Journal of Bacteriology and Mycology

Open Access

Austin Publishing Group

Research Article

Epidemiological Aspects and Antibiotic Resistance Profile of *Pseudomonas aeruginosa* in Fann CHNU

Ka R[1,2]*, Diagne R[2], Niang AA[1,3], Ndiaye M[1], Diop A[3], Dièye B[3], Dia ML[1,3], Sow AI[1,3]

[1]Laboratoire de Bactériologie, CHU de Fann, Dakar, Sénégal

[2]UFR des Sciences de la Santé, Université de Thiès, Fann, Dakar, Sénégal

[3]Faculté de Médecine, Pharmacie et Odontologie, UCAD, Fann, Dakar, Sénégal

***Corresponding author:** Pr Roughyatou Ka, Laboratoire de Bactériologie, CHU de Fann. BP 15117 Dakar Fann, Dakar, Sénégal

Received: April 09, 2020; **Accepted:** May 01, 2020; **Published:** May 09, 2020

Abstract

Pseudomonas aeruginosa is a gram-negative bacillus, opportunistic pathogen, saprophyte of humid environments in hospitals. This bacteria, naturally resistant to several antibiotics, is often involved in the occurrence of care-associated infections.

P.aeruginosa is notorious for being intrinsically resistant to many structurally unrelated antimicrobial agents. These bacteria is one of those bacteria which are listed in the antimicrobial resistance survey. The objective of our study was to study the frequency of isolation of *P. aeruginosa* and to determine the evolution of antibiotic resistance in CHNU de Fann between 2012 and 2016. This is a retrospective, descriptive study of strains of *Pseudomonas aeruginosa* isolated from the Bacteriology Laboratory of Fann's Hospital. Bacteria were isolated according to current procedures. For each isolated strain, an antibiogram was performed following the recommendations of the CA-SFM. The average number of strains found was 151 per year. Most of them were isolated from patients over the age of sixty. The isolates came mainly from suppurations samples (49.1%) followed by urines (26.8%) and respiratory samples (16.2%). The study of global resistance showed rates of 40.6% for ticarcillin, 36.1% for gentamicin, 22.3% for ceftazidime, 25% for imipenem and 10% for ciprofloxacin. Regarding the sensitivity according to the pathological product, there was no noticeable difference for beta-lactams, whereas for aminoglycosides, isolated strains of blood cultures had higher resistance levels. *Pseudomonas aeruginosa* is a pathogen that is increasingly isolated in the laboratory. Its many virulence factors and its multi-resistance to antibiotics justify the surveillance that is essential to update the therapeutics protocols.

Keywords: *Pseudomonas aeruginosa*; Multi-Drug Resistant Bacteria; Antibiotics; Nosocomial Infections; Senegal

Introduction

Pseudomonas aeruginosa, also known as pyocyanic bacteria, is a non-fermentative, Gram-negative and a rode-shaped bacteria associated with a large variety of infections. It is an opportunistic pathogen, commonly found in the moist environments in the hospital, where it is often involved in the occurrence of nosocomial infections [1].

P. aeruginosa displays natural resistance to a large variety of antibiotics that belong to a broad range of families. This natural resistance is often associated with lower outer membrane permeability, efflux pumps that physically sequester incoming antibiotics and expel them out of the cell [2], or production of antibiotic inactivating enzymes [2]. Hence, antibiotic resistance, acquired through mutational changes or horizontal transfer of antimicrobial resistance genes, have also been described with *P. aeruginosa* [3]. Moreover, *P. aeruginosa* induces adaptive antimicrobial resistance by producing a biofilm that act as protective barriers against antibiotic penetration [4,5]. In addition, this adaptive resistance is often associated with generation, in the biofilm, of bacterial persister cells, tolerant to high concentrations of antibiotic, that contribute to the recalcitrance of *P. aeruginosa* caused chronic infections [6]. The multiplicity of the pathways employed by this bacteria to develop antibiotic resistance could explain the high frequency of the occurrence of acquired antipseudomonal resistance. This *P. aeruginosa* -mediated antimicrobial resistance could lead to a drastic therapeutic resource limitation drawback as very few or no conventional antibiotics are still effective in infections caused by multiresistant strains of *P. aeruginosa* [7]. Intriguingly, this hurdle appears difficult to overcome as the discovery of news drug is still very slow whereas the emergence of *P. aeruginosa* Multi-Drug-Resistant (MDR) strains is overwhelming [8]. Therefore, this bacteria rises a major public health concern and is thus, listed by the World Health Organization (WHO), among the pathogens to be monitored in the context of antimicrobial resistance surveillance [9].

