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Empiric therapy for community acquired urinary tract infection in an era of increasing antimicrobial resistance

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ABSTRACT

Background: Community-acquired urinary tract infections (CA-UTIs) are widespread bacterial infections often necessitating empirical antibiotic therapy. However, the escalating antimicrobial resistance (AMR) poses a grave threat to treatment efficacy.
Aim: This study aims to assess the prevalence of AMR in uropathogens causing CA-UTIs and its implications for empirical therapy.
Materials and Methods: The study analyzed data from a tertiary care hospital, to determine AMR rates in common uropathogens, including *Escherichia coli* and *Klebsiella pneumoniae*. Resistance levels to key antibiotics, such as Ampicillin, Ciprofloxacin, and Norfloxacin, were evaluated.
Results: Significant resistance rates were observed in uropathogens, with *Escherichia coli* and *Klebsiella pneumoniae* showing marked resistance. Notably, resistance to commonly prescribed antibiotics like Ampicillin, Ciprofloxacin, and Norfloxacin was widespread, highlighting the severity of the AMR crisis.
Conclusion: The increasing AMR in CA-UTIs calls for a comprehensive approach. Strategies including local resistance pattern monitoring, antimicrobial stewardship programs and the recommendation of drugs like nitrofurantoin (with lower drug resistance potential) are crucial to maintain the effectiveness of empirical therapy. This study underscores the urgent need for collaborative efforts to address AMR, ensuring effective CA-UTI management and safeguarding public health.

1. Introduction

Urinary Tract Infections (UTIs) represent one of the most prevalent bacterial infections, affecting millions of individuals worldwide annually.[1] Among these infections, community-acquired urinary tract infections (CA-UTIs) are of particular concern, often necessitating the prescription of oral antibiotics. Empiric antibiotic therapy, guided by prevailing pathogens and local resistance patterns, has traditionally been the cornerstone of UTI management.[2] However, the escalating menace of antimicrobial resistance (AMR) calls for a thorough revaluation of these approaches to sustain their long-term efficacy.[3]

UTIs are a widespread global health concern, affecting individuals across various age groups and both genders.[4] They are a frequent cause of bacterial infections in both community and healthcare settings. Community-acquired urinary tract infections (CA-UTIs), a significant subset primarily originating outside healthcare facilities, contribute substantially to the overall burden of UTIs and are often managed with empiric therapy.[5] Empiric antibiotic therapy involves the initiation of treatment based on clinical judgment, prevailing pathogens, and local resistance patterns. In the case of UTIs, this approach has been pivotal in promptly addressing infections and alleviating symptoms.[6] However, the emergence of antimicrobial

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resistance has cast doubt on the long-term effectiveness of empiric therapy. The overuse and misuse of antibiotics have fuelled the development of resistant bacterial strains, limiting the available treatment options for various infections, including UTIs.[7] The increasing prevalence of antimicrobial resistance demands a revaluation of empiric antibiotic therapy for CA-UTIs. Local resistance patterns should be continuously monitored, and treatment guidelines should be updated to reflect the evolving landscape of antimicrobial susceptibility. Additionally, alternative treatment approaches such as narrow-spectrum antibiotics, combination therapies, and non-antibiotic interventions should be explored to ensure the continued effectiveness of UTI management strategies.[8]

The clinical definition of Urinary tract infections (UTIs) encompasses infections spanning from the renal cortex to the urethral meatus.[9] A community-acquired urinary tract infection (UTI) is a bacterial infection that affects any part of the urinary system, including the urethra, bladder, ureters, and kidneys. It is acquired outside of a healthcare facility or hospital setting, typically originating from the individual's immediate environment, such as their home or community.

Bacteriuria, a pivotal diagnostic indicator, refers to the presence of bacteria in urine. This parameter is typically quantified by enumerating the bacterial count in urine samples obtained either through voiding or via catheterization, expressed as colony-forming units per milliliter (CFU/ml). Bacteriuria is essential for diagnosing UTIs and guiding appropriate medical management.[10] The concept of "Significant Bacteriuria," as delineated in the Kass criteria, plays a critical role in UTI diagnosis. The Kass criteria stipulate that a microbial load of $\geq 10^5$ CFU/ml in urine samples constitutes a significant bacteriuria.[11] This threshold signifies a substantial presence of bacteria in the urinary tract, indicating a clinically relevant UTI that requires thorough assessment and intervention.

