A COMPARATIVE STUDY OF ANTIMICROBIAL SENSITIVITY IN PATIENTS WITH ACUTE PYELONEPHRITIS AND EMPHYSEMATOUS PYELONEPHRITIS

Original Research

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ABSTRACT

Background: Urinary tract infections (UTIs) commonly affect men and can lead to serious complications such as acute pyelonephritis (APN) and emphysematous pyelonephritis (EPN). APN typically impacts the renal pelvis and parenchyma, often exacerbated by conditions like obesity, diabetes, or immunosuppression. EPN, characterized by gas formation within the renal tissues, is predominantly caused by Escherichia coli and Klebsiella pneumoniae.

Objective: This study aims to identify the pathogens responsible for emphysematous pyelonephritis, compare their prevalence with acute pyelonephritis, and evaluate their antimicrobial sensitivity patterns.

Methods: A comparative study was conducted over twelve months, from July 2023 to June 2024, involving 145 patients diagnosed with APN and EPN at the Institute of Kidney Disease, Peshawar. Urine samples were collected and cultured to determine the causative microorganisms and assess their antibiotic sensitivities. Data analysis was performed using SPSS 23.

Results: Among the patients, 72.4% (n=105) were diagnosed with APN and 27.6% (n=40) with EPN. Escherichia coli was the most common pathogen in both conditions. Antimicrobial sensitivity testing showed high effectiveness of colistin (90.4%), amikacin (88.0%), piperacillin/tazobactam (82.4%), imipenem (82.4%), and gentamicin (82.4%) for APN. However, sensitivities were lower in EPN, reflecting a concerning rise in antimicrobial resistance.

Conclusion: The prevalence of antimicrobial resistance, especially in EPN cases, poses significant challenges. Although colistin, aminoglycosides, and carbapenems remain largely effective, their misuse is contributing to increased resistance. Adhering to WHO guidelines for antimicrobial prescriptions is critical to manage and prevent the escalation of multidrug resistance.

Keywords: Acute Pyelonephritis, Antimicrobial Resistance, Antimicrobial Sensitivity, Carbapenems, Emphysematous Pyelonephritis, Escherichia coli, Urinary Tract Infections

INTRODUCTION

Urinary tract infections (UTIs) rank among the most common infections acquired either in the community or within hospital settings, affecting a significant number of individuals annually. These infections range from asymptomatic bacteriuria to severe renal infections that may lead to sepsis. Women are particularly more susceptible to UTIs than men due to anatomical differences such as a shorter urethra, which is in closer proximity to the anal orifice (2). Acute pyelonephritis (APN) is an infection of the renal pelvis and parenchyma, primarily resulting from an ascending infection from the lower urinary tract, though it can also arise from hematogenous spread. Individuals with conditions such as obesity, diabetes mellitus, urinary obstruction, or those who are immunosuppressed, are at an increased risk of developing complications like renal abscesses and emphysematous pyelonephritis (EPN) (3). Emphysematous pyelonephritis is a severe, gas-producing infection of the renal tissues that predominantly affects individuals with diabetes mellitus, which is present in over 90% of the cases (4). The infection is usually caused by bacteria from the Enterobacteriaceae family, with Escherichia coli and Klebsiella pneumoniae being the most common pathogens. Other organisms, including Proteus, Enterococcus, Pseudomonas, Clostridium, Aspergillus, and occasionally Candida species, have also been implicated (7). The management of UTIs typically begins with empirical antimicrobial therapy, which is adjusted based on culture and sensitivity reports. This preemptive approach is crucial as it allows for immediate management of the infection, potentially averting severe outcomes.

