ISSN: 2977-4047

Journal of Life Sciences Research and Reviews

SCIENTIFIC Research and Community

Research Article

Open Access

# Prevalence of Pseudomonas Aeruginosa in ICU Patients Clinical Isolates in Khartoum State Hospitals, Sudan, 2023

**Abdelrhman Akram Kamal Eldin Ahmed[1], Ahmed Mohammed Elhassan Elamin Ibrahim[1], Malaz Abdelrhman Taj Alsir Mohammed Khair[1], Mohaira Omer Abdallrsool Ataa Almnan[1], Wafa Mohammed Hussein Abuelgasim[2], Ahmed Mohamed Farah Shadoul[3], Ayman Anwar Mohammed osman[4] and Muslih Haroun Elhussien Gamea[5*]**

[1]Department of Microbiology, Faculty of Medical Laboratory Sciences Program, Nile University, Sudan

[2]Faculty Deen of Nile university, Medical Laboratory Sciences, Assistant Professor of Medical Microbiology, Sudan

[3]Secretary General Sudan Medical Specialization Board, Sudan

[4]Forensic Science Institute, Sudan

[5]Sudan International University, Register of the National Council for Medical and Health Professions, Sudan

## ABSTRACT

**Background:** Pseudomonas aeruginosa is one of the most frequent Gram-negative pathogens responsible for nosocomial pneumonia.

**Methods:** This is a cross-sectional analytical study was carried out on the target population (Khartoum state) (2023). The study included a total of (320) people of different ages, all volunteers were verbally informed about the study and their consent form were obtained, sample was collected, IBM statistic SPSS (V 25) was used for statistical analysis.

**Results:** our study was designed to estimate the prevalence of Pseudomonas aeruginosa in ICU patients which revealed that among participants a high percent of females (78.4%) was diagnosed by pseudomonas with a majority source in urine, a fair of them aged between 31 – 40 years, most of them were single with 53.8%, results revealing that less than 20.3% were treated with antibiotics all samples were resistance to Meropenem and Imipenem, and for 1 – 3 months period of treatments.

**Conclusion:** This finding highlights the necessity of continuous antimicrobial resistance surveillance for this bacterium is necessary for guiding antimicrobial treatment and finding new treatments, providing workshops and ensuring the level of knowledge remains high among health worker specially. Additionally, more effort should be made to educate people about the risk of drug resistance of these bacteria, more effort should be done by hospital staff in sterilization specially ICU wards.

***Corresponding author**

Muslih Haroun Elhussien Gamea, Sudan International University, Register of the National Council for Medical and Health Professions, Sudan.

**Received:** November 10, 2025; **Accepted:** November 18, 2025; **Published:** November 24, 2025

## Introduction

Pseudomonas *aeruginosa* is one of the most frequent Gram-negative pathogens responsible for nosocomial pneumonia [1]. According to data reported by the National Healthcare Safety Network (NHSN), P. aeruginosa (16.6%) ranked second in the USA among the pathogens isolated from VAP patients from 2009 to 2010 [2]. In comparison, the prevalence of P. aeruginosa in CAP is much lower. P. aeruginosa was the pathogen in only 0.05% of patients with CAP [3].

Initial empirical antimicrobial therapy is commonly recommended in guidelines for the management of pneumonia [4]. The initial management of a suspected P. aeruginosa infection should include a selected β-lactam plus either an antipseudomonal quinolone or an aminoglycoside [4].

Recent trends show an increase in the prevalence of nosocomial pneumonia (NP) caused by multidrug-resistant (MDR) Gram-negative bacteria, most commonly Pseudomonas aeruginosa with documented resistance to β-lactams, carbapenems, aminoglycosides, and fluoroquinolones [5]. Consequently, the therapeutic effectiveness of current therapies for bacterial NP is becoming increasingly limited, emphasizing the need for development of new and effective antimicrobials as well as novel strategies to prevent resistance emergence [6].

Nosocomial pneumonia due to P. aeruginosa (Pa-NP) is associated with considerable morbidity, prolonged hospitalization, increased costs, and mortality [7]. P. aeruginosa is one of the few pathogens independently associated with increased mortality among patients with sepsis or pneumonia in the ICU setting [8]. The mortality associated with Pa-NP is further increased when inappropriate

initial antibiotic therapy (IIAT) is prescribed, usually due to the presence of MDR pathogens [9].

The overall impact of Pa-NP on clinical outcomes and healthcare costs underscores the importance of this nosocomial infection.

**Justification**

P. aeruginosa pneumonia is becoming difficult to treat because of the increasing prevalence of drug resistance and the resultant limited therapeutic options [10]. Studying the current prevalence of the bacteria will be useful in future therapeutic studies. There a few previous studies conducted about this study in Sudan.

**Objectives**

**General Objective**

- To estimate the prevalence of *Pseudomonas aeruginosa* in Khartoum hospitals, 2202-2023.

**Specific Objectives**

- To estimate the prevalence of Pseudomonas aeruginosa in ICU Patients Clinical Isolation.
- To detect resistance of antimicrobial sensitivity among isolation.
- To identify clinical risk factors associated with MDR Pa-NP
- To compare the results with the patient demographic data and clinical status.

**Literature Review**

**Introduction**

*P. aeruginosa* is the most commonly encountered gram-negative species that is not a member of the family Enterobacteriaceae and is an uncommon member of the normal human flora. The organism survives in various environments in nature and in homes and hospitals. Because of the ubiquitous nature of *P. aeruginosa*, the transmission of to humans can occur in a variety of ways. *P. fluorescens*, *P. putida*, and *P. stutzeri* are environmental inhabitants, but they are much less commonly found in clinical specimens than is *P. aeruginosa.* The other pseudomonads are also environmental organisms. Because they are rarely encountered in patient specimens, the mode of transmission to humans remains uncertain [11]. Pseudomonas aeruginosa, the primary human pathogen in the genus *Pseudomonas*, is widely distributed in nature. It may colonize healthy humans without causing diseases, but is also a significant opportunistic pathogen, and a major cause of nosocomial (hospital acquired) infections [12]. Pseudomonas aeruginosa is regularly a cause of nosocomial pneumonia, nosocomial urinary tract infections, surgical site infections, infections of severe burns, and infections patients undergoing either chemotherapy for neoplastic diseases or antibiotic therapy [13].

Pseudomonas aeruginosa is one of the most important microorganisms which causes problems clinically as a result of its high resistance to antimicrobial agents [14].

