MedCrave
Step into the World of Research

Journal of Microbiology & Experimentation

Research Article

Open Access

CrossMark

Retrospective comparative study of *Pseudomonas aeruginosa* antibiotic resistance isolated from intensive care units (ICUs) patients from tertiary hospital in Nepal

Abstract

This finding has examined the persistent emergence of resistance among *P. aeruginosa* strains to common antimicrobial drugs vis a-vis the increasing number of reports documented world-wide. Our study objectives were finding the antimicrobial resistance patterns of *P. aeruginosa* from clinical isolates obtained from hospitalized patients. The main purpose of this study was aimed to perform antibiotic resistance patterns among the *P aeruginosa* isolates from ICU units in tertiary hospitals in Nepal.

Two hundred and fifty strains of *P. aeruginosa* were isolated from different clinical specimens and fully characterized by regular standard bacteriological proceedings between March 1998 and November 2003. Antimicrobial susceptibility patterns of each isolate were carried out by the Kirby- Bauer disk diffusion method as per guidelines of CLSI. These initial laboratory findings of antibiotic resistance of *P. aeruginosa* isolates have been compared for next successive 17 years to find the significant antimicrobial resistances rise if any from the data.

Primarily for the initial 3 years of study, Majority of high antibiotic resistance isolates of *P. aeruginosa* were obtained from specimens of pus, sputum, urine, and tracheal aspirates. The isolated pathogens showed resistance to amikacin (18.45%), ciprofloxacin (28.32%) and Cefoperazon-sulbactam (36.42%). Resistance rates to Co-trimoxazole, piperacillin, ceftriaxone and chloramphenicol varied from 49.00% to 71.00%. Most of the isolates were susceptible to imipenem. 21.67% of *P. aeruginosa* isolates were found to be multi-drug resistant. The results also established clear evidence of drug resistant strains of *P. aeruginosa*. Imipenem, amikacin, and ciprofloxacin were found to be the mainly effective antibiotics. From ICUs isolates, resistance rates were found to be the highest. It therefore demands a very well thought-out and cognizance treatment regimen by the general practitioners to hinder the further spread of *P. aeruginosa* antimicrobial resistance. We therefore analyzed current and long-term trends of antibiotic resistance within our hospitals, including separate analysis of trends for ICUs.

Secondly, pathogenic *P. aeruginosa* species isolated at the tertiary teaching hospital throughout the 17-year period from the records was analyzed. There was a considerable rise in resistance over a decade in the bacterial species of *P. aeruginosa* in the successive years. The tendency of ciprofloxacin resistance was on the rise for the entire tertiary teaching hospital from 2.5% in 2003 to 12.5% in 2011 ($P<0.01$, Spearman rank order correlation). In addition to this, there was an increase in resistance in the ICUs, but in common lower than that for the whole hospital. A remarkable resistance increase was observed for imipenem first and foremost noticeable in the ICUs compared to the other hospital units. Similarly, the resistance to ceftazidime, piperacillin and gentamicin at the tertiary teaching hospital noticed a noticeable rise, specifically in the ICUs.

Keywords: antimicrobial resistance, intensive care unit clinical isolates, Nepal, *Pseudomonas aeruginosa*

Volume 10 Issue 2 - 2022

Tarani Prasad Paneru
Department of Microbiology, Tri Chandra Campus, Nepal

Correspondence: Tarani Prasad Paneru, Department of Microbiology, Trichandra Campus, TU, Nepal and University of the Sunshine Coast, Sunshine Coast, Australia, Tel +61410999619, Email tppaneru@gmail.com

Received: March 28, 2022 | **Published:** April 20, 2022

Abbreviations: APACHE, acute physiological assessment and chronic health evaluation; CCUG, culture collection university of Goteborg, Sweden; CI, confidence interval; CLSI, clinical and laboratory standard institute; CNS, central nervous system; COPD, chronic obstructive pulmonary disease; CVC, central venous catheter; CSL, corn-steep liquor (A method of Antibiotic production); ICU, intensive care unit; IQR, interquartile range; MDR, multidrug-resistant; MDRPA, multidrug-resistant *Pseudomonas aeruginosa;* MRSA, methicillin-resistant *Staphylococcus aureus;* OR, odds ratio; PDR, pandrug-resistant; PDRPA, pandrug resistant *Pseudomonas aeruginosa;* PFGE, pulsed field gel electrophoresis; SOFA, sequential organ failure assessment; SPSS, statistical package for the social sciences; VRE, vancomycin-resistant enterococci; XDR, extensively drug-resistant

Introduction

P. aeruginosa is an opportunistic pathogen in human ubiquitous organisms in numerous different environmental situations, and it can be isolated from different living materials, including plants, people, and animals. The organism can also be isolated in the emergency

hospital clinics from various surface or material sources, including respiratory treatment equipment, disinfectants, cleanser, sinks, mops, medications, and various physiotherapy and hydrotherapy tools.[1]

Many virulence factors, including exotoxins and enzymes are produced by *P aeruginosa* by which it is a particularly virulent pathogen.[2] The production of a biofilm protects the organism from harsh environmental conditions. The film additionally safeguards from host antibodies and phagocytes providing resistance to the organism.[3]

It is common in hospitalized patients though rarely causes disease in healthy persons. As outlined by The National Nosocomial Infections Surveillance (NNIS) System, *P. aeruginosa* to be the second most commensal pathogen form confined in nosocomial pneumonia, regularly serious and severe, particularly in immunocompromised patients, the third most is isolated from urinary tract infection (UTI) and sites to the surgical operations detached from all locales of nosocomial contamination.[4] It is related to nosocomial transmission that prompts to progressive lung diseases in cystic fibrosis sometimes complexed by antimicrobial resistance.[11]

Epidemiology

Gessard found *P. aeruginosa,* first in 1882 from green discharge in wounds. Individuals can transmit the *P. aeruginosa* from various sources like fresh water as well as restrooms, respiratory medical equipment though it doesn't typically colonize epithelium. Accordingly, it could be found as a feature of typical gastrointestinal commensal even in healthy individuals. They are not effectively eliminated from the areas that become contaminated, for example, operating theater rooms, emergency clinical units.[5]