Even though *P. aeruginosa* is increasingly isolated in the Fann University Hospital's laboratory, nationwide studies addressing its epidemiological characteristics, its antibiotic susceptibility profile as well as its spread conditions in the hospitals are still lacking in Senegal. Therefore, there is a crucial need to launch studies that address the mechanism that underline this striking phenomenon and its epidemiological aspects. Such studies would rule out the impact of *P. aeruginosa* mediated antibiotic resistance in patient's clinical outcomes.

Citation: Ka R, Diagne R, Niang AA, Ndiaye M, Diop A, Dièye B, et al. Epidemiological Aspects and Antibiotic Resistance Profile of Pseudomonas aeruginosa in Fann CHNU. J Bacteriol Mycol. 2020; 7(1): 1125.

It is in this particular context that we set to conduct this study that aimed at: (i) determining the frequency of isolation of the strains of *P. aeruginosa* circulating in the Fann University Hospital, (ii) establishing their epidemiological (iii) and their antibiotic susceptibility profiles.

Material and Method

To reach the goals assigned above, we conducted a retrospective cross-sectional study on the strains of *P. aeruginosa* isolated in the Bacteriology Laboratory of the Fann University Hospital (Dakar, Senegal) from January 2012 to December 2016.

Ethics

The study was approved by the Institutional Ethics committee of the "Université Cheikh Anta Diop de Dakar". As the data was collected as part of routine laboratory tests, informed consent was waived. No additional risk was possessed on behalf of the patients and all precautions needed was taken to keep their identification unrevealed.

Patients

All patients (inpatients and outpatients) attending the microbiology laboratory of the Fann University Hospital, to whom a cytobacteriological examination was prescribed, during the time of our study, were enrolled.

Samples

All the specimens including inter alia suppurations, blood, urine, respiratory specimen, harvested from the patients involved in our study, were used.

Isolation and identification of *Pseudomonas aeruginosa*

The isolation of the strains from the pathological products was performed by inoculating the clinical samples onto Mueller Hinton (MH) agar (BIORAD) and Eosin Methylene Blue (EMB) selective agar plates (BIORAD). The cultures were then grown at 37˚C for 18-24 hours. Subsequent to that, the plates were observed and the bacteria that form big, irregular, flat and translucent single colonies with a green fluorescent pigment which diffuses through the culture medium, and have a syringe-like odor, were assumed *P. aeruginosa*. To further identify the isolated colonies, to genus and species level, the suspected ones were peaked and used to perform Gram staining, motility test and biochemical tests (oxidase tests, sugar fermentation tests etc.). Ultimately, the aforementioned presumptive isolates were identified as *P. aeruginosa* based on their cultural and biochemical characteristics.

Susceptibility testing

The susceptibility to antipseudomonal drugs was carried out on Mueller Hinton agar, according to the Bauer-Kirby disc diffusion method [10] with respect to the National Committee for Clinical Laboratory Standards (NCCLS) [10]. To this end, the isolated colonies from the culture conditions described above, were picked and suspended in a tube containing 2-3 ml of a 0.85% sterile saline solution. The turbidity was then adjusted to 0.5 McFarland standards. This preparation was thereafter spread uniformly onto the Mueller Hinton agar (BIORAD) using sterile cotton swabs. The antibiotics discs were placed on the plates following a setting that allows for direct detection of a potential extended spectrum beta-lactamase.