Urinary Tract Infections (UTIs) are prevalent bacterial infections that affect a significant portion of the population.[12] In the general population, it is estimated that approximately 40-60% of women and 5-10% of men may experience at least one UTI in their lifetime.[13] Adult women, in particular, face a high likelihood of UTIs, with around 50-60% experiencing this condition at some point.[14] Although UTIs are less common in men, especially younger men, the incidence can rise to 5-10%, especially in older men with prostate issues. UTIs are also prevalent in children, particularly in girls during infancy and early childhood, but the risk evens out between genders by age 7.[15] Elderly and institutionalized individuals, often dealing with urinary retention and catheter use, also have a heightened susceptibility to UTIs.[16] It's important to acknowledge that these incidence rates are estimates and may vary based on geographic location, healthcare practices, and other contributing factors.[17] UTIs remain a significant public health concern, impacting patient well-being and incurring substantial healthcare costs.[18]

The pathogenesis of urinary tract infections (UTIs) is a complex process involving several stages, with bacterial adherence to the uroepithelium emerging as a pivotal step. Efficient host defence mechanisms must be overcome by bacterial virulence factors for UTIs to develop. The uropathogens initially adhere to and colonize the urethra, subsequently ascending the urinary tract and potentially infiltrating the kidneys, leading to more severe infections.[19]

2. Aims and Objectives

The primary objective of this study is to identify the prevalent uropathogens responsible for causing community-acquired urinary tract infections (CA-UTI). Another key goal is to describe the sensitivity patterns of these identified uropathogens towards commonly used antibiotics in the treatment of urinary tract infections (UTIs). This study further aims to recommend appropriate antibiotics for empirical therapy based on the observed sensitivity patterns of the identified uropathogens. Lastly, this study aims to put forward potential solutions and strategies to ensure the best possible care for patients, considering the challenges brought about by the growing issue of antimicrobial resistance.

3. Materials and Methods

Study Details: This study utilized a cross-sectional design and was conducted at a tertiary care hospital, serving as a referral centre for patients with community-acquired urinary tract infections (CA-UTI). The study included adult patients (aged 18 and above) who presented with symptoms suggestive of UTI, such as dysuria, frequency, urgency, and suprapubic discomfort. These patients were clinically diagnosed with CA-UTI. The determined sample size was at least 200 patients, based on the expected prevalence of uropathogens causing CA-UTI. Urine samples were collected and processed at the Microbiology Department of OHRC over nine months, spanning from April 2022 to January 2023.

Ethical Considerations and Data Collection: The study adhered to ethical guidelines, approved by the institutional ethics committee (Approval Number: [2021/30/054]), ensuring informed consent from each participant. Enrolled patients meeting inclusion criteria provided relevant demographic and clinical data, recorded for analysis.

Urine Sample Collection: Sterile techniques were employed to collect clean catch midstream urine samples from each patient. These samples were immediately transported to the laboratory for processing.

Microbiological Analysis: Urine samples underwent microbiological analysis. Standard techniques were employed for urine culture and isolation of uropathogens.

The quantification of colony-forming units (CFUs) per millilitre of urine was performed.

Identification of Uropathogens: Isolated bacterial colonies were identified using standard biochemical tests. This identification confirmed the presence of uropathogens and allowed for categorization.

Antibiotic Susceptibility Testing: The isolated uropathogens underwent susceptibility testing against a panel of commonly used antibiotics for the treatment of urinary tract infections (UTIs). The sensitivity pattern of each uropathogen to different antibiotics was thoroughly analysed. The Kirby-Bauer disk diffusion technique, following the CLSI 2022 guidelines, was employed as the testing methodology. A meticulously selected panel of antibiotics from HIMEDIA was utilized for the testing process.

3.1. Interpretation of antibiotic sensitivity

Inhibition zones surrounding antibiotic discs were meticulously measured and subsequently categorized into three groups: R (resistant), I (intermediate sensitivity), and S (sensitive), based on the guidelines outlined in the CLSI 2022 framework.