P. aeruginosa is effectively versatile in clinic and ICU conditions and can obtain resistance from numerous common sanitizers and antimicrobials solutions, *P. aeruginosa* can be isolated from hand-washing sinks, hand moisturizers, cleaning agents, respiratory multi-use vials and artificial fingernails. The organism could keep on existing in a few antiseptic solutions used to sanitize endoscopes and various surgical instruments.[6,7]

Neutropenic patients are a very real threat in those cases of *P. aeruginosa* in febrile when infection's predominant mortality is essentially as high as 50-70 %.[8] The cases of *P. aeruginosa* have been continuously more perceived as nosocomial and community acquired diseases among pediatric patients and adults with HIV/AIDS, with low CD4 lymphocyte counts.[9,10] Fundamental driver of morbidity and mortality in cystic fibrosis particularly persistent by airway route contamination *P. aeruginosa* is the main microbe.[11,12] Ocular infections occur when an inner tubing arrangement of automated cataract when surgical equipment gets contaminated with the organism.[13,14] Disease by *P. aeruginosa* in all untimely newborn children connected with 52.3% mortality, significantly higher than the 13.7% to 23.8% fatality from other gram-negatives.[15]

Clinical manifestations

P. aeruginosa mainly causes Community-Acquired Pneumonia (CAP), still infrequent essentially in HIV patients, organ or bone marrow transplant patients, or patients with neutropenia.[16] *P. aeruginosa* is the most related to the ventilator-related emergency unit) where pneumonia is obtained in around 21% of cases. Common infection in those patients who have chronic infection requiring respiratory and ventilatory help, immunocompromised, malignant growth and neutropenia or potentially hypogammaglobulinemia and cystic fibrosis.[17,18] Inconsistently, *P. aeruginosa* is related by circulatory system disease, septic shock, and acute respiratory distress syndrome (ARDS) as a complexity. *P. aeruginosa* can turn into a typical microbe among those patients with tracheostomy getting mechanical ventilation, for short periods.[19]

Generally, endocarditis following long term hospitalization related with prosthetic endovascular gadgets (for example pacemakers) has been found.[20,21] Meningitis is incredibly occasional because of *P. aeruginosa* including the Central nervous system (CNS).[22] *P. aeruginosa* disease in Orbital cellulitis and endophthalmitis has been revealed as a complexity of sepsis in children, HIV/AIDS patients, and patients with hematologic malignancy.[23]

Likewise, it causes a localized infection of the outer ear canal regularly known as swimmers' ear, otitis media externa. Necrotizing otitis media outside is a subset of osteomyelitis brought about by *P. aeruginosa* in which the temporal bone and skull base is involved.[24] Hot tub folliculitis is a disease frequently pertaining to the hair follicles that can emerge as an outcome of washing in a contaminated tub bath.[25] Delicate tissue involvement, Puncture Wounds as well as septic joint diseases, osteochondritis, and osteomyelitis of the damaged bone or joint might occur. Individuals including regular water submerging get clammy interdigital regions of the feet are the destinations for colonization with *P. aeruginosa*.

Green nail disorders with persistent oncolytic nails who have drawn out drenching openness to fresh water leading to a characteristic green staining is quite often in onycholysis or a persistent paronychia and is generally confined to a couple of nails.[26] Ecthyma gangrenosum is found as a cutaneous sign of severe infection as *P. aeruginosa* commonly connected with bacteremia and sepsis. Necrotizing fasciitis has been portrayed in diabetic hosts and neutropenic patients.[27] Serious burn wounds Pseudomonas is obtained, and their colonization happens when ordinary skin, respiratory, gastrointestinal flora is replaced by nosocomial organism like *P. aeruginosa* colonize a little while after a few weeks of initial burn.[28]

Pathogenesis

The pathogenesis by *P. aeruginosa* typically includes localized inflammation and destruction of tissues, enabling the organism to get the supplements to live by there, and attack the host. The predisposing antimicrobial resistance of *P. aeruginosa* is the main complication in treatment and the biofilm development gives protection from antibiotic agents.[29]

Objectives

The main reason for this study was intended to perform antimicrobial resistance patterns among the *P aeruginosa* isolated from ICU units in tertiary hospitals in Nepal.

Study review

Recently antimicrobial resistance increased constantly whereas the number of irresistible illnesses that could be relieved or controlled fifteen years prior. Additionally, the premier advance in the rise of antimicrobial resistance is the exact problem, detailing and research of the resistance inside the hospital acquired infections.[30,31]

Various surveillance of antimicrobial resistance and antibiotic consumption was principal concern to assess what is happening concerning antibiotic resistance notwithstanding the setting up of a standard for controlling the further emergence of antibiotic resistance at the European Union (EU) gathering.[32] Also, simultaneously effective treatment for severe infections is of most significance for the

prophylaxis.[33,34] We hence came to a choice to investigate current and long-haul tendency of antibiotic resistance inside hospitals, including separate assessment of patterns for ICUs.

