Evaluation of the Antibiotic Resistance Pattern at the Medical Services Administration Hospital in Khartoum, Sudan, 2021

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ABSTRACT

The number of antibiotics available is limited and does not cover the growing antibiotic resistance challenge. Misuse and overuse of antibiotics act as factors that help in improving and increasing the problem of resistance to those currently being prescribed by doctors. The study was carried out at the Medical Services Administration Hospital (MSAH) in Khartoum, Sudan to investigate the antibiotic resistance pattern for the period between Dec. 2020 and Jan. 2022. The results showed that, in a total of different clinical samples that were collected and processed, a total number of 980 organisms were isolated. The result indicated that 345 out of the total isolates (35.20%) were Klebsiella pneumonia, 326 (33.27%) Escherichia coli, 154 (15.71%) Pseudomonas aeruginosa, 130 (13.27%) Proteus mirabilis, and 25 (2.55%) Staphylococcus aureus. The results showed that K. pneumonia was quite resistant to piperacillin, cefuroxime, and azithromycin. The amikacin, imipenem, and meropenem antibiotics showed significant activity against K. pneumonia. The isolates of E. coli showed significant resistance to azithromycin and were more sensitive to imipenem and meropenem. P. aeruginosa was resistant to penicillin, amoxicillin/clavulanic acid, and azithromycin in a big way, but it was very sensitive to cefuroxime, the drug used to treat strep throat infections. P. mirabilis was found to be resistant to nalidixic acid, nitrofurantoin, amoxicillin/clavulanic acid, and azithromycin. It showed good sensitivity to amikacin, imipenem, and meropenem. It was clear that S. aureus was resistant to cefuroxime, ceftriaxone, nitrofurantoin, and norfloxacain, while tests showed that it was sensitive to imipenem.

Keywords - Antibiotics, resistance, MSA hospital, Sudan.

I. INTRODUCTION

Antibiotics are a crucial line of defense against bacterial infections by suppressing the growth of or killing other microorganisms at very low concentrations. Most bacteria are becoming resistant to various antibiotics, which creates a limitation for treating minor and major infectious diseases (Dugassa and Shukuri 2017).

Antibiotic resistance is occurring due to various causes like widespread use of antibacterial drugs, incorrect use of antibiotics, patient-related factors, prescriber’s prescription habits, veterinary prescriptions, commercial promotion, over the counter sale of antibiotics, underuse of microbiological testing, globalization, and incorrect use of antibiotics such as too short a time/improper use like too low dose, at inadequate potency, or wrong diagnosis (Pinder et al. 2015).

The antibiotic resistance consequences lead to prolonged illness and a greater risk of death; longer periods of hospitalization and infections, which increase the number of infections spread in the community (Friedman, Temkin, and Carmeli 2016). Nosocomial infections are becoming more and more common because doctors are doing more invasive procedures on patients and using more antimicrobials to save their lives (Friedrich 2019).

The impact of resistance on public health and the economy leads to a large pool of resistant genes and an increased burden on society regarding morbidity, mortality, and cost (Friedman, Temkin, and Carmeli 2016). The current situation demonstrates that a significant number of second- and third-line medicines are proving to be ineffective in clinical settings due to alterations in bacterial or host genes (Pulingam et al. 2021). The Centers for Disease Control and Prevention...
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II. METHODOLOGY

2.1. Study Area.

The Medical Services Administration Hospital (MSA hospital) in Khartoum, Sudan, served as the site of this retrospective investigation. The MSA hospital is one of the largest hospitals in Khartoum and serves as a referral center for both public and private hospitals in Khartoum and also for the neighboring states. The hospital serves more than four million people by providing clinical services. The MSA hospital also functions as a teaching facility for medical students.

2.2. Study design

This study was a hospital-based retrospective analysis of antimicrobial drug susceptibility data obtained from the microbiology lab for the time period between December 2020 to January 2022. Records and data were gathered from the MSA hospital's central laboratory's microbiology department.