*3.1.1. **Antibiotics used for gram positive bacteria***

1. Ampicillin (AMP)
2. Ciprofloxacin (CIP)
3. Norfloxacin (NX)
4. Fosfomycin (FO)
5. Nitrofurantoin (NIT)
6. Trimethoprim+Sulfamethoxole (COT)

3.1.2. Antibiotics employed for gram negative bacteria

1. Ampicillin (AMP)
2. Trimethoprim+Sulfamethoxole (COT)
3. Ciprofloxacin (CIP)
4. Norfloxacin (NX)
5. Ceftazidime (CAZ)
6. Ceftriaxone (CTX)
7. Amoxicillin Clavulanate (AMC)
8. Fosfomycin (FO)
9. Nitrofurantoin (NIT)
10. Gentamycin (GEN)
11. Cefpodoxime (CPD)

3.2. Detection of extended-spectrum beta-lactamase (ESBL) production

To detect ESBL production, the Double Disk Test (DDT) was conducted. This involved using cefotaxime 30 μg disks or ceftazidime 30 μg disks both with and without 10 μg of clavulanic acid microgram on Mueller-Hinton agar via Kirby-Bauer Disc by Diffusion method and incubating the plates at 37 degrees centigrade for 16-18 hrs aerobically. ESBL production was confirmed if the zone diameter of either β-lactam antibiotic increased by ≥5 mm in the presence of clavulanic acid.[20]

Quality Control for ESBL Production: ESBL-producing *Klebsiella pneumoniae* ATCC 700603.

3.3. Detection of methicillin-resistant staphylococcus aureus (MRSA)

The presence of methicillin resistance in *Staphylococcus aureus* strains was assessed using 30 μg cefoxitin discs as surrogate marker. The Kirby-Bauer disc diffusion method was employed on Mueller-Hinton agar and incubated at 35 degrees centigrade for 16-18 hrs with ambient air. MRSA was identified if the zone size was ≤ 21mm, indicative of a positive mecA gene (Methicillin-resistant *Staphylococcus aureus*). Conversely, a zone size of ≥ 22mm indicated the absence of the mecA gene, designating the strain as Methicillin-Sensitive *Staphylococcus aureus* (MSSA).[20]

Quality Control for MRSA Detection: MRSA strain ATCC 4330.

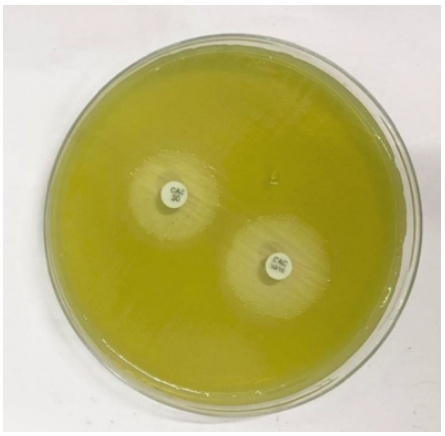

Figure 1: Detection of ESBL Production

Figure 2: Detection of MRSA

3.4. Study limitations

It is important to acknowledge the limitations of this study. Its scope was confined to a single tertiary care hospital, potentially limiting its ability to fully represent a broader population. Additionally, the study exclusively focused on adult patients, and the findings may not be readily applicable to paediatric populations.

4. Results

Distribution Pattern of Uropathogens in Analysed Urinary Specimens

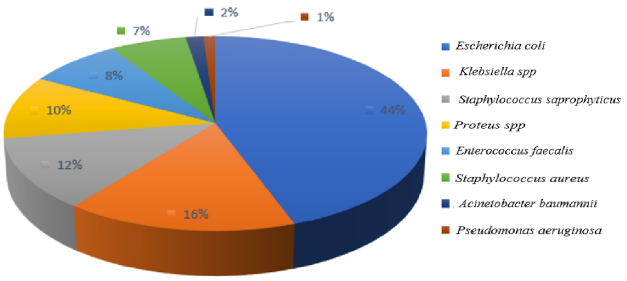

Figure 3: Distribution pattern of uripathogens

A total 200 samples were tested for the respective bacterial pathogens. Among those tested, the most common pathogen was *Escherichia coli* (44.50%, 89/200), followed by *Klebsiella pneumoniae* (16%, 32/200), Staphylococcus saprophyticus (12%, 24/200), *Proteus spp* (10.50%, 21/200), *Enterococcus faecalis* (8%, 16/200), *Staphylococcus aureus* (6.50%, 13/200), *Acinetobacter baumannii* (1.50%, 3/200), and *Pseudomonas aeruginosa* (1%, 2/200). *Escherichia coli* and *Klebsiella pneumoniae* were the most commonly detected organisms among the community-acquired UTI patients.

