SSR Institute of International Journal of Life Sciences
ISSN (O): 2581-8740 | ISSN (P): 2581-8732
Bharty *et al*., 2024
DOI: 10.21276/SSR-IIJLS.2024.10.3.7

Research Article

open access

Extended Spectrum Beta Lactamase-Producing *Pseudomonas aeruginosa*: Phenotypic Identification and Antimicrobial Resistance Pattern

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Received: 19 Dec 2023/ Revised: 05 Feb 2024/ Accepted: 06 Apr 2024

ABSTRACT

Background: *Pseudomonas aeruginosa* is the most prevalent Gram-negative bacteria associated with nosocomial infections. It is therefore necessary to study its trend of antimicrobial resistance. Few therapeutic alternatives are available as Extended spectrum Beta lactamases (ESBL)-producing organisms exhibit co-resistance to several antibiotics' classes. To study's aim is to study the prevalence, ESBL production, and resistance pattern of *P. aeruginosa* isolates obtained from respiratory samples employing phenotypic methods.

Methods: This study was conducted on 560 clinical respiratory samples from patients presented to the School of Excellence in Pulmonary Medicine, NSCB Medical College, Jabalpur, India**.** It was a prospective study conducted in the Department of Microbiology on 100 *P. aeruginosa* samples obtained from respiratory samples of both patient's in-patient department (IPD) and out-patient department (OPD).

Result: Among the 560 samples subjected to identification and isolation of aerobic growth, 385 samples were positive for bacterial growth. Of these, 100 (26%) samples were positive for *P. aeruginosa*. Antibiotic sensitivity pattern was determined for all the isolated strains. *P. aeruginosa* isolates showed maximum resistance to ticarcillin/clavulanic acid (79%), aztreonam (78%), and ceftazidime (74%). However, *P. aeruginosa* strains showed maximum sensitivity to piperacillin/tazobactam (88%). The same isolates were also examined using the double disc synergy method for phenotypic characterization of ESBL against ceftazidime and clavulanic acid using the CLSI standards. About 49% of the resistant *P. aeruginosa* strains isolated from sputum samples were positive for ESBL.

Conclusion: The current work strongly suggests further research on *P. aeruginosa* antibiotic-resistant strains for ESBL phenotypic characterization.

Key-words: Antimicrobial, Extended-spectrum ß-lactamases, Pseudomonal infection, *P. aeruginosa*, Susceptibility test

How to cite this article
Bharty SS, Gupta MK, Dhakar JS, Kumar V, Bharty SK. Extended Spectrum Beta Lactamase-Producing *Pseudomonas aeruginosa*: Phenotypic Identification and Antimicrobial Resistance Pattern. SSR Inst Int J Life Sci., 2024; 10(3): 5448-5455.

Access this article online
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INTRODUCTION

The well-known opportunistic bacterium *Pseudomonas aeruginosa* has an inherent resistance to several medicines and disinfectants. The lungs act as a primary site for bacterial colonization and infection. This could be either in the form of chronic, progressively deteriorating infectious and inflammatory pulmonary disease like cystic fibrosis (CF) or in a more acute situation such as

severe pneumonia in the case of immunocompromised patients [1].

P. aeruginosa is one of the most prevalent Gram-negative pathogens linked to infections and demonstrates a high degree of intrinsic resistance to antimicrobial medications, having the capacity to develop even greater drug resistance [2,3]. Nowadays, this bacterial species is producing resistance to all antibiotics which could be attributed to the production of ESBL due to overproduction of broad spectrum β-lactamases, active efflux, and decreased outer membrane permeability [4]. Extended-spectrum β-lactamase strains and multidrug resistance are highly prevalent in hospitals [5].

An interesting class of plasmid-mediated enzymes is called ESBL. Frankfurt, Germany described the first oxyimino beta lactamase or ESBL 1983 [6]. These enzymes produce resistance to extended-spectrum cephalosporins, carbapenems, and monobactums but do not impact cephamycins (cefoxitin and cefotetan) or carbapenems (meropenem or imipenem) [7].

