceptibility of P. aeruginosa against cefurixime. Carbapenems the most significant group of antibiotics against MDR P. aeruginosa but the development of Carbapenems resistance is becoming a challenge for health care professionals and limited the therapeutic options. Sufficient measures are required to prevent the spread of Carbapenemase encoding gene to other bacteria(23). The current study demonstrated that 60% P. aeruginosa were resistant against Carbapenem antibiotics (Imepenem, Meropenem). Rodríguez-Martínez JM et al, showed that 87% of strains of P. aeruginosa were resistant against Imepenem(24).Another study reported 100% resistance against Carbapenems,20 it is very obvious that efficacy of this particular antibiotic is declining. Clonal spread contributes lesser importance in the statistics and epidemiology of infections caused by P. aeruginosa, and the main mechanism associated with increased resistance to Imipenem was reduced expression of OprD (outer membrane protein) found in the isolates(25).

This investigation found that an aggregate of 7527 experiment were broke down, yielding 46 *P. aeruginosa,* detaches. pus, wound swab, sputum, and tracheal suction were utilized to detach *Pseudomonas aeruginosa*. *P. aeruginosa* showed, Ceftazidime 63.04 percent, 65.21 percent in Cefixime, 56.52 percent in Ceftriaxone and Cefotaxime, and 56.52 percent in Piperacillin, resilient behavior. Antibiotics, for example, Imipenem,

Meropenem, Piperacillin/Tazobactam, Ciprofloxacin, Gentamicin, Amikacin, and Tobramycin have likewise been demonstrated to be successful in the treatment of this bacterial infection. *(26)* However, as per the current examination, *P. aeruginosa* is challenging to Imipenem, Meropenem, and Ciprofloxacin. In 254 cultures, *P. aeruginosa* was isolated (5.4 percent). Ceclor (100 percent) and Cefizox (100 percent) were the most resistant medications, followed by amoxil/ampicillin (99.6%), ceflixime (99.6%), doxycycline (99.6%), cefuroxime (99.2%), cephradine (99.2%), cotrimoxazole (99.2%), nalidixic acid (98.8%), pipemidic acid (98.6%), and augmentin (98.6%). (97.6 percent) (27).*P. aeruginosa* was collected from a sum of 5,960 samples. Wound swabs had a 35% growth rate, urine had a 28%, sputum had a 14%, tracheal suction had a 10%, blood had a 7%, and broncho-alveolar lavage had a 4% growth rate of *P. aeruginosa*. Carbapenems (meropenem n=440 (35%), imipenem n=436 (34%), and beta-lactam + beta-lactamase inhibitor mix (piperacillin+tazobactam n=437 (34%) had low ratio of resisitance, yet cephalosporins (ceftazidime n=716 (56%), fluoroquinolones (ciprofloxacin (52%)*(28)*.Previous study gives subjective evidence of the viability of ceftazidime-avibactam for the remedy of CRE and MDR *P. Aeruginosa* contaminations in hospitalized sufferers with limited remedy choices.Most of preliminaries demonstrated excellent results for ceftazidime-avibactam remedy (medical achievement prices went from 45 to a hundred%, and 30-day mortality went from zero to 63 percentage), which were clearly higher than comparator drugs in positive examinations *(29)*

As indicated by a new report, showed that the general predominance of MDR- *P. aeruginosa* was 8.1 percent (205/2533); most of them (85.4 percent, 177/205) came from patients who had been presented to anti-bacterial agents in the 90 days before segregation, and the diseases were for the most part medical clinic gained (95.1 percent, 195/205) with just 4.9 percent from the local area. Cefepime (96.6 percent, 198/205), ciprofloxacin, piperacillin/tazobactam (91%, 186/205), and meropenem (90%, 184/205) resistance was found in most of MDR-*P.aeruginosa*. Diabetes mellitus (47.3 percent, n=97), malignant growth (17.1 percent, n=35), end-stage renal infection (13.7 percent, n=28), and cardiovascular breakdown (10.7 percent, n=22) were the most widely recognized patient comorbidities with MDR-*P. aeruginosa*.).*(30)*. This is in accordance with our current examination, which has reconsidered *P. aeruginosa* resistant to carbapenem and ciprofloxacine.

The molecular investigation in the current study show the presence of *ParC gene* among carbanaem, ciprofloxacine, gentamicine resistant 20 strains. It is reported previously that from *P. aeruginosa* ATCC 27853, the EC-PARC-A and EC-PARC-B primers yielded the predicted 234-bp DNA fragment. The deduced 62-amino-acid sequence had 93.5 percent identity with the *E. coli ParC* protein, while the 186-bp nucleotide sequence had 76.3 percent similarity to the *E. coli parC* gene, excluding the primers (31).