2.3. Data collection

The culture and sensitivity data were collected from the microbiology department records in the central laboratory of the MSA hospital for the period between December 2020 and January 2022 after official permission from the hospital administration. The targeted data includes the species of the isolated pathogens and the results of antibiotic culture and sensitivity tests.

The samples of urine, pus, blood, ear discharge, eye swab, genital swab, stool, cerebrospinal fluid (CSF), sputum, and nasal swab samples suspected of any bacterial infection are usually sent from different wards in MSA hospital to the microbiology department at the central lab to perform culture and sensitivity tests. Based on standard operating procedures and the most recent clinical and laboratory Standard Institute guidelines, the lab uses standard techniques and biochemical analytical methods for culturing and identifying microorganisms.

The antibiotic culture and sensitivity tests are carried out using the Kirby–Bauer disc diffusion method according to the Clinical Laboratory Standards Institute (CLSI) guidelines. Descriptive statistics were used for analysis, and the results were expressed as frequency and percentage. Microsoft Excel 2016 software was used to analyze the data.

2.4. Ethical consideration

Ethical approval was not obtained as this study is a retrospective study involving the collection of secondary data on the antimicrobial susceptibility of bacterial isolates, which does not require ethical approval in Sudan. No patient information was accessed during this research. For the use of the data, official permission was obtained from the MSA hospital administration to collect the antimicrobial susceptibility data from the microbiology lab registration book. All data obtained during the study was kept confidential and used only for this study.

III. RESULT AND DISCUSSION

3.1. The percentages of isolated and identified microbes in the samples processed at the microbiology department in the central lab.

Based on the antimicrobial culture and sensitivity data from the records of the microbiology
department at the central laboratory of MSA hospital from December 2020 to January 2022, the current research showed that Klebsiella pneumoniae, Escherichia coli, Pseudomonas aeruginosa, Proteus mirabilis, and Staphylococcus aureus were the most common pathogens found in the processed samples.

In a total of different clinical samples that were processed during the study period, 980 organisms were isolated. The results showed that out of the 980 isolated bacteria, 345 (35.20%) were K. pneumoniae, 326 (33.27%) were E. coli, 154 (15.71%) were P. aeruginosa, 130 (13.27%) were P. mirabilis, and 25 (2.55%) were S. aureus (Figure 1).

![Figure 1: The percentages of isolated and identified microbes in the samples processed at the central lab of MSA hospital](image)

### 3.2. The antimicrobial resistance pattern of Klebsiella pneumoniae at the MSA hospital

The results showed that K. pneumoniae was highly resistant to azithromycin (100% of the total cases were resistant), piperacillin (98.8%), cefuroxime (98.2%), amoxicillin/clavulanic (96.2%), colistin (93.6%), ceftazidime (91.3%), cefixime (90.1%), and cefpime (86.9%), as shown in figure (2). On the other hand, K. pneumoniae was found to be more sensitive to imipenem (78.8% of the total cases were sensitive), meropenem (76.5%), and amikacin (77.6%) as shown in figure (2).

**Klebsiella pneumoniae** is one of the multi-drug resistant (MDR) organisms and it has been identified as an urgent threat to human health by the World Health Organization, the US Centers for Disease Control and Prevention and the UK Department of Health (Navon-Venezia, Kondratyeva, and Carattoli 2017).

In hospitals, K. pneumoniae infections are most common in newborns, the elderly, and people with weak immune systems. This organism is also the cause of a lot of infections that people get from other people, like pneumonia and sepsis (Khan, Ahmad, and Mehboob 2015).

Antibiotic resistance in K. pneumoniae is associated with high rates of morbidity and mortality in clinical patients. Acquisition of antibiotic resistance genes and intrinsic resistance to several classes of antibiotics limits treatment options for infections caused by K. pneumoniae (Bassetti et al. 2018). Currently, K. pneumoniae strains producing Extended Spectrum Beta-Lactamases (ESBLs) and carbapenemases have spread globally (Younas et al. 2018).