Generally, the prevalence of beta-lactamases and ESBL is increasing and posing a serious threat with the increase in higher-generation cephalosporins [8]. There are many types of ESBL:

TEM beta-lactamases (class A) or TEM-1 is the predominant beta-lactamase in Gram-negative bacteria. It produces up to 90% ampicillin resistance in *E. coli* [9]. The amino acid changes that cause the ESBL phenotype group together around the enzyme's active region and alter its structure to provide substrates such as oxyimino beta-lactam access. About 140 TEM-type enzymes have been described based on different combinations of changes. Some of the most prevalent types found in the USA are TEM-10, TEM-12, and TEM-26 [10-12].

SHV beta-lactamases (class A) or SHV-1 share a similar overall structure and 68% of the same amino acids as TEM-1. The SHV 1 beta-lactamase causes most plasmid-mediated ampicillin resistance in *Klebsiella pneumoniae*, accounting for as much as 20% of the resistance. The amino acids surrounding the active site of ESBLs in this family are also altered; these modifications typically occur at positions 238 or 239 and 240. About 60 SHV variants are reported, with SHV 12 and SHV 5 as the two most prevalent variants [10].

The most prevalent variants of CTX-M beta-lactamases (class A) included CTX-M-14, CTX-M-3, and CTX-M-2. Currently, CTX-M-15 is the most widely prevalent type in the community, with its prevalence in *E. coli* in the UK [13]. The chromosome of *K. pneumoniae* ATCC BAA 2146 has recently been found to have transposed beta-lactamases CTX M 15 and ISEcp1[14]. For a considerable time, OXA beta-lactamases (class D) were acknowledged as a plasmid-mediated beta-lactamase variation that was less frequent but still capable of hydrolyzing oxacillin and related antistaphylococcal penicillins. Other plasmid-mediated ESBLs, including PER, GES, VEB, and IBC beta-lactamases, have been reported; however, these are rare and mostly found in *P. aeruginosa* and only a few geographic locations [14].

MATERIALS AND METHODS

The study was conducted on 560 clinical respiratory samples from patients presented to the School of Excellence in Pulmonary Medicine, Department of Microbiology, NSCB Medical College, Jabalpur, India. It was a prospective study involving 100 *P. aeruginosa* isolates from respiratory samples of the out-patient department (OPD) and in-patient department (IPD).

Inclusion criteria- Samples that showed growth of *P. aeruginosa.*

Exclusion criteria- Isolates other than *P. aeruginosa* were considered as exclusion criteria.

Inoculation of Samples- Routine cultures of all the isolates were done on nutrient and blood agar plates (Fig. 1a and b). The culture plates were incubated aerobically at 37°C overnight. Bacterial growth was checked after overnight incubation, and the microbes were identified using biochemical tests as per the standard laboratory methods [15]. Antibiotic sensitivity test was conducted on the National Committee for the clinical Laboratory Standard lines using Kirby Bauer disc diffusion method on Muller Hinton agar (MHA) [15].

Antibiotic Susceptibility Testing- All the *P. aeruginosa* isolates were tested for antibiotic susceptibility as per the standard CLSI guidelines for antimicrobials [16] including Piperacilin, Gentamycin, Ciproflaxacin, Amikacin, Cotrimoxazole, Tobramycin, Cefepime, Cefoperazone, Ceftazidime, Ceftazidieme + Clavulanic acid, Colistin, Meropenem, and Imipenem. According to CLSI guidelines, all the isolates with reduced

susceptibility to a third-generation cephalosporin were investigated for ESBL production [15].

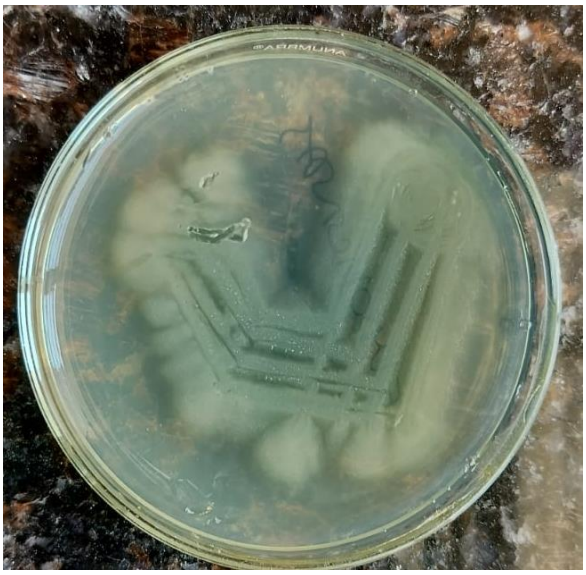

Fig. 1(a): Nutrient agar showing growth of *P. aeruginosa*

Fig. 1(b): Blood agar showing growth of *P. aeruginosa*

ESBL Detection- Phenotypic test was used for ESBL detection using combined disc diffusion method as per the CLSI guidelines. ESBL detection was done using following steps [16]:

