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RESEARCH ARTICLE

ANTIMICROBIAL RESISTANCE PROFILES AMONG UROPATHOGENS: A JUDICIOUS SELECTION OF ANTIBIOTICS TO MINIMIZE ANTIMICROBIAL RESISTANCE (AMR) ASSISTS THE CLINICIAN

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ABSTRACT

Introduction: Urinary tract infections (UTIs) are a significant health concern, necessitating accurate identification of causative agents and their antimicrobial susceptibility patterns for effective treatment. Antibiotic resistance among uropathogens threaten to greatly increase the economic burden of these infections.^{1,6} The emergence of antimicrobial resistance (AMR) among uropathogens has become a global concern, leading to limited treatment options and increased healthcare costs. This study aimed to investigate the antimicrobial resistance profiles of uropathogens and emphasize the importance of judicious antibiotic selection to minimize AMR and assist clinicians in effective treatment decisions. Most common organisms isolated causing UTI in present study were *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Enterococcus faecalis*. **Objective:** The objective of this study was to identify the most frequently involved pathogen in the causation of urinary tract infections (UTIs) in patients, determine the common causative agents, and assess their antimicrobial susceptibility patterns. **Methodology:** This retrospective study was conducted at Healthians Lab, Gurugram, India, to determine the common causative agents and antimicrobial susceptibility patterns of UTIs using microbiologic laboratory data from urine culture samples tested over a one-year period. Bacterial identification and antibiotic sensitivity is done by automated system BD phoenix. The minimal inhibitory concentration (MIC) of each antibiotic was determined and judged to be susceptible, intermediate, or resistant following the breakpoints of Clinical and Laboratory Institute (CLSI). **Conclusion:** The study provides important data on the most commonly isolated organisms from urine samples. The analysis and comparison of the antimicrobial susceptibility patterns of these organisms provide valuable insights for clinicians. Based on this information, they can choose the most appropriate empirical treatment options for UTIs.

INTRODUCTION

Urinary tract infections (UTIs) are a significant public health concern worldwide, with high recurrence rates and increasing antimicrobial resistance posing challenges in their management. The emergence of antibiotic resistance among uropathogens has the potential to escalate the economic burden associated with UTIs.^{1,2} Infection is commonly observed in young and mature adults, with a higher prevalence among females. Risk factors for UTIs include catheterization, anatomical abnormalities, and behavioral factors. If left untreated, UTIs can progress to pyelonephritis, and transmission of microbes to the gastrointestinal tract or kidneys can lead to further complications.² Although UTIs can occur in any season, a spike in infection rates is often observed during warm summer months. Common uropathogens are *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas*

aeruginosa, *Enterococcus faecalis*, these pathogens have been consistently identified in various studies and are known for their ability to cause urinary tract infections. Present study aims in better understanding of the etiology and antibiotic susceptibility pattern of the isolates.

Objective: The objective of this study was to identify the most frequently involved pathogen in the causation of urinary tract infections (UTIs) in patients, determine the common causative agents, and assess their antimicrobial susceptibility patterns.

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METHODOLOGY

A retrospective study was conducted by reviewing the data of patients diagnosed with UTIs over a specified period. This data- driven study was conducted in the Healthians Lab, Gurugram India laboratory. To achieve this objective, the following methodology was employed:

All urine cultures requested within the one-year period, specifically from 1st February 2021 to 1st February 2022, were included in the analysis. Only patients with positive culture results were considered for further analysis. Sample Selection: Urine samples from patients diagnosed with UTIs were included in the study. Samples with a bacterial count of $\geq 10^5$ colony-forming units per ml (CFU /mL) were considered. Bacterial Identification: Bacterial identification was performed using the automated BD Phoenix M50 system. Gram-negative and Gram-positive ID panels were used for bacterial identification. The system utilizes advanced technology to accurately identify different bacterial species present in the urine samples.

Antibiotic Sensitivity Testing: After bacterial identification, antibiotic sensitivity testing was conducted using the BD Phoenix M50 system. This system assesses the susceptibility of identified pathogens to various antibiotics, providing valuable information on the most effective treatment options. Antimicrobial susceptibility testing for gram negative bacteria was conducted BD planes-NID 500, NID55. The tested antimicrobial agents included: amikacin, ampicillin, cefepime, ceftriaxone, ciprofloxacin, gentamicin, imipenem, meropenem, nitrofurantoin, piperacillin-tazobactam, trimethoprim-sulfamethoxazole, and fosfomycin. PMIC ID 70 panels were used for gram positive bacteria and antimicrobial agents included were levofloxacin, linezolid, nitrofurantoin, penicillin G, teicoplanin, tetracycline, and vancomycin. The minimal inhibitory concentration (MIC) of each antibiotic was determined by the BD Phoenix M50 system. The results were interpreted as susceptible, intermediate, or resistant following the breakpoints recommended by the Clinical and Laboratory Standards Institute (CLSI).

