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Changing Trends in Uropathogen Distribution and Antibiotic Resistance Patterns in Nairobi, Kenya: A Longitudinal Study

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A B S T R A C T

Introduction: Urinary tract infections (UTIs) remain a significant global health challenge, exacerbated by the increasing prevalence of antibiotic resistance. This study aimed to investigate the changing trends in uropathogen distribution and antibiotic resistance patterns in Nairobi, Kenya, over a five-year period. **Methods:** A retrospective longitudinal study was conducted using laboratory records from three major hospitals in Nairobi. Data on uropathogens isolated from urine cultures and their antibiotic susceptibility profiles were collected from January 2018 to December 2023. Descriptive statistics, chi-square tests, and logistic regression analysis were used to analyze the data. **Results:** A total of 12,475 urine cultures were analyzed. *Escherichia coli* was the most prevalent uropathogen (48.2%), followed by *Klebsiella pneumoniae* (18.6%), *Staphylococcus saprophyticus* (12.5%), *Proteus mirabilis* (8.7%), and *Enterococcus faecalis* (7.1%). A significant increase in the prevalence of *K. pneumoniae* ($p<0.001$) and a decrease in *E. coli* ($p=0.023$) were observed over the study period. Resistance rates to commonly used antibiotics, including ampicillin, trimethoprim-sulfamethoxazole, and ciprofloxacin, increased significantly for most uropathogens. Multidrug resistance was observed in 32.1% of isolates, with a significant increase over time ($p<0.001$). Conclusions: This study highlights the dynamic nature of uropathogen distribution and antibiotic resistance patterns in Nairobi. The increasing prevalence of *K. pneumoniae* and the rise of multidrug resistance pose a serious threat to public health. **Conclusion:** surveillance and the implementation of antimicrobial stewardship programs are crucial to guide empirical treatment and preserve the effectiveness of available antibiotics.

1. Introduction

Urinary tract infections (UTIs) represent a persistent and significant global health challenge, affecting millions of individuals annually and imposing a considerable burden on healthcare systems worldwide. These infections encompass a spectrum of clinical presentations, ranging from the relatively benign, such as asymptomatic bacteriuria and cystitis, to the potentially life-threatening, such as pyelonephritis and urosepsis. While UTIs can affect individuals of all ages and genders, they are particularly prevalent among women, with an estimated 50-60% experiencing at least one UTI in their lifetime. This increased susceptibility in females is attributed to a complex interplay of anatomical, hormonal, and behavioral factors. The pathogenesis of UTIs typically involves the ascension of bacteria from the periurethral area into the urinary tract, where they adhere to and colonize the uroepithelium, triggering an inflammatory response. Uropathogenic *Escherichia coli* (UPEC) is the predominant etiological agent, accounting for approximately 75-90% of community-acquired UTIs. This bacterium possesses a remarkable arsenal of virulence factors, including adhesins, toxins, and iron acquisition systems, which enable it to successfully establish infection in the urinary tract.

Other commonly encountered uropathogens include *Klebsiella pneumoniae*, *Staphylococcus saprophyticus*, *Proteus mirabilis*, *Enterococcus faecalis*, and *Pseudomonas aeruginosa*. These pathogens exhibit diverse virulence mechanisms and antibiotic resistance profiles, contributing to the complexity of UTI management.[1-4]

The cornerstone of UTI management is prompt and appropriate antibiotic therapy, guided by clinical presentation, urine culture results, and local antibiotic resistance patterns. However, the escalating prevalence of antibiotic resistance among uropathogens poses a formidable challenge to effective treatment. Antibiotic resistance arises from the selective pressure exerted by the misuse and overuse of antibiotics in human and animal healthcare, agriculture, and the environment. This selective pressure favors the survival and proliferation of resistant strains, leading to the dissemination of resistance genes through various mechanisms, including horizontal gene transfer. The consequences of antibiotic resistance are far-reaching and profound. Resistant infections are associated with increased treatment failure rates, necessitating the use of broader-spectrum and often more toxic antibiotics. This can lead to a cascade of adverse effects, including disruption of the normal microbiota, Clostridium difficile infection, and the selection of multidrug-resistant organisms. Moreover, antibiotic resistance contributes to prolonged hospital stays, increased healthcare costs, and higher morbidity and mortality rates.[5-7]

Surveillance of uropathogen distribution and antibiotic resistance patterns is paramount for informing empirical treatment decisions, optimizing antibiotic use, and implementing effective infection control measures. Longitudinal studies, which track these trends over time, provide invaluable insights into the evolving dynamics of uropathogens and their resistance profiles, enabling the identification of emerging threats and the development of targeted interventions. These studies are particularly crucial in resource-limited settings, where the burden of UTIs and antibiotic resistance is disproportionately high. In Kenya, UTIs constitute a significant public health concern, particularly among women and children. The country faces numerous challenges in combating UTIs, including limited access to healthcare, inadequate sanitation, and the widespread availability of over-the-counter antibiotics. These factors contribute to the high prevalence of UTIs and the emergence of antibiotic resistance. However, data on the changing trends in uropathogen distribution and antibiotic resistance patterns in Kenya are scarce, hindering the development of evidence-based strategies for UTI prevention and management.[8-10] This study aimed to address this knowledge gap by conducting a comprehensive longitudinal analysis of uropathogen prevalence and antibiotic resistance profiles in Nairobi, Kenya, over a five-year period.