1. About 4–5 colonies of the test strain were added to 1 ml of normal saline to maintain standard turbidity of 0.5 McFarland.
2. The inoculum on cation-balanced MHA plate was used to prepare lawn culture using a sterile cotton swab.
3. The cotton swab was rotated against the inner edge of the suspension tube to express any extra broth.
4. The antibiotic disc was placed after the inoculum had been allowed to dry for 15 minutes.
5. Phenotypic confirmation test for ESBL was conducted according to the CLSI guidelines using ceftazidime and ceftazidime + clavulanic acid on MHA [15].

Statistical Analysis- The study was conducted by SPSS 25.0 software. Statistical analysis, including comparisons of resistance patterns and prevalence rates among different demographic groups, was conducted to elucidate significant findings. The study's methodology likely involved standard microbiological techniques for isolate identification and antimicrobial susceptibility testing, with data analysis performed using appropriate statistical methods to draw meaningful conclusions about antimicrobial resistance patterns and their association with ESBL production. ANOVA was used as a statistical tool and $p<0.05$ was the level of significance.

Ethical Consideration- The institutional ethical committee granted ethical approval to conduct the current study.

RESULTS

Among the 385 bacterial isolates from 560 respiratory samples, 26% isolates were *P. aeruginosa*; rest isolates were *Streptococcus* (0.8%), *S. aureus* (22.6%), *E. coli* (11.8%), *K. pneumoniae* (28.2%), and *Enterococcus sp.* (10.6%) (Fig. 2). The present study revealed *Pseudomonas* infection as 69% and 31% among male and female, respectively. Table 1 shows the distribution of *Pseudomonas* infection in the in-patient and out-patient departments, with 65% of cases occurring indoors, whereas 35% are occurring in outdoor patients. It was observed that infection was prevalent in the age group 30-45 years. *Pseudomonal* infection was predominant in the urban population as compared to the rural population (Table 1).

Table 1: Sociodemographic characteristics of all patients with *Pseudomonas* infection.

Variables	**Percentage of culture-positive *Pseudomonas* samples (%)**
Gender	
Male	69
Female	31

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Place of presentation	
IPD	65
OPD	35
Age group (in years)	
15–30	19
30–45	34
45–60	30
60–75	17
Residential status	
Urban	53
Rural	47

IPD: in-patient department; OPD: out-patient department

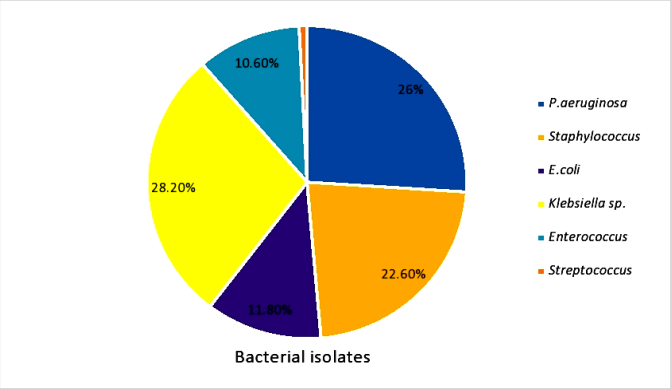

Fig. 2: Different isolates from the respiratory samples.

Table 2 shows the antimicrobial resistance pattern of all the *P. aeruginosa* isolates. The β-lactams group showed maximum resistance to ticarcillin/clavulanic acid (79%). This was followed by aztreonam (78%), ceftazidime (74%), cefoxitin (70%), meropenem (68%), imipenem (72%), ceftizoxime (55%), ceftriaxone (50%), and cefepime (48%). However, only 12% of isolates showed resistance to piperacillin/tazobactam. Aminoglycosides group showed maximum resistance to gentamicin (74%). This was followed by amikacin (69%), and netilmicin (64.0%). In the fluoroquinolones group, *P. aeruginosa* isolates showed maximum resistance to levofloxacin (67%), followed by ciprofloxacin (64%).

