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To evaluate the resistivity of Klebsiella pneumonia against present antibiogram: Case report study

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***Abstract*---**Klebsiella pneumoniae has become a health care concern due to its production of extended-spectrum beta-lactamase (ESBL) and its resistance to carbapenem. In February 2022, a 28-year-old female patient was admitted to the CCU private ward at Anil Bhagi Hospital in Firozpur, Punjab, India. The urine sample was inoculated with CLED agar medium for microbiological investigation. B D Phoenix sophisticated automated microbiology system was utilised for identification and sensitivity of bacteria for 24 hours for confirmation of bacteria and antibiotic sensitivity. Fosfomycin, teigocyclin and colistin were sensitive whereas other antibiotics were resistant. The observed radiuses were 13mm, 12mm, and 8mm, respectively. A urine culture revealed a highly resistant K. pneumoniae strain with over 1100,000 colony-forming units (cfu) per mL. In February 2022, a 38-

year-old female patient was admitted to the CCU private ward. The 7-8 ml blood sample was collected in blood culture bottles for microbiological examination and cultured for 5 days in the B D Phoenix sophisticated automated microbiology equipment. Fosfomycin, teigocyclin and colistin were sensitive while other antibiotics were resistant. The radius observed was 9mm, 4 mm and 8 mm respectively. Due to the scarcity of new antibacterial medications under development, we must maximise the effectiveness of current antibacterial treatments.

***Keywords*---**Klebsiellapneumoniae, pan-drug resistance, infection, intensive care unit.

Introduction

Antimicrobial resistance (AMR) is a fast growing concern in today's healthcare facilities across the globe. Pathogenic bacteria, such as Klebsiellapneumoniae, are rapidly evolving multidrug resistant (MDR) strains and often represent a major hazard to patients owing to an elevated mortality risk due to therapeutic alternatives' decreasing efficiency. K. pneumoniae is known to cause community-acquired infections, but it has recently been identified as a significant source of hospital-acquired diseases. Through the synthesis of enzymes such as Extended Spectrum Lactamase (ESBLs) and Carbapenemase, K. pneumoniae has been reported to acquire antibiotic resistance more quickly than most bacteria. [1-3] Antibiotic exposure is the most major risk factor for AMR. The intense and extended use of antibiotics in the hospital environment is one of the major factors to the establishment and spread of highly resistant bacteria for health-care associated illnesses (HAIs). [4] K. pneumoniae is also crucial in the transmission of antibiotic resistance genes from environmental bacteria to clinically significant bacteria. [5] There are several pathways of antibiotic resistance that will have a detrimental impact on treatment results. Antibiotic resistance has been identified as one of the world's three major issues by the World Health Organization (WHO). 3 K. pneumoniae is a Gram-negative encapsulated bacterium that thrives on mammalian mucosal surfaces as well as in soil, plants, and water. K. pneumoniae typically colonises the oropharynx and gastrointestinal tract in humans, from which it can easily enter the circulation and other tissues and cause infections such as bacteremia, septicemia, surgical site infection, urinary tract infection, hospital acquired pneumonia, and ventilator-associated pneumonia. It also contributes to the high prevalence of opportunistic infections in immunocompromised individuals, such as those with bladder neuropathy or diabetes mellitus. [6,7]K. pneumoniae is also renowned for its propensity to create biofilms, which are bacterial populations embedded in an extracellular matrix. Proteins, exopolysaccharides, DNA, and lipopeptides make up this matrix. [8]LeChevallier et al. were the first to report K. pneumoniae and the biofilm-forming process in 1988. [9] K. pneumoniae possesses virulence factors such as capsule polysaccharide, lipopolysaccharide, type 1 and type 3 fimbriae, outer membrane proteins, and iron acquisition and nitrogen source utilisation determinants. K. pneumoniae exploited these virulence factors to survive and avoid detection by the immune system during infection, as well as for biofilm development. [10,11] K.