Last, our research has several limitations. First, we did not conduct a multivariate discussion of disease status and treatment. Second, this is a single-centre study conducted in a Lahore. The number of P. aeruginosa samples was relatively small; therefore, our results may not be extrapolated to other hospitals and regions of the country. In addition, because this is a retrospective study, we cannot rule out unmeasurable uncertainties.However, we will continue to perform new research, and track the disease and treatment. In addition, this study lacks relevant research on drug resistance mechanisms. In future studies, we will perform a related analysis of the drug resistance mechanisms of P. aeruginosa in accordance with disease to obtain a more comprehensive understanding of this issue.

Conclusion

We finished up by writing survey and by aftereffect of current examination that *P. aeruginosa* (MDR) collected from critically ill patients showed different resistivity pattern against carbapenem and ciprofloxacine. Furthermore examines uncovered that *Psudomonase* will be viewed as more dangerous microbe on account of it resistivity design. Persistent usage of antibiotics due to consistent infection may cause resistivity pattern of *Psudomonase*. In this study also elaborate usage of same antibiotic on multiple times may also made *Psudomonase* resistant. In this condition multi drug resistant *Psudomonase* should be treated with combination of antibiotics that were concluded sensitive to *P. aeruginosa* in this study i.e. carbapenem and ciprofloxacine.

References

1. Kerr KG, Snelling AM. Pseudomonas aeruginosa: a formidable and ever-present adversary. The Journal of hospital infection. 2009;73(4):338-44.
2. Thi MTT, Wibowo D, Rehm BHA. Pseudomonas aeruginosa Biofilms. Int J Mol Sci. 2020;21(22).
3. Jurado-Martín I, Sainz-Mejías M, McClean S. Pseudomonas aeruginosa: An Audacious Pathogen with an Adaptable Arsenal of Virulence Factors. Int J Mol Sci. 2021;22(6).
4. Peix A, Ramírez-Bahena MH, Velázquez E. Historical evolution and current status of the taxonomy of genus Pseudomonas. Infection, genetics and evolution : journal of molecular epidemiology and evolutionary genetics in infectious diseases. 2009;9(6):1132-47.
5. Bisht K, Baishya J, Wakeman CA. Pseudomonas aeruginosa polymicrobial interactions during lung infection. Curr Opin Microbiol. 2020;53:1-8.
6. Rasoulinejad SA, Sadeghi M, Montazeri M, Hedayati Goudarzi H, Montazeri M, Akbarian N. Clinical Presentation and Microbial Analyses of Contact Lens Keratitis; an Epidemiologic Study. Emergency (Tehran, Iran). 2014;2(4):174-7.
7. Sousa AM, Pereira MO. Pseudomonas aeruginosa Diversification during Infection Development in Cystic Fibrosis Lungs-A Review. Pathogens (Basel, Switzerland). 2014;3(3):680-703.
8. Gellatly SL, Hancock REW. Pseudomonas aeruginosa : new insights into pathogenesis and host defenses. Pathogens and disease. 2013;67(3):159-73.
9. Azam MW, Khan AU. Updates on the pathogenicity status of Pseudomonas aeruginosa. Drug Discov Today. 2019;24(1):350-9.
10. Yaslianifard S, Mobarez AM, Fatolahzadeh B, Feizabadi MM. Colonization of hospital water systems by Legionella pneumophila, Pseudomonas aeroginosa, and Acinetobacter in ICU wards of Tehran hospitals. Indian journal of pathology & microbiology. 2012;55(3):352-6.
11. Chai YH, Xu JF. How does Pseudomonas aeruginosa affect the progression of bronchiectasis? Clin Microbiol Infect. 2020;26(3):313-8.
12. Chegini Z, Khoshbayan A, Taati Moghadam M, Farahani I, Jazireian P, Shariati A. Bacteriophage therapy against Pseudomonas aeruginosa biofilms: a review. Ann Clin Microbiol Antimicrob. 2020;19(1):45.
13. Hilliam Y, Kaye S, Winstanley C. Pseudomonas aeruginosa and microbial keratitis. J Med Microbiol. 2020;69(1):3-13.
14. de Sousa T, Hébraud M, Dapkevicius M, Maltez L, Pereira JE, Capita R, et al. Genomic and Metabolic Characteristics of the Pathogenicity in Pseudomonas aeruginosa. Int J Mol Sci. 2021;22(23).
15. Mielko KA, Jabłoński SJ, Milczewska J, Sands D, Łukaszewicz M, Młynarz P. Metabolomic studies of Pseudomonas aeruginosa. World J Microbiol Biotechnol. 2019;35(11):178.
16. Pang Z, Raudonis R, Glick BR, Lin TJ, Cheng Z. Antibiotic resistance in Pseudomonas aeruginosa: mechanisms and alternative therapeutic strategies. Biotechnol Adv. 2019;37(1):177-92.
17. Liaqat I, Liaqat M, Tahir HM, Haq I, Ali NM, Arshad M, et al. Motility effects biofilm formation in Pseudomonas aeruginosa and Enterobacter cloacae. Pakistan journal of pharmaceutical sciences. 2019;32(3):927-32.
18. Tenover FC, Nicolau DP, Gill CM. Carbapenemase-producing Pseudomonas aeruginosa -an emerging challenge. Emerg Microbes Infect. 2022;11(1):811-4.
19. Doi Y. Treatment Options for Carbapenem-resistant Gram-negative Bacterial Infections. Clinical Infectious Diseases. 2019;69(Supplement_7):S565-S75.
20. Cerceo E, Deitelzweig SB, Sherman BM, Amin AN. Multidrug-Resistant Gram-Negative Bacterial Infections in the Hospital Setting: Overview, Implications for Clinical Practice, and Emerging Treatment Options. Microbial drug resistance (Larchmont, NY). 2016;22(5):412-31.
21. Kaye KS, Pogue JM. Infections Caused by Resistant Gram-Negative Bacteria: Epidemiology and Management. Pharmacotherapy. 2015;35(10):949-62.