The distribution of ESBL-producing *P. aeruginosa* isolates as per CLSI method using discs of third-generation cephalosporins alone and combined with clavulanic acid was also studied. All the 100 isolates of *P. aeruginosa* were found positive with reduced susceptibility to one or the other third-generation cephalosporins. Out of the total 100 *P. aeruginosa* isolates tested, about 49% and 51% of isolates were ESBL producers and non-ESBL producers, respectively.

Table 3 compares the antimicrobial resistance pattern of ESBL-producing and non-ESBL-producing *P. aeruginosa* isolates against various antibiotics. On comparing the Significant difference was observed in the resistance pattern among ESBL-producing and non-ESBL-producing *P. aeruginosa* isolates against β-lactam drugs such as ceftazidime, ceftriaxone, cefepime, ceftizoxime, imipenem, and meropenem ($p<0.05$). However, aztreonam and cefoxitin showed a nonsignificant association ($p>0.05$). A non-significant relationship was observed between the resistance pattern of β-lactam/β-lactamase inhibitor combinations among ESBL-producing and non-ESBL-producing isolates when tested for piperacillin/tazobactam and ticarcillin/clavulanic acid ($p>0.05$). On analyzing the resistance pattern of aminoglycosides in ESBL-producing and non-ESBL-producing *P. aeruginosa* isolates, this study showed significant differences for amikacin, gentamicin, and netilmicin ($p<0.05$). On comparing the resistance to fluoroquinolones, a significant difference was seen in ciprofloxacin ($p<0.05$) as compared to levofloxacin ($p>0.05$), which was found to be non-significant.

Table 2: Antimicrobial resistance pattern of *P. aeruginosa* clinical isolates.

Antimicrobial drugs	***P. aeruginosa* isolates (n= 100)**	
	Number of resistant isolates (n)	**Percentage of resistant isolates (%)**
β-lactams		
Ceftizoxime (30 µg)	55	55
Ceftazidime (30 µg)	74	74
Ceftriaxone (30 µg)	50	50
Cefepime (30 µg)	48	48
Cefoxitin (30 µg)	70	70
Aztreonam (30 µg)	78	78
Imipenem (10 µg)	72	72
Meropenem (10 µg)	68	68
Piperacillin/Tazobactam (100/10 µg)	12	12
Ticarcillin/Clavulanic acid (75/10 µg)	79	79

Aminoglycosides		
Gentamicin (10 µg)	74	74
Amikacin (30 µg)	69	69
Netilmicin (30 µg)	64	64
Fluoroquinolones		
Ciprofloxacin (5 µg)	64	64
Levofloxacin (10 µg)	67	67

Table 3: Antimicrobial resistance pattern of ESBL-producing and ESBL non-producing *P. aeruginosa* isolate against various antibiotics

Antimicrobial drugs	**ESBL producers (n=49)**		**ESBL non producers (n=51)**		**p-value**
	n	**%**	**n**	**%**	
β- lactams					
Ceftazidime	49	100.0	25	49.1	<0.05
Ceftizoxime	49	100.0	6	11.8	<0.05
Ceftriaxone	48	97.9	2	3.9	<0.05
Cefepime	35	71.3	13	35.5	<0.05
Cefoxitin	32	65.3	38	74.6	>0.05
Aztreonam	42	85.72	36	70.6	>0.05
Imipenem	32	65.3	40	78.4	<0.05
Meropenem	28	57.1	40	78.4	<0.05
Piperacillin /tazobactam	3	6.1	9	17.6	<0.05
Ticarcillin/ clavulanic acid	40	81.6	39	76.5	>0.05
Aminoglycosides					
Gentamicin	34	69.4	40	78.4	<0.05
Amikacin	29	59.2	40	78.4	<0.05
Netilmicin	27	55.1	37	72.5	<0.05
Fluoroquinolones					
Ciprofloxacin	25	51.0	39	76.5	<0.05
Levofloxacin	16	32.7	17	33.3	>0.05