2. Methods

This investigation into the evolving landscape of uropathogen distribution and antibiotic resistance patterns in Nairobi, Kenya, employed a robust methodological framework designed to ensure both scientific rigor and ethical integrity. The study adopted a retrospective longitudinal design, capitalizing on the wealth of information contained within the laboratory records of three major hospitals in Nairobi. These hospitals, namely Kenyatta National Hospital, Aga Khan University Hospital, and Nairobi Hospital, were strategically selected to represent a diverse patient population and a significant proportion of healthcare services within the city. This approach aimed to enhance the generalizability of the study findings to the broader population of Nairobi. The study period spanned five years, commencing on January 1st, 2018, and concluding on December 31st, 2023. This extended timeframe allowed for the capture of temporal trends and the identification of any significant shifts in uropathogen prevalence and antibiotic resistance profiles over time. The longitudinal nature of the study design conferred a distinct advantage over cross-sectional studies, enabling the researchers to discern not only the prevalence of specific uropathogens and resistance patterns but also the trajectory of their evolution over the study period.

The lifeblood of this study was the data extracted from the laboratory information systems of the participating hospitals. These systems, repositories of a vast amount of clinical and laboratory data, provided the raw material for the analysis. The data extraction process was meticulously executed, ensuring the capture of all relevant information for each urine culture record. This information encompassed a range of variables, including patient demographics such as age and gender, the date of urine culture, the specific uropathogen isolated, and the results of antibiotic susceptibility testing. To ensure the integrity and reliability of the data, stringent inclusion and exclusion criteria were applied. All urine cultures from patients of all ages and genders were considered for inclusion, reflecting the study's commitment to inclusivity and representation. However, to avoid the potential for bias introduced by duplicate entries, only the first urine culture per patient during the study period was included in the final analysis. Furthermore, cultures with no uropathogen isolated or with incomplete antibiotic susceptibility data were excluded from the analysis to maintain the quality and completeness of the dataset.

The determination of antibiotic susceptibility patterns constituted a pivotal component of this investigation. Antibiotic susceptibility testing was performed by the participating laboratories using standardized and validated methods, ensuring the reliability and comparability of the results. The Kirby-Bauer disk diffusion method, a widely accepted and robust technique, was employed in this study. This method involves the inoculation of a standardized bacterial suspension onto an agar plate and the subsequent placement of antibiotic-impregnated disks onto the agar surface. The antibiotics diffuse into the agar, creating a concentration gradient, and the zone of bacterial growth inhibition around each disk is measured. The size of the zone of inhibition is inversely proportional to the minimum inhibitory concentration (MIC) of the antibiotic, which is the lowest concentration of an antibiotic that prevents visible bacterial growth. In addition to the Kirby-Bauer method, some laboratories employed automated systems for antibiotic susceptibility testing. These systems, while based on the same principles as the disk diffusion method, offer the advantages of increased throughput, reduced turnaround time, and automated interpretation of results. Regardless of the method used, the interpretation of susceptibility results adhered to the Clinical and Laboratory Standards Institute (CLSI) guidelines, which provide standardized breakpoints for defining susceptibility and resistance based on the MIC values. The adherence to these guidelines ensured consistency and comparability of the results across different laboratories and testing methods. The panel of antibiotics included in the analysis was carefully selected to reflect the most commonly used antibiotics for the treatment of UTIs in both community and hospital settings. This panel comprised ampicillin, amoxicillin-clavulanate, ceftriaxone, ceftazidime, ciprofloxacin, gentamicin, nitrofurantoin, trimethoprim-sulfamethoxazole, and piperacillin-tazobactam. This comprehensive selection allowed for a thorough assessment of the resistance profiles of the isolated uropathogens and provided valuable insights into the current state of antibiotic resistance in Nairobi.

The vast amount of data collected in this study necessitated a robust statistical framework to extract meaningful insights and identify significant trends. The statistical analysis was conducted using a combination of descriptive statistics, chi-square tests, and logistic regression analysis. These methods were strategically employed to address the specific research questions and objectives of the study. Descriptive statistics were used to summarize the key characteristics of the study population and the prevalence of different uropathogens. These descriptive measures included frequencies, percentages, means, and standard deviations. The use of descriptive statistics provided a clear and concise overview of the data, laying the foundation for more advanced statistical analyses. Chi-square tests, a non-parametric statistical method, were employed to assess the significance of trends in uropathogen distribution and antibiotic resistance over time. This method is particularly suited for analyzing categorical data, such as the prevalence of different uropathogens

or the proportion of isolates resistant to a particular antibiotic. By comparing the observed frequencies with the expected frequencies, chi-square tests determine whether there is a statistically significant association between the variables under investigation. In this study, chi-square tests were used to determine whether the observed changes in uropathogen distribution and antibiotic resistance patterns over the five-year study period were statistically significant. Logistic regression analysis, a powerful statistical technique, was used to identify factors associated with multidrug resistance (MDR). MDR, defined as resistance to three or more classes of antibiotics, is a significant clinical challenge and a key indicator of the severity of antibiotic resistance. Logistic regression analysis allows for the assessment of the relationship between a binary outcome variable, such as the presence or absence of MDR, and multiple predictor variables, such as uropathogen species, year of isolation, and hospital of isolation. By estimating the odds ratios and their associated confidence intervals, logistic regression analysis identifies the factors that are independently associated with the outcome variable. This analysis provided valuable insights into the factors contributing to the development and spread of MDR among uropathogens in Nairobi. All statistical analyses were performed using SPSS software version 26 (IBM Corp, Armonk, NY, USA), a widely used statistical software package. The choice of SPSS was based on its comprehensive suite of statistical tools, user-friendly interface, and extensive support resources. A p-value of less than 0.05 was considered statistically significant, indicating that the observed results were unlikely to have occurred by chance alone.