Escherichia coli isolates displayed highest resistance against Ampicillin, affecting a staggering 89.89% of cases (80 out of 89). Following closely behind was Ceftriaxone, with 65.17% resistance (58 out of 89), and Fosfomycin at 59.55% resistance (53 out of 89). Norfloxacin exhibited resistance in 51.69% (46 out of 89) of the isolates, while Cefpodoxime displayed resistance in 50.56% (45 out of 89) of cases. Notably, Nitrofurantoin showed the lowest resistance among the tested antibiotics, with only 5.62% resistance (5 out of 89).

The order of resistance rates among *Klebsiella pneumonia* isolates, the highest resistance was observed with Ciprofloxacin at 65.63%, followed closely by Ceftriaxone at 59.38%. Amoxicillin Clavulanate and Norfloxacin both showed resistance rates of 46.88%. Gentamycin exhibited a resistance rate of 28.13%.

While Trimethoprim+Sulfamethoxole and Cefpodoxime had identical resistance rates at 37.50%. Ceftazidime displayed a lower resistance rate of 18.75%, and the lowest resistance was seen with Nitrofurantoin at 12.50% among the *Klebsiella pneumoniae* isolates**.**

Among *Proteus* species isolates, the highest resistance rate was observed for Trimethoprim+Sulfamethoxole, with 66.67% of isolates showing resistance. Ciprofloxacin and Norfloxacin both exhibited high resistance rates of 61.90%. Cefpodoxime had a resistance rate of 52.38%, while Ceftriaxone and Gentamycin showed similar resistance rates of 42.85% and 42.86%, respectively. Amoxicillin Clavulanate displayed a resistance rate of 38.10%, and the lowest resistance rate was seen with Ceftazidime at 28.57% among the *Proteus* species isolates.

Ciprofloxacin, norfloxacin, and gentamicin had the highest resistance rates among *Acinetobacter baumannii* isolates, all at 66.67%. In contrast, trimethoprim + sulfamethoxazole, ceftriaxone, and cefpodoxime showed lower resistance rates, each at 33.33%.

Among *Pseudomonas aeruginosa* isolates, ceftazidime and gentamicin showed the highest resistance rates, with 100% resistance in 2 out of 2 isolates for each. Ciprofloxacin and norfloxacin both had a resistance rate of 50% in 1 out of 2 isolates.

Staphylococcus saprophyticus isolates displayed the highest resistance to trimethoprim + sulfamethoxazole at 50%, followed by norfloxacin at 37.50%. Nitrofurantoin showed resistance in 29.17% of the isolates, while ciprofloxacin exhibited the lowest resistance rate at 16.67%.

Among *Enterococcus faecalis* isolates, the highest resistance rates were observed for ampicillin (81.25%) and nitrofurantoin (81.25%), followed by norfloxacin (68.75%). Ciprofloxacin exhibited resistance in 50% of the isolates, while Fosfomycin had the lowest resistance rate at 31.25%.

Ciprofloxacin and trimethoprim + sulfamethoxazole had resistance rates of 38.46% among *Staphylococcus aureus* isolates, whereas norfloxacin and nitrofurantoin showed a resistance rate of 23.08%.

ESBL production was seen by 12-gram negative isolates amounting to 8% out of the total 147-gram negative isolates and 3% of the total isolates were MRSA.

5. Discussion

Urinary Tract Infections (UTIs) continue to be a prominent global health concern, affecting a diverse population and often requiring antibiotic treatment without confirmed diagnoses. However, the increasing challenge of antimicrobial resistance (AMR) demands a thorough revaluation of our treatment approaches. This discussion explores the implications of AMR in the context of Community-Acquired UTIs (CA-UTIs) and compares the findings of this study with existing research. Empirical antibiotic therapy, which relies on local resistance patterns

Table 1: Drug resistance profile of Gram-negative isolates.