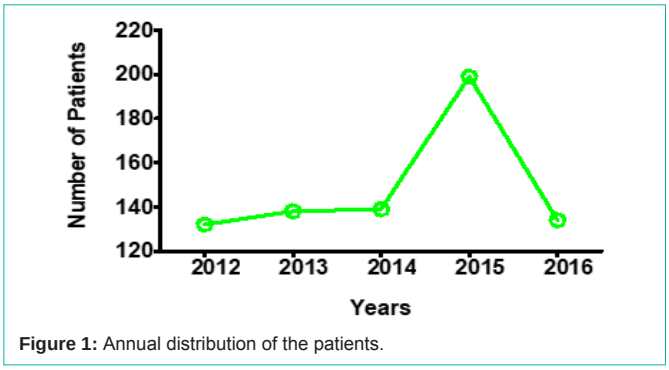

Figure 1: Annual distribution of the patients.

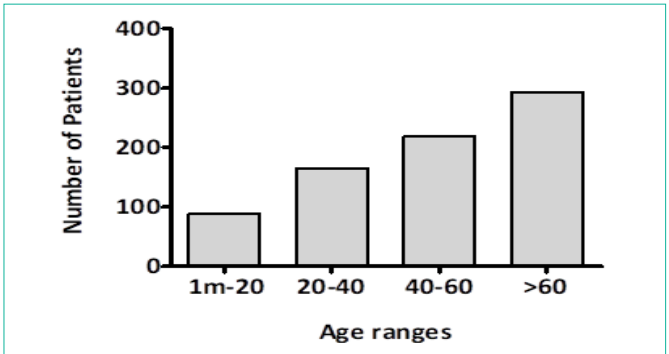

Figure 2: Distribution per age of the patients.

These latter were then inverted and incubated at 35-37˚C for 16 to 18 hours. Following overnight incubation, a bacterial lawn appeared on the plates with zones of inhibition around the antibiotic discs. The diameters of the inhibition zones were measured and the results were recorded as susceptible (S) intermediate (I) and resistant (R). The data were interpreted according to the 2017 CA-SFM recommendations [10]. A systematic search for extended spectrum beta-lactamase was done using the synergy test.

The following antibiotics all purchased from BIORAD, were used at the indicated concentrations, in our study: Ticarcillin (TIC; 75 µg), Ticarcillin-clavulanic acid (TCC; 75-10 µg), Aztreonam (ATM; 30 µg), Cefepime (FEP; 30 µg), Ceftazidine (CAZ; 10 µg), Ciprofloxacin (CIP; 100 µg), Colistin (CST; 10 µg), Imipenem (IPM; 10 µg), Piperacillin (PIP; 100 µg), Fosfomycin (FOS; 200 µg), Kanamycin (K; 30 µg), Piperacilline+tazobactam (PPT; 30/06 µg), Gentamicine (GN; 10 µg), Tobramycine (TM; 10 µg), Amikacin (AK; 30 µg), Levofloxacin (LEV; 5 µg). *P. aeruginosa* ATCC 27853 was used as quality control reference strain for the verification of our procedures.

Statistical analysis

Data were collected and analyzed using the Excel and the GraphPad Prism softwares. Discrete variables were expressed as frequencies and percentages. The chi-squared test was used at 5% ($P \leq 0.05$) significance level, to compare proportions of categorical variables.

Results

Patients

A total of 755 patients with a yearly average number of 148 ± 28 strains were involved in our study. The year 2015 was the year with

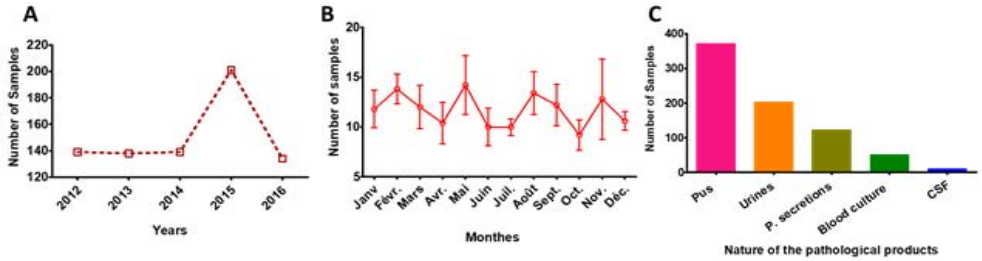

Figure 3: Characteristics of samples collected during the study.

Table 1: Pathological products collected from the patients included in our study.