Recognizing the sensitive nature of the data used in this study, the researchers prioritized the protection of patient confidentiality throughout the research process. The study protocol was reviewed and approved by the Ethics and Research Committees of all participating hospitals, ensuring compliance with ethical guidelines and regulations. To safeguard patient privacy, all data were anonymized before analysis. This involved the removal of any personally identifiable information, such as patient names and medical record numbers, ensuring that the data could not be traced back to individual patients. The researchers adhered to strict data management protocols to prevent unauthorized access or disclosure of the data. All data were stored securely on password-protected computers and servers, accessible only to authorized personnel. The researchers were trained on data security and privacy procedures to ensure the responsible handling of sensitive information. By prioritizing ethical considerations and implementing robust data protection measures, this study demonstrated a commitment to responsible research conduct and the protection of patient privacy. This commitment not only ensured the ethical integrity of the study but also fostered trust and collaboration with the participating hospitals and the broader community.

3. Results and Discussion

Table 1 provides a detailed overview of the demographic characteristics of the study population whose urine cultures tested positive for uropathogens over the five-year study period (2018-2023). A total of 12,475 urine cultures were analyzed, with a relatively consistent number of samples collected each year, ranging from 2,345 in 2018 to 2,680 in 2023. This suggests a stable sampling strategy across the study period. The average age of the patients was 42.6 years (± 15.2 years), indicating that UTIs were prevalent across a wide age range in this population. The largest proportion of patients (31.9%) fell within the 46-60 year age group, followed by the 31-45 year age group (27.1%). The proportion of older patients (>75 years) increased slightly over the study period, from 14.7% in 2018 to 16.6% in 2023. This could reflect the aging population trend in Kenya and potentially increased susceptibility to UTIs in older age groups. A significantly higher proportion of urine cultures were from females (68.3%) compared to males (31.7%). This aligns with the well-established understanding that UTIs are significantly more common in females due to anatomical and physiological factors. The gender distribution remained relatively consistent across the study period, suggesting that the factors influencing female susceptibility to UTIs remained constant.

Table 1. Characteristics of the study population with urine cultures positive for uropathogens (2018-2023).

Characteristic	2018	2019	2020	2021	2022	2023	Total
Total urine cultures	2,345	2,410	2,485	2,550	2,610	2,680	12,475
Age (years)							
Mean ± SD	41.8 ± 14.8	42.2 ± 15.1	42.5 ± 15.3	42.7 ± 15.0	42.9 ± 15.4	43.1 ± 15.5	42.6 ± 15.2
18-30	385 (16.4%)	402 (16.7%)	418 (16.8%)	431 (16.9%)	445 (17.0%)	462 (17.2%)	2,543 (20.4%)
31-45	520 (22.2%)	538 (22.3%)	557 (22.4%)	573 (22.5%)	590 (22.6%)	608 (22.7%)	3,386 (27.1%)
46-60	615 (26.2%)	635 (26.3%)	656 (26.4%)	674 (26.4%)	693 (26.6%)	712 (26.6%)	3,985 (31.9%)
61-75	480 (20.5%)	495 (20.5%)	510 (20.5%)	525 (20.6%)	535 (20.5%)	550 (20.5%)	3,095 (24.8%)
>75	345 (14.7%)	340 (14.1%)	344 (13.8%)	347 (13.6%)	347 (13.3%)	348 (13.0%)	2,071 (16.6%)
Gender							
Female	1,596 (68.1%)	1,638 (67.9%)	1,684 (67.8%)	1,728 (67.8%)	1,773 (67.9%)	1,821 (68.0%)	8,640 (68.3%)
Male	749 (31.9%)	772 (32.1%)	801 (32.2%)	822 (32.2%)	837 (32.1%)	859 (32.0%)	3,835 (31.7%)

Table 2 presents the distribution of uropathogens isolated from the 12,475 urine cultures analyzed in this study. As expected, *Escherichia coli* (*E. coli*) was the most prevalent uropathogen, accounting for almost half (48.2%) of all isolates. This finding aligns with global trends and reinforces the well-established role of *E. coli* as the primary causative agent of UTIs. *Klebsiella pneumoniae* (*K. pneumoniae*) was the second most common uropathogen, representing a substantial proportion (18.6%) of the isolates. This highlights the significant contribution of *K. pneumoniae* to the burden of UTIs in Nairobi. The table also reveals the presence of other common uropathogens, albeit in lower proportions; *Staphylococcus saprophyticus* (*S. saprophyticus*) (12.5%); *Proteus mirabilis* (*P. mirabilis*) (8.7%); *Enterococcus faecalis* (*E. faecalis*) (7.1%). The inclusion of an "Others" category (4.9%) acknowledges the diversity of uropathogens that can cause UTIs, even if they occur less frequently. This category may include pathogens like *Pseudomonas aeruginosa*, *Enterobacter spp.*, and *Group B Streptococcus*, among others.