However, the indiscriminate use of antimicrobials has led to the development of resistance among bacterial populations, creating a significant challenge in the treatment of infections. Antimicrobial resistance not only leads to higher treatment costs and prolonged hospital stays but also affects the overall quality of patient care. In many developing countries, the cost of medication remains a significant concern, compounded by the widespread misuse of antimicrobial drugs, which research indicates happens in approximately 50% of prescriptions (10). This misuse has accelerated the emergence of resistant bacterial strains, necessitating the development and use of new, more expensive antimicrobial agents (11). This study aims to delineate the patterns of antimicrobial resistance in patients with emphysematous pyelonephritis compared to those with acute pyelonephritis and to recommend appropriate empiric antimicrobial therapy based on these findings. Understanding these patterns is essential for developing targeted therapies that can effectively manage these infections and reduce the burden of antimicrobial resistance.

METHODS

This single-centered comparative study was conducted over a twelve-month period from July 2023 to June 2024 at the Urology Department of the Institute of Kidney Disease in Peshawar. The study employed a non-probability convenience sampling method to select 145 patients. Ethical approval was granted by the departmental ethical committee, adhering to the Declaration of Helsinki to ensure ethical standards were maintained throughout the research. Participants selected for this study were those diagnosed with either acute pyelonephritis (APN) or emphysematous pyelonephritis (EPN), based on comprehensive clinical evaluations which included medical history and physical examination. The exclusion criteria were stringent: individuals under the age of 18, pregnant women, those who had taken antibiotics within the previous 14 days, patients with chronic kidney diseases, known urogenital structural abnormalities, or incomplete data were not considered for this study.

Upon presentation, several diagnostic tests were performed which included complete blood count, renal function tests, HbA1c, urine analysis, and imaging studies such as abdominal radiography, abdominopelvic ultrasound, and computerized tomography (CT scan). APN was defined according to clinical signs such as a temperature of ≥38.0°C accompanied by symptoms like urgency, frequency, dysuria, suprapubic tenderness, or flank pain, along with a positive urine dipstick test for leukocyte esterase or nitrate, or a microscopic examination showing >5 to 9 white blood cells per high-power field (12). EPN was characterized as a necrotizing infection of the renal parenchyma that produces gas, confirmed by CT findings as per criteria established by Huang and Tseng (14). Aseptic mid-stream urine samples were collected from the diagnosed patients and sent to the pathology department for culture and sensitivity testing. The urine was inoculated on Cysteine Lactose Electrolyte Deficient agar using a semi-quantitative strip method and incubated at 37°C for 24 to 48 hours. Microorganisms were identified using Gram staining, biochemical tests, and serology, with the Enterobacteriaceae and related organisms identified by the Analytical Profile Index API20E (Biomerieux, France) (15). Antibacterial susceptibility was assessed through the Kirby-Bauer disk diffusion method, adhering to the Clinical and Laboratory Standards Institute (CLSI) guidelines. The results were classified into categories such as multidrug-sensitive (Multi-S), monodrug-resistant (MoDR), multidrug-resistant (MDR), and extensively drug-resistant (XDR) based on their antibiotic sensitivity patterns (17). Data were entered and analyzed using SPSS version 23. Descriptive and inferential statistics were employed to describe the variables and compare the results, respectively, with statistical significance set at a p-value < 0.05. The findings were presented in various formats, including tables, figures, and percentages. This meticulous methodology ensures the reliability and validity of the study's outcomes, providing valuable insights into the antimicrobial resistance patterns in patients with APN and EPN.

RESULTS

In a study conducted over a year involving 145 patients with pyelonephritis, 64.1% were males and 35.9% were females, with an overall mean age of 43.3 ± 14.5 years, ranging from 18 to 75 years. Of these, the majority, 72.4%, were diagnosed with acute pyelonephritis, while the remaining 27.6% had emphysematous pyelonephritis. The investigation highlighted significant differences in age distribution between the two conditions, with the mean age for acute pyelonephritis at 38.7 years compared to 55.3 years for emphysematous pyelonephritis, suggesting a correlation between age and the severity of the infection (p-value: 0.01).