Data Analysis: The data obtained from the study includes information on the commonly isolated uropathogens from urine cultures over a one- year period. A total of 15,497 urine samples were received, out of which 2,122 samples exhibited the presence of pathogenic organisms. The most commonly isolated uropathogens from urine cultures were as follows: Escherichia coli: 1549 cases (72.9%), Klebsiella pneumoniae: 389 cases (18.3%), Pseudomonas aeruginosa: 81 cases (3.8%), Citrobacter koseri: 68 cases (3.2%), Proteus mirabilis: 35 cases (1.6%), Enterococcus faecalis: 34 cases (2%). Same has been depicted in the Figure 1.1

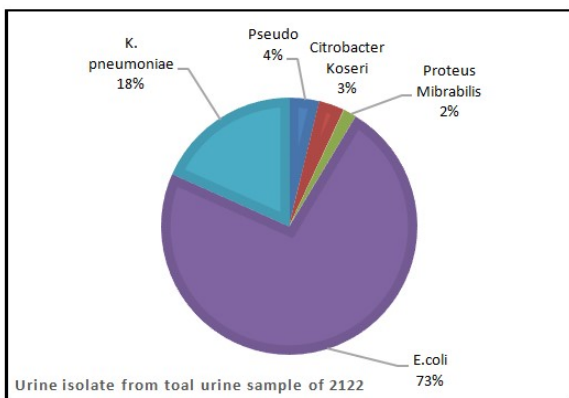


Figure 1.1

Antibiotic sensitivity pattern of the different isolate as follows:

Escherichia coli: Out of total 1549, E. coli isolated (630) 73% were ESBL producers and approximately (230) 27% were carbapenemase producers which is depicted in Figure 1.2 fosfomycin is $\geq 80\%$ effective against E. coli depicted in Figure 1.3

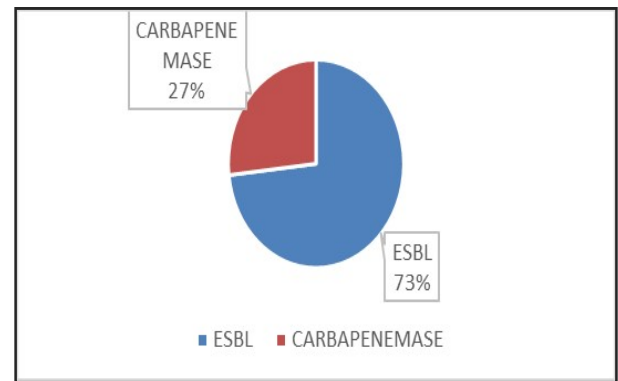


Figure 1.2

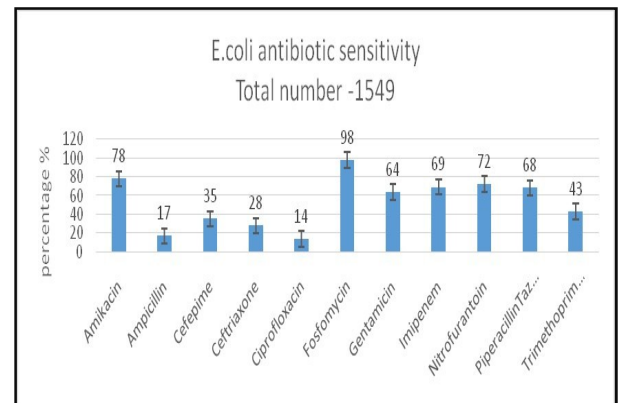


Figure 1.3

Klebsiella pneumoniae: Amikacin is most effective against Klebsiella pneumoniae depicted in Figure 1.4

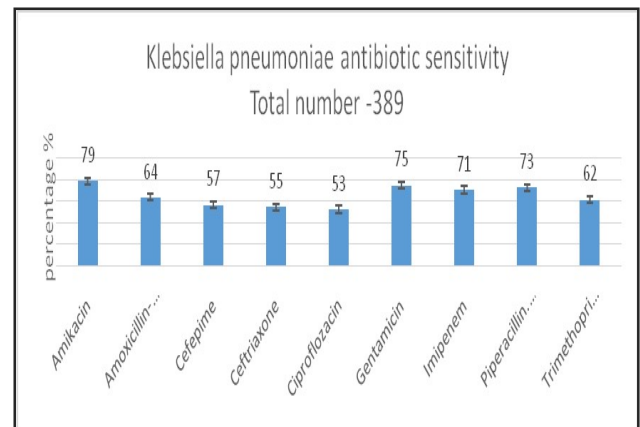


Figure 1.4

Pseudomonas aeruginosa: amikacin, piperacillin-tazobactam are most effective against Pseudomonas aeruginosa depicted in Figure 1.5