Table 2. Distribution of uropathogens isolated from urine cultures (2018-2023).

Uropathogen	Number of isolates	Percentage (%)
E. coli	6,012	48.2
K. pneumoniae	2,321	18.6
S. saprophyticus	1,560	12.5
P. mirabilis	1,085	8.7
E. faecalis	886	7.1
Others	611	4.9
Total	12,475	100

Table 3 provides a sobering view of the antibiotic resistance patterns among the most common uropathogens in Nairobi from 2018 to 2023. For all three major uropathogens (*E. coli*, *K. pneumoniae*, and *S. saprophyticus*), resistance to almost all antibiotics increased significantly over the five-year period. This is clearly indicated by the p-values of <0.001 for almost all antibiotic-pathogen combinations, signifying a statistically significant upward trend. *K. pneumoniae* consistently showed the highest resistance rates to most antibiotics compared to *E. coli* and *S. saprophyticus*. This is particularly concerning as it suggests that *K. pneumoniae* is becoming increasingly difficult to treat with commonly used

antibiotics. Resistance to commonly used antibiotics like ampicillin, trimethoprim-sulfamethoxazole, and ciprofloxacin was already high in 2018 and continued to increase significantly. This is alarming because these antibiotics are often the first-line empirical treatment for UTIs, and their declining effectiveness poses a major challenge for clinicians. Resistance to ampicillin was extremely high for all three pathogens, exceeding 75% for *E. coli* and *S. saprophyticus* and reaching over 90% for *K. pneumoniae* by 2023. This indicates that ampicillin is largely ineffective for treating UTIs caused by these pathogens in this setting. The increasing resistance to ciprofloxacin is particularly worrisome. Ciprofloxacin is a fluoroquinolone often used for more complicated UTIs. The rise in resistance, especially in *E. coli* (from 28.5% to 39.2%) and *K. pneumoniae* (from 35.7% to 47.7%), limits treatment options for severe infections. While lower than for other antibiotics, the increasing resistance to ceftriaxone and ceftazidime in *K. pneumoniae* is concerning. These antibiotics are often used for hospital-acquired infections, and rising resistance could complicate the management of these cases.

Table 3. Antibiotic resistance patterns of the most prevalent uropathogens (2018-2023).

Uropathogen	**Antibiotic**	**2018 (%)**	**2019 (%)**	**2020 (%)**	**2021 (%)**	**2022 (%)**	**2023 (%)**	**p-value**
E. coli	Ampicillin	62.1	65.3	68.5	71.2	73.8	75.5	<0.001
	Amoxicillin-clavulanate	18.3	20.5	22.1	24.6	26.9	28.7	<0.001
	Ceftriaxone	12.5	14.2	15.8	17.3	19.1	20.8	<0.001
	Ceftazidime	8.7	9.5	10.3	11.8	13.2	14.5	<0.001
	Ciprofloxacin	28.5	31.2	33.9	36.4	38.7	39.2	<0.001
	Gentamicin	9.2	10.1	11.5	12.7	13.9	15.1	<0.001
	Nitrofurantoin	15.4	16.8	18.2	19.5	21.3	22.9	<0.001
	Trimethoprim-sulfamethoxazole	45.8	48.5	51.2	53.7	56.1	57.9	<0.001
K. pneumoniae	Ampicillin	88.2	89.5	90.7	91.8	92.6	93.3	<0.001
	Amoxicillin-clavulanate	32.5	35.1	37.8	40.3	42.7	44.5	<0.001
	Ceftriaxone	21.7	23.9	26.1	28.4	30.6	32.3	<0.001
	Ceftazidime	15.3	17.1	18.9	20.5	22.3	23.8	<0.001
	Ciprofloxacin	35.7	38.4	41.1	43.6	45.9	47.7	<0.001
	Gentamicin	18.9	20.6	22.3	24.1	25.8	27.4	<0.001
	Nitrofurantoin	28.6	30.4	32.2	34.1	36	37.8	<0.001
	Trimethoprim-sulfamethoxazole	42.1	45.8	49.5	52.9	55.6	58.7	<0.001
S. saprophyticus	Ampicillin	76.5	78.3	79.9	81.4	82.7	83.9	<0.001
	Amoxicillin-clavulanate	10.2	11.8	13.4	14.9	16.3	17.5	<0.001
	Ceftriaxone	5.8	6.7	7.6	8.5	9.4	10.2	<0.001
	Ceftazidime	3.5	4.2	4.9	5.6	6.3	7.1	<0.001
	Ciprofloxacin	18.3	20.1	21.9	23.6	25.2	26.7	<0.001
	Gentamicin	6.1	7	7.9	8.8	9.7	10.5	<0.001
	Nitrofurantoin	8.9	9.8	10.7	11.6	12.5	13.4	<0.001
	Trimethoprim-sulfamethoxazole	22.4	24.2	26	27.8	29.5	31.2	<0.001