The β-lactamases in antibiotic-resistant K. pneumoniae are varied, and penicillin-binding proteins (PBP s) expression is variable in the β-lactam system. In addition, PBPs and β-lactamases are two important resistance mechanisms in K. pneumoniae caused by the frequent use of antibiotics in patients with pneumonia (Wang et al. 2020).

### 3.3. The antimicrobial resistance pattern of Escherichia coli at the MSA hospital

The results as shown in figure (2) indicated that E. coli was highly resistant to azithromycin (100% of the total cases were resistant), amoxicillin/clavulanic (98.7% of the total cases), piperacillin (98.4%), cefuroxime (98.1%), colistin (97.4%), ceftazidime (94.1%), cefixime (93.8%), cefotaxime (93.8%), and cefpime (92.6%). Regarding the pattern of sensitivity, it was found that E. coli was more sensitive to amikacin (81.9% of all cases were sensitive), meropenem (78.2%), and imipenem (73.9%), as shown in figure (3).
The acquired, or extrinsic, and continuously increasing resistance of *E. coli* to antibiotics is already considered a major public health problem around the world (Galindo-Méndez 2020). In 2018, more than half of the *E. coli* isolates sent to the European Centre for Disease Prevention and Control were resistant to at least one group of antimicrobials that were being watched. Often, they were resistant to more than one group (Peñalva et al. 2019).

The ability of *E. coli* to colonize different environments, including the guts of humans and animals, has provided this organism with the evolutionary advantage of acquiring antibiotic resistance traits from other bacteria within its environment, as well as being easily transmitted via the fecal-oral route (Lee, Lee, and Choe 2018). People can have more than a thousand commensals, to human pathogens (Mairi et al. 2018; Son et al. 2021).

### 3.4. The antimicrobial resistance pattern of *Pseudomonas aeruginosa* at the MSA hospital

The results indicated that *Pseudomonas* was found to be highly resistant to Azithromycin (100% of the total cases were resistant), amoxicillin/clavulanic (99.2%), nalidixic acid (98.4%), ofloxacin (98.4%), nitrofurantoin (97.6%), norfloxacin (95.3%), colistin (94.6%), and cefuroxime (93% of total cases were resistant). On the other hand, *P. aeruginosa* was highly resistant to azithromycin (100% of the total cases were resistant), amoxicillin/clavulanic (99.2%), nalidixic acid (98.4%), ofloxacin (98.4%), nitrofurantoin (97.6%), norfloxacin (95.3%), colistin (94.6%), and cefuroxime (93% of total cases were resistant). On the other hand, *P. mirabilis* showed good sensitivity to imipenem (82.3% of the total cases were sensitive) and amikacin (81.5% of the total cases were sensitive) as shown in figure (4).
The emergence and spread of antibiotic resistance determinants, including colistin, and shows reduced susceptibility to imipenem. However, higher levels of resistance to imipenem commonly occur in *P. mirabilis* isolates consecutively to the loss of porins, reduced expression of penicillin binding proteins (PBP), PBP1a, PBP2, or acquisition of several antibiotic resistance genes, including carbapenemase genes (Hammoudi Halat and Ayoub Moubareck 2020; Girlich et al. 2020).

A lot of bacteria are also resistant to drugs that aren’t lactamases, like fluoroquinolones and nitrofurans, which are used to treat UTIs. The emergence and spread of multidrug-resistant *P. mirabilis* isolates, such as those producing ESBLs, AmpC cephalosporinases, and carbapenemases, is also becoming more common (Girlich et al. 2020).

Concerning antibiotic resistance determinants, *P. mirabilis* has integrative and conjugative elements (ICEPm) and other ICEs in the SXT/R391 family that can self-replicate and self-transfer to other strains and species, transferring virulence genes and antibiotic resistance as well (Girlich et al. 2020).