**Pathogenesis**

*P. aeruginosa* can cause infection in almost any part of the body, although it does not membranes or skin have become compromised such that they no longer serve as a physical barrier to typically cause infection in a healthy host. People who are most susceptible to P. aeruginosa infections are those who's mucous infection (e.g. in burn patients) [15] Being neutropenic or otherwise immunodeficient predisposes patients to infection with many different organisms of which *P. aeruginosa* is one. The unique lung environment that occurs in patients with cystic fibrosis fosters a chronic infection with P. aeruginosa in which the organism displays a characteristic mucoid phenotype due to the production of alginate that surrounds microcolonies of the organism [16]. Hospitalized patients who have cardiovascular disease, cancer or diabetes and especially patients on mechanical respirators are likely to acquire pneumonia or bacteremia due to P. aeruginosa in hospitalized patients lead to increased length of stay (LOS) and increased costs as well as significant morbidity and mortality [17]. The type of infection caused by P. aeruginosa varies by whether the person is healthy or has underlying disease or had some type of healthcare intervention [18].

The pathogenesis of pseudomonal infections are both invasive and toxigenic. The 3 stages are bacterial attachment and colonization, local infection, and bloodstream dissemination and systemic disease [19].

In order for P. aeruginosa to cause any type of infection it must first enter the host and colonize. Entry is often via inhalation into the respiratory tract, but the organism is so ubiquitous that is hard to tell exactly how the organism is acquired in all cases [20].

**Virulence Factors**

*P. aeruginosa* is able to adapt to the adverse environment in hosts by secreting a variety of virulence factors, which contribute to successful infection and causing disease [21].

The virulence factors produced by *P. aeruginosa* can be divided into two functional groups: factors that aid in the attachment of the organism to host cells, which are the fimbriae and flagella; and factors that aid in the invasion of tissue and the inhibition of the immune response. All of the virulence factors used by *P. aeruginosa* are also produced by other microorganisms except for pyocyanin which is uniquely produced by *P. aeruginosa* [22].

**Lipopolysaccharides (LPS)**

LPS, a component of the outer membrane, acts as an endotoxin and contributes to the bacterium's ability to cause inflammation and evade the host immune system. It is also involved in antibiotic resistance by serving as a physical barrier to antimicrobial agents [23].

**Type III Secretion System (T3SS)**

The T3SS is a needle-like structure that injects effector proteins directly into host cells. These proteins disrupt host cellular processes, leading to cell death and immune evasion. Four types of toxins are produced, including ExoS, ExoT, ExoU, and ExoY. These toxins wield diverse capabilities, such as GTPase-activating proteinase (GAP) activity, ADP-ribosyl transferase activity (ADPRT), adenylate cyclase activity, and even membrane phospholipid cleavage, an effect seen in ExoU potent phospholipase A2 (PLA2) activity. These toxins collectively initiate inflammation and subvert host cell functions. The T3SS is crucial for causing acute infections, such as pneumonia and sepsis [24].

**Exotoxins**

P. aeruginosa produces several exotoxins, including ExoS, ExoT, ExoU, and ExoY, which are delivered via the T3SS. These toxins interfere with host cell signaling, cytoskeleton dynamics, and immune responses, contributing to tissue damage and disease severity. Exotoxin A (ETA), an ADP-ribosyl transferase is the most toxic virulence factor of *P. aeruginosa* causing necrotizing at the site of colonization and inhibiting host cell protein synthesis. The various extracellular proteolytic enzymes and lipolytic enzymes all secreted by the type II secretion system are also weapons for P. aeruginosa invasion. Elastase A (LasA), a serine protease secreted

by P. aeruginosa is proven to be relevant to antibiotic resistance in clinical isolates. The most abundant protease elastase B (LasB) is the major virulence factor. Due to its protein cleavage activity, LasB could interfere with bacterial clearance, disrupt epithelial junctions, and affect biofilm formation [25].

**Biofilm Formation**

Biofilm is a structure built primarily of autogenous extracellular polymeric substances (EPS) that serves as a scaffold to wrap bacteria on a surface and shield them from external pressures and hinder phagocytosis [26]. The EPS of P. *aeruginosa* biofilms matrix attached to a variety of surfaces or tissues consists of proteins, exopolysaccharides (Psl, Pel, and alginate), and extracellular DNA (eDNA) which can be hydrolyzed by DNase I [27]. The process of biofilm formation by *P. aeruginosa* progresses begins with attachment to the surfaces suitable for growth including medical instruments and food, followed by the formation of microcolonies, and finally, maturation involving the expression of matrix polymers [28].

**Quorum Sensing**

Quorum sensing is a form of bacterial communication that enables *P. aeruginosa* to regulate gene expression allowing the microbes to coordinate activity against the host in the setting of infection. *P. aeruginosa* has several well-defned quorum sensing pathways, such as Ls, Rhl, and Pqs that all generate autoinducers, which difuse into bacterial and host cells leading to transcriptional regulation that benefits continued bacterial survival and decreased immune response to infection [29].

**Flagella and Pili**

Flagella are responsible for motility, helping the bacterium to reach and colonize host tissues. Pili, particularly type IV pili, are involved in adhesion to host cells and surfaces, initiating biofilm formation and facilitating twitching motility on solid surfaces. The polar flagellum responsible for motility in liquid or on solid surfaces is also an important virulence factor. The attachment ability of the flagellum aids initial binding to the cystic fibrosis epithelia and initiates biofilm establishment [30].

**Alginate**

This exopolysaccharide is a major component of the biofilm matrix in mucoid strains of *P. aeruginosa*. Alginate production is upregulated in chronic infections and contributes to the bacterium's resistance to phagocytosis and antibiotics [31].

**Proteases**

*P. aeruginosa* secretes various proteases, such as elastase and alkaline protease, which degrade host tissues and immune components, promoting infection and inflammation. These enzymes also play roles in nutrient acquisition and biofilm development [32].

**Pyocyanin and Pyoverdine**

the blue-green pigment pyocyanin plays a pivotal role in pathogenicity by inducing oxidati vestress within host cells. It disrupts host catalase and the electron transport system (ETS), suppressing phagocytosis [33]. Pyoverdine also interferes with host electron transport pathways and the redox cycling system, impairing immune system function [34].

**Isolation**

Isolation of *Pseudomonas aeruginosa* involves several steps, from sample collection to identification on selective media. Here is a detailed procedure

**Sample Collection**

Collect samples from potential infection sites or environments. Clinical specimens can include sputum, urine, blood, wound swabs, or other bodily fluids. Environmental samples can include water, soil, or surfaces.

**Inoculation onto Selective Media**

Several types of media can be used to selectively isolate *P. aeruginosa*:

Cetrimide Agar: This medium contains cetrimide, which inhibits the growth of most bacteria except *Pseudomonas* species. *P. aeruginosa* produces characteristic greenish-blue colonies due to pyocyanin production.

MacConkey Agar: This differential medium helps differentiate *P. aeruginosa* based on its ability to grow and produce non-lactose fermenting colonies, which appear pale or colorless.