Pathological products	Numbers	Percentages (%)
Pus	371	49,1
Urines	202	26,8
Pulmonary secretions	122	16,2
Blood culture	50	6,6
CSF	10	1,3
Total	**755**	**100**

the highest number of patients (199 patients) registered (Figure 1). Our patients included outpatients (20%; n=152) and inpatients (80%; n=603). Among them, 60.2% (n=455) were males and 39.8% (n=300) were females displaying thereby, a male preponderancy translated into a sex ratio of 1.5. The mean age was 46 ± 16 years with ages ranging from 1 month to 85 years while the median age was 49 years. Hence, 29% (n=219) of the patients were in the 40-60 years age groups while 37.8% (n=283) of the patients aged over 60 years (Figure 2).

Samples

A total number of 755 clinical samples, for a cytobacteriological examination, were received, in the laboratory, during the time of the study (Table 1). The average number of samples was 151 ± 27 yearly with the highest number of samples received in 2015 (Figure 3). Comparing the number of samples received per month, no significant difference was noticeable between the different months (Figure 3). Of the clinical samples received, the most frequent type of pathological products were the suppurations (49.1%; n=371), followed by the urines (26.8%; n=202) and the respiratory specimens (16.2%; n=122) (Table 1, Figure 3).

Pseudomonas aeruginosa isolation

Overall, 755 isolates of *P. aeruginosa* were collected over the 5 year's timeframe. The analysis of the frequency of isolation over time revealed that 152 ± 33 strains were isolated yearly in the laboratory with the highest frequency (211/year) registered in 2015. The great majority (80%; n = 603) of the bacterial strains were isolated from inpatients more precisely from those hospitalized in the surgery departments (45%; n=271) (Figure 4). Only 20% (n=152) of the isolates were recovered from outpatients.

With regard to patient's age, the clinical samples collected from the patients aged over 60 years old, yielded 40% (300 strains) of the isolates.

Analysing the distribution of the isolates according to the different types of clinical samples, we discovered that *P. aeruginosa*

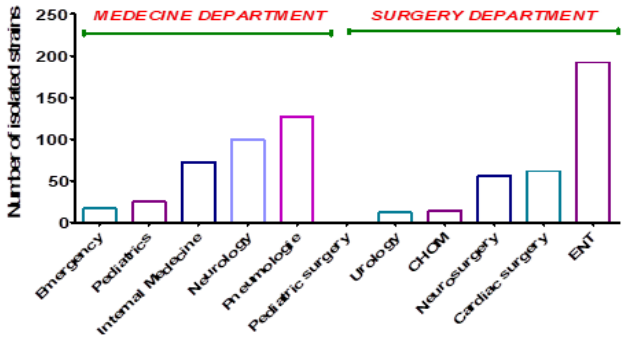

Figure 4: Number of *P. aeruginosa* strains isolated according to the clinical unit.

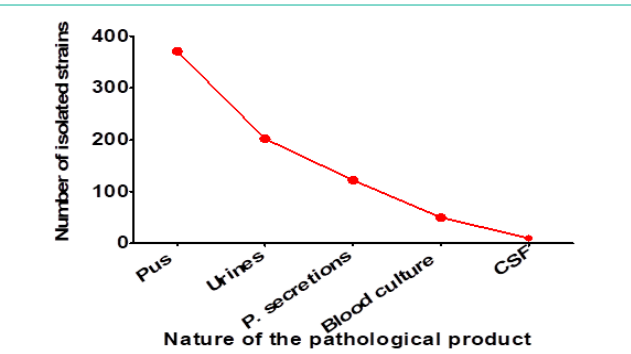

Figure 5: Number of *P. aeruginosa* strains isolated according to the type of clinical sample.

was more prevalent in the suppurations (49.1%; n=371) followed by the urine (26.8%; n=202) and respiratory specimens (16.2% n=122) whereas the blood (6.6%; n=50) and the CSF (1.3% n=10) contributed poorly to that distribution (Figure 5).