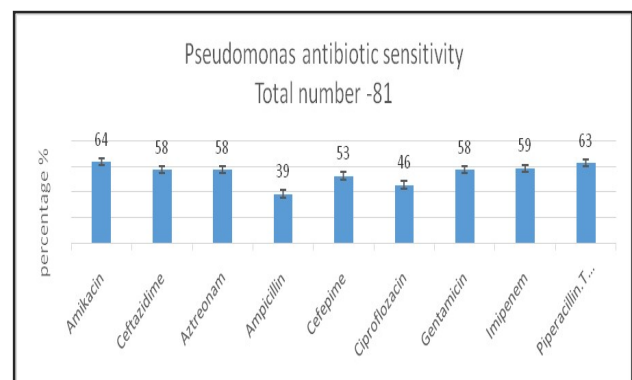


Figure 1.5

Citrobacter koseri: amikacin, ceftriaxone, gentamicin were $\geq 80\%$ effective against *Citrobacter koseri* depicted in Figure 1.6

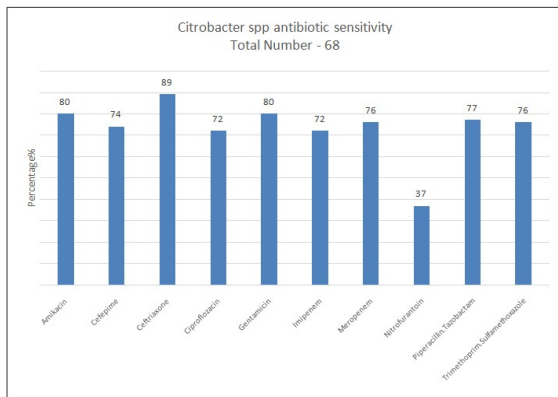


Figure 1.6.

Proteus mirabilis: imipenem, piperacillin-tazobactam are most effective against *Proteus mirabilis* depicted in Figure 1.7

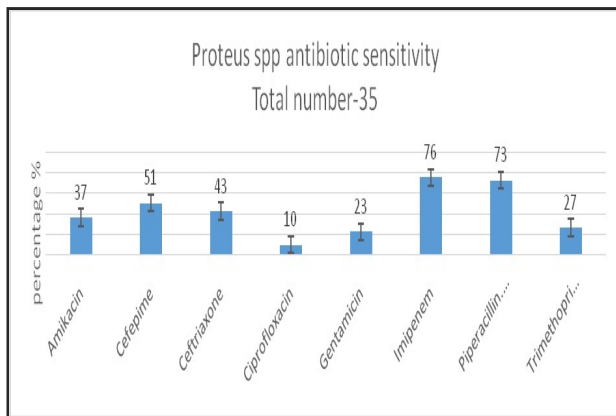


Figure 1.7.

Enterococcus faecalis: penicillin, ampicillin, linezolid, nitrofurantoin, teicoplanin, vancomycin were $\geq 80\%$ effective against *Enterococcus faecalis* depicted in Figure 1.8

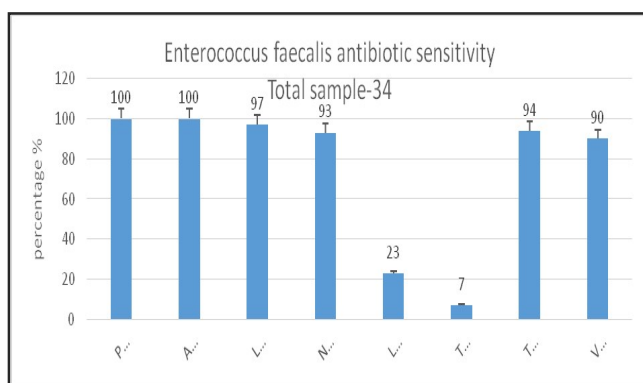


Figure 1.8

DISCUSSION

The data obtained from this study aligns with findings from other studies conducted in India and worldwide, indicating that the spectrum of organisms causing urinary tract infections (UTIs) is similar. Among the uropathogens, *Escherichia coli* (specifically uropathogenic *E. coli* or UPEC) is reported as the predominant cause of UTIs in various populations.^{1,3,4,5,6} A study in South India also found *E. coli*, *K. pneumoniae* and *P. aeruginosa* to be the most common gram-negative isolates associated with community acquired UTI.⁹ In the present study out of total 549 *E. coli* isolated 630 were