Table: Comparison of acute pyelonephritis and emphysematous pyelonephritis

Factors		Acute pyelonephritis n=105	Emphysematous pyelonephritis n=40	p-value
Age (mean, in years)		38.7	55.3	0.01
Gender (%)	Male	74 (70.5)	19 (47.5)	0.01
	Female	31 (29.5)	21 (52.5)	
BMI (mean, kg/m2)		27.3	32.0	0.05
Diabetes mellitus (%)		19 (18.1)	33 (82.5)	0.00
Obstructive uropathy (%)		16 (15.2)	13 (32.5)	0.03

Regarding risk factors, diabetes mellitus was notably more prevalent in patients with emphysematous pyelonephritis (82.5%) compared to those with acute pyelonephritis (18.1%), underlining its significant association with the more severe form of the disease. Obstructive uropathy was also more common in emphysematous pyelonephritis (32.5%) than in acute pyelonephritis (15.2%), both statistically significant with p-values of 0.00 and 0.03, respectively.
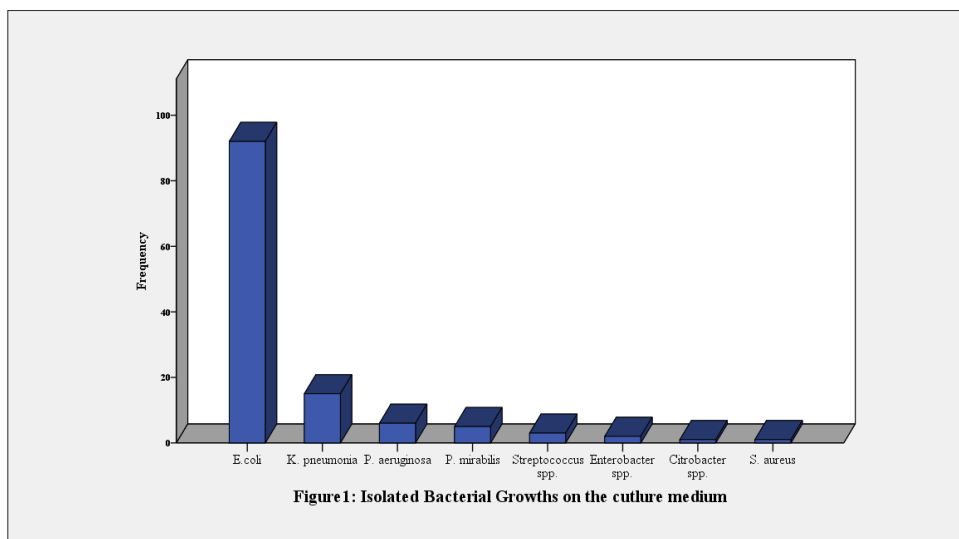

Figure1: Isolated Bacterial Growths on the cutlure medium

Table: Isolated bacterial growth in patients of acute pyelonephritis and emphysematous pyelonephritis

Bacteria	Acute pyelonephritis n=105 (%)	Emphysematous pyelonephritis n=40 (%)
Escherichia coli	68 (64.8)	24 (60.0)
Klebsiella pneumonia	7 (6.7)	8 (20.0)
Pseudomonas aeruginosa	1 (1.0)	5 (12.5)
Proteus mirabilis	4 (3.8)	1 (2.5)
Streptococcus spp.	3 (2.8)	0
Enterobacter spp.	2 (1.9)	0
Citrobacter spp.	1 (1.0)	0
Staphylococcus aureus	1 (1.0)	0

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Cultural analysis showed bacterial growth in 86.2% of cases, with Escherichia coli being the predominant pathogen in 63.4% of the cultures, followed by Klebsiella pneumoniae, and other less frequent bacteria such as Pseudomonas aeruginosa, Proteus mirabilis, and Streptococcus spp. The patterns of bacterial prevalence and their resistance to antimicrobials were also examined. Colistin, amikacin, and piperacillin/tazobactam were among the antimicrobials showing the highest sensitivity across both conditions. The study further categorized the bacterial isolates based on their drug resistance patterns, identifying 28.0% as multidrug-sensitive, 24.8% as monodrug-resistant, 31.2% as multidrug-resistant, and 16.0% as extensively drug-resistant. The analysis did not reveal a statistically significant difference in resistance patterns between the two conditions, suggesting a generalized high level of resistance across all bacteria types.