Doctors come up short of appreciation for the likely significance of Pseudomonas aeruginosa in the hospitals. A review was directed to isolate and assess the rate of multidrug resistance of *P. aeruginosa* (MDRPA) and pan-drug resistant *P. aeruginosa* (PDRPA) from the ICU units. A cross-sectional review was performed for a long time at the ICUs of Shahid Gangalal National Heart Center, Kathmandu. In general out of 1,060 samples were handled in which 700 were clinicals from inpatients while 360 were the surface swab samples. The tracking down uncovered that *P. aeruginosa* was found from 66 (9.43%) clinical examples though 60 (16.67%) were surface swab tests. Among clinical isolates, Antibiotic susceptibility testing (AST) by Kirby Bauer plate dissemination method in which 56 (84.8%) were sensitive to Cefoperazon and sulbactam combination (CSL) following by 42 (63.6%) to polymyxin-B and 36 (54.5%) to piperacillin-tazobactam (PT), while among surface swab test isolates over 90% were found sensitive to the greater part of the common antibiotic agents utilized. Around 59 (89.4%) MDRPA were isolated from clinical samples instead it was just 7 (11.7%) from surface swab tests. Just isolated from clinical samples (6.1%) revealed PDRPA. The results made clear that it can get rid of the threat of MDRPA and PDRPA in the ICUs.[35]

Another review researched the further antimicrobial resistance pattern of *P. aeruginosa* isolated from the patients in the mid and far western area of Nepal. The review was directed on a total 917 patients with prior suspicion with *P. aeruginosa* diseases, going to outpatient and inpatients of Nepalgunj Medical College Teaching Hospital, Banke, Nepal from September 2011 to January 2014. The outcome uncovered those one hundred 94 isolates were distinguished as *P. aeruginosa*. Resistance patterns to Chloramphenicol (74.23%), Ceftriaxone (69.56%), Cefepime (57.22%), Cefoperazon-Sulbactam (54.12%) and Co-trimoxazole (53.02%) was revealed. Every single one of the isolates were susceptible to Imipenem, 48 (24.74%) of *P. aeruginosa* isolates were multi-drug resistant to >3 classes of antibiotics. Out of 194 isolates, 88 (45.36%) were from the patients of 21-40 years age class, which was measurably huge ($P<0.05$) contrasted with the other age class. Antibiotic misuse may be elevated degrees of antibiotic resistance in many isolates.[36]

From March 1998 to November 2001, all patients hospitalized in the clinical ICU of college who lived in the unit for no less than 3 days were tentatively included in the review. Methodical choice for the identification of resistance or possibly resistance microbes was carried out during the initial 3 years of its execution in this prospective review. The review was an examination utilizing clinical and microbiological data gathered for the length of the prospective evaluation program for *P. aeruginosa* through the point of examining the risk factors acquisition. All through a 17-year time, we had the option to deliberately acquire multisite surveillance isolates from patients who were admitted to ICU units. We examined exhaustively the factors related to the acquisition of various resistance phenotypes of *P. aeruginosa* and considered both huge exposures to antibiotics and colonization pressure.

Materials and methods

From different clinical specimens' 250 strains of *P. aeruginosa* were isolated and fully characterized by regular standard bacteriological proceedings between March 1998 and November 2001. Further by the method of Kirby- Bauer disk diffusion under the guidelines of CLSI, isolated organisms were carried out antimicrobial susceptibility patterns of each such isolates. For assessments of resistance rates the specimens from the burns unit ICU, the general surgery ICU, the neurosurgery ICU, and the thoracic surgery ICU, were included.

At preliminary tests were oxidase test positive, a triple sugar iron agar (TSI) reaction of alkaline over no change, and growth at 37 'C through these tests from which *P. aeruginosa* can be distinguished and affirmed. Extra key biochemical characteristics contain oxidation of glucose however not disaccharide, decrease of nitrates to nitrogen gas and hydrolysis of acetamide. The characteristics for *P. aeruginosa* incorporate fruity sweet-grape smell, rarely taco-like scent, dispersion of green pigment, the mix of the yellow (pyoverdine) and blue (pyocyanin) pigments, making the culture a radiant green color. The mucoid appearance of *P. aeruginosa* strains is because of constant colonization of organisms in cystic fibrosis respiratory pneumonic sicknesses.

For review concentrate on antibiotic susceptibility test consequences of clinical isolates from the seventeen-year time frame 2000-2017 were taken from the lab everyday record file documents and PC database set. The absolute number bacterial isolates from culture assessed was between 15 00-24 00 records were included every year for our analysis, which included organisms collected from a wide range of specimens obtained from patients. To avoid repetition of isolates, a single isolate of similar species and sort of specimen was taken in from every patient during every year. There were no patterns inside the quantity of specimens taken all through the review period.

This choice of strategy worked with the inclusion of all blood isolates in which extended antibiotic susceptibility results were accessible. The legitimacy of this procedure was checked by contrasting and a strategy for including only one isolates of every species per patient regardless of specimen while there was no differentiation in resistance rates aside from Pseudomonas aeruginosa and imipenem, which showed somewhat higher resistance figures with our choice technique. Identification and isolation of organisms from culture media was finished utilizing standard methods.[37]

The antibiotic sensitivities of isolates were performed by the disk diffusion method followed by the Swedish Reference Group for Antibiotics (SRGA), with interpretation adjusted to species groups.[38,39] The strains were cultured onto Oxoid Iso-Sensitivity test Agar (Oxoid AB, Sollentuna, Sweden) or PDM agar (AB Biodisk, Solna, Sweden). The susceptibility interpretation (SIR system: S = susceptible, I = intermediate susceptibility, R = resistant) followed guidelines from the SRGA.

The guidelines have embraced species-related MIC limits, as well as species-related zone width breakpoints.[40] With species-related zone breakpoints, the I rate is minimized. Just isolates that were listed as R were included for the tables as level of resistant isolates percentages. Control strains *E. coli* ATCC 25922 (CCUG 17620), *Staphylococcus aureus* ATCC 29213 (CCUG 15915), *E. faecalis* ATCC 29212 (CCUG 9997), and *P. aeruginosa* ATCC 27853 (CCUG 17619) (ATCC, American Type Culture Collection; CCUG) were included to assure the guarantee of the antibiotic susceptibility testing procedure.[41]

Sample swab from pharynx, nasal cavities, and rectum, as well as respiratory emissions like tracheobronchial suction, bronchoscopy or sputum were taken in 48 hours of admission and multiple times in seven days from that point until release or the initial 2 months of the ICU remaining and straightforwardly acquired as necessity going to doctor. For isolation and identification of the organism, tests were cultured in routine agar media. Intermediate susceptibility was considered as resistance with the end goal of analysis. Molecular typing was performed by pulse-field gel electrophoresis by standard

method directed by procedure manual in Ananda ban Leprosy Hospital Lele, Lalitpur. Multiple antibiotics Resistance was named MDR, extensively drug-resistant (XDR) or pan-drug-resistant (PDR) as described elsewhere.[42]