Antibiotic susceptibility

***P. aeruginosa* susceptibility to beta-lactam antibiotics:** An average number of 466 ± 143 strains of *P. aeruginosa* was tested for their susceptibility to a broad range of beta-lactam antibiotics. The results gathered from this antibiotic susceptibility testing revealed that, 25.6 ± 10.2% ($P < 0.005$) of the isolates of *P. aeruginosa* encountered in the Fann University Hospital, displayed antipseudomonal resistance toward the antibiotics tested in our setting. In contrast, 68.03 ± 11.7% ($P < 0.005$) of the strains were susceptible to the tested antibiotics while only 6.35 ± 4.9% ($P < 0.005$) of them were showing intermediate resistance (Figure 5).

Table 2: *P. aeruginosa* susceptibility to beta-lactam antibiotics.

Antibiotics	Number of strains	Susceptible (%)	Intermediate (%)	Resistant (%)
Ticarcillin	569	54	5,4	40,6
Ticarcillin + Clavulanic Acid	426	59,6	2,3	38
Piperacillin	260	82,3	1,5	16,2
Piperacillin + Tazobactam	515	84,7	2,5	12,8
Ceftazidime	515	58	9,7	32,3
Aztreonam	606	60,1	16,2	23,7
Cefepim	246	72,8	8,1	19,1
Imipenem	590	72,8	5,1	22,1
Mean ± STD	**466 ± 143**	**68,03 ± 11,7**	**6,35 ± 4,9**	**25,6 ± 10,2**

Table 3: *P. aeruginosa* susceptibility to non-beta-lactam antibiotics.

Antibiotics	Number of strains	Susceptible (%)	Intermediate (%)	Resistant (%)
Gentamicin	455	83,3	0,44	16,26
Amikacin	660	95,45	0	4,55
Ciprofloxacin	634	88,8	1,26	9,93
Levofloxacin	336	88,7	1,78	9,52
Colostin	353	95,46	0	4,53
Mean ± STD	**488 ± 153**	**90,34 ± 5,2**	**0,70 ± 0,79**	**8,95 ± 4,83**

Table 4: *P. aeruginosa* susceptibility according to the type of the pathological product.

Antibiotics	Blood (%)	Urin (%)	Pus of otitis (%)	SSI (%)	Mean ± STD
Ticarcillin	31,3	50,4	58	42,7	45,6 ± 11,4
Ceftazidime	51,8	62,8	69,8	58	60,6 ± 6,6
Imipenem	80,5	87,8	91	80,5	84,95 ± 9,26
Amikacin	75,6	98,2	95,7	96,8	91,575 ± 9,26
Ciprofloxacin	85,3	90,7	86,7	92,4	88,775 ± 2,88
Colistin	80,3	98,9	96,4	96,4	93 ± 7,40
Mean ± STD	**67,46 ± 21,3**	**81,46 ± 20,11**	**82,93 ± 15,6**	**77,8 ± 22,59**	**77,41 ± 19,61**

With 40.6% (n=227) of the isolated strains resistant to it, Ticarcillin was the antibiotic the mostly affected by the *P. aeruginosa* mediated antimicrobial resistance (Table 2). Pseudomonal Ticarcillin resistance was slightly lowered (38%; n=216) when Clavulanic Acid was associated with Ticarcillin. The testing of the other related antibiotics such as Ceftazidime, Aztreonam and Imipenem, in the same setting, resulted in 32.3%, 23.7% and 22.1% resistance frequencies respectively (Table 2).

Determining the antibiotic resistance phenotype, we discovered that 40% of the strains were secreting a penicillinase, 25% were producing an Extended Spectrum Beta-Lactamase (ESBL) while 14% of them were presenting low outer membrane permeability to Imipenem (IMPR).

***P. aeruginosa* susceptibility to non-beta-lactam antibiotics:** Overall 488 ±153 isolates of *P. aeruginosa* were tested for their susceptibility to various non-bata-lactamin antibiotics. This testing have depicted a high overall susceptibility (90, 3 ± 5%) to the tested non-beta lactam antibiotics. For instance, the lowest susceptibility rated were observed with Levofloxacin (88.7%), Gentamicin (83.3%) and Ciprofloxacin (88.8%) (Table 3).