Nutrient Agar: Though non-selective, nutrient agar can support the growth of *P. aeruginosa*, which typically produces a distinctive grape-like odor and greenish pigment.

**Incubation**

Incubate the inoculated plates at 37°C for 24-48 hours under aerobic conditions. *P. aeruginosa* colonies are usually large, flat, with a rough surface, and may exhibit a metallic sheen.

**Preliminary Identification**

Observe the colonies for typical *P. aeruginosa* characteristics:
Greenish-blue pigmentation due to pyocyanin production.
Fluorescence under UV light due to pyoverdine production.
Grape-like or corn tortilla odor.

**Biochemical Tests**

Confirm the identification of P. aeruginosa using the following biochemical tests:

Oxidase Test: P. aeruginosa is oxidase-positive. A small amount of bacterial colony is placed on filter paper soaked with oxidase reagent (tetramethyl-p-phenylenediamine). A positive reaction results in a purple color within a few seconds.

Catalase Test: P. aeruginosa is catalase-positive. A colony is mixed with a drop of hydrogen peroxide ($H_2O_2$). Bubbling indicates the presence of catalase enzyme.

Glucose Oxidation: P. aeruginosa can oxidize glucose but does not ferment it. The oxidation-fermentation (O-F) test can differentiate between oxidative and fermentative metabolism. In O-F medium, P. aeruginosa will produce acid in the open tube (with air) but not in the closed tube (without air).

Nitrate Reduction: P. aeruginosa reduces nitrate to nitrogen gas. In the nitrate reduction test, the bacteria are grown in nitrate broth, and reagents (sulfanilic acid and alpha-naphthylamine) are added after incubation. A red color indicates the presence of nitrites.

Pigment Production: Observe for the production of pigments like pyocyanin (blue-green) and pyoverdine (yellow-green) on nutrient agar or specific media like King's A and B media.

**Drug Resistance Mechanisms**

main mechanisms through which *P. aeruginosa* exhibits drug resistance:

**Efflux Pumps**

Efflux pumps are transport proteins that actively expel a wide range of antibiotics out of the bacterial cell, reducing the intracellular concentration of the drug to sub-lethal levels. *P. aeruginosa*

possesses several multidrug efflux pumps, including:
MexAB-OprM: Confers resistance to beta-lactams, fluoroquinolones, and aminoglycosides.
MexXY-OprM: Provides resistance to aminoglycosides and fluoroquinolones [35].

**Beta-Lactamases**
These enzymes hydrolyze the beta-lactam ring of beta-lactam antibiotics, rendering them ineffective. *P. aeruginosa* produces various beta-lactamases, including:

- **AmpC cephalosporinase:** Induced by exposure to beta-lactams and confers resistance to cephalosporins.
- **Extended-spectrum beta-lactamases (ESBLs):** Degrade a wide range of beta-lactams, including penicillin's and cephalosporins [36].
- **Carbapenemases:** Such as VIM, IMP, and KPC, which hydrolyze carbapenems [37].

**Porin Channel Alterations**
Porins are proteins that form channels in the outer membrane of Gram-negative bacteria, allowing the passage of small molecules, including antibiotics [38]. *P. aeruginosa* can alter the expression or function of porins to reduce drug uptake:
OprD downregulation: Specifically reduces uptake of carbapenems like imipenem [39].

**Target Site Modifications**
Alterations in the target sites of antibiotics can reduce drug binding and efficacy. Examples include:
Mutations in DNA gyrase and topoisomerase IV: Confer resistance to fluoroquinolones by reducing drug binding affinity [40].
Modifications in penicillin-binding proteins (PBPs): Reduce binding of beta-lactam antibiotics [41].

**Biofilm Formation**
Biofilms are structured communities of bacteria encased in a self-produced extracellular matrix. Biofilms protect *P. aeruginosa* from antibiotics and the host immune system by:
Providing a physical barrier to antibiotic penetration.
Creating a microenvironment with nutrient and oxygen gradients that reduce bacterial growth rate and metabolic activity, making the bacteria less susceptible to antibiotics.
Promoting the exchange of resistance genes among bacterial cells [42].

**Enzyme Modification**
*P. aeruginosa* wields a formidable weapon, antibiotic-inactivating enzymes. These enzymes possess the ability to dismantle or modify antibiotics, rendering them powerless. This intrinsic defense mechanism presents a significant hurdle for clinicians combating *P. aeruginosa* infections. One of the most critical classes of antibiotic inactivating enzymes in *P. aeruginosa* is β-lactamases. β-lactam antibiotics, including penicillin and cephalosporins, target bacterial cell walls by inhibiting PBP. *P. aeruginosa* has honed its β-lactamase production to counteract these antibiotics by hydrolyzing the b-lactam ring that is present in b-lactam antibiotics. β-lactamases are categorized into four classes: A, B, C, and D, depending on theiramino acid sequences [43].

**Epidemiological Studies**
Epidemiological studies on *Pseudomonas aeruginosa* have provided valuable insights into the distribution, infection rates, resistance patterns, and risk factors associated with this pathogen.

**Prevalence in Healthcare Settings**
P. aeruginosa is a significant cause of hospital-acquired infections, particularly in intensive care units (ICUs). Studies indicate that it is responsible for a substantial proportion of infections such as ventilator-associated pneumonia (VAP), bloodstream infections (BSI), and urinary tract infections (UTIs). For instance, one study highlighted that *P. aeruginosa* accounts for about 10% of all hospital-acquired infections [44].

**Antimicrobial Resistance Trends**
Surveillance data from the National Healthcare Safety Network (NHSN) and the Centers for Disease Control and Prevention (CDC) show that *P. aeruginosa* exhibits high rates of resistance to multiple antibiotics, including carbapenems, fluoroquinolones, and cephalosporins. The prevalence of multidrug-resistant (MDR) *P. aeruginosa* has been a growing concern, with reports indicating that 26-30% of isolates from ICUs are MDR [45,46].

**Impact on Cystic Fibrosis Patients**
Epidemiological data from cystic fibrosis (CF) registries, such as the Cystic Fibrosis Foundation Patient Registry and the European Cystic Fibrosis Society Registry, show that *P. aeruginosa* is one of the most common pathogens isolated from CF patients [47]. Despite aggressive treatment regimens, a significant percentage of CF patients continue to be colonized with *P. aeruginosa*, particularly as they age. Studies report a prevalence of 29.8% to 49.6% in different age groups within CF populations [48].

**Infections in Immunocompromised Hosts**
*P. aeruginosa* poses a high risk to immunocompromised patients, including those with neutropenia, hematological malignancies, and those undergoing transplantation [49]. It is a major cause of morbidity and mortality in these populations, with bloodstream infections caused by *P. aeruginosa* associated with high mortality rates. Epidemiological studies have found that *P. aeruginosa* is responsible for a significant proportion of Gram-negative bacteremia's in these patients [50].