Statistical analysis

Investigation and analysis intended to design for continuous variables, implies alongside standard deviations and medians with interquartile ranges (IQRs) were utilized for estimation of their scattering in central tendency. Continuous variables were looked at by utilizing the t-test or Mann-Whitney U test and denominators in proportions were as the count of patients. The proportions were compared through utilizing the Fisher's accurate test or $\chi 2$ test. To assess attributes of acquisition of *P. aeruginosa* and acquisition of resistance from piperacillin-tazobactam, ceftazidime, carbapenems and quinolones, multivariable logistic regression analysis (step-forward procedure) was applied. All things considered, the entire group was considered after we analyzed the risk factors for the securing of protection from antipseudomonal antibiotics, on the grounds that acquisition of resistance in strains of *P. aeruginosa* could be introduced during admission. APACHE II score, SOFA score and age of the patients were incorporated in the models analysis as binary variables, taking consideration that the median at the same time as the cut off value, whereas colonization pressure was fractionalized by the peak observed value (95th percentile). Inside multivariate models determining the acquisition of resistant strains to each antipseudomonal agent and multiple drugs, a cutoff of 72 hours was applied to fractionalized antibiotic exposure characterizing the minimal duration of exposure related to resistance.[43] Variables by means of a *P*-value<0.3 in the univariate analysis were considered for the multivariate model. Calculations were finished utilizing the IBM SPSS version 20.0 statistical software package (IBM).

Observation

The observation was made based on the data obtained from the routine laboratory test observation of antibiotic disc diffusion method and the data was plotted and analyzed with various statistical tools.

The trend of ciprofloxacin resistance was on the increase for the entire tertiary teaching hospitals from 2.5% in 2003 to 12.5% in 2011 ($P < 0.01$, Spearman rank order correlation). It was also an increase in resistance in the ICUs, in any case; overall lower than that for the entire medical hospitals with little variations noted. A noticeable resistance increment was seen for imipenem significantly noticeable in the ICUs, where it fluctuates, but with peaks in 2003-04 and 2010-11, shored at 25% and 28% for the last two years. In the surgical ICU, 16 patients in 2010 and 12 patients in 2011 were infected with bacteria that were shown by PFGE analysis to belong to one single clone representing nosocomial outbreaks of immune-resistant isolates. It is probable that the increase in resistance in 2003-04 was also due to an outbreak. The ceftazidime resistance was in no way above 1.5% at the tertiary teaching hospital for the duration of the study period. Similarly, the resistance to ceftazidime, piperacillin and gentamicin did not exceed 2.2% at the tertiary teaching hospital as a whole and 4.9% in the ICUs after 2003 (Table 1).

Table 1 *Pseudomonas aeruginosa* during 1988-99 shown as percentages

	Piperacillin S ≥ 21/R ≤ 17		Gentamicin S ≥ 21/R ≤ 17		Ciprofloxacin S ≥ 32/R ≤ 24		Ceftazidime S ≥ 23/R ≤ 19		Imipenem S ≥ 23/R ≤ 19	
Year	**TH**	**ICU**	**TH**	**ICU**	**TH**	**ICU**	**TH**	**ICU**	**TH**	**ICU[a]**
2000	0.7	0	0.6	4.5	–	–	1.3	0	0	–
2001	0.8	2.6	0.4	0	–	–	0.4	2.6	–	–
2002	4.4	16.3	6	16.2	–	–	0.51	0	4.5	–
2003	1.7	4.9	2	4.9	2.5	0	0.4	0	2.5	10.3
2004	1.5	4.1	1.5	1.3	3.6	1.5	0.6	1.4	5.7	14.7
2005	0.5	0	1.8	1.3	8.8	2.9	1	1.3	4.3	6.6
2006	0.8	1.5	1.7	1.5	9.7	10.3	0.6	0.5	6.3	6.2
2007	0.6	1.9	0.9	3.8	7.8	6.4	0.3	0	3.7	3.8
2008	0.8	1.7	1.3	1.7	13.6	2	0.5	3.5	1.6	0
2009	0.9	2.3	1.6	4.4	8.9	6.2	0.2	0	5	13.3
2010	1.2	0.9	1.1	2.8	12	8.9	0.2	0	9	27.8
2011	2.2	3.5	1	0	12.5	3.9	1.5	2.3	9.9	25.3
N [b]	379	67	379	66			378	67		

TH, tertiary hospital

[a]Number of isolates equal to or below 20.

[b]mean number of isolates per year.

Out of the strains almost all antibiotics were susceptible in 62 patients (53%), XDR in 18 (16%), PDR in 1(1%), MDR in 4 (4%) and 1 or 2 groups of antibiotics in 28 (26%) found resistant. Resistance acquisition to carbapenems, piperacillin-tazobactam, ceftazidime, fluoroquinolones and amikacin was observed in 40 (37%), 18 (18%), 31 (29%), 29 (28%) and 1 (1%) strain, correspondingly.

Emergence of resistance to a given antibiotics from a prior susceptible strain after exposure to itself occurred in 6 (46%) of 13 exposed to carbapenems (vs 1 (3%) of 95 non-exposed; $P < 0.001$), 8 (29%) of 28 exposed to fluoroquinolones (vs 2 (3%) of 94 non-exposed; $P < 0.001$), 4(20%) of 20 patients exposed to ceftazidime (vs 8 (8%) of 106 non-exposed; $P = 0.1$), and 3 (15%) of 20 exposed to piperacillin-tazobactam (vs 9 (8%) of 117 non-exposed; $P=0.3$). From the data analysis for almost a decade registry, a greater part of isolates of *P. aeruginosa* (83.75%) were received from specimens of sputum, urine, tracheal aspirates and pus. The isolated pathogens showed resistance to amikacin (19.25%), ciprofloxacin (26.59%) and Cefoperazon-sulbactam (35.48%). Resistance rates to Co-trimoxazole, piperacillin, ceftriaxone and chloramphenicol varied from 49.00% to 74.00%. In contrast almost 50% isolates were susceptible to imipenem. The most crucial part is that about 32 (22.73%) of *P. aeruginosa* isolates were found to be multi-drug resistant. From the table 1 above it was found that the antibiotic resistance was found to be increased at the end of the years (Figure 1).