DISCUSSION

Antibiotic resistance has been identified as a concern to public health and is currently endangering the efficacy of several antibiotic medicines. It has been found that *P. aeruginosa*, which has a special tendency to develop treatment resistance, is linked to higher rates of morbidity and mortality [17]. This study was conducted on 100 *P. aeruginosa* isolates from several respiratory samples. Out of these, 69% and 31% isolates were obtained from male and female patients, respectively. These results agreed with the study by Uslan *et al.* and Kothari *et al*. [17,18]. This might be attributed to males being more exposed to various environmental factors than females. Thus, males are more prone to *Pseudomonas* infection.

Among 100 isolates, about 65% of patients were from IPD, while 35% of cases were from OPD in the hospital (Table 1). These results concurred with the study by Kothari *et al.* [18] with 69% *P. aeruginosa* isolates from the IPD. Infection in the present study was predominant in the age group of 30-45 years, like the study by Kothari *et al*. [18]. However, Shiny *et al.*[19] reported predominant Pseudomonal isolates in the age group 61–75 years. The possible reason could be that this age group (46-60 years) moves out of the house and is at utmost risk of acquiring infection. Urban populations are more prone to *Pseudomonas* infection than rural populations. These results were similar to the study by Kothari *et al*.[18] and contradictory to the study by Shiny *et al.*[19]. The possible reason could be the lower exposure of rural people to various environmental conditions (air pollution, water pollution, etc.) compared to urban people. About 26% of isolates in this study were positive for *P. aeruginosa,* while 74% were other bacterial species. It is a well-known fact that *P. aeruginosa* is a common environmental contaminant with the highest percentage of positivity in respiratory samples of the present study; these results were like the study by Shiny *et al*. [19].

Pseudomonas sp. presents a significant challenge in nosocomial infection as this species is inherently resistant to many antimicrobial agents. The present study analyzed the antimicrobial susceptibility patterns of a hundred clinical isolates of *P. aeruginosa* from respiratory samples using culture and sensitivity tests. In the β-lactams group, *P. aeruginosa* isolates showed maximum resistance to ticarcillin/clavulanic acid (79%). This was followed by aztreonam (78%), ceftazidime (74%), imipenem (72%), cefoxitin (70%), meropenem (68%), ceftizoxime (55%), ceftriaxone (50%), and cefepime (48%). Resistance was observed with piperacillin/ tazobactam in 12% of isolates. Shiny *et al*.[19] Their study showed lower resistance to these antibiotics, possibly because it included only respiratory patients who had already taken several antibiotics before and,

thus, developed resistance. Similar results were depicted concerning these antibiotics on *P. aeruginosa* isolates. Basak *et al*.[20] in their study reported 64% and 66% resistance to ceftazidime and cefepime, respectively. Similarly, Behera *et al*.[21] reported high resistance to β-lactams, 70% and 81% resistance to ceftazidime and cefepime, respectively. High resistance of about 97%, 82.7%, and 89.1% to cefoxitin, ceftazidime, and ceftizoxime was reported by Upadyay *et al*.[22]. These results were also to the findings of Kumar *et al*.[23] who reported 66.8%, 68.3%, and 48.5% resistance to ceftazidime, cefepime, and ceftriaxone, respectively. However, Agarwal *et al*.[24] reported low resistance to ceftazidime (10.35%) compared to the present study's results. Similarly, Khan *et al*.[25] also found low resistance to ceftazidime (30.2%), cefepime (31.7%), and aztreonam (37%) as compared to the present study. This disagreement in the results could be due to high usage of cephalosporins for empirical therapy in almost every patient admitted to this institute.

The present study showed a higher level of resistance to β-lactam/β-lactamase inhibitor combination with maximum resistance (79%) to ticarcillin/clavulanic acid and minimum resistance (12%) to piperacillin /tazobactam combination. Our results were in agreement with those of Lambert *et al*.[26] who reported 9% resistance to piperacillin/tazobactam in cystic fibrosis patients. Similarly, Behera *et al*.[21] reported 82% resistance to ticarcillin/clavulanic acid and Lister *et al*.[27] reported 11% resistance to piperacillin/tazobactam combination.