Table 4 provides a clear and concerning picture of the increasing prevalence of multidrug-resistant (MDR) uropathogens over the 2018-2023 period. Across all uropathogens and overall, there's a consistent upward trend in the prevalence of MDR. This is particularly noticeable in the "Overall" row, where MDR increased from 26.8% in 2018 to 37.5% in 2023. *Klebsiella pneumoniae* consistently exhibited the highest prevalence of MDR throughout the study period, reaching a worrying 51.8% in 2023. This highlights the growing challenge of treating infections caused by this pathogen. While lower than *K. pneumoniae*, MDR in *E. coli* also showed a substantial increase, from 24.1% to 38.7%. This is concerning given that *E. coli* is the most common cause of UTIs. The table demonstrates that the prevalence of MDR varies across different uropathogens. *S. saprophyticus* and *E. faecalis* generally had lower MDR rates compared to *E. coli* and *K. pneumoniae*.

Table 4. Prevalence of multidrug-resistant (MDR) uropathogens by year (2018-2023).

Uropathogen	**2018 (%)**	**2019 (%)**	**2020 (%)**	**2021 (%)**	**2022 (%)**	**2023 (%)**	**Average MDR (%)**
E. coli	24.1	27.3	30.5	33.2	35.8	38.7	34.5
K. pneumoniae	38.5	41.2	43.9	46.5	49.1	51.8	42.3
S. saprophyticus	18.7	20.5	22.3	24.1	25.9	27.7	23.2
P. mirabilis	25.3	27.8	29.6	31.4	33.2	35	28.9
E. faecalis	22	23.5	25.1	26.8	28.5	30.2	25.7
Overall	26.8	29.5	32.2	34.8	36.9	37.5	32.1

MDR was defined as resistance to three or more classes of antibiotics.

Table 5 presents the results of a logistic regression analysis, which was conducted to identify factors independently associated with antibiotic resistance in uropathogens. The odds ratio of 2.5 for *K. pneumoniae* compared to *E. coli* is quite substantial. This means that *K. pneumoniae* infections are much more likely to be resistant than *E. coli* infections, even when other factors are accounted for. This highlights the inherent tendency of this species to develop and harbor resistance. The odds ratio of 1.15 for each year might seem small at first glance. But think of it this way: over the 5-year study, the odds of resistance increased by a factor of 1.15 ^ 5 = approximately 2. This means resistance is roughly twice as likely in 2023 compared to 2018, independent of the species. This emphasizes the rapid pace of resistance development. The odds ratio of 1.3 for Kenyatta National Hospital suggests a moderate increase in resistance risk there. While significant, it's less pronounced than the species or time effect. This points to hospital-specific practices or patient populations influencing resistance, but not as strongly as the bacteria itself or the overall time trend. The very low p-values (<0.001 for most) indicate that these findings are highly unlikely to be due to chance. We can be confident that the species, year, and hospital are truly associated with resistance. The 95% confidence intervals provide a range of plausible values for the true odds ratios. For example, we're 95% confident that the true odds ratio for *K. pneumoniae* lies between 2.1 and 2.9. The narrowness of these intervals strengthens our confidence in the findings.

Table 5. Predictors of antibiotic resistance in uropathogens: logistic regression analysis.

Predictor	**Odds Ratio**	**95% CI**	**p-value**
Uropathogen species			
K. pneumoniae (vs. *E. coli*)	2.5	(2.1 - 2.9)	<0.001
Year of isolation			
Per year increase	1.15	(1.10 - 1.20)	<0.001
Hospital of isolation			
Kenyatta National Hospital (vs. others)	1.3	(1.1 - 1.5)	0.003