**Previous Studies**
A study conducted by **Elsheikh Mohammed et al, 2023** in Sudan, aim of this study is to determine the prevalence of MDR, XDR and PDR-P. aeruginosa clinical isolates in Khartoum State-Sudan. Materials and Methods. A multihospital laboratory-based study was conducted to collect P. aeruginosa clinical isolates from various clinical specimen's culture during eighteen-month period from March 2020 to December 2021. The P. aeruginosa strains were reidentified by conventional biochemical methods and genotypically by amplification of 16S rRNA gene by Polymerase chain reaction (PCR) assay. Antimicrobial susceptibility testing was done by Kirby-Bauer disc diffusion method. MDR, XDR and PDR were determined according to new recommendation of the Clinical and Laboratory Standards Institute and the European Committee for Antimicrobial Susceptibility Testing. Results showed of 512 P. aeruginosa clinical isolates were recovered from various clinical specimen's culture, only 289(66.4%) of the isolates were confirmed as P. aeruginosa strains genotypically, out of those P. aeruginosa strains were categorized regarding antimicrobial resistance to 98(33.9%) MDR, 61(21.1%) XDR and 2(0.7%) PDR. The XDR strains were exhibited significant overall resistance to all used antibiotic classes, whereas MDR strains were insignificant resistant to fluoroquinolones and polymyxins. Patients prior of hospitalized for 1-2weeks, uses of companied antibiotics therapy with duration of one week and source of isolation from wound swab and blood specimen ($P < 0.05$), remained independently associated with an increased

likelihood of antimicrobial resistant in clinical P. aeruginosa isolates. Conclusion. The study highlights the increase prevalence of MDR and XDR P. aeruginosa clinical isolates in both hospital and community settings, along with emerged two pandrug resistant strains. Thus, continuous antimicrobial resistance surveillance for this bacterium is necessary for guiding antimicrobial treatment and stewardship as well as based knowledge for future comparative studies [51].

**A Second Study by SAVAŞ, LÜTFÜ; DURAN et al 2005, in Turkey** showed that intensive care units (ICUs) are burdened with a high frequency of nosocomial infections often caused by multiresistant nosocomial pathogens. Pseudomonas aeruginosa has emerged as one of the most problematic Gram-negative pathogens. The objective of this study was to identify frequency of Pseudomonas aeruginosa from the various clinical samples in ICUs, and to investigate resistance patterns against various antibiotics widely used for treatment. This study was carried out between September 2000-September 2002. Antimicrobial susceptibility testing was performed by the disc diffusion method according to NCCLS (National Commitee for Clinical and Laboratory Standards) guidelines. The following antibiotics were tested: imipenem, meropenem, aztreonam, ciprofloxacin, ceftazidime, cefepime, piperacillin, norfloxacin and the aminoglycosides (gentamicin, netilmicin,tobramycin, and amikacin). Pseudomonas aeruginosa were isolated from 16.4 % (152/928) of the patients in ICUs. The highest Pseudomonas aeruginosa isolation was obtained in the burns unit (26.9%, 78/290) followed by, cardiovascular surgical ICU (17.6%, 13/74) general surgical ICU (24/164, 14.6 %), internal ICU (17/180, 9.4%) and coronary ICU (20/220, 9.1%). There is a statistically significant difference between surgical ICU and medical internal ICU ($P < 0.05$). The most effective antibiotics were carbapenems (imipenem and meropenem) and the resistance rates were detected as 15% and 20.4%, respectively among 152 Pseudomonas aeruginosa strains. In conclusion, the frequency of Pseudomonas aeruginosa was found to be high in patients treated at ICUs. The results demonstrate that the resistance rates are alarmingly high. To reduce the emergence and spread of antimicrobial-resistant pathogens in ICUs, monitoring and optimisation of antimicrobial use should be considered carefully. These findings suggest that the resistance rates of aminoglycosides, 3th generation antibiotics and quinolone are increasing progressively in Turkey [52].

A third study by **Saman Nadeem, Faisal Hanif, Yasmeen Taj, et al (2019) in Karachi**, to evaluate the antibiotic resistance pattern of Pseudomonas aeruginosa and its prevalence from samples received from Intensive Care Units (adult and neonatal) at PNS Shifa Hospital Karachi. across sectional study was carried out at PNS SHIFA hospital. Samples including blood, pus, wound swab, sputum and endobronchial washing were received for culture and sensitivity. Isolates were cultured on blood and MacConkey agar. Antibiotic susceptibility testing was performed by Kirby-Bauer and broth microdilution and then analyzed on SPSS version 23. Results were confirmed by VITEK 2. Out of 674 positive clinical specimens 97(14.39%) were positive for Pseudomonas aeruginosa growth. The most susceptible antibiotic against Pseudomonas aeruginosa was Polymixin b (94.854%). The least effective antimicrobial was aztreonam (40.21%sensitive). prevalence of Pseudomonas aeruginosa from the samples of Intensive Care Units was found to be 14.39%. The most susceptible antibiotic against pseudomonas was Polymixin B. The least effective antimicrobial was aztreonam [53].

A fourth study by Sara E Mohammed, Omnia M Hamid, Sababil S Ali, et al (2023) aimed to determine the prevalence of MDR, XDR and PDR-P. aeruginosa clinical isolates in Khartoum State-Sudan. A multihospital laboratory-based study was conducted to collect *P. aeruginosa* clinical isolates from various clinical specimen's culture during eighteen-month period from March 2020 to December 2021. The *P. aeruginosa* strains were reidentified by conventional biochemical methods and genotypically by amplification of 16S rRNA gene by Polymerase chain reaction (PCR) assay. Antimicrobial susceptibility testing was done by Kirby-Bauer disc diffusion method. MDR, XDR and PDR were determined according to new recommendation of the Clinical and Laboratory Standards Institute and the European Committee for Antimicrobial Susceptibility Testing. **Results showed** of 512 *P. aeruginosa* clinical isolates were recovered from various clinical specimen's culture, only 289(66.4%) of the isolates were confirmed as *P. aeruginosa* strains genotypically, out of those *P. aeruginosa* strains were categorized regarding antimicrobial resistance to 98(33.9%) MDR, 61(21.1%) XDR and 2(0.7%) PDR. The XDR strains were exhibited significant overall resistance to all used antibiotic classes, whereas MDR strains were insignificant resistant to fluoroquinolones and polymyxins. Patients prior of hospitalized for 1-2weeks, uses of companied antibiotics therapy with duration of one week and source of isolation from wound swab and blood specimen ($P < 0.05$), remained independently associated with an increased likelihood of antimicrobial resistant in clinical *P. aeruginosa* isolates. study highlighted the increase prevalence of MDR and XDR P. aeruginosa clinical isolates in both hospital and community settings, along with emerged two pandrug resistant strains. Thus, continuous antimicrobial resistance surveillance for this bacterium is necessary for guiding antimicrobial treatment and stewardship as well as based knowledge for future comparative studies [54].