Table: Sensitivities of antimicrobial drugs in both groups, acute pyelonephritis and emphysematous pyelonephritis

Antimicrobial drugs	Acute pyelonephritis n=87 (%)	Emphysematous pyelonephritis n=38 (%)
Colistin	84 (96.5)	29 (76.3)
Imipenem	81 (93.1)	22 (57.9)
Amikacin	81 (93.1)	29 (76.3)
Meropenem	80 (91.9)	20 (52.6)
Piperacillin/tazobactam	79 (90.8)	24 (63.2)
Gentamicin	79 (90.8)	24 (63.2)
Fosfomycin	79 (90.8)	15 (39.5)
Nitrofurantoin	69 (79.3)	10 (26.3)
Trimethoprim/sulfamethoxazole	66 (75.9)	9 (23.7)
Levofloxacin	63 (72.4)	4 (10.5)
Cefoperazone/sulbactam	61 (70.1)	6 (15.8)
Ciprofloxacin	59 (67.8)	6 (15.8)
Ceftriaxone	58 (66.7)	6 (15.8)
Amoxicillin/clavulanic acid	55 (63.2)	4 (10.5)
Ampicillin	50 (57.5)	5 (13.2)

This comprehensive data analysis underscores the critical nature of demographic factors like age and underlying conditions such as diabetes and obstructive uropathy in influencing the course of pyelonephritis. The findings stress the need for targeted antimicrobial therapy based on sensitivity patterns to manage both acute and emphysematous pyelonephritis effectively.

Gender Distribution of Patients

Average Age by Condition

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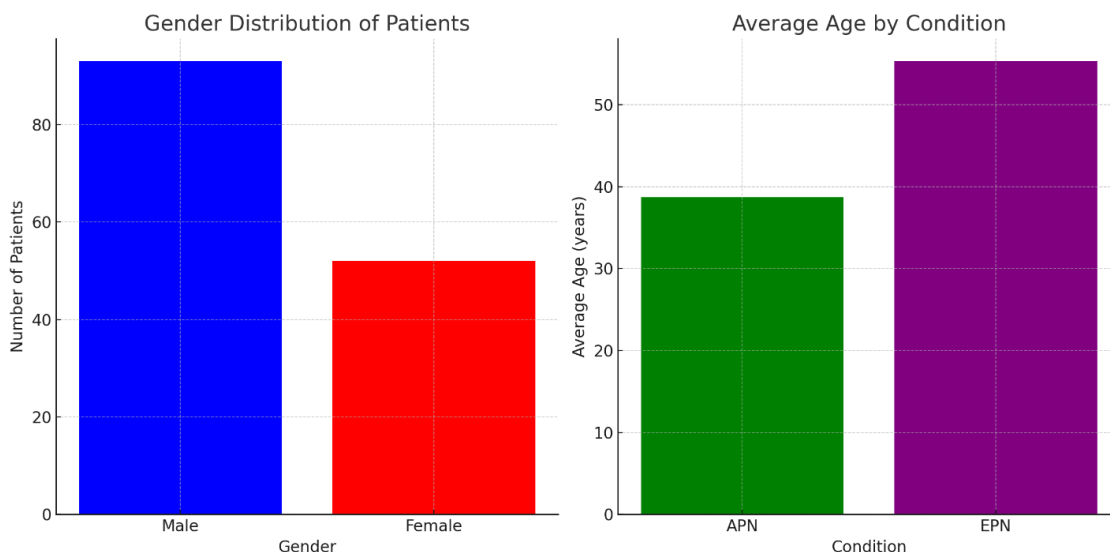
DISCUSSION