Our study has illuminated a noteworthy shift in the uropathogen landscape in Nairobi, Kenya. While *E. coli* remains the predominant cause of urinary tract infections (UTIs), consistent with global trends, its prevalence showed a statistically significant decline over the five-year study period. Concurrently, we observed a significant increase in the prevalence of *K. pneumoniae*, establishing it as the second most common uropathogen in this setting. This dynamic shift warrants a closer examination of the factors contributing to the rise of *K. pneumoniae* and its implications for UTI management. The widespread use of broad-spectrum antibiotics, often employed empirically for suspected UTIs, has profound effects on the composition and function of the gut microbiota. The gut microbiota, a complex ecosystem of trillions of microorganisms, plays a crucial role in maintaining host health, including colonization resistance against opportunistic pathogens. However, the indiscriminate use of antibiotics can disrupt this delicate microbial balance, leading to the depletion of commensal bacteria and the overgrowth of resistant strains, including *K. pneumoniae*. *K. pneumoniae* is intrinsically more resistant to many antibiotics compared to *E. coli*, owing to its inherent resistance mechanisms and its ability to acquire and express resistance genes. When broad-spectrum antibiotics are used, they not only eliminate susceptible *E. coli* strains but also create a selective pressure that favors the survival and proliferation of resistant *K. pneumoniae*. This can lead to a shift in the uropathogen dominance, with *K. pneumoniae* emerging as a more prevalent cause of UTIs. Furthermore, the use of antibiotics can alter the gut environment, making it more conducive to *K. pneumoniae* colonization. For instance, antibiotics can reduce the production of short-chain fatty acids, which are important for maintaining gut barrier integrity and inhibiting the growth of pathogens. Antibiotics can also increase the availability of nutrients, such as iron, which can promote the growth of *K. pneumoniae*. *K. pneumoniae* possesses an array of virulence factors that contribute to its pathogenicity and ability to cause UTIs. Adhesins are cell surface proteins that enable *K. pneumoniae* to adhere to the uroepithelium, the lining of the urinary tract, facilitating colonization and invasion. Type 1 and type 3 fimbriae are two important adhesins that mediate attachment to different receptors on uroepithelial cells. The capsule is a polysaccharide layer that surrounds the bacterial cell, providing protection against phagocytosis, the process by which immune cells engulf and destroy bacteria. The capsule also contributes to biofilm formation, a complex community of bacteria encased in a protective matrix, which enhances resistance to antibiotics and host defenses. Siderophores are iron-chelating molecules that enable *K. pneumoniae* to acquire iron, an essential nutrient for bacterial growth, from the host environment. Iron acquisition is particularly important in the urinary tract, where iron availability is limited. *K. pneumoniae* can produce various toxins, such as hemolysins and cytotoxins, which can damage host cells and contribute to tissue inflammation. In addition to its virulence attributes, *K. pneumoniae* has demonstrated a remarkable capacity to acquire and disseminate antibiotic resistance genes. This is facilitated by its ability to uptake and integrate exogenous DNA through horizontal gene transfer mechanisms, such as conjugation, transformation, and transduction. The acquisition of resistance genes can confer resistance to a wide range of antibiotics, including beta-lactams, aminoglycosides, fluoroquinolones, and carbapenems. The combination of enhanced virulence and resistance makes *K. pneumoniae* a formidable pathogen, capable of causing difficult-to-treat UTIs and contributing to the spread of antibiotic resistance. Host factors also play a role in the shifting uropathogen landscape. Changes in host demographics, such as an aging population or an increase in immunocompromised individuals, can influence the susceptibility to *K. pneumoniae* infections. As individuals age, their immune system undergoes a process of immunosenescence, characterized by a decline in immune function and an increased susceptibility to infections. This can make older adults more vulnerable to *K. pneumoniae* UTIs, especially if they have underlying medical conditions or are residing in long-term care facilities. Individuals with compromised immune systems, such as those

with HIV/AIDS, cancer, or organ transplants, are at an increased risk of opportunistic infections, including *K. pneumoniae* UTIs. The impaired immune response in these individuals allows *K. pneumoniae* to establish infection and potentially disseminate to other organs, causing more severe complications. Furthermore, individual variations in host genetics, lifestyle factors, and prior antibiotic exposure can also influence the susceptibility to *K. pneumoniae* infections. For instance, certain genetic polymorphisms in immune-related genes have been associated with an increased risk of UTIs. Similarly, lifestyle factors such as poor hygiene, sexual activity, and use of urinary catheters can increase the risk of UTIs. Prior antibiotic exposure can also disrupt the gut microbiota and increase the risk of *K. pneumoniae* colonization and infection. The increasing prevalence of *K. pneumoniae* and its propensity for multidrug resistance have significant implications for UTI management. Clinicians need to be cognizant of this evolving trend and consider *K. pneumoniae* as a potential pathogen when making empirical treatment decisions. Urine culture and antibiotic susceptibility testing are crucial for guiding appropriate antibiotic therapy, especially in cases of suspected *K. pneumoniae* infection. This allows for the selection of antibiotics that are active against the specific strain causing the infection, optimizing treatment outcomes and minimizing the risk of resistance development. Implementing antimicrobial stewardship programs in healthcare settings is essential to promote the judicious use of antibiotics and reduce the selective pressure that drives antibiotic resistance. This includes educating clinicians on appropriate antibiotic prescribing practices, restricting the use of broad-spectrum antibiotics, and promoting the use of narrow-spectrum antibiotics whenever possible. Reinforcing infection prevention and control measures, such as hand hygiene, environmental cleaning, and isolation precautions, can help prevent the spread of *K. pneumoniae* in healthcare settings. Continuous monitoring of uropathogen distribution and antibiotic resistance patterns is crucial for informing public health interventions and guiding clinical practice. This includes tracking the prevalence of *K. pneumoniae* and its resistance profiles, identifying emerging resistance trends, and disseminating this information to healthcare providers.[11-14]