Aminoglycosides group showed maximum resistance to gentamicin (74%), followed by amikacin (69%), and netilmicin (64%). Similar results were reported by Kumar *et al*. [23]. However, low resistance to these antibiotics was reported by Shiny *et al*.[19] and Kothari *et al*.[18] This might be due to the varying usage of antibiotics from place to place. Among the fluoroquinolones group, *P. aeruginosa* isolates showed maximum resistance to levofloxacin (67%), followed by ciprofloxacin (64%). Comparable results were observed by Pitout *et al.* [28].

Of the 100 isolates of *P. aeruginosa* tested in the present study, 49% and 51% were ESBL and non-ESBL producers, respectively. Similar results were found in studies by Kothari *et al*.[18] and Shiny *et al*.[19] which showed 42.2% and 59% of ESBL producers, respectively. However, Chaudhari *et al*.[29] reported much higher ESBL production in 77.3% of *P. aeruginosa* than in the present study. This difference could be attributable to the study environment under which the study was conducted. Umadevi *et al*.[30] reported ESBL production in 19.4% of the *P. aeruginosa* isolates. Extensive use of β-lactam antibiotics in the given hospital causing selection pressure could be the reason behind such a high rate of ESBL production in the present study.

A comparative analysis of the antimicrobial resistance pattern of ESBL-producing and ESBL-non-producing *P. aeruginosa* isolates was conducted. The results indicated resistance to ceftazidime, ceftriaxone, cefepime, ceftizoxime, imipenem, and meropenem as 100%, 97.9%, 71.3%, 100%, 65.3%, and 57.1% in ESBL producing isolates of *P. aeruginosa,* respectively. Whereas, the resistance to ceftazidime, ceftriaxone, cefepime, ceftizoxime, imipenem, and meropenem was 49.1%, 3.9%, 35.5%, 11.8%,78.4%, and 78.4% in non-ESBL producing isolates of *P. aeruginosa* isolates, respectively. Statistical analysis showed a highly significant difference ($p<0.05$) in resistance to these drugs in non-ESBL and ESBL-producing *P. aeruginosa* isolates. Many authors reported high antibiotic resistance in ESBL-producing *P. aeruginosa* isolates [31,32]. Resistance to antibiotics such as piperacillin, cefotaxime, ceftriaxone, imipenem, ceftazidime, and aztreonam in 42.9%, 71.4%, 57.1%, 28.5%, 57.1%, and 42.9% ESBL producing *P. aeruginosa* isolates was observed by Tavajjohi *et al*. respectively [31]. However, these authors did not compare antibiotic resistance among ESBL and non-ESBL producers [31,32].

This study indicated a significant association ($p<0.05$) between resistance to aminoglycosides and fluoroquinolones in ESBL and non-ESBL-producing *P. aeruginosa* isolates. Resistance to gentamicin, amikacin, netilmicin, ciprofloxacin was observed in 69.4%, 59.2%, 55.1%, and 51% ESBL-producing *P. aeruginosa* isolates, respectively. Resistance to gentamicin, amikacin, netilmicin, and ciprofloxacin was observed in 78.4%, 78.4%, 72.5%, and 76.5% non-ESBL-producing *P. aeruginosa* isolates, respectively. Other authors reported high antibiotic resistance to these antibiotics in ESBL-producing *P. aeruginosa* isolates [31,32]. Resistance to antibiotics such as gentamicin and ciprofloxacin in 42.9% and 17.4% ESBL-producing *P. aeruginosa* isolates was reported by Tavajjohi *et al*.[31]. Pagani *et al*.[32] reported that PER-1 ESBL producers represent the nine outbreaks in Italy. It shows a multidrug resistance (MDR)

phenotype, including resistance to extended-spectrum cephalosporins, meropenem, aminoglycosides, aztreonam, and most commonly, ciprofloxacin and imipenem. However, the study did not compare antibiotic resistance patterns among non-ESBL and ESBL producers. Rates of drug resistance are higher among non-ESBL producers in aminoglycosides and fluoroquinolones. This may be due to different drug resistance mechanisms in ESBL non-producers and less prevalence of co-resistance for aminoglycosides and fluoroquinolones among these isolates [31].