pneumoniae may form a thick coating of extracellular biofilm that aids bacterial adhesion to living or non-living surfaces, therefore shielding antibiotic penetration and limiting its effects. [12]

Case Study No. 1

In February 2022, a 28-year-old female patient was admitted to the CCU private ward at Anil Bhagi Hospital in Firozpur, Punjab, India. She had symptoms such as chest discomfort when breathing and coughing up phlegm, fatigue, fever, sweating, and trembling chills. She was on a ventilator at the time. All samples (blood, urine, and sputum) were collected from the patient and submitted to the laboratory for microbiological, haematological, and biochemical analysis.

The urine sample was inoculated with CLED agar medium for microbiological investigation. (Cystiene lactose electrolyte deficient agar medium) was then incubated for 24 hours at 37°C. On the CLED agar medium, a mucoid colony was found after incubation. Gram staining was used to further investigate the ananysis. Under the microscope, we noticed gram-negative rod-shaped creatures. B D Phoenix sophisticated automated microbiology system was utilised for identification and sensitivity of bacteria for 24 hours for confirmation of bacteria and antibiotic sensitivity. All antibiotics were shown to be resistant when the B D Phoenix procedure was completed.

Disc diffusion techniques of antibiotics (Imipenem, Meropenem, cefepim, Ciprofloxacin, Amikacin, Ceftazidime, Ceftriaxon, Cefotaxime, Ampicilin, Colistine, Fosfomycin, and tigecyclin) were employed for manual assessment of K. pneumoniae sensitivity and resistance. The disc technique involves placing a little volume of culture on Mueller hinton agar medium and a standardised antibiotic disc on the plate surface and incubating the culture media plate overnight. If the antibiotic is able to block the development of the microorganism, it does not grow around the bacterial disc, indicating that it is sensitive; if the microorganism grows around the antibiotic disc, indicating organism resistance to this antibiotic. The diameter of the colony as measured in millimetres was used to detect and distinguish between sensitive and resistant conditions.

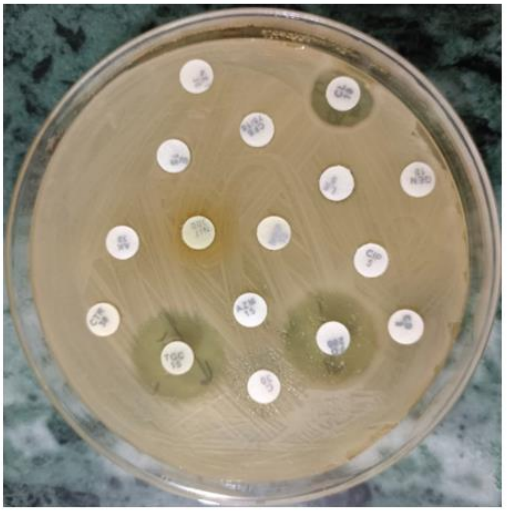

Fig 1 demonstrated that fosfomycin, teigocyclin and colistin were sensitive whereas other antibiotics were resistant. The observed radiuses were 13mm, 12mm, and 8mm, respectively. A urine culture revealed a highly resistant K. pneumoniae strain with over 1100,000 colony-forming units (cfu) per mL.

Fig 1.

The therapy began with fosfomycin and was terminated after 7 days of treatment.

Case Study No. 2

In February 2022, a 38-year-old female patient was admitted to the CCU private ward at Anil Bhagi Hospital in Firozpur, Punjab, India. She was exhibiting indications of pneumonia. A blood sample was collected from the patient and submitted to the laboratory for microbiological, haematological, and biochemical analysis.

The 7-8 ml blood sample was collected in blood culture bottles for microbiological examination and cultured for 5 days in the B D Phoenix sophisticated automated microbiology equipment. But the blood culture was positive for microorganisms after 3 days, we removed the blood culture bottled from the system and transferred the 1mi blood culture from the blood culture bottled to MacConkey agar under aseptic conditions. This MacConkey agar plate was incubated for another 24-48 hours at 370 degrees Fahrenheit. We discovered a mucoid colony on a MacConkey agar plate after 24 hours. Gram staining was used to further investigate the ananysis. Under the microscope, we noticed gram-negative rod-shaped creatures.