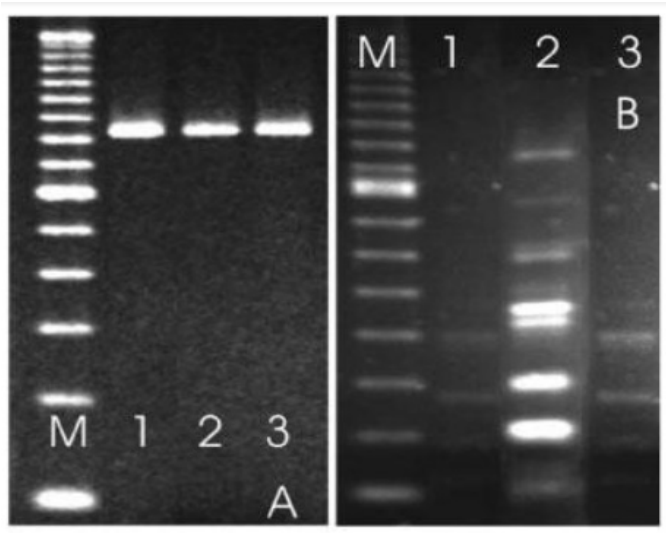

Figure 3 - Amplification products of two bacterial isolates from the same patient. A. rDNA-PCR of *P. aeruginosa* ATCC 9027 (lane 1), bacterial isolate 21 (lane 2) and bacterial isolate 23 (lane 3). B. tDNA-PCR of *P. aeruginosa* ATCC 9027 (lane 1), bacterial isolate 21 (lane 2) and bacterial isolate 23 (lane 3). The molecular marker 100 bp ladder is shown in lane M.

Figure 1 Photograph of pulsed field gel electrophoresis of antibiotic resistance *P. aeruginosa.*

Result

P. aeruginosa obtained from ICUs patient's samples were lower antimicrobial sensitivity than other isolates from the hospital. Most of the antibiotics used were found to be rise in resistant to *P. aeruginosa*. It was also found that most of the antibiotics decreased their sensitivity pattern from 1st to 4th week of culture and at the end of 4th week, nearly all the isolates of *P. aeruginosa* were only sensitive to polymyxin B and resistant to all antibiotics. Subsequently, pathogenic *P. aeruginosa* species isolated and identified at the tertiary teaching hospital from a data pool throughout the period was analyzed but total number of other bacterial species Both numbers and proportions of the whole number of bacterial isolates was out of the extent of this review. There was a huge increase after some time in the bacterial types of *P. aeruginosa* in the sequential years. There was also significant rise antibiotic resistance in the ICUs, regardless, in general lower than that for the other medical units with little varieties noted. A recognizable resistance was seen for imipenem noticeably perceptible in the ICUs by the statistical analysis.

Discussion

The most quintessential outcome in our analysis was the resistance levels in between the entire hospital and the ICUs with variation. Chief proof tracked down that the resistance from ciprofloxacin among *P. aeruginosa* strains was on the increment. The resistance levels were transcending at top in the ICUs for certain antibiotics, however much higher in different divisions of the hospitals. According to a worldwide perspective, in ICUs the prevalence of infections is generally higher than in other words, and nosocomial are additionally more regular in ICUs therefore antibiotic utilization is moderately high in ICUs. Just a couple of similar studies have been done about antibiotic resistance in ICUs and different wards accordingly, this study was intended to contrast ICUs and the entire hospital, is of importance.[44]

Our outcomes correspond to certain comparable studies by Archibald et al and others archived differentiation between other medical care facilities and ICUs. In general, their outcomes called attention to higher resistance in hospitals than in outpatient clinics. The larger antimicrobial resistance was to be found in the ICUs of the emergency hospital.

There are different outcomes where resistant rates in clinical hospitals were for the most part seen in the Intensive care units. As opposed to these reports, by one hospital, there were higher resistance rates for *P. aeruginosa* against imipenem in outpatients. Fridkin et al. has additionally shown comparative investigations of *P. aeruginosa* in outpatient areas who tracked down a higher predominance of quinolone resistance than ICUs.

Definite guidelines ought to be applied to forestall nosocomial transmission of organisms alongside colonization with resistant organisms for this isolation care unit is fundamental overall. From analytical studies, a few published works on antibiotic resistance are concentrated around limited time spans.[45] ICU corresponding to the entire hospital bolsters our view. Then again, the fluctuations can't be altogether made sense by outbreaks. Such a long way to address these questions further extensive analysis of antibiotic resistance in ICUs ought to be performed at these hospitals.

These sorts of studies with high paces of predominance with *P. aeruginosa* having imipenem resistance among isolates from the ICUs have been analyzed by numerous researchers.[45] Tsakris et al. found the high resistance rates because of nosocomial episodes.[46] Likewise, Archibald et al represented the high resistant rates of 28% in 1998 and 25% in 1999 inside ICU were viewed as aftereffects of a gradual accreditation of isolates from nosocomial outbreaks in the hospital and operational intensive care units. The resistance prevalence was viewed as significant fluctuations during the study time. In this manner, it is basic to put more efforts on including all areas of a hospital in resistance surveillance studies, especially in the ICUs, emphasizing the significance of expanded reconnaissance periods.[45]

There may be more tendency to choose resistant mutants in patients previously colonized or infected by *P. aeruginosa*, carbapenems and fluoroquinolones than additional agents. Prior exposures to anti pseudomonal agents can acquire resistance either by confining mutants infected by more susceptible phenotypes or recently colonized in patients.[47,48] In addition, acquiring resistant strains by irrelevant antibiotics and various medications has as a rule related to the earlier exposure to fluoroquinolones or carbapenems.[49] However, there are a couple of exceptions.