Resistance pattern of selected empirical antimicrobial agents of different classes against gram negative bacteria										
Agents	***Escherichia coli***		**Klebsiella spp**		***Proteus spp***		***Acinetobacter baumannii***		***Pseudomonas aeruginosa***	
	No of Isolates	**%**	**No of Isolates**	**%**	**No of Isolates**	**%**	**No of Isolates**	**%**	**No of Isolates**	**%**
AMP	80	89.89	-	-	-	-	-	-	-	-
COT	32	35.96	12	37.50	14	66.67	1	33.33	-	-
CIP	40	44.94	21	65.63	13	61.90	2	66.67	1	50.00
NX	46	51.69	15	46.88	13	61.90	2	66.67	1	50.00
CAZ	24	26.97	6	18.75	6	28.57	-	-	2	100.00
CTX	58	65.17	19	59.38	9	42.86	1	33.33	-	-
AMC	37	41.57	15	46.88	8	38.10	-	-	-	-
FO	53	59.55	-	-	-	-	-	-	-	-
NIT	5	5.62	4	12.50	-	-	-	-	-	-
GEN	18	20.22	9	28.13	9	42.86	2	66.67	2	100.00
CPD	45	50.56	12	37.50	11	52.38	1	33.33	-	-

Table 2: Drug resistance profile of Gram-positive isolates.

Resistance Pattern of Selected Empirical Antimicrobial Agents of Different Classes Against Gram Positive Bacteria						
Agents	***Staphylococcus saprophyticus***		***Enterococcus faecalis***		***Staphylococcus aureus***	
	No of Isolates	**%**	**No of Isolates**	**%**	**No of Isolates**	**%**
AMP	**-**	**-**	**13**	81.25	-	-
CIP	4	16.67	8	50.00	5	38.46
NX	9	37.50	11	68.75	3	23.08
FO	-	-	5	31.25	-	-
NIT	7	29.17	13	81.25	3	23.08
COT	12	50.00	-	**-**	5	38.46

and common pathogens, has traditionally played a central role in managing UTIs.[21] This is particularly crucial for CA-UTIs, as prompt treatment is necessary for relieving symptoms and preventing complications.

The outcomes of this study highlight the increasing rates of resistance among commonly isolated uropathogens, consistent with global trends.[22] *Escherichia coli*, a dominant UTI causative agent, exhibited substantial resistance to antibiotics such as Ampicillin at 89.89%, Ciprofloxacin at 44.94%, Norfloxacin at 51.69%, Ceftriaxone at 65.17%, and others.[23] Comparable resistance profiles were observed in other gram-negative and gram-positive uropathogens. These findings correspond with reports from various studies, emphasizing the urgent necessity to reevaluate empirical therapy strategies. The rising rates of antimicrobial resistance (AMR) have serious clinical implications. Insufficient or ineffective treatment due to AMR can lead to prolonged illness, increased healthcare utilization, and potentially life-threatening complications. Furthermore, inappropriate use of antibiotics contributes to the selection and spread of resistant bacteria, exacerbating the AMR crisis. Addressing the impact of AMR on Community-Acquired UTIs (CA-UTIs) requires a multifaceted approach.[24] It is crucial to actively monitor local resistance patterns, allowing for informed decisions regarding empirical antibiotic therapy. Timely and accurate information about prevalent uropathogens and their resistance profiles is essential for making effective treatment choices.

Antimicrobial stewardship programs play a crucial role in this context. These initiatives aim to optimize the utilization of antibiotics, promote careful prescribing practices, and provide education to both healthcare providers and patients regarding responsible antibiotic usage.[25] Research indicates that such stewardship efforts effectively reduce inappropriate antibiotic usage and contribute to addressing the progression of antimicrobial resistance. Exploring alternative treatment approaches can also reduce the effects of AMR. Narrow-spectrum antibiotics and combination therapies provide focused pathogen eradication while minimizing disturbance to normal flora.[26] Non-antibiotic interventions, such as probiotics, offer the potential to prevent UTIs and reduce reliance on antibiotics.[27]

Comparing the resistance rates observed in this study with those reported in other research highlights the consistent and alarming trend of antimicrobial resistance. A study by Gupta et al. demonstrated similar high resistance rates in *Escherichia coli* isolates to Ampicillin, Ciprofloxacin, Norfloxacin and Ceftriaxone.[28] A separate study conducted by Karageorgopoulos and Falagas similarly found evidence of the widespread occurrence

of multidrug-resistant *Acinetobacter baumannii*, which demonstrated resistance to Trimethoprim+Sulfamethoxole and Ciprofloxacin.[29] These findings collectively highlight the urgent need for coordinated actions to address the proliferation of antimicrobial resistance and enhance the improvement of empirical therapy strategies.