**Fifth study by Al-Orphaly M, Hadi HA, Eltayeb FK, et al (2021),** showed over the last decades, there has been a dramatic global increase in multidrug-resistant (MDR) pathogens particularly among Gram-negative bacteria (GNB). Pseudomonas aeruginosa is responsible for various health care-associated infections, while MDR P. aeruginosa causes significant morbidity and mortality. Middle East and North Africa (MENA) represent an unexplored geographical region for the study of drug resistance since many of these countries are at crossroads of high volume of travel, diverse expatriate populations, as well as high antibiotic consumption despite attempts to implement antimicrobial stewardship programs. This minireview analyzes epidemiology, microbiological, and genomic characteristics of MDR P. aeruginosa in the MENA region. Published data on MDR P. aeruginosa prevalence, antimicrobial resistance patterns, and genetic profiles from studies published during the past 10 years from 19 MENA countries have been included in this minireview.

There is wide variation in the epidemiology of MDR P. aeruginosa in the MENA region in terms of prevalence, antimicrobial characteristics, as well as genetic profiles. Overall, there is high prevalence of MDR P. aeruginosa seen in the majority of the countries in the MENA region with similarities between neighboring countries, which might reflect comparable population and antibiotic-prescribing cultures. Isolates from critical care units are significantly resistant particularly from certain countries such as Saudi Arabia, Egypt, Libya, Syria, and Lebanon with high-level resistance to cephalosporins, carbapenems, and aminoglycosides. Colistin susceptibility patterns remains high apart from countries with high-level antibiotic resistance such as Saudi Arabia, Syria, and Egypt [55].

## Methodology

### Methodology

A cross-sectional analytical study was carried out on the target population (Khartoum state).

### Study Area

Different clinical isolates in Khartoum hospitals include: Khartoum teaching hospital, , Sudan. Omdurman teaching hospital and Bahry hospital.

3.2 STUDY POPULATION

This study was covered 300 patients at Khartoum locality who fulfilled.

### Sample Size

Due to time factor, any cooperating persons in health care fields in the area of Khartoum were considered to give results, finally a sample of 320 was taken.

### Inclusion Criteria

- Males and females who are clinically diagnosed patients in ICU beds from different ages.

### Exclusion Criteria

- Patients who are clinically healthy or with mild diseases.

### Sample Frame

A sample of (320) person who are a residence in Khartoum area in Mar 2023

### Sample Technique

Stratified random sampling method of selection.

### Sample Method

Blood and urine, swab samples will be obtained from Hospitals in Khartoum state and samples will be transported in cold ice box to laboratory and tested after up to 1 hour from taking the samples. Questionnaire will be used to collect demographic data from participants.

### Data Collection Tools

Data was collected anonymously through a self-administered questionnaire, prepared in English, and a blood sample is collected.

### Data Analysis

Data entry and analysis will be done using statistical package of social science program SPSS version 25.0 (IBM SPSS Inc. Chicago, IL). Descriptive statistics (i.e., frequencies, percentages, mean, p. value and correlation) will be performed.

### Ethical Consideration

Approval will be taken from research committee, Al-Madain College for Medical Sciences and Technology. Participants' consent will be taken while collecting the data for the study.

Participants will be informed about the objective and purpose of the study in the informed consent. And only participant voluntarily willing to take part will be included. No financial benefits will be offered to participants.

## Data Presentation, Analysis Results

### Introduction

This is chapter deals with the study findings, analysis data and discussion; the researcher used methods of quantitative in nature. The quantitative analysis used to generate interpretation from the questionnaire. The researcher has presented the findings that answer the study questions. The findings presented in line with the study objectives "samples of 320".

The population size was 320 samples; the data had analyzed using the SPSS (statistical package for social science).

### Methods

- Frequencies and percentages have used to know the statistics with mean and STD.

### Gender

**Table 1: Shows the Population's Gender**

| Answer | Frequency | Percent |
|---|---|---|
| Male | 69 | 21.6% |
| Female | 251 | 78.4% |
| Total | 320 | 100 % |

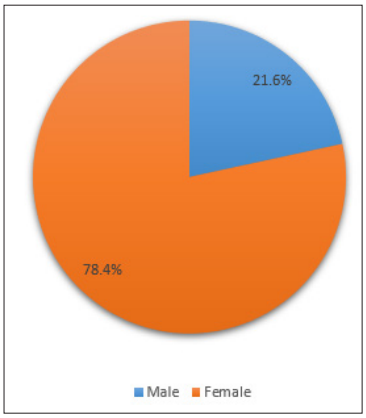


**Figure 1:** The Population's Gender Age

**Table 2: Shows the Population's Age**

| Answer | Frequency | Percent |
|---|---|---|
| Less than 20 years | 45 | 14.1% |
| 20 – 30 years | 102 | 31.9% |
| 31 – 40 years | 122 | 38.1% |
| More than 40 years | 51 | 15.9% |
| Total | 320 | 100 % |

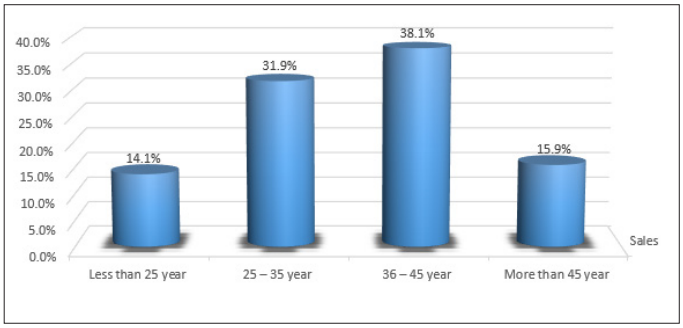


**Figure 2:** Age Educational Level

**Table 3: Shows the Population's Education**

| Answer | Frequency | Percent |
|---|---|---|
| Primary school | 175 | 54.7% |
| Secondary school | 40 | 12.5% |
| University degree | 80 | 25.0% |
| Master degree | 25 | 7.8% |
| Total | 320 | 100.0% |

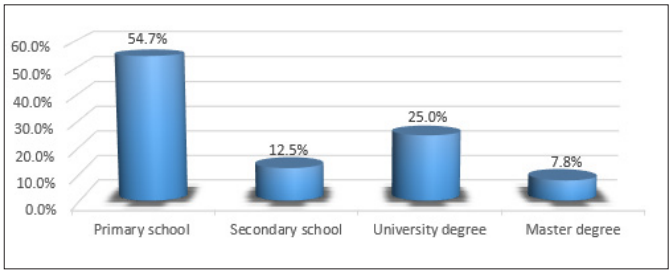


**Figure 3:** Educational level Marital Status

**Table 4: Shows the Population's Marital Status**

| Answer | Frequency | Percent |
|---|---|---|
| Single | 172 | 53.8% |
| Married | 130 | 40.6% |
| Widow | 18 | 5.6% |
| Total | 320 | 100.0% |