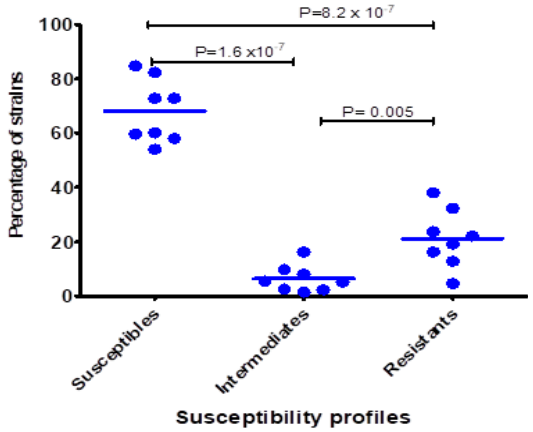

Figure 6: Distribution of antibiotics susceptibility of Pseudomonal strains.

***P. aeruginosa* susceptibility over the type of pathological product:** When comparing the strains of *P. aeruginosa* isolated from various types of pathological products, no significant difference in the susceptibility rates was noticeable between the strains isolated

from the urine (81.5 ± 20%), the Otitis (82.9 ±15%) and surgery site infection (SSI) (77.8 ± 22.59%) (Figure 5A). Whereas, lower levels of antibiotic susceptibility (67.46% ± 21, 3; P=0.04) was exhibited by the strains isolated from the blood samples (Figure 5A).

This difference in susceptibility rates was more pronounced when Ticarcillin, Ceftazidime and Amikacin, tested on strains derived from various clinical samples, (Table 4) were compared. For instance, 31.3% of the strains derived from blood were susceptible to Ticarcillin while this frequency was estimated at 50, 4%, 58% and 42,7% in the strains derived from the urine, the Otitis suppuration, and SSI respectively. Similar magnitudes of difference in susceptibility rates were also observed with, Ceftazidime and Amikacin when comparing strains recovered from the listed clinical samples (Table 4). This discrepancy in antibiotic susceptibility *P. aeruginosa* isolates derived from different clinical samples was not observed with the other antibiotics tested in this settings.

Discussions

Pseudomonas aeruginosa is a large bacterium that causes care-associated infections with complex virulence [11]; this pathogen continues to cause therapeutic challenges because with high morbidity and mortality rate associated with infections of *P. aeruginosa* and the possibility of developing drug resistance during treatment [12]. Prevalence surveys of nosocomial infections conducted here and elsewhere show that this bacteria generally occupies second place after broad-spectrum Beta-Lactamase Secreting Enterobacteria (ESBL) [12,13,14]. In our study, we found on average 136 strains / year except in 2015 where there were 211 isolates; after investigations, two outbreaks of nosocomial *P. aeruginosa* infections occurred in this year in a unit of the hospital. The majority of patients were over 60 years old in our series. Older age is not a risk factor, but it is the common underlying conditions that weaken defenses in older people make them more susceptible to infectious risks [11]. Forty-five percent of the isolates were from surgical patients. Indeed, it is known that *P. aeruginosa* is a bacterium feared by surgeons because often involved in the occurrence of superinfection of surgical wounds [12,15]. It is a bacterium that is also responsible for urinary tract infections, especially in elderly patients with indwelling catheters [16,17,18]. Pathoogen also found in bacteremia [19,20], which is a serious disorder with significant morbidity and mortality worldwide and is one of the most common Health-Related Infections (HAI). Their incidence is correlated with the increase of central or peripheral venous catheters use. Long term in intensive care unit and non-compliance with basic rules of asepsis and hygiene are additional risk factors [18]. *Pseudomonas aeruginosa* can be isolated from pulmonary specimens that reflect or reveal a debilitated area such as superinfection in the field of chronic bronchopneumopathy or cystic fibrosis [21,22,23].