For a situation study,[50] the primary indicators of a multidrug resistant (MDR) phenotype were cephalosporins and aminoglycosides yet in an accomplice study,[51] quinolones were defensive against the obtaining of resistant phenotypes or played no part in the earlier resistant strain in *P. aeruginosa.* However, not satisfactory data have been provided to guarantee the evidence which of the previously mentioned process is specially connected with such factors.[52]

Antimicrobial resistance is an existing issue in Nepal, as contributing factors to raise in treatment costs, staying hospital, morbidity and mortality as infectious illnesses are a typical sickness. The certain level of the issue is in dilemma since the greater part of the published works received from patients or hospitals.[53] The utilization of antibiotic agents with imprudent practices in human infection treatment as well as indiscriminate prophylaxis in animals cultivation might add to the rise of multidrug resistant (MDR) strains remarkably.[54] Proper management of the emerging of drug resistance

and its outbreaks is best directed by an active coordinated infection control program in the hospitals which can assess designated cohorts of infected patients, isolation or rigorous barriers precautionary measures, improved reconnaissance, early discharge of patients, and modification in use of antimicrobial therapy.[55]

Notwithstanding the improvement of direct inhibitors of resistant mechanism systems, i.e., β-lactamase inhibitors, another technique is to focus on the regulation of gene expression. Albeit a lot of information has been acquired toward understanding the method of mechanism by which *P. aeruginosa* regulates AmpC, OprD, and efflux pumps. Clearly, we have a difficult experience ahead and have a lot to find out about how this ingenious microorganism regulates different resistant mechanisms to address the problem as it faces.[56]

In the acquisition of a given strain when cross-transmission is involved, it is estimated that colonization pressure ought to be a related risk factor. While defined by an alternate way, where in the ICU setting colonization pressure has been independently related by the acquisition of MRSA, VRE, Clostridium difficile, Acinetobacter baumannii and *P. aeruginosa.*[57]

A few other non-antibiotic related cofactors are exposure to medical equipment, duration of critical illness and severity of the underlying conditions have been reported as risk factors for the acquisition of any *P. aeruginosa* or strains with single-drug resistant or MDR phenotypes.[58]

Moreover, the number of results vis-a-vis the different resistance phenotypes and MDR were meager, subsequently leading to a long dilemma concerning the nature of the multivariate models. On the other hand, as responsiveness of observation probably won't be completed, the colonization status of certain patients could have been miscounted. Moreover, information regarding consistency with infection control measures in the review time and reconnaissance of the study might not be accessible promptly.

Conclusion

Our comparative study based on first three years laboratory routine antibiotic disc diffusion tests to the next successive 17 years data reviewed study shows that the rate of antibiotic resistance is in increasing order, specifically nosocomial transmitted *P aeruginosa* related infections in ICUs.

Antibiotic resistance acquisition in *P. aeruginosa* in critical care units might be with a high rate of antibiotic consumption, colonization pressure and non-antibiotic exposures might be the key variables.[59] For the acquisition of resistant strains to fluoroquinolones, piperacillin-tazobactam and multiple drugs, exposures to amikacin might be an auxiliary factor in this review than recorded in the past. Previously sensitive strains of *P. aeruginosa,* rise of resistance happens even more frequently after exposure to fluoroquinolones and carbapenems than to ceftazidime or piperacillin-tazobactam. The result affirmed the long-laid out incidence of drug resistant strains of *P. aeruginosa.* All in all, the best antimicrobial drugs were revealed as Imipenem, amikacin, and ciprofloxacin. Diminution of the further spread of antimicrobial resistance among the *P. aeruginosa* strains is imperative. It is hence requiring an extremely prudent, rational regimen prescription by the general practitioners.[60]

Infected with *P. aeruginosa* patients ought to get Standard Transmission Precautions in the medical facilities and hospital setting, isolation for a patient with MDR-*P. aeruginosa* is obligatory required. Investigation of evidenced outbreaks of infection by molecular epidemiologic techniques, such as pulsed field gel electrophoresis should be a proper application. Along these lines, we suggest sensible utilization of antibiotic therapy by the general practitioners to hinder the increasing multidrug resistance of *P. aeruginosa* strains in Nepal.

Acknowledgments

None.

Conflicts of interest

Author declares that there is no conflict of interest.