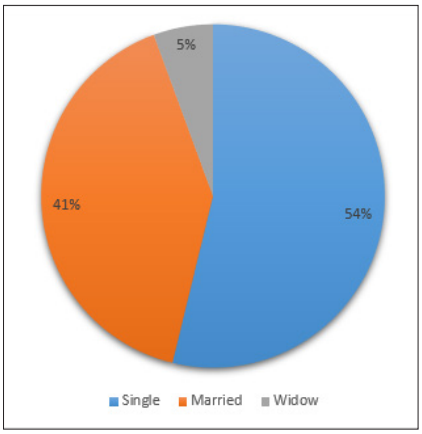


**Figure 4:** Marital Status

**Table 5: Shows the Population's Antibiotic Treatment**

| Answer | Frequency | Percent |
|---|---|---|
| Yes | 65 | 20.3% |
| No | 255 | 79.7% |
| Total | 320 | 100.0% |

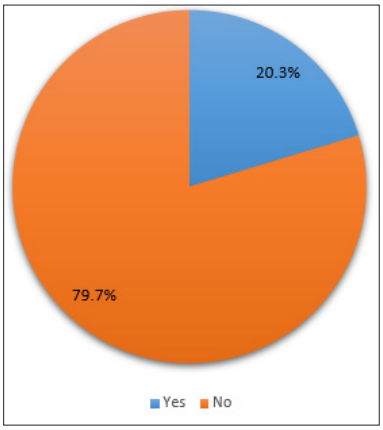


**Figure 5:** Antibiotic Treatment

**If yes for How Long?**

**Table 6: Shows the Population's Period of Treatment**

| Answer | Frequency | Percent |
|---|---|---|
| Less than 1 month | 23 | 35.4% |
| 1 - 3 months | 24 | 36.9% |
| More than 3 months | 18 | 27.7% |
| Total | 65 | 100 % |

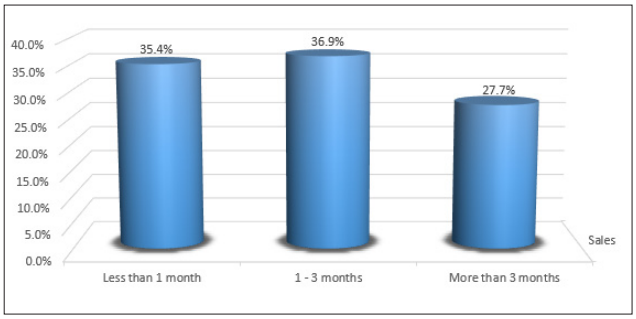


**Figure 6:** Change when taken from Nutrient

**Source of Sample**

**Table 7: Shows the Population's Sample Source**

| Answer | Frequency | Percent |
|---|---|---|
| Urine | 130 | 40.6% |
| Wound swab | 63 | 19.7% |
| Serious fluid | 23 | 7.2% |
| Sputum | 43 | 13.4% |
| Blood | 61 | 19.1% |
| Total | 65 | 100% |

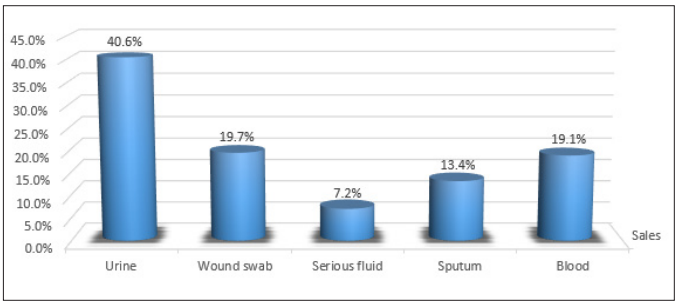


**Figure 7:** Change when taken from Nutrient.

**Cross Tabulation of Antibiotic Treatment with Age and Gender and Age**

**Table 8: Treatment with Gender**

| | | Antibiotic treatment | | Total | P. value | Sig |
|---|---|---|---|---|---|---|
| | | Yes | No | | | |
| Gender | Male | 19 | 50 | 69 | 0.080 | Non-sig |
| | Female | 50 | 201 | 251 | | |
| Total | | 69 | 251 | 320 | | |

**Table 9: Treatment with Age**

| | | Antibiotic treatment | | Total | P. value | Sig |
|---|---|---|---|---|---|---|
| | | Yes | No | | | |
| **Age** | Less than 20 years | 19 | 26 | 45 | 0.037 | Sig |
| | 20 - 30 years | 50 | 52 | 102 | | |
| | 31 - 40 years | 0 | 122 | 122 | | |
| | More than 40 years | 0 | 51 | 51 | | |
| Total | | 69 | 251 | 320 | | |

**Table 10: Cross Tabulation of Source of Infection with Gender**

| | | Gender | | Total | P. value | Sig |
|---|---|---|---|---|---|---|
| | | Male | Female | | | |
| Source | Urine | 25 | 105 | 130 | 0.045 | Sig |
| | Wound swab | 13 | 50 | 63 | | |
| | Serious fluid | 4 | 19 | 23 | | |
| | Sputum | 11 | 32 | 43 | | |
| | Blood | 16 | 45 | 61 | | |
| Total | | 69 | 251 | 320 | | |

***P. value considered significant when < 0.05.**

## Discussion, Conclusion and Recommendations

### Discussion

Over the last decades, there has been a dramatic global increase in multidrug-resistant (MDR) pathogens particularly among Gram-negative bacteria (GNB). Pseudomonas aeruginosa is responsible for various health care-associated infections, while MDR P. aeruginosa causes significant morbidity and mortality [55].

Therefore, our study was designed to estimate the prevalence of Pseudomonas aeruginosa in ICU patients which revealed that among participants a high percent of females (78.4%) was diagnosed by pseudomonas with a majority source in urine, a fair of them aged between 31 – 40 years, Most of them were single with 53.8%, results revealing that less than 20.3% were treated with antibiotics all samples were resistance to Meropenem and Imipenem, and for 1 – 3 months period of treatments, in compare with other studies those results were similar as study done in Sudan by Elsheikh Mohammed et al (2023) [51] and study by Saman Nadeem, (2019) [53] Unlike the study done in turkey by SAVAŞ, LÜTFÜ; DURAN et al (2005) which showed a low rate of infection in ICU 16.4%, this non similarity may be due to geographical differences between the countries [52].

### Conclusion

The study concluded that there is a high rate of infection among ICU patients, mostly in urinary tract infections, high rate among females in middle age, results demonstrate that the resistance rates are alarmingly high.