The resistance rates of *P. aeruginosa* in the bacteriology laboratory vary according to geographical location, community or nosocomial nature of the infection, type of hospital service and type of sampling [24,25]. *Pseudomonas aeruginosa* is a naturally multi-resistant bacterium, and the most commonly prescribed antibiotics in the first line of therapy are ticarcillin and ceftazidime. But there are fairly high levels of resistance (40.6% for ticarcillin and 42% for ceftazidime which is a marker of multi-resistance); studies in other countries, such as Spain and Togo, show fairly similar rates [16,26, 27]. We found a resistance rate of 22% for imipenem, resistance also reported by other studies [18,27]; the mechanisms involved are the impermeability which results in an isolated resistance to imipenem and which concerned 14.6% of our strains and the secretion of carbapenemases appeared as a result of the abusive or inappropriate use of carbapenems for the treatment of multi drug resistant bacteria [19]. Aminoglycosides were generally active with fairly low levels of resistance (gentamicin: 16.3% and amikacin: 4.5%): these antibiotics are essentially parenterally administered molecules, which explains their limited use. We have noted good sensitivity of the latest-generation fluoroquinolones, which is also found in other studies [15, 18]; and these critical antibiotics are used to treat multidrug-resistant *P. aeruginosa* infections [24,25].

Conclusion

The evaluation and monitoring of bacterial resistance to antibiotics is one of the roles of the bacteriology laboratory. *Pseudomonas aeruginosa* is a ubiquitous germ that can cause multiple opportunistic infections that can occur as epidemics in healthcare settings. Its medical interest lies mainly in the fact that the opportunistic infections caused are often serious and difficult to cure, because of a strong resistance to many antibiotics. This study revealed high levels of resistance to antibiotics (including beta-lactam antibiotics) with 25% resistance to imipenem, a molecule used for the treatment of multi-resistant bacterial infections. It is a pathogen of clinical and epidemiological importance due its increasing frequency and the problems of therapeutic involved.

References

1. Nauciel C, Vilate JL. Bactériologie médicale connaissances et pratiques 2e Edition. Paris: Masson. 2000; p140-141.
2. Miryala SK, Anbarasu A, Ramaiah S. Systems biology studies in *Pseudomonas aeruginosa* PA01 to understand their role in biofilm formation and multidrug efflux pumps. Microb Pathog. 2019; 136: 103668.
3. Buhl M, Kästle C, Geyer A, Autenrieth IB, Peter S, Willmann M. Molecular Evolution of Extensively Drug-Resistant (XDR) *Pseudomonas aeruginosa* Strains from Patients and Hospital Environment in a Prolonged Outbreak. Front Microbiol. 2019; 10: 1742.
4. Müller L, Murgia X, Siebenbürger L, Börger C, Schwarzkopf K, Sewald K, Häussler S, Braun A, Lehr CM, Hittinger M, Wronski S. Human airway mucus alters susceptibility of *Pseudomonas aeruginosa* biofilms to tobramycin, but not colistin. J Antimicrob Chemother. 2018; 73: 2762-2769.
5. Eliana Drenkard. Antimicrobial resistance of *Pseudomonas aeruginosa* biofilms. Microbes and Infection. 2003; 5: 1213-1219.
6. Patrick K. Taylor, Amy T.Y. Yeung, Robert E.W. Hancock. Antibiotic resistance in *Pseudomonas aeruginosa* biofilms: Towards the development of novel anti-biofilm therapies. Journal of Biotechnology. 2014; 19: 121-130.
7. Gowri Raman, Esther E. Avendano, Jeffrey Chan, Sanjay Merchant & Laura Puzniak. Risk factors for hospitalized patients with resistant or multidrug-resistant *Pseudomonas aeruginosa* infections: a systematic review and meta-analysis. Antimicrobial Resistance & Infection Control. 2018; 79.
8. Pang Z, Raudonis R, Glick BR, Lin TJ, Cheng Z. Antibiotic resistance in *Pseudomonas aeruginosa*: mechanisms and alternative therapeutic strategies. Biotechnol Adv. 2019; 37: 177-192.
9. Organisation Mondiale de la santé: Guide pour établir la surveillance en laboratoire. Available at www.afro.who.int › sites › default › files › guide-for-establishing-lab-survey.
10. Détermination de la sensibilité aux antibiotiques. In: CASFM/EUCAST:

Société Française de Microbiologie Ed. 2016; 08-15.

11. Bentzmann S, Plesiat P. *Pseudomonas aeruginosa*: une virulence complexe. Revue Francophone des Laboratoires. 2011; 435: 73-81.

12. Floret N, Bertrand X, Thouverez M, Talon D. Infections nosocomiales à *Pseudomonas aeruginosa*: origine endogène ou exogène de la bactérie? Pathologie Biologie. 2009; 57: 9-12.