Community-acquired bacterial urinary tract infections (UTIs) are a significant health concern, commonly prompting medical consultation. Effective management hinges on the precise identification of the causative organism and the subsequent selection of appropriate antibiotics. The study corroborates existing literature indicating a high prevalence of UTIs among sexually active females due to anatomical predispositions, such as a short urethra closely situated to the anal orifice, or a high bacterial load in the urothelial mucosa (18). Additionally, factors like pregnancy and urinary tract obstructions further exacerbate the risk (19). This research highlights that emphysematous pyelonephritis, while also common in females, is predominantly influenced by diabetes mellitus, with up to 95% of such cases historically linked to this condition in literature (20)(22). In this study, approximately 80% of patients with emphysematous pyelonephritis had diabetes mellitus, underscoring its significant role as a risk factor. Furthermore, the interplay of obstructive uropathy, diabetes mellitus, and advancing age has been documented to increase the risk of developing this severe form of pyelonephritis (23).

The demographic and clinical profile of the study population indicates a marked susceptibility among older adults and individuals with comorbid conditions like diabetes mellitus, aligning with previous findings (20)(23). The pathogen spectrum identified in this study, predominantly Escherichia coli followed by Klebsiella pneumoniae, mirrors the global pathogen distribution in UTIs (6)(8)(24). Notably, Pseudomonas aeruginosa was more prevalent in emphysematous pyelonephritis cases than in acute cases, differing from some prior research which suggested a lesser role for this pathogen (28). The antimicrobial sensitivity pattern observed illustrates a significant resistance trend, with colistin, amikacin, and piperacillin/tazobactam showing the highest effectiveness. This finding is particularly alarming considering the comparative data from Peshawar indicating previously higher sensitivity rates (29). The decline in antimicrobial effectiveness over time suggests an urgent need for ongoing surveillance and the development of novel therapeutic strategies to manage these infections effectively.

The study also demonstrates a robust rate of drug resistance, with 16% of pathogens exhibiting extensive drug resistance, reflecting the growing global challenge of antimicrobial resistance (24)(30). Despite these concerning trends, the resistance patterns did not show statistical significance between groups, which might be indicative of the study's methodological limitations rather than a true lack of variation. Limitations of this study include its single-center design and the relatively small sample size, particularly of patients with emphysematous pyelonephritis, which may not fully represent the broader patient population. Additionally, the retrospective verification of antibiotic use prior to admission was not feasible, which could influence the observed antimicrobial resistance patterns. This study provides valuable insights into the epidemiology and antimicrobial resistance patterns of UTIs, particularly highlighting the critical role of underlying conditions such as diabetes mellitus. The findings underscore the necessity for targeted antibiotic stewardship programs and the importance of integrating comprehensive diabetic care into the management strategies for patients at risk of severe UTIs. Further multicentric studies with larger sample sizes are essential for corroborating these findings and enhancing the generalizability of the study results.

CONCLUSION

The study effectively underscores the persistent efficacy of colistin, aminoglycosides, and carbapenems against the hardy uropathogens causing urinary tract infections, particularly emphysematous pyelonephritis. However, it concurrently highlights the growing issue of extensive drug resistance, primarily due to the misuse of these potent antimicrobials. The findings advocate for strict adherence to WHO guidelines on prescribing practices, emphasizing the necessity for hospital management to establish a rigorous antibiotic use protocol for emphysematous pyelonephritis. Implementing such measures is crucial to curbing the spread of multidrug resistance and ensuring the continued effectiveness of existing antibiotic therapies.

AUTHOR CONTRIBUTIONS

Author	Contribution
Ahmad Nawaz	Conceptualization, Methodology, Formal Analysis, Writing - Original Draft, Validation, Supervision
Muzzamil Sohail	Methodology, Investigation, Data Curation, Writing - Review & Editing
Sulaiman Shah	Investigation, Data Curation, Formal Analysis, Software
Muhammad Idrees Khan	Software, Validation, Writing - Original Draft
Junaid Shah	Formal Analysis, Writing - Review & Editing
Usama Saeed	Writing - Review & Editing, Assistance with Data Curation

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