### Recommendations

This finding highlights the necessity of continuous antimicrobial resistance surveillance for this bacterium is necessary for guiding antimicrobial treatment and finding new treatments, providing workshops and ensuring the level of knowledge remains high among health worker specially. Additionally, more effort should be made to educate people about the risk of drug resistance of these bacteria, more effort should be done by hospital staff in sterilization specially ICU wards.

## Appendix

### Appendix I

**Al-Madain College for Medical Sciences and Technology**
**Medical laboratory sciences**

**1. Gender:**
Male ( ) Female ( )

**2. Age in years:**
20 ( ) 20 – 30 ( )
30 – 40 ( ) < 40 ( )

**3. Educational level:**
Primary ( ) Secondary ( )
University ( ) Master ( )

**4. Marital status:**
Single ( ) Married ( )
Widow ( )

**5. Have you been administrated to ICU before?**
Yes ( ) NO ( )

**6. Have you had antibiotics treatments before?**
Yes ( ) NO ( )

**7. If yes, for how long?**
Less than 1 month ( ) 1 – 3 months ( )
5 – 10 months ( )

**References**

1. Gaynes R, Edwards JR (2005) National Nosocomial Infections Surveillance System. Overview of nosocomial infections caused by Gram-negative bacilli. Clin Infect Dis 41: 848-854.
2. Sievert DM, Ricks P, Edwards JR, Schneider A, Patel J (2013) Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009-2010. Infect Control Hosp Epidemiol 34: 1-14.
3. Fujitani S, Sun HY, Yu VL, Weingarten JA (2011) Pneumonia due to Pseudomonas aeruginosa part I: epidemiology, clinical diagnosis, and source. Chest 139: 909-919.
4. Chinese Society of Critical Care Medicine, Guidelines for the diagnosis, prevention and treatment of ventilator-associated pneumonia. Chinese Journal of Internal Medicine (2013) 52: 524-543.
5. Sievert DM, Ricks P, Edwards JR, Schneider A, Patel J. National Healthcare Safety Network (NHSN) Team and Participating NHSN Facilities, et al. Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009–2010 (2013) Infect Control Hosp Epidemiol 34: 1-14.
6. Kollef MH, Micek ST (2014) Rational Use of Antibiotics in the ICU: Balancing stewardship and clinical outcomes. JAMA 312: 1403-1404.
7. Parker CM, Kutsogiannis J, Muscedere J, Cook D (2008) Ventilator-associated pneumonia caused by multidrug-resistant organisms or Pseudomonas aeruginosa: prevalence, incidence, risk factors, and outcomes. J Crit Care 23: 18-26.
8. Vincent JL, Sakr Y, Sprung CL, Ranieri VM, Reinhart K (2006) Sepsis Occurrence in Acutely Ill Patients Investigators. Sepsis in European intensive care units: results of the SOAP study. Crit Care Med 34: 344-353.
9. Micek ST, Reichley RM, Kollef MH (2011) Health care-associated pneumonia (HCAP): empiric antibiotics targeting methicillin-resistant Staphylococcus aureus (MRSA) and Pseudomonas aeruginosa predict optimal outcome. Medicine (Baltimore) 90: 390-395.
10. Nathwani D, Raman G, Sulham K, Gavaghan M (2014) Menon. Clinical and economic consequences of hospital-acquired resistant and multidrug-resistant Pseudomonas aeruginosa infections: a systematic review and meta-analysis. Antimicrob Resist Infect Control 3: 32.
11. BAILEY & SCOTT'S DIAGNOSTIC MICROBIOLOGY 13th edition pp336-337.
12. Erdem B (1999) Pseudomonas. In: Ustacelebi S. Basic Clin Microbiol. Ankara, Gunes Publication: 551-558.
13. Gilligan PH: Pseudomonas and Burkholderia. In Manual of Clinical Microbiology (Eds. Mur ray RR, Baron EJ, Pfaler MA, Tenover FC, Yolken RH) American Society for Microbiology, Washington DC, 1995: 509-19.
14. Jarvis WR, Martone WJ (1992) Predominant pathogens in hospital infections. J Antimicrob Chemother A: 19-24.
15. Kiska DL, Gilligan PH (2003) Pseudomonas. In: Murray PR, Baron EJ, Jorgensen JH, Pfaller MA, and Yolken RH, editors. Manual of Clinical Microbiology, 8th ed. Washington DC: ASM Press: 719-728.
16. Qarah S, Cunha BA, Dua P, Lessnau K-D Pseudomonas aeruginosa infections. eMedicine accessed 10: 28-10.
17. Chen SP, Rodoy R. Pseudomonas infection. Accessed online at <http://emedicine.medscape.com/article/970904-overview> on October 28, 2010. 3. Chen SP, Rodoy R. Pseudomonas infection. Accessed online at <http://emedicine.medscape.com/article/970904-overview> on October 28, 2010.
18. Weinstein MP, Towns ML, Quartey SM (1997) The clinical significance of positive blood cultures in the 1990s: a prospective comprehensive evaluation of the microbiology, epidemiology, and outcome of bacteremia and fungemia in adults. Clin Infect Dis 24: 584-602.
19. Pollack M (2000) Pseudomonas Aeruginosa. Mandell GL, Bennett JE, Dolin R, eds. Principles and Practice of Infectious Diseases. 5th ed. New York, NY: Churchill Livingstone: 2310-2327
20. Sadikot RT, Blackwell TS, Christman JW, Prince AS (2005) Pathogen-host interactions in Pseudomonas aeruginosa pneumonia. Am J Respir Crit Care Med 171: 1209-1223.
21. Vidaillac C, Chotirmall SH (2021) Pseudomonas aeruginosa in bronchiectasis: infection, inflammation, and therapies. Expert Rev Respir Med 15: 649-662.
22. Driscoll JA, Brody SL, Kollef MH (2007) The epidemiology, pathogenesis and treatment of Pseudomonas aeruginosa infections. Drugs 67: 351-368.
23. Kühn MJ, Talà L, Inclan YF, Patino R, Pierrat X, Vos I (2021) Mechanotaxis directs Pseudomonas aeruginosa twitching motility. Proc Natl Acad Sci USA 118: e2101759118.
24. Hardy KS, Tessmer MH, Frank DW, Audia JP (2021) Perspectives on the pseudomonas aeruginosa type iii secretion system effector exou and its subversion of the host innate immune response to infection. Toxins (Basel) 13: 880.
25. Barken KB, Pamp SJ, Yang L, Gjermansen M, Bertrand JJ, Klausen M (2008) Roles of type IV pili, flagellum-mediated motility and extracellular DNA in the formation of mature multicellular structures in Pseudomonas aeruginosa biofilms. Environ Microbiol 10: 2331-2343.
26. Ma LZ, Wang D, Liu Y, Zhang Z, Wozniak DJ (2022) Regulation of biofilm exopolysaccharide biosynthesis and degradation in Pseudomonas aeruginosa. Annu Rev Microbiol 76: 413-433.
27. Swartjes JJ, Das T, Sharifi S, Subbiahdoss G, Sharma PK (2013) A functional DNase I coating to prevent adhesion of bacteria and the formation of biofilm. Adv Funct Mater 23: 2843-2849.
28. Sauer K, Camper AK, Ehrlich GD, Costerton JW, Davies DG (2002) Pseudomonas aeruginosa displays multiple phenotypes during development as a biofilm. Am Soc Microbiol 184: 1140-1154.
29. Papenfort K, Bassler BL (2016) Quorum sensing signal-response systems in Gram-negative bacteria. Nat Rev Microbiol 14: 576-88.
30. Jurado-Martin I, Sainz-Mejias M, McClean S (2021) Pseudomonas aeruginosa: an audacious pathogen with an adaptable arsenal of virulence factors. Int J Mol Sci 22: 3128.
31. Boyd A, Chakrabarty AM (1995) Pseudomonas aeruginosa biofilms: role of the alginate exopolysaccharide. J Ind Microbiol 15: 162-168.
32. Cabana C, Castandet J, Sprynski N, Melessike M, Beyria L (2021) Pseudomonas aeruginosa elastase contributes to the establishment of chronic lung colonization and modulates the immune response in a murine model. Front Microbiol 11: 620819.
33. Hall S, McDermott C, Anoopkumar-Dukie S, McFarland AJ, Forbes A (2016) Cellular effects of pyocyanin, a secreted virulence factor of Pseudomonas aeruginosa. Toxins (Basel) 8: 236.
34. Durán O, Ramos C, Chen O, Castillo J, de Mayorga B (2022) "Pyoverdine as an important virulence factor in Pseudomonas aeruginosa antibiotic resistance" in The global antimicrobial resistance epidemic-innovative approaches and cutting-edge