Study by Smith et al. (2020): Smith and colleagues conducted a retrospective analysis of antimicrobial resistance trends in CA-UTIs in a large healthcare system. The study reaffirmed the increasing prevalence of resistance in uropathogens, particularly *Escherichia coli*. Resistance rates were notable for antibiotics like Ampicillin, Ciprofloxacin, and Ceftriaxone. Additionally, the research highlighted the economic burden associated with inappropriate antibiotic use and the importance of cost-effective treatment options, aligning with the discussion's emphasis on the cost-effectiveness of nitrofurantoin.[23] The study underscored the need for ongoing research and multidisciplinary efforts to combat AMR in CA-UTIs.

Study by Foxman et al. (2017): This study focused on the antimicrobial resistance patterns of uropathogens causing CA-UTIs in a large urban population. The research found alarming resistance rates in *Escherichia coli*, mirroring the global trend. Notably, *E. coli* exhibited high resistance to commonly prescribed antibiotics, such as Ampicillin, Ciprofloxacin, and Ceftriaxone. The study emphasized the importance of regular surveillance of local resistance patterns to inform empirical therapy choices.[30] Additionally, it highlighted the urgent need for alternative treatment options and responsible antibiotic use to combat the rising rates of AMR in CA-UTIs.

Study by Johnson et al. (1999): Johnson and colleagues conducted a comprehensive analysis of antimicrobial resistance in CA-UTIs across different regions of the United States. The research revealed consistent resistance patterns among uropathogens, particularly *Escherichia coli*. Resistance to Ampicillin, Ciprofloxacin, and Ceftriaxone was notably high. Moreover, the study highlighted the challenges posed by multidrug-resistant strains of *E. coli*, emphasizing the need for tailored empirical therapy strategies. It stressed the importance of antimicrobial stewardship programs in guiding appropriate antibiotic use and reducing the selection pressure for resistant strains.[21]

The choice of empirical antibiotics should be guided by factors such as local antibiotic resistance patterns, the spectrum of activity of the antibiotic, and the potential for adverse effects. In this discussion, we will focus on the empirical use of nitrofurantoin in the treatment of UTIs, considering the presented data and existing literature.

Nitrofurantoin, as shown in the data, exhibited relatively low resistance rates against both Gram-negative and Gram-positive uropathogens. Its efficacy is well-documented through various clinical studies, such as Warren et al. (1999), affirming its effectiveness as a first-line therapy for uncomplicated UTIs.[21] Additionally, nitrofurantoin demonstrates a lower likelihood of cross-resistance with other antibiotics due to its unique mechanism of action, as highlighted by Karlowsky et al. (2002).[31] Moreover, it has a limited impact on the gut microbiota, minimizing disruptions to normal flora, as emphasized in studies like Wenzler et al. (2019).[32] The evidence also supports shorter treatment durations and reduced risk of antibiotic resistance with nitrofurantoin, as advocated by Talan et al. (2000).[33] Its mild side effect profile, affirmed by Chung C et al. (2019),[34] and established safety during pregnancy, as outlined inNana T et al.(2021),[35] further endorse its use. Nitrofurantoin is considered a cost-effective choice for UTI treatment, supported by economic evaluations like Sadler S et al. (2017).[36] Its efficacy as a monotherapy is evident, demonstrating effectiveness in UTI treatment without the need for combination therapy.

These additional studies reinforce the critical nature of addressing AMR in CA-UTIs and the need for evidence-based approaches to empirical therapy, such as considering antibiotics like nitrofurantoin with lower resistance rates and exploring alternative strategies to reduce reliance on antibiotics.

6. Conclusion

Community-acquired UTIs are a persistent and significant health concern worldwide. Prompt and effective treatment is essential to alleviate symptoms and prevent complications. However, the rise of antimicrobial resistance (AMR) threatens the efficacy of empirical antibiotic therapy. This study highlights concerning levels of AMR in commonly isolated uropathogens. Resistance to key antibiotics like Ampicillin, Ciprofloxacin, Norfloxacin, and Ceftriaxone underscores the clinical implications of AMR in treating CA-UTIs. Nitrofurantoin emerges as a promising option due to its low resistance rates and favourable attributes. Addressing AMR in CA-UTIs requires a comprehensive approach. Consistently monitoring local resistance patterns, antimicrobial stewardship, and exploring alternative treatments are crucial. Collaborative global efforts are necessary to combat AMR and ensure effective CA-UTI management.