13. Dia NM, Ka R, Dieng C et al. Résultats de l'enquête de prévalence des infections nosocomiales au CHU de Fann (Dakar, Sénégal). Médecine et Maladies Infectieuses. 2008; 38: 270-274.

14. Deguenonvo LF, Traore K, Dia Badiane NM, Ka R, Cissoko Y. Résultats d'une enquête d'incidence des cas d'infections nosocomiales à bactéries multi résistantes dans un Centre Hospitalier à Dakar (Sénégal). Revue Malienne d'Infectiologie et de Microbiologie. 2015; 5: 8.

15. Rapport d'activité de l'Observatoire National de l'Epidémiologie de la Résistance Bactérienne aux Antibiotiques (ONERBA). France. 2016.

16. Salou MDS, Ekouevi DK, Nyasenu T, Lack F, Loko K, Tigossou S, Prince David M, Dagnra. Aspects phénotypiques de la résistance aux β-lactamines des souches de *Pseudomonas aeruginosa* isolées au laboratoire de Bactériologie médicale du CHU Sylvanus Olympio (CHU SO) de Lomé, Togo. J. Rech. Sci. Univ. Lomé (Togo). 2014; 16: 157-162.

17. Drissi M, Baba Ahmed Z, Dehecq B, Bakour R, Plésiat P, Hocquet D. Antibiotics susceptibility and mechanisms of β-lactams resistance among clinical strains of *Pseudomonas aeruginosa*: First report in Algeria. Médecine et maladies infectieuses. 2008; 38: 187-191.

18. Frikh M, Maleb A, Nyaledome Ablavi I, Elouennass M, Lemouer A. *Pseudomonas aeruginosa*: épidémiologie et état actuel des résistances: étude rétrospective sur trois ans. Journal Marocain des Sciences Médicales. 2017; 21: 33-40.

19. Gellen-Dautremer J. Bactériémie à *Pseudomonas aeruginosa*. Antibiotiques. 2010; 12: 75-81.

20. Ebongue CO, NdaMefo'o JP, Ngouadjeu Dongho, Eboumbou Moukoko EC, Adiogo D, Beyiha G. Profil bactériologique et sensibilité aux antibiotiques des isolats d'hémoculture (2006-2011) à Douala, Cameroun C. Revue malienne d'infectiologie et de microbiologie. 2014; 2: 27-39.

21. Meite S, Cisse CB, Monemo P, Babo CJ, Mlan Tanou AP, Faye-Kette H, Dosso M, Amonkou A. Profil de résistance des bactéries isolées des prélèvements bronchiques protégés chez des patients sous ventilation assistée en réanimation au CHU de Yopougon. Médecine d'Afrique noire. 2011; 415-422.

22. Hoiby N, Fredericksen B, Pressler T. Eradication of early *Pseudomonas aeruginosa*. Journal of cysticfibrosis. 2005; 4: 49-54.

23. Lenoir G, Vrielynck S, Clairicia M, Fezaa DA, Sorin M, Sermet Gandelus I. Infection bactérienne et mucoviscidose. Revue Francophone des Laboratoires. 2007; 397: 49-57.

24. Merens A, Delacour H, Plesiat P, Cavallo JD, Jeannot K. *Pseudomonas aeruginosa* et résistance aux antibiotiques. Revue Francophone des Laboratoires. 2011; 435: 49-62.

25. Chatterjee M, Anju CP, Biswas L, Anil Kumar V, Gopi Mohan C, Biswas R. Antibiotic resistance in *Pseudomonas* and alternative therapeutic options. Int J Med Microbiol. 2016; 306: 48-58.

26. Sevillano E, Valderrey C, Canduela MJ, Umaran A, Calvo F, Gallego L. Resistance to antibiotics in clinical isolates of *Pseudomonas aeruginosa*. Pathologie Biologie. 2006; 54: 493-497.

27. Gonsu Kamga H, Toukam M, Sando Z, Ndifo Ngamba JM, Mbakop CD, Adiogo D. Caractérisation phénotypique des souches de *Pseudomonas aeruginosa* isolées dans la ville de. 2015.