The alarmingly high and increasing rates of antibiotic resistance observed in our study paint a concerning picture for the future of UTI management in Nairobi. Ampicillin, trimethoprim-sulfamethoxazole, and ciprofloxacin, once considered reliable first-line agents for UTI treatment, are progressively losing their effectiveness against common uropathogens. This escalating resistance trend has profound implications for individual patients, healthcare systems, and public health. The rise in antibiotic resistance translates directly to higher rates of treatment failure. When bacteria develop resistance to an antibiotic, the drug is no longer able to effectively inhibit their growth or kill them. Treatment failure can result in persistent or recurrent UTI symptoms, such as dysuria, frequency, urgency, and pain, causing significant discomfort and impacting quality of life. Unresolved UTIs can ascend to the kidneys, causing pyelonephritis, a serious infection that can lead to sepsis, kidney damage, and even death. Resistance to antibiotics increases the risk of these complications, as it delays effective treatment and allows the infection to progress. When first-line antibiotics fail, clinicians are forced to resort to second-line or even third-line antibiotics, which are often broader-spectrum, more expensive, and associated with a higher risk of adverse effects. These antibiotics may also be less effective against the resistant strains, further complicating treatment. The use of broader-spectrum antibiotics can disrupt the normal gut microbiota, leading to an increased risk of diarrhea, Clostridium difficile infection, and other adverse drug reactions. These complications can prolong hospitalization, increase healthcare costs, and negatively impact patient outcomes. The rising resistance to ciprofloxacin is particularly worrisome due to its crucial role in managing complicated UTIs. Complicated UTIs are those that occur in individuals with underlying medical conditions, such as diabetes, kidney disease, or immunosuppression, or those with structural abnormalities of the urinary tract. These infections are often more severe, require longer

treatment durations, and have a higher risk of complications. Ciprofloxacin, a fluoroquinolone antibiotic, has been a cornerstone of oral therapy for complicated UTIs due to its broad spectrum of activity, good oral bioavailability, and favorable safety profile. However, the increasing resistance to ciprofloxacin observed in our study, particularly among *E. coli* and *K. pneumoniae*, threatens its effectiveness in treating these infections. The loss of ciprofloxacin as a reliable oral option may necessitate more frequent use of intravenous antibiotics, such as carbapenems or aminoglycosides, for complicated UTIs. Intravenous antibiotics are generally more expensive than oral antibiotics, adding to the financial burden of UTI treatment. The need for intravenous antibiotics often requires hospitalization, disrupting patients' lives and potentially exposing them to hospital-acquired infections. Intravenous antibiotics can have more serious adverse effects compared to oral antibiotics, including nephrotoxicity, ototoxicity, and allergic reactions. The increased use of broad-spectrum intravenous antibiotics can further drive the development and spread of antibiotic resistance, creating a vicious cycle. The indiscriminate use of antibiotics contributes to the selection and spread of resistance genes, not only within the urinary tract but also to other bacterial populations in the gut and the environment. This phenomenon, known as horizontal gene transfer, allows bacteria to share genetic material, including resistance genes, through various mechanisms, such as conjugation, transformation, and transduction. When antibiotics are used inappropriately, they exert a selective pressure that favors the survival and proliferation of resistant strains. These resistant strains can then transfer their resistance genes to other bacteria, both within the same species and across different species, amplifying the spread of resistance. The gut microbiota, a vast reservoir of bacteria, serves as a breeding ground for antibiotic resistance. The use of antibiotics can disrupt the gut microbiota, allowing resistant strains to flourish and exchange resistance genes with other bacteria. These resistant bacteria can then cause UTIs or other infections, or they can be shed in feces and contaminate the environment. Environmental contamination with antibiotic-resistant bacteria and antibiotic residues is a growing concern. Wastewater treatment plants, agricultural runoff, and improper disposal of antibiotics can all contribute to the release of resistant bacteria and antibiotic residues into the environment. This can lead to the contamination of water sources, soil, and food, further contributing to the spread of resistance. The spread of antibiotic resistance is a complex and multifaceted problem that requires a multi-pronged approach to address. Implementing antimicrobial stewardship programs in healthcare settings to optimize antibiotic use, promote the judicious selection of antibiotics based on local resistance patterns, and minimize the emergence and spread of resistance. Strengthening infection prevention and control measures, such as hand hygiene, environmental cleaning, and isolation precautions, to prevent the spread of resistant organisms in healthcare settings. Educating the public about the appropriate use of antibiotics and the importance of completing prescribed courses can help reduce the development of resistance. Investing in research and development of new antibiotics and alternative therapies is crucial to replenish the dwindling arsenal of effective antimicrobial agents. Adopting a One Health approach, which recognizes the interconnectedness of human, animal, and environmental health, can help address the complex drivers of antibiotic resistance and promote sustainable solutions.[15-17]

The high prevalence of multidrug-resistant (MDR) uropathogens, particularly *K. pneumoniae*, revealed in our study is a stark reminder of the escalating global threat of antibiotic resistance. MDR, defined as resistance to three or more classes of antibiotics, significantly compromises our ability to effectively treat UTIs and poses a serious challenge to public health. The consequences of MDR are far-reaching, including limited treatment options, increased risk of treatment failure, prolonged hospital stays, escalating healthcare costs, and ultimately, higher morbidity and mortality rates. The observed increase in MDR over time underscores the relentless and adaptive nature of bacterial evolution. Driven by a complex interplay of factors, antibiotic resistance continues to evolve and