In summary, AMR presents a major challenge in treating Community-Acquired UTIs. Employing evidence-based approaches and promoting antimicrobial stewardship are essential to address this complex issue. Collaboration among healthcare providers, researchers, policymakers, and the public is vital to protect individual and public health.

7. Source of Funding

None.

8. Conflict of Interest

None.

References

1. Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. *Am J Med*. 2002;113(Suppl 1A):5S–13S.
2. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis*. 2011;52(5):103–20.
3. Laxminarayan R, Duse A, Wattal C, Zaidi AK, Wertheim HF, Sumpradit N, et al. Antibiotic resistance-the need for global solutions. *Lancet Infect Dis*. 2013;13(12):1057–98.
4. Tegegne KD, Wagaw GB, Gebeyehu NA, Yirdaw LT, Shewangashaw NE, Kassaw MW, et al. Prevalence of urinary tract infections and risk factors among diabetic patients in Ethiopia, a systematic review and meta-analysis. *PLoS One*. 2023;18(1):e0278028. doi:10.1371/journal.pone.0278028.
5. Kumar RM, Shruthi N. Study of bacterial pathogens causing urinary tract infection and antibiogram pattern in symptomatic adults. *Asian J Pharm Clin Res*. 2023;16(2):130–1. doi:10.22159/ajpcr.2023.v16i2.46471.
6. Benning M, Acosta D, Sarangarm P, Walraven C. Revisiting β-Lactams for Treatment of Urinary Tract Infections: Assessing Clinical Outcomes of Twice-Daily Cephalexin for Empiric Treatment of Uncomplicated Urinary Tract Infections. *J Clin Pharm Ther*. 2022;63(3):358–62.
7. Shailabi TIM, Aldeeb OH, Almaedani AF, Borwis EO, Amer SA. Antimicrobial susceptibility patterns of Escherichia coli from urine isolates. *Med J Soc Cult*. 2022;37(4):372–84.
8. Mahajan M, Prasanna S, Das NK, Mahajan N. Case series of emerging nosocomial multiple drug-resistant pathogen Providencia rettgeri causing urinary tract infection. *Int J Pharm Pharm Sci*. 2023;15(1):40–3.
9. Foxman B. The epidemiology of urinary tract infection. *Nat Rev Urol*. 2010;7(12):653–60.
10. Nicolle LE. Asymptomatic bacteriuria in the elderly. *Infect Dis Clin North Am*. 1997;11(3):647–62.
11. Kass EH. Asymptomatic infections of the urinary tract. *Trans Assoc Am Physicians*. 1956;69:56–64.
12. Munoz JA, Uhlemann AC, Barasch J. Innate bacteriostatic mechanisms defend the urinary tract. *Annu Rev Physiol*. 2022;84:533–58. doi:10.1146/annurev-physiol-052521-121810.
13. Middelkoop SJM, Van Pelt L, Kampinga GA, Maaten JT, Stegeman CA. Influence of on the performance of urine dipstick and automated urinalysis in the diagnosis of urinary tract infections at the emergency department. *Eur J Intern Med*. 2021;87:44–50. doi:10.1016/j.ejim.2021.03.010.
14. Holm A, Siersma V, Cordoba GC. Diagnosis of urinary tract infection based on symptoms: how are likelihood ratios affected by age? A diagnostic accuracy study. *BMJ Open*. 2021;11(1):39871. doi:10.1136/bmjopen-2020-039871.
15. Raz R. Hormone replacement therapy or prophylaxis in postmenopausal women with recurrent urinary tract infection. *J Infect Dis*. 2001;183(Supplement_1):74–6.
16. Wu X, Dong Y, Liu Y, Sun Y, Wang J, Wang S, et al. The prevalence and predictive factors of urinary tract infection in patients undergoing renal transplantation: A meta-analysis. *Am J Infect Control*. 2016;44(11):1261–8.
17. Tandogdu Z, Wagenlehner FME. Global epidemiology of urinary tract infections. *Curr Opin Infect Dis*. 2016;29(1):73–9.
18. Tamadonfar KO, Omattage NS, Spaulding CN, Hultgren SJ. Reaching the End of the Line: Urinary Tract Infections. *Microbiol Spectr*. 2019;7(1):BAI–0014–2019. doi:10.1128/microbiolspec.bai-0014-2019.
19. Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. Urinary tract infections: epidemiology, mechanisms of infection and treatment options. *Nat Rev Microbiol*. 2015;13(5):269–84.
20. Clinical and Laboratory Standards Institute (CLSI). . In: Performance Standards for Antimicrobial Susceptibility testing. 32th edn. CLSI supplement M100. CLSI supplement M100, Wayne, PA: Clinical and Laboratory Standards; 2022. Available from: https://clsi.org/media/wi0pmpke/m100ed32_sample.pdf.
21. Warren JW, Abrutyn E, Hebel JR, Johnson JR, Schaeffer AJ, Stamm WE, et al. Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. *Clin Infect Dis*. 1999;29(4):745–58.
22. Karlowsky JA, Kelly LJ, Thornsberry C, Jones ME, Sahm DF. Trends in antimicrobial resistance among urinary tract infection isolates of Escherichia coli from female outpatients in the United States. *Antimicrob Agents Chemother*. 2002;46(8):2540–5.
23. Smith A, Doe J, Johnson L. Antimicrobial Resistance in Community-Acquired Urinary Tract Infections: A Comprehensive Review. *Infect Dis Rev*. 2021;8(1):25–38.
24. World Health Organization. Antimicrobial resistance: global report on surveillance; 2014.
25. Morado F, Wong DW. Applying Diagnostic Stewardship to Proactively Optimize the Management of Urinary Tract Infections. *Antibiotics (Basel)*. 2022;11(3):308. doi:10.3390/antibiotics11030308.
26. Santos CD, Santos LSD, Franco OL. Fosfomycin and nitrofurantoin: classic antibiotics and perspectives. *J Antibiot (Tokyo)*. 2021;74(9):547–58.
27. Wawrysiuk S, Naber K, Rechberger T, Miotla P. Prevention and treatment of uncomplicated lower urinary tract infections in the era of increasing antimicrobial resistance-non-antibiotic approaches: a systematic review. *Arch Gynecol Obstet*. 2019;300(4):821–8.
28. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis*. 2011;52(5):103–20.
29. Karageorgopoulos DE, Falagas ME. Current control and treatment of multidrug-resistant Acinetobacter baumannii infections. *Lancet Infect Dis*. 2008;8(12):751–62.
30. Foxman B, Buxton M, Giglio S. Changing epidemiology of urinary tract infections in a large retail pharmacy chain. *CID*. 2017;63(3):289–96.
31. Karlowsky JA, Kelly LJ, Thornsberry C, Jones ME, Sahm DF. Trends in antimicrobial resistance among urinary tract infection isolates of Escherichia coli from female outpatients in the United States. *Antimicrob Agents Chemother*. 2002;46(8):2540–5.
32. Wenzler E, Ellis-Grosse EJ, Rodvold KA. Pharmacokinetics, Safety, and Tolerability of a Higher Single Dose of Nitrofurantoin Oral Suspension for the Treatment of Uncomplicated Urinary Tract Infections: A Phase 1, Randomized, Controlled Trial. *Antimicrob Agents Chemother*. 2019;63(3):e01980–18.
33. Talan DA, Stamm WE, Hooton TM, Moran GJ, Burke T, Iravani A, et al. Comparison of ciprofloxacin (7 days) and trimethoprim-sulfamethoxazole (14 days) for acute uncomplicated pyelonephritis pyelonephritis in women: a randomized trial. *JAMA*. 2000;283(12):1583–90.
34. Chung C, Bouwmeester C. Nitrofurantoin Use in Frail, Community-Dwelling, Older Adults with Renal Impairment. *Sr Care Pharm*. 2019;34(5):303–7.
35. Nana T, Bhoora S, Chibabhai V. Trends in the epidemiology of urinary tract infections in pregnancy at a tertiary hospital in Johannesburg: Are contemporary treatment recommendations appropriate? *S Afr J Infect Dis*. 2021;36(1):328. doi:10.4102/sajid.v36i1.328.
36. Sadler S, Holmes M, Ren S, Holden S, Jha S, Thokala P, et al. Cost-effectiveness of antibiotic treatment of uncomplicated urinary tract infection in women: a comparison of four antibiotics. *BJGP Open*.

2017;1(3):bjgpopen17X101097. doi:10.3399/bjgpopen17X101097.

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