ESBL producers and 230 were carbapenemase producers^{7,8}. The main mechanism of carbapenem resistance of *E. coli* and *K. pneumoniae* is production of various carbapenemases.¹ A study in East India in 2012 reported ESBL strains in 23.2% *E. coli* and 9.4% *K. pneumoniae*.¹⁰ Researchers from Jaipur reported an increasing trend of ESBL producing *Escherichia coli* strains (from 9.52% to 30.08%) over a period of 3 years (2007-2009)¹¹. A study in South India conducted in 2008 reported an MDR prevalence of 8.4% in *E. coli* isolates¹². In present study fosfomycin was $\geq 80\%$ effective against *E. coli*. Amikacin was most effective against *Klebsiella pneumoniae*. A study in East India showed *E. coli* and *Klebsiella* isolates to be quite sensitive to aminoglycosides (72-76%) and nitrofurantoin (52%). However, the study reported high resistance to all quinolones except levofloxacin (52%) and all cephalosporins and cotrimoxazole¹⁰ amikacin, piperacillin-tazobactam were approximately 80% effective against *Pseudomonas aeruginosa*. Amikacin, Ceftriaxone, Gentamicin were $\geq 80\%$ effective against *Citrobacter koseri*. Imipenem, piperacillin-tazobactam were most effective against *Proteus mirabilis*.^{1,3,8} penicillin, ampicillin, linezolid, nitrofurantoin, teicoplanin, vancomycin were $\geq 80\%$ effective against *Enterococcus faecalis*. Antibiotic resistance is becoming a serious global health problem, and updated surveillance of antimicrobial susceptibility of a specific type of infection is of great importance for initial empirical therapy⁴.

Resistance observed to commonly prescribed antibiotics like fluoroquinolones, third generation cephalosporins and cotrimoxazole is an important finding as these are the antibiotics recommended for empirical therapy of urinary tract infections in various national and international guidelines. The National Centre for Disease Control (NCDC) guidelines recommend nitrofurantoin, cotrimoxazole or ciprofloxacin for the treatment of acute uncomplicated cystitis and amikacin or gentamicin for acute uncomplicated pyelonephritis^{8,14}.

CONCLUSION

This study provides valuable insights into the antimicrobial susceptibility trends among uropathogens and emphasizes the importance of monitoring and comparing these trends with other studies. By periodically conducting similar studies on a larger scale in different regions, healthcare providers can frame empiric antibiotic therapy guidelines tailored to local antimicrobial susceptibility patterns. This approach can significantly improve patient outcomes and minimize the misuse of antibiotics. The increasing difficulty in treating UTIs is primarily attributed to the widespread emergence of antibiotic resistance mechanisms. This study highlights the sensitivity profiles of various antibiotics, with fosfomycin and nitrofurantoin demonstrating good susceptibility among the isolates analyzed. These oral drugs with limited renal penetration can be considered as suitable options for the empiric treatment of uncomplicated low UTIs. Enterobacteriaceae members, including *Escherichia coli* and *Klebsiella pneumoniae*, which have acquired plasmids encoding extended-spectrum β -lactamases (ESBLs). These enzymes confer resistance to a broad range of β -lactam antibiotics, further limiting treatment options. The rising prevalence of ESBL-producing uropathogens emphasizes the urgent need for judicious antibiotic use and infection control measures to curb the spread of resistance. Continued surveillance and research efforts are crucial in addressing the challenges posed by antimicrobial resistance in UTIs. By identifying emerging resistance patterns and evaluating the effectiveness of different antibiotics, healthcare providers can make informed decisions regarding empirical treatment. Additionally, promoting public awareness about the appropriate use of antibiotics and the importance of preventive measures, such as hygiene practices, can contribute to the overall management of UTIs and reduction of antimicrobial resistance. Tendency to self-medicate, noncompliance to treatment, financial constraints and lack of education on part of patient, sale of antibiotic drugs without proper prescription and failure to educate patient on part of pharmacists, negligible surveillance of susceptibility patterns, poor regulatory controls over antibiotics and lack of will to make change on part of health care system, and

administering antibiotics before obtaining sample for culture, failure to educate patient and poor prescribing practices on part of physicians are among many factors that lead to injudicious and inappropriate use of antibiotics in India, hence causing rapid development of resistance³. In conclusion, this study highlights the significance of monitoring and comparing antimicrobial susceptibility trends among uropathogens in guiding empirical treatment of UTIs. Optimum therapeutic antimicrobial management should target a specific pathogen with a precise dose and treatment duration in order to effectively combat causative microbes, reduce the risk of complications, minimize adverse drug reactions. Regular large-scale studies, tailored to regional contexts, can aid in formulating effective guidelines for clinicians, leading to improved patient outcomes and lower the risk of AMR. Addressing the challenges posed by antibiotic resistance in UTIs requires a comprehensive approach involving healthcare providers, researchers, and public education initiatives.

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