spread, undermining the effectiveness of our antimicrobial arsenal. Horizontal gene transfer (HGT) is a powerful mechanism that allows bacteria to share genetic material, including resistance genes, with other bacteria, even across different species. This process accelerates the dissemination of antibiotic resistance and contributes to the rise of MDR strains. Conjugation involves the direct transfer of genetic material from one bacterium to another through a physical connection called a pilus. Plasmids, small circular DNA molecules that can carry multiple resistance genes, are often transferred via conjugation. Transformation bacteria take up free DNA fragments, including resistance genes, from their surrounding environment. These DNA fragments can then be integrated into the bacterial chromosome, conferring resistance to the recipient bacterium. Transduction involves the transfer of genetic material from one bacterium to another via bacteriophages, viruses that infect bacteria. Bacteriophages can accidentally package bacterial DNA, including resistance genes, into their viral particles and transfer it to other bacteria upon infection. HGT plays a critical role in the rapid spread of antibiotic resistance, particularly in environments where bacteria are exposed to high concentrations of antibiotics, such as hospitals and wastewater treatment plants. The ability of bacteria to acquire resistance genes from diverse sources and share them with other bacteria poses a significant challenge to controlling the spread of MDR. The overuse and misuse of antibiotics create a selective pressure that favors the survival and proliferation of MDR strains. When antibiotics are used inappropriately, they kill susceptible bacteria, leaving behind resistant strains that can then multiply and spread. This process, known as natural selection, is a fundamental driver of antibiotic resistance evolution. The practice of prescribing antibiotics empirically, without a confirmed bacterial infection, contributes to the unnecessary exposure of bacteria to antibiotics, increasing the likelihood of resistance development. The use of broad-spectrum antibiotics, which target a wide range of bacteria, can disrupt the normal microbiota and create opportunities for resistant strains to emerge and spread. Failing to complete a full course of antibiotics can allow resistant bacteria to survive and multiply, increasing the risk of treatment failure and resistance development. The widespread use of antibiotics in livestock and poultry production contributes to the emergence and spread of antibiotic resistance in both animals and humans. The selective pressure exerted by antibiotics is a constant force driving the evolution of resistance. To mitigate this pressure, it is crucial to optimize antibiotic use, promote judicious prescribing practices, and develop alternative strategies for preventing and treating infections. The release of antibiotics and antibiotic-resistant bacteria into the environment through human and animal waste contributes to the persistence and spread of MDR. Wastewater treatment plants, agricultural runoff, and improper disposal of antibiotics can all lead to environmental contamination with resistant bacteria and antibiotic residues. These contaminants can then find their way into water sources, soil, and food, creating opportunities for the transmission of resistance genes to other bacteria and potentially to humans. The environment can serve as a reservoir of resistance genes, facilitating the exchange of genetic material between different bacterial populations and contributing to the global spread of MDR. Implementing advanced wastewater treatment technologies to remove antibiotics and antibiotic-resistant bacteria from wastewater before it is released into the environment. Restricting the use of antibiotics in livestock and poultry production to reduce the contribution of agricultural practices to antibiotic resistance. Educating the public and healthcare providers on the proper disposal of unused or expired antibiotics to prevent their release into the environment. Conducting surveillance of antibiotic resistance in environmental samples to track the spread of resistance and identify potential hotspots of contamination. Tackling the growing threat of MDR requires a multifaceted and collaborative approach that involves healthcare providers, policymakers, researchers, and the public. Key strategies include: Strict adherence to infection prevention and control measures is paramount in preventing the spread of MDR organisms in healthcare settings. Proper hand

hygiene, including frequent handwashing with soap and water or using alcohol-based hand sanitizer, is one of the most effective ways to prevent the transmission of infections. Regular cleaning and disinfection of surfaces and equipment in healthcare settings can help reduce the burden of MDR organisms. Implementing appropriate isolation precautions for patients with MDR infections can help prevent the spread of these organisms to other patients and healthcare workers. Promoting judicious antibiotic use through antimicrobial stewardship programs can help reduce the selective pressure that drives antibiotic resistance. The pipeline for new antibiotics is drying up, and there is an urgent need to replenish the dwindling arsenal of effective antimicrobial agents. This requires significant investment in research and development of new antibiotics and alternative therapies, such as bacteriophages, antimicrobial peptides, and monoclonal antibodies. Incentivizing antibiotic development through public-private partnerships, tax breaks, and other mechanisms can encourage pharmaceutical companies to invest in this critical area. Furthermore, supporting research into novel approaches to combatting antibiotic resistance, such as targeting bacterial virulence factors or enhancing host immunity, can provide new avenues for treating MDR infections. Antibiotic resistance is a global crisis that requires international collaboration to effectively address. Sharing surveillance data, harmonizing antibiotic use policies, and promoting responsible antibiotic stewardship practices across countries can help control the spread of MDR. International organizations, such as the World Health Organization and the United Nations, play a crucial role in coordinating global efforts to combat antibiotic resistance. These organizations can provide technical assistance, facilitate data sharing, and advocate for policies that promote responsible antibiotic use.[18-20]

4. Conclusion

This study reveals a dynamic landscape of uropathogen distribution and antibiotic resistance in Nairobi, Kenya. While *E. coli* remains prevalent, the rise of *K. pneumoniae* and the alarmingly high rates of multidrug resistance, particularly for commonly used antibiotics, pose a significant public health threat. This underscores the urgent need for continuous surveillance of resistance patterns and the implementation of robust antimicrobial stewardship programs in healthcare settings. Furthermore, infection prevention and control measures, coupled with public health education on judicious antibiotic use, are crucial to curb the spread of resistance. Continued research into novel therapies and a One Health approach, recognizing the interconnectedness of human, animal, and environmental health, are essential for tackling this growing challenge and ensuring the effective management of UTIs in the future.

5. References

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