CONCLUSIONS

Routine screening and detection of β-lactamases by phenotypic methods in clinical isolates of *P. aeruginosa* could provide a practical guide to clinicians to avoid therapeutic failures. In addition, appropriate treatment options must be introduced to reduce the spread of these resistant strains and reduce mortality in hospitalized patients.

To further reduce the emergence of MDR *P. aeruginosa* isolates, stringent antibiotic policies and steps to restrict the careless use of cephalosporins and carbapenems in the hospital setting should be implemented.

CONTRIBUTION OF AUTHORS

Research concept- Sonia Sharma Bharty, Manish Kumar Gupta

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Final approval- Sanjay Kumar Bharty

REFERENCES

[1] Knapp S, Schultz MJ, van der Poll T. Pneumonia Models and Innate Immunity to Respiratory Bacterial Pathogens. Shock. 2005; 24: 12-18.

[2] Nseir S, Di Pompeo C, Brisson H, Dewavrin F, Tissier S, et al. Intensive care unit-acquired Stenotrophomonas maltophilia: Incidence, risk factors, and outcome. Crit Care., 2006; 10: R143.

[3] Aloush V, Navon-Venezia S, Seigman-Igra Y, Cabili S, Carmeli Y. Multidrug-resistant *Pseudomonas aeruginosa*: Risk factors and clinical impact. Antimicrob Agents Chemother., 2006; 50: 43-48.

[4] Poole K. Efflux Pumps as Antimicrobial Resistance Mechanism. Annals of Medicine., 2007; 39: 162-76. doi: 10.1080/07853890701195262.

[5] Govan JR, Deretic V. Microbial Pathogenesis in Cystic Fibrosis: Mucoid *Pseudomonas aeruginosa* and *Burkholderia cepacia*. Microbiol Rev., 1996; 60: 539-74.

[6] Jacoby GA, Carreras I. Activities of beta-lactam antibiotics against *Escherichia coli* strains producing extended-spectrum beta-lactamases. Antimicrob Agents Chemother., 1990; 34: 858-62.

[7] Falagas ME, Karageorgopoulos DE. Extended-spectrum β-lactamase-producing organisms. JHI., 2009; 73: 345-54.

[8] Cooksey R, Swenson J, Clark N, Gay E, Thornsberry C. Patterns and mechanisms of beta-lactam resistance among isolates of Escherichia coli from hospitals in the United States. Antimicrob Agents Chemother., 1990; 34: 739-45.

[9] Paterson DL, Hujer KM, Hujer AM, Yeiser B, Bonomo MD, et al. Extended-spectrum beta-lactamases in *Klebsiella pneumoniae* bloodstream isolates from seven countries: Dominance and widespread prevalence of SHV- and CTX-M-type beta-lactamases. Antimicrob Agents Chemother., 2003; 47: 3554-60.

[10] Bradford PA. Extended-spectrum beta-lactamases in the 21st century: Characterization, epidemiology, and detection of this important resistance threat. Clin Microbiol Rev., 2001; 14: 933-51.

[11] Jacoby GA, Munoz-Price LS. The new beta-lactamases. N Engl J Med., 2005; 352: 380-91.

[12] Woodford N, Ward E, Kaufmann ME, Turton J, Pearson A, et al. Molecular Characterisation of Escherichia coli isolates producing CTX-M-15 Extended-spectrum beta-lactamases (ESBL) in United Kingdom. Health Protection Agency, 2006; 4: 11-19.

[13] Hudson CM, Bent ZW, Meagher RJ, Williams KP. Resistance determinants and mobile genetic

elements of an NDM-1-encoding *Klebsiella pneumoniae* strain. PLoS One, 2014; 9: e99209.

[14]Van Eldere J. Multicentre surveillance of *Pseudomonas aeruginosa* susceptibility patterns in nosocomial infections. J Antimicrob Chemother., 2003; 51: 347-52.

[15]Clinical and Laboratory Standard Institute. Performance standards for antimicrobial susceptibility testing 23rd informational supplement CLSI document M100-s23. Wayne, PA: Clinical and Laboratory Standards Institute; 2013.

[16]Bauer AW, Kirby WMM, Sherries JC, Jurek M. Antibiotic Susceptibility Testing by a Standardized Single. Method. Am J Clin Pathol., 1996; 54: 493-96.