22. Camus L, Vandenesch F, Moreau K. From genotype to phenotype: adaptations of Pseudomonas aeruginosa to the cystic fibrosis environment. Microb Genom. 2021;7(3).
23. Diggle SP, Whiteley M. Microbe Profile: Pseudomonas aeruginosa: opportunistic pathogen and lab rat. Microbiology (Reading). 2020;166(1):30-3.
24. Ma LZ, Wang D, Liu Y, Zhang Z, Wozniak DJ. Regulation of Biofilm Exopolysaccharide Biosynthesis and Degradation in Pseudomonas aeruginosa. Annu Rev Microbiol. 2022;76:413-33.
25. Marei EM. Isolation and Characterization of Pseudomonas aeruginosa and its Virulent Bacteriophages. Pak J Biol Sci. 2020;23(4):491-500.
26. Pokharel K, Dawadi BR, Bhatt CP, Gupte S. Prevalence of Pseudomonas Aeruginosa and its Antibiotic Sensitivity Pattern. Journal of Nepal Health Research Council. 2019;17(1):109-13.
27. Shah DA, Wasim S, Abdullah FE. Antibiotic resistance pattern of Pseudomonas aeruginosa isolated from urine samples of Urinary Tract Infections patients in Karachi, Pakistan. Pakistan journal of medical sciences. 2015;31(2):341.
28. Saeed M, Rasheed F, Afzal RK, Hussain S, Riaz S, Ahmad A. Pseudomonas aeruginosa: Evaluation of Pathogen Burden and Drug-Resistance Trends in a Tertiary Care Hospital. Journal of the College of Physicians and Surgeons--Pakistan : JCPSP. 2018;28(4):279-83.
29. Soriano A, Carmeli Y, Omrani AS, Moore LSP, Tawadrous M, Irani P. Ceftazidime-Avibactam for the Treatment of Serious Gram-Negative Infections with Limited Treatment Options: A Systematic Literature Review. Infectious Diseases and Therapy. 2021:1-46.
30. Sid Ahmed MA, Hassan AAI, Abu Jarir S, Abdel Hadi H, Bansal D, Abdul Wahab A, et al. Emergence of Multidrug- and Pandrug- Resistant Pseudomonas aeruginosa from Five Hospitals in Qatar. Infect Prev Pract [Internet]. 2019 2019/12//; 1(3-4):[100027 p.]. Available from: http://europepmc.org/abstract/MED/34368684
31. Nakano M, Deguchi T, Kawamura T, Yasuda M, Kimura M, Okano Y, et al. Mutations in the gyrA and parC genes in fluoroquinolone-resistant clinical isolates of Pseudomonas aeruginosa. Antimicrob Agents Chemother. 1997;41(10):2289-91.