B D Phoenix sophisticated automated microbiology system was utilized for identification and sensitivity of bacteria for 24 hours for confirmation of bacteria and antibiotic sensitivity. After the B D Phoenix procedure, all antibiotics were found to be resistant, and K. pneumonia was identified as an infectious bacterium. Disc diffusion techniques of antibiotics (Imipenem, Meropenem, cefepim, Ciprofloxacin, Amikacin, Ceftazidime, Ceftriaxon, Cefotaxime, Ampicilin, Colistine, Fosfomycin, and tigecyclin) were employed for manual assessment of K. pneumoniae sensitivity and resistance.

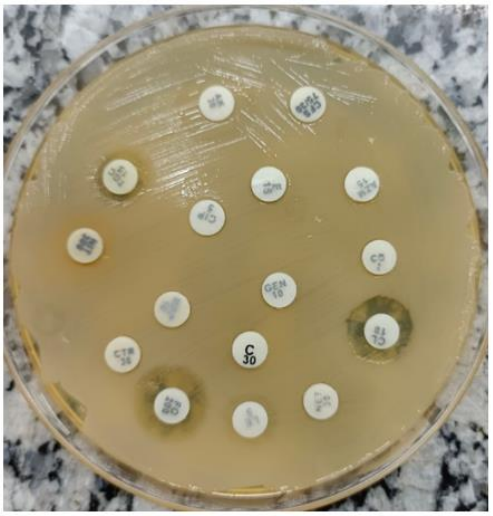

Fig 2 showed that fosfomycin, teigocyclin and colistin were sensitive while other antibiotics were resistant. The radius observed was 9mm, 4 mm and 8 mm respectively.

The treatment begin with fosfomycin and discontinued after 5 days of treatment, and discharged. After 5 days, the symptoms were disappeared.

Table 1
Antibiotic sensitivity pattern on K. pneumoniae

	Case 1	Case 2
Antibiotic	Avg MIC/Diameter	Avg MIC/Diameter
Fosfomycin	**13mm**	**9mm**
Teigocyclin	**12mm**	**4mm**
Colistin	**8mm**	**8mm**
Amikacin	**>**32	**>**32
Amoxycillin-clavulanate	>64	>64
Ampicillin	16	16
Aztreonam	>16	>16
Cefazolin	2	2
Cefepime	>32	>32
Cefotaxime	8	8
Cefoxitin	>16	>16
Ceftadizime	8	8
Chloramphenicol	>2/38	>2/38
Ciprofloxacin	8	8
Gentamicin	<=8	<=8
Imipenem	<=2	<=2
Levofloxacin	>2	>2
Meropenem	8	8
Piperacillin	>16	>16
Piperacillin-tazobactum	16/8	16/8
Tetracycline	>4	>4
Trimethoprim-sulfamethoxazole	<=4/4	<=4/4

Discussion

The most significant aspect of research aimed at preventing the emergence of antibiotic resistance is to provide more institutions and individuals with access to data produced via evidence-based medical practises. It is not sufficient to report merely antibiotic resistance/susceptibility in research since notifying about all antibiotics used during reporting may not always result in correct findings. As a result, it is vital to be selective about notifications within the scope of preventative actions for resistance development and to adopt the NAS strategy. [13] The primary goal of this technique is to test for the most appropriate antimicrobials, to report the most appropriate treatment alternatives within the framework of test findings in a restricted fashion, and to minimise resistance development as much as possible. In our study, which was intended to be a meta-analysis, diverse findings on antibiotic resistance of K. pneumoniae discovered by separate researchers who did not know each other were methodically analysed in order to generate evidence-based data. Because there was no specific standards when the resistance was reported, the majority of the work done in the databases was omitted. Otherwise, research that do not meet our criteria will raise the standard deviation of the findings, rendering them meaningless.