References

1. Pollack M. *Pseudomonas aeruginosa*. *In* G. L. Mandell, R. Dolan, and J. E. Bennett (ed.), Principles and practices of infectious diseases. Churchill Livingstone: New York, NY; 1995. 1820–2003 p.
2. CA Hart. Antibiotic resistance: an increasing problem? It always has been, but there are things we can do. *BMJ.* 1998;316(7140):1255–1256.
3. Shigeki Fujitani, Hsin-Yun Sun, Yu VL, et al. Pneumonia Due to Pseudomonas aeruginosa: Part I: Epidemiology, Clinical Diagnosis, and Source. *Chest.* 2011;139(4):909–919.
4. Richards MJ, Edwards JR, Culver DH, et al. Nosocomial infections in medical intensive care units in the United States, National Nosocomial Infections Surveillance System. *Crit Care Med.* 1999;27(5):887–892.
5. Engleberg NC dV, Dermondy TS. *Pseudomonas aeruginosa*. Fourth ed: Lippincott Williams & Wilkins; 2007.
6. Centers for Disease Control and Prevention. Pseudomonas dermatitis/folliculitis associated with pools and hot tubs-Colorado and Maine, 1999-2000. *MMWR Morb Mortal Wkly Rep.* 2000;49(48):1087–1091.
7. Kennedy AM, Elward AM, Fraser VJ. Survey of knowledge, beliefs, and practices of neonatal intensive care unit healthcare workers regarding nosocomial infections, central venous catheter care, and hand hygiene. *Infect Control Hosp Epidemiol*. 2004;25(9):747–752.
8. El-Solh AA, Sikka P, Ramadan F, et al. Etiology of severe pneumonia in the very elderly. *Am J Respir Crit Care Med.* 2001;163(3 Pt 1):645–651.
9. Afessa B, Green B. Bacterial pneumonia in hospitalized patients with HIV infection: the Pulmonary Complications, ICU Support, and Prognostic Factors of Hospitalized Patients with HIV (PIP) Study. *Chest.* 2000;117(4):1017–1022.
10. Vidal F, Mensa J, Martinez JA, et al. Pseudomonas aeruginosa bacteremia in patients infected with human immunodeficiency virus type 1. *Eur J Clin Microbiol Infect Dis.* 1999;18(7):473–477.
11. Burns JL, Emerson J, Stapp JR, et al. Microbiology of sputum from patients at cystic fibrosis centers in the United States. *Clin Infect Dis.* 1998;27(1):158–163.
12. *Cystic Fibrosis Foundation*, Seventh ed. Bethesda, MD: Approved Standard; 1994.
13. Cruciani M, Malena M, Amalfitano G, et al. Molecular epidemiology in a cluster of cases of postoperative Pseudomonas aeruginosa endophthalmitis. *Clin Infect Dis.* 1998;26(2):330–333.
14. Keene WE, Markum AC, Samadpour M. Outbreak of Pseudomonas aeruginosa infections caused by commercial piercing of upper ear cartilage. *JAMA.* 2004;291(8):981–985.
15. Gordon A, Isaacs D. Late onset neonatal Gram-negative bacillary infection in Australia and New Zealand: 1992-2002. *Pediatr Infect Dis* J. 2006;25(1):25–29.
16. Hatchette TF, Gupta R, Marrie TJ. Pseudomonas aeruginosa community-acquired pneumonia in previously healthy adults: case report and review of the literature. *Clin Infect Dis.* 2000;31(6):1349–1356.

17. Arancibia F, Bauer TT, Ewig S, et al. Community-acquired pneumonia due to gram-negative bacteria and pseudomonas aeruginosa: incidence, risk, and prognosis. *Arch Intern Med.* 2002;162(16):1849–1858.

18. Baltch A, Smith R. *Pseudomonas aeruginosa: infections and treatment*. New York, NY: Marcel Dekker; 1994.

19. Rello J, Lorente C, Diaz E, et al. Incidence, etiology, and outcome of nosocomial pneumonia in ICU patients requiring percutaneous tracheotomy for mechanical ventilation. *Chest.* 2003;124(6):2239–2243.

20. Apple J, Hunt JL, Wait M, et al. Delayed presentations of aortic valve endocarditis in patients with thermal injury. *J Trauma.* 2002;52(2):406–409.

21. Rodgers GL, Mortensen J, Fisher MC, et al. Predictors of infectious complications after burn injuries in children. *Pediatr Infect Dis J.* 2000;19(10):990–995.

22. Chang WN, Lu CH, Huang CR, et al. Mixed infection in adult bacterial meningitis. *Infection.* 2000;28(1):8–12.

23. Menon J, Rennie IG. Endogenous Pseudomonas endophthalmitis in an immunocompetent patient: a case for early diagnosis and treatment. *Eye.* 2000;14(Pt 2):253–254.

24. Green S, Nathwani D, Gourlay Y, et al. Nebulized colistin (polymyxin E) for AIDS-associated Pseudomonas aeruginosa pneumonia. *Int J STD AIDS.* 1992;3:130–131.

25. Centers for Disease Control and Prevention. Pseudomonas aeruginosa infections associated with transrectal ultrasound-guided prostate biopsies-Georgia, 2005. *MMWR Morb Mortal Wkly Rep.* 2006;55(28):776–777.

26. Greenberg JH. Green fingernails: a possible pathway of nosocomial pseudomonas infection. *Mil Med.* 1975;140(5):356–357.

27. Kusne S, Eibling DE, Yu VL, et al. Gangrenous cellulitis associated with gram-negative bacilli in pancytopenia patients: dilemma with respect to effective therapy. *Am J Med.* 1988;85(4):490–494.

28. Williams HB, Breidenbach WC, Callaghan WB, et al. Are burn wound biopsies obsolete? A comparative study of bacterial quantitation in burn patients using the absorbent disc and biopsy techniques. *Ann Plast Surg.* 1984;13(5):388–395.

29. Engleberg NC dV, Dermondy TS. Fourth ed: Lippincott Williams & Wilkins; 2007.

30. DA Goldmann, RA Weinstein, RP Wenzel, et al. Strategies to prevent and control the emergence and spread of antimicrobial-resistant microorganisms in hospitals. A challenge to hospital leadership. *JAMA.* 1996;275:234–240.

31. A Tomasz. Multiple-antibiotic-resistant pathogenic bacteria. A report on the Rockefeller University Workshop. *N Engl J Med.* 1994;330(17):1247–1251.

32. Wise R, Hart T, Cars O, et al. Antimicrobial resistance. Is a major threat to public health. *BMJ.* 1998;317(7159):609–610.

33. C Bornet, A Davin-Regli, C Bosi, et al. Imipenem resistance of enterobacter aerogenes mediated by outer membrane permeability. *J Clin Microbiol.* 2000;38(3):1048–1052.

34. MH Kollef, G Sherman, S Ward, et al. Inadequate antimicrobial treatment of infections: a risk factor for hospital mortality among critically ill patients. *Chest.* 1999;115:462–474.

35. Shiva Bhandari, Megha R Banjara, Binod Lekhak, et al. Multi-Drug and Pan-Drug Resistant Pseudomonas aeruginosa: A Challenge in Post- Antibiotic Era. *Nepal Journal of Science and Technology.* 2012;13(2):197–202.

36. Salman Khan, Priti Singh, Ms. Rashmi, et al. Recent trend of multi-drug resistance in Pseudomonas aeruginosa. *Bangladesh Journal of Medical Science.* 2014;13(4):438–442.