3.6. The antimicrobial resistance pattern of *Staphylococcus aureus* at the MSA hospital

The results revealed that *S. aureus* was highly resistant to cefuroxime, nitrofurantoin, ceftriaxone and norfloxacin (100% of the tested samples were resistant), ceftaxime, amoxicillin/clavulanic and colistin (96% of the tested samples were resistant), cefepime, ceftazidime and nalidixic acid (92% of the tested samples were resistant), piperacillin/tazobactam, cefotaxime, and piperacillin (88% of the tested samples were resistant). The study findings indicated that *S. aureus* was most sensitive to imipenem (84% of the total cases were sensitive, as shown in figure (6)).

**Figure 5:** The number of resistant cases of *P. mirabilis* to the assessed antibiotics.

*P. mirabilis* is a commensal member of the Enterobacteriaceae in the human digestive tract. At the same time, *P. mirabilis* is commonly involved in urinary tract infections (UTI) (Behzadi et al. 2020). *P. mirabilis* is naturally resistant to several antibiotics, including colistin, and shows reduced susceptibility to imipenem. However, higher levels of resistance to imipenem commonly occur in *P. mirabilis* isolates consecutively to the loss of porins, reduced expression of penicillin binding proteins (PBP), PBP1a, PBP2, or acquisition of several antibiotic resistance genes, including carbapenemase genes (Hammoudi Halat and Ayoub Moubareck 2020; Girlich et al. 2020).

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**Figure 6:** The number of resistant cases of *S. aureus* to the assessed antibiotics.

*Staphylococcus aureus* shows the adaptive evolution of bacteria in the antibiotic era better than any other human pathogen. It has a unique ability to quickly adapt to each new antibiotic, from penicillin and methicillin to the most recent ones, linezolid and daptomycin (Guo et al. 2022; Silva et al. 2022).

The mechanisms of *S. aureus* resistance include enzymatic inactivation of the antibiotic (penicillinase and aminoglycoside-modification enzymes); alteration of the target with decreased affinity for the antibiotic (notable examples being penicillin-binding protein 2a of methicillin-resistant *S. aureus* and D-Ala-D-Lac of peptidoglycan precursors of vancomycin-resistant strains), trapping of the antibiotic (for vancomycin and possibly daptomycin) and efflux pumps (fluoroquinolones and tetracycline) (Peterson and Kaur 2018).

Complex genetic arrays (staphylococcal chromosomal cassette mec elements or the vanA operon) have been acquired by *S. aureus* through horizontal gene transfer, while resistance to other antibiotics, including some of the most recent ones (e.g., fluoroquinolones, linezolid, and daptomycin), has developed through spontaneous mutations and positive selection. Detection of the resistance mechanisms and their genetic basis is an important support for antibiotic susceptibility surveillance in *S. aureus* (Partridge et al. 2018; Gheorghe, Popa, and Măruțescu 2018).

**IV. CONCLUSION**

Misuse and overuse of antibiotics worldwide has transformed antibiotic-resistant bacteria into a global health crisis. The present retrospective study, which has been carried out at the microbiology department in the
central laboratory of MSA hospital, indicated that all the isolated bacteria had developed significant rates of resistance to most of the antibiotics that are frequently used in the hospital. Our research offers significant information on the bacterial spectrum, with the main isolated pathogens being K. pneumoniae, E. coli, P. aeruginosa, P. mirabilis, and S. aureus. Besides the most resistant bacteria, the current study highlighted the antibiotics that showed decreased antimicrobial activities against the isolates, which constitute a major challenge for antibiotics' empirical use. As a result, the current study assists doctors at MSA hospital with empirical treatment by prescribing appropriate antibiotics based on drug susceptibility reports. Moreover, this study helps the hospital at the managerial level to evaluate and continually track the use of antibiotics and to regularly apply hospital antibiograms analysis to ensure sustained efficacy of the routinely used antibiotics as well as to assist manual empiric antimicrobial remedies and track trends in antimicrobial resistance.

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AUTHOR CONTRIBUTIONS

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation; or taking part in drafting, revising, or critically reviewing the article. All authors gave final approval of the version to be published agreed on the journal to which the article has been submitted, and agreed to be accountable for all aspects of the work.

CONFLICT OF INTEREST

The authors declare no conflicts of interest for this work.

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