[17]Uslan DZ, Crane SJ, Steckelberg JM, et al. Age- and sex-associated trends in bloodstream infection: A population-based study in Olmsted County, Minnesota. Arch Intern Med., 2007; 167: 834-39.

[18]Kothari A, Kumar S, Omar BJ, Kiran K. Detection of extended-spectrum beta-lactamase (ESBL) production by disc diffusion method among Pseudomonas species from various clinical samples. J Family Med Prim Care, 2020; 9: 683-93.

[19]Shiny P, Rajendran S, Sarayu Y. A Study on Isolation and Antibiotic Sensitivity Testing of *Pseudomonas aeruginosa* Isolated from Patients with Respiratory Tract Infection with Special Reference to Phenotypic and Genotypic Characterization of Extended Spectrum Beta Lactamases (ESBL). Open J Med Microbiol., 2016; 6: 80-86.

[20]Basak S, Khodke M, Bose S, Mallick SK. Inducible AmpC beta-lactamase producing *Pseudomonas aeruginosa* isolated in a rural hospital of central India. J Clin Diagnostic Res., 2009; 3: 1921-27.

[21]Behera B, Mathur P, Das A, Kapil A, Sharma V. An evaluation of four different phenotypic techniques for detection of metalo-β-lactamase producing *Pseudomonas aeruginosa.* Indian J Med Microbiol., 2008; 26: 233-37.

[22]Upadhyay S, Sen MR, Bhattacharjee A. Presence of different beta-lactamase classes among clinical isolates of *Pseudomonas aeruginosa* expressing AmpC beta-lactamase enzyme. J Infect Dev Ctries., 2010; 4: 239-42.

[23]Kumar V, Sen MR, Nigam C, Gahlot R, Kumari S. Burden of different β- lactamase classes among clinical isolates of AmpC producing *P. aeruginosa* in burn patients: A prospective study. Indian J Crit Care Med., 2012; 16: 136-40.

[24]Agarwal G, Lodhi RB, Kamalakar UP, Khadse RK, et al. Study of metallo-beta lactamase production in clinical isolates of *Pseudomonas aeruginosa.* Indian J Med Microbiol., 2008; 26: 349-51.

[25]Khan JA, Igbal Z, Rahman SU, Farzana K, Khan A. Prevalence and resistance pattern of *Pseudomonas aeruginosa* against various antibiotics. Pak J Pharm Sci., 2008; 21: 311-15.

[26]Lambert PA. Mechanisms of antibiotic resistance in *Pseudomonas aeruginosa*. J R Soc Med., 2002; 95: 22-26.

[27]Lister PD. Chromosomally-encoded resistance mechanisms of *Pseudomonas aeruginosa*: Am J Pharmacogenomics., 2002; 2: 235-43.

[28]Pitout JDD, Gregson DB, Poirel L, MaClure JA, Le P, et al. Detection of *Pseudomonas aeruginosa* producing MBLs in a large centralized laboratory. J Clin Microbiol., 2005; 43: 3129-35.

[29]Chaudhari U, Bhaskar H, Sharma M. The Imipenem–EDTA disk method for the rapid identification of metallo-β-lactamase producing gram negative bacteria. Indian J Med Res., 2008; 127: 406-407.

[30]Umadevi S, Joseph NM, Kumari K, et al. Detection of extended spectrum beta lactamases, ampc beta lactamases and metallo beta lactamases in clinical isolates of ceftazidime resistant *Pseudomonas aeruginosa*. Braz J Microbiol., 2011; 42: 1284-88.

[31]Tavajjohi Z, Moniri R, Khorshidi A. Detection and characterisation of multidrug resistance and extended spectrum beta lactamases producing *Pseudomonas aeruginosa* isolates in teaching hospital. Afr J Microbiol Res., 2011; 5: 3223-28.

[32]Pagani L, Mantengoli E, Migliavacca R, Nucleo E, Pollini S, et al. Multifocal Detection of Multidrug Resistant *Pseudomonas aeruginosa* Producing The PER-1 Extended-Spectrum β-Lactamase in Northern Italy. J Clin Microbiol., 2004; 42: 2523-29.