37. RE Murray, EJ Bdron, MA Pfdller, et al. *Manual of clinical microbiology*. ASM Press: Washington, DC; 1999.

38. Martínez JA, Delgado E, Martí S, et al. Influence of antipseudomonal agents on Pseudomonas aeruginosa colonization and acquisition of resistance in critically ill medical patients. *Intensive Care Med*. 2009;35:439–447.

39. Nazaret Cobos-Trigueros, Mar Solé, Pedro Castro, et al. Acquisition of *Pseudomonas aeruginosa* and its resistance phenotypes in critically ill medical patients: role of colonization pressure and antibiotic exposure. *Crit Care*. 2015;19(1):218.

40. B Olsson-Liljequist, A Forsgren. Antimicrobial susceptibility testing in Sweden. I. The work of the Swedish Reference Group for Antibiotics (SRGA and SRGA-M). *Scand J Infect Dis Suppl.* 1997;105:5–7.

41. G Kahlmeter, B Olsson-Liljequist, S Ringertz. Antimicrobial susceptibility testing in Sweden. IV. Quality assurance. *Scand J Infect Dis Suppl*. 1997;105:24–31.

42. Magiorakos A, Srinivasan A, Carey RB, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect*. 2012;18(3):268–281.

43. Patel N, McNutt LA, Lodise TP. Relationship between various definitions of prior antibiotic exposure and piperacillin-tazobactam resistance among patients with respiratory tract infections caused by Pseudomonas aeruginosa. *Antimicrob Agents Chemother.* 2008;52(8):2933–2936.

44. L Archibald, L Phillips, D Monnet, et al. Antimicrobial resistance in isolates from inpatients and outpatients in the United States: increasing importance of the intensive care unit. *Clin Infect Dis.* 1997;24(2):211–215.

45. M Söurberg, A Farra, U Ransjöu, et al. Different trends in antibiotic resistance rates at a university teaching hospital. *Clinical Microbiology and Infection.* 2003;9(5):388–396.

46. A Tsakris, S Pournaras, N Woodford, et al. Outbreak of infections caused by Pseudomonas aeruginosa producing VIM-1 carbapenemase in Greece. *J Clin Microbiol*. 2000;38(3):1290–1292.

47. Carmeli Y, Troillet N, Eliopoulos GM, et al. Emergence of antibiotic-resistant Pseudomonas aeruginosa: comparison of risks associated with different antipseudomonal agents. *Antimicrob Agents Chemother*. 1999;43(6):1379–1382.

48. Riou M, Carbonnelle S, Avrain L, et al. In vivo development of antimicrobial resistance in Pseudomonas aeruginosa strains isolated from the lower respiratory tract of Intensive Care Unit patients with nosocomial pneumonia and receiving antipseudomonal therapy. *Int J Antimicrob.* 2010;36(6):513–522.

49. Akhabue E, Synnestvedt M, Weiner MG, et al. Cefepime-resistant Pseudomonas aeruginosa. *Emerg Infect Dis*. 2011;17(6):1037–1043.

50. Aloush V, Navon-Venezia S, Seigman-Igra Y, et al. Multidrug-resistant Pseudomonas aeruginosa: risk factors and clinical impact. *Antimicrob Agents Chemother*. 2006;50(1):43–48.

51. Montero M, Sala M, Riu M, et al. Risk factors for multidrug-resistant Pseudomonas aeruginosa acquisition: impact of antibiotic use in a double case–control study. *Eur J Clin Microbiol Infect Dis*. 2010;29(3):335–339.

52. DalBen MF, Basso M, Garcia CP, et al. Colonization pressure as a risk factor for colonization by multi-resistant Acinetobacter spps and carbapenem-resistant Pseudomonas aeruginosa in an intensive care unit. *Clinics (Sao Paulo)*. 2013;68(8):1128–1133.

53. Antimicrobial resistance in India: current scenario. *APUA Newsletter*. 2008; 26 p.

54. APUA. Multidrug-resistant Escherichia coli from apparently healthy children in Kenya. APUA Newsletter. 2007; 25(1). (11) APUA. *Infection control: a potent antimicrobial resistance containment strategy. APUA Newsletter;* 2008.

55. PB Crichton. Enterobacteriaceae; *Escherichia, Klebsiella, Proteus* and other genera. JG Collee, AG Fraser, BP Marmion, A Simmons (Eds.), Mackie and McCartney, practical medical microbiology. Churchill Livingstone, New York; 1996. 369 p.

56. Philip D Lister, Daniel J Wolter, Nancy D Hanson. Antibacterial-Resistant Pseudomonas aeruginosa: Clinical Impact and Complex Regulation of Chromosomally Encoded Resistance Mechanisms. *Clin Microbiol Rev*. 2009;22(4):582–610.

57. Venier AG, Leroyer C, Slekovec C, et al. Risk factors for Pseudomonas aeruginosa acquisition in intensive care units: a prospective multicenter study. *J Hosp Infect*. 2014;88(2):103–108.

58. Bhat S, Fujitani S, Potoski BA, et al. Pseudomonas aeruginosa infections in the intensive care unit: can the adequacy of empirical β-lactam antibiotic therapy be improved? *Int J Antimicrob Agents*. 2007;30(5):458–462.

59. Richards MJ, Edwards JR, Culver DH, et al. Nosocomial infections in medical intensive care units in the United States. National Nosocomial Infections Surveillance System. *Crit Care Med.* 1999;27(5):887–892.

60. Anil Chander, Mohammad Shahid Raza. Antimicrobial susceptibility patterns of *Pseudomonas aeruginosa* clinical isolates at a tertiary care hospital in Kathmandu. *Asian Journal of Pharmaceutical and Clinical Research*. 2013;6(Suppl 3):235–238.

Citation: Paneru TP. Retrospective comparative study of *Pseudomonas aeruginosa* antibiotic resistance isolated from intensive care units (ICUs) patients from tertiary hospital in Nepal. *J Microbiol Exp.* 2022;10(2):65–72. DOI: 10.15406/jmen.2022.10.00355