solutions. ed. G. Tellez-Isaias (Rijeka: IntechOpen) Ch. 8.
35. Pang Z, Raudonis R, Glick BR, Lin T-J, Cheng Z (2019) Antibiotic resistance in Pseudomonas aeruginosa: mechanisms and alternative therapeutic strategies. Biotechnol. Adv 37: 177-192.
36. Castanheira M, Simner PJ, Bradford P A (2021) Extended-spectrum β-lactamases: an update on their characteristics, epidemiology and detection. JAC Antimicrobial Resist 3: dlab092.
37. Tooke CL, Hinchliffe P, Bragginton EC, Colenso CK (2019) β-Lactamases and β-lactamase inhibitors in the 21st century. J Mol Biol 431: 3472-03500.
38. Welte W, Nestel U, Wacker T, Diederichs K (1995) Structure and function of the porin channel. Kidney Int 48: 930-940.
39. Fang Z, Zhang LY, Huang YM, Qing Y, Cao KY (2014) OprD mutations and inactivation in imipenem-resistant Pseudomonas aeruginosa isolates from China. Infect. Genet Evol 21: 124-128.
40. Hooper DC, Jacoby GA (2016) Topoisomerase inhibitors: fluoroquinolone mechanisms of action and resistance. Cold Spring Harb Perspect Med 6: a025320.
41. Sethuvel DPM, Bakthavatchalam YD, Karthik M, Irulappan M (2023) β-Lactam resistance in ESKAPE pathogens mediated through modifications in penicillin-binding proteins: an overview. Infect Dis Ther 12: 829-841.
42. Vestby LK, Grønseth T, Simm R, Nesse LL (2020) Bacterial biofilm and its role in the pathogenesis of disease. Antibiotics 9: 59.
43. Bush K, Bradford PA (2016) β-Lactams and β-lactamase inhibitors: an overview. Cold Spring Harb. Perspect Med 6: a025247.
44. Caffrey AR, Appaneal HJ, Liao JX, Piehl EC, Lopes V (2022) Treatment heterogeneity in Pseudomonas aeruginosa pneumonia. Antibiotics 11: 1033.
45. CDC. Multidrug-resistant Pseudomonas aeruginosa. 2021. https://arpsp.cdc.gov/profle/antibiotic-resistance/mdr-empseudomonas-aeruginosaem.
46. Weiner-Lastinger LM (2020) Antimicrobial-resistant pathogens associated with adult healthcare-associated infections: summary of data reported to the National Healthcare Safety Network, 2015-2017. Infect Control Hosp Epidemiol 41: 1-18.
47. Hatziagorou E (2020) Changing epidemiology of the respiratory bacteriology of patients with cystic fbrosis-data from the European cystic fbrosis society patient registry. J Cyst Fibros 19: 376-383.
48. Salsgiver EL (2016) Changing epidemiology of the respiratory bacteriology of patients with cystic fibrosis. Chest 149: 390-400.
49. Tofas P (2017) Pseudomonas aeruginosa bacteraemia in patients with hematologic malignancies: risk factors, treatment and outcome. Diagn Microbiol Infect Dis 88: 335-341.
50. Carvalho AS (2020) Bloodstream infections in neutropenic patients with haematological malignancies. Infect Dis Health 25: 22-29.
51. Elsheikh Mohammed, Sara & Hamid, Omnia & Ali, Sababil & Allam, Mushal & Elhussein, Abdelrahim & Robert, Steve. Prevalence of Multidrug-Resistant, Extensively Drug-Resistant and Pandrug-Resistant Pseudomonas aeruginosa Clinical Isolates in Khartoum State, Sudan. 11. 1-7. 10.12691/ajidm-11-1-1.
52. Savaş, Lütfü, Duran, Nizami, Savaş (2005) the prevalence and resistance patterns of pseudomonas aeruginosa in intensive care units in a university hospital. Turkish journal of medical sciences 35: 317-322.
53. Saman Nadeem, Faisal Hanif, Yasmeen Taj, Sana Yousuf (2019) Emergence and Management of Muti-Drug Resistant Pseudomonas Aeruginosa Isolated from Intensive-Care Unit. JBUMDC 9: 137-140.
54. Sara E Mohammed, Omnia M Hamid, Sababil S Ali, Mushal Allam, A M Elhussein (2023) Prevalence of Multidrug-Resistant, Extensively Drug-Resistant and Pandrug-Resistant Pseudomonas aeruginosa Clinical Isolates in Khartoum State, Sudan. American Journal of Infectious Diseases and Microbiology 11: 1-7.
55. Al-Orphaly M, Hadi HA, Eltayeb FK, AlHail H, Samuel BG (2021) Epidemiology of multidrug-resistant Pseudomonas aeruginosa in the Middle East and North Africa region. mSphere 6: e00202-21.