ESBL-producing bacteria are resistant to beta-lactam antibiotics as well as drugs from other classes, and they play an important role in MDR microorganisms. Many nations have lately reported an upsurge in the number of ESBL generating microbes. In multicenter investigations, the rate of ESBL in K. pneumoniae isolates was reported to be 48.7 percent. [14]

Infections with multidrug resistant gramme negative bacilli have been linked to considerable morbidity and death.[15] Bacterial isolates containing carbapenemases may hydrolyze a wide range of -lactams, including penicillins, cephalosporins, carbapenems, and monobactam. The bulk of these bacteria are members of the ESCAPE group (Enterococcusfaecium, Staphylococcus aureus, Clostridium difficille, Acinetobacterbaumannii, Pseudomonas aeruginosa, and Enterobacteriacae species) and are responsible for the majority of hospital- and community-acquired illnesses. [16] They have a proclivity to "elude" eradication by all presently available antibacterial agents. This was noted in a recent assessment by the Infectious Diseases Society of America (IDSA) titled "terrible bugs, no medicines." This has becoming increasingly concerning, particularly because no promising new antimicrobial medicines are on the horizon. The growing use of carbapenems to treat organisms generating extended-spectrum beta lactamase (ESBL), which leads to resistance to these drugs, is a key risk factor for this rise. [17]

The increasing number of immunocompromised people has resulted in a rise in the frequency of infections with these highly resistant pathogens. The use of oxyimino group antibiotics (cefuroxime, ceftriaxone, cefotaxime, ceftazidime, or aztreonam) is a well-known risk factor for ESBL acquisition.[18]The best way to treat Carbapenemase-producing Klebsiellapneumoniae pathogens remains uncertain. Using few novel antimicrobials in development, physicians have resorted to treating these infections with older, previously abandoned antimicrobials such as colistin and tigecycline. This method has lately resulted in

the creation of microbes resistant to all known antibiotic classes, including polymyxins. [19] and its associated toxins Thebacteriostaticglycylcyclinetigecycline is a glycylcycline having broad action against numerous enterobacteraceae, including ESBLs and Klebsiellapneumoniaecarbapenemases (KPCs). However, because of its low serum levels, it should be used with care for treating bacterial infections. The most serious side effects of colistin treatment include nephrotoxicity and neurotoxicity. Neurotoxicity may be difficult to detect, particularly in severely sick individuals who are unable to disclose paraesthesia.

Klebsiellapneumoniae generating carbapenemase has been effectively treated with single or combination antibiotic treatments. Neuneret al[20] showed varying susceptibilities in vitro to tigecycline (98%), colistin (86%), amikacin (45%), and gentamicin (22%), among 60 patients with carbapenemase-producing Klebsiellapneumoniae bloodstream infections. Clinicians have been obliged to utilise alternate antibiotics such as tigecycline and polymyxins(polymyxin B or colistin) to treat infections caused by carbapenemase resistant Enterobacteriacae, as was the case in this instance.

Conclusion

Klebsiellapneumoniae isolates resistant to all frequently used antimicrobial drugs have been identified as becoming clinically significant infectious agents. The worldwide proliferation of this agent is a challenge for doctors, since there are limited treatment alternatives for combating these viruses. Furthermore, improved procedures for isolating these infections and screening persons who they colonise are required while we wait for the development of new efficacious medications against resistant Gram-negative bacteria. Due to the scarcity of new antibacterial medications under development, we must maximise the effectiveness of current antibacterial treatments. While these requirements are being addressed, it is also vital to have antimicrobial stewardship guidelines in place, improve monitoring, and implement effective infection control initiatives to restrict the spread of these infections. We are sharing this instance to highlight some worrisome aspects that may soon be relevant to an increasing number of clinicians and patients worldwide.

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