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Microbiological analysis of complicated urinary tract infections in a specialised urology unit in KwaZulu-Natal Province, South Africa, 2021 - 2023

S Konar,[1,2] MB ChB, DTM&H; **M Pye Han,**[3] MB ChB; **Y Mahabeer,**[1,2] MB ChB, FC Path (Micro); **K Swe Swe-Han,**[1,2] FCPath (Micro), PhD (Med Micro)

[1] *Department of Medical Microbiology, Inkosi Albert Luthuli Central Hospital Laboratory, National Health Laboratory Service, Durban, South Africa*
[2] *Department of Medical Microbiology, School of Pathology, Faculty of Health Sciences, University of KwaZulu-Natal, Durban, South Africa*
[3] *Department of Urology, St Aidan's Hospital, Durban, South Africa*

Corresponding author: *S Konar (selinakonar@gmail.com)*

Background. Complicated urinary tract infections (cUTIs) are a growing burden in urological patients, particularly those with prior catheterisation or surgical procedures. Appropriate empirical antimicrobial therapy is an essential component in the management of these patients; therefore, treatment guidelines need to be reviewed periodically.
Objectives. To evaluate the microbiological causes and antimicrobial resistance (AMR) patterns of cUTIs in a specialised urology department in KwaZulu-Natal Province, South Africa.
Method. A retrospective study was conducted on all positive urine cultures of patients attending a urology clinic and ward from 1 January 2021 to 31 December 2023. Samples were processed according to standard operating procedures.
Results. A total of 820 specimens were analysed in this study. *Escherichia coli* was the most common causative agent of cUTIs, accounting for 47% of all isolates, followed by *Klebsiella* spp. (15%). *Enterococcus* spp. was the most prevalent Gram-positive uropathogen. Notably, high resistance patterns were observed, with ciprofloxacin resistance rates of 79.4% in *E. coli* and 50.8% in *Klebsiella* spp. Extended-spectrum beta-lactamase-producing bacteria were detected in 43.3% of *E. coli* and 40.2% of *Klebsiella* spp. isolates, while carbapenem resistance was detected in 15.3% of *Klebsiella* spp.
Conclusion. Our study shows the importance of antibiotic surveillance to guide empirical antimicrobial therapy based on local microbiological data. Owing to the increase in resistance of common uropathogens to commonly used antimicrobials, we advocate revised guidelines for the empirical treatment of cUTIs.

Keywords: antimicrobial resistance, complicated urinary tract infection, *Escherichia coli*, multidrug-resistant organism, urology department

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In 2019, the global burden of urinary tract infections (UTIs) was >400 million, resulting in 200 000 deaths.[1] These infections can be classified as uncomplicated, where there are no functional or structural abnormalities, or complicated, where these abnormalities are present or where the patient has underlying comorbidities.[2] Complicated urinary tract infections (cUTIs) are a common reason for hospital attendance and admission. In the USA, cUTIs accounted for >100 000 admissions in 2000. However, data on the true prevalence of these infections globally are lacking.[3] In Uganda, the prevalence of UTIs in patients attending a hospital was found to be 32%.[4]

The most common organism causing cUTI is uropathogenic *Escherichia coli*, followed by *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Enterococcus* spp. and *Staphylococcus* spp.[5] Nosocomial pathogens, such as *P. aeruginosa*, are common in healthcare-associated infection, while Enterobacterales, particularly *E. coli*, are the predominant causative agents in urological patients.[6,7] However, non-*E. coli* pathogens, including *Klebsiella* spp. and *Enterococcus* spp., are frequently isolated, especially from immunocompromised patients or those with pre-existing urinary catheters.[8] Notably, these pathogens exhibit high resistance rates, with extended-spectrum beta-lactamase (ESBL)-producing bacteria and multidrug-resistant organisms increasingly reported.[9,10]

Management of cUTIs requires early and targeted antibiotic therapy to improve outcomes, as delays in initiating appropriate treatment in septic patients are linked to higher mortality.[11] This highlights the importance of understanding local microbiological causes and resistance profiles to develop appropriate empirical treatment protocols. Current national treatment guidelines for cUTIs in South Africa (SA) advocate the use of fluoroquinolones with gentamicin or ceftriaxone as alternative agents for pyelonephritis.[12] However, a lack of local susceptibility data for uropathogens causing cUTIs, especially in the context of urology patients, is evident.

The purpose of this study was to identify the microbiological causes of cUTIs and analyse antimicrobial resistance trends in a specialised urology department in KwaZulu-Natal Province, SA. The findings aim to inform the optimisation of current empirical treatment protocols, contributing to improved patient outcomes and better stewardship of antibiotic use.

Methods

Setting

Urine samples from the urology department at St Aidan's hospital in Durban, SA, were analysed. All patients who seek urological services here need to be referred from other healthcare facilities. General outpatients are not seen in this hospital.

Study design and data collection

A retrospective, descriptive study was conducted on all positive urine cultures of patients attending the urology clinic and ward from 1 January 2021 to 31 December 2023. All patients who attended the urology department were considered to have a cUTI, as this is a specialist urology hospital where patients with uncomplicated infections are not seen. Urine specimens were analysed by the National Health Laboratory Service (NHLS) according to the standard operating procedures. Laboratory number, age, gender, type of urine specimen, clinical history, organism and antimicrobial susceptibility were extracted from the laboratory information system. Data were deduplicated. Urinary samples from the same patient were removed if they had the same organism, same resistance patterns and if they were taken within 21 days of the first sample. Patient details were removed for confidentiality.

Urine samples with a single organism of $>10^5$ CFU/mL from a midstream urine specimen and a colony count of $>10^2$ CFU/mL were used for urinary catheter and suprapubic specimens. Identification and antimicrobial susceptibility testing were performed using Vitek 2 (bioMérieux, France). If two organisms were present in equal quantities, then identification and susceptibility testing were performed on both organisms, using the same platform. If there were two organisms and one was predominant, the decision to conduct further work-up on the organism was made by the pathologist. Urine samples in which ≥3 organisms were isolated were considered contaminated and were excluded from the study.

Antibiotics were selectively reported by the pathologist in accordance with Clinical and Laboratory Standards Institute guidelines.[13-15] ESBL-producing organisms were defined as those isolates that were resistant to third-generation cephalosporins, i.e. ceftriaxone, cefotaxime and ceftazidime. Carbapenem-resistant *Enterobacterales* (CRE) was defined as those isolates that were resistant to any of the carbapenems: ertapenem, imipenem or meropenem. Detection of specific carbapenemases was not conducted.

Data analysis

Statistical analyses were conducted using the Kruskal-Wallis equality-of-populations rank test for continuous data, and the *z*-column proportional test and χ^2 goodness-of-fit test for categorical variables. $P<0.05$ was considered statistically significant. Data were analysed using the Statistical Package for Social Sciences (SPSS) version 29 for Windows (IBM Corp, USA), with appropriate tests applied based on data type.

Ethical considerations

Ethics approval was granted by the University of KwaZulu-Natal Biomedical Research Ethics Committee (ref. no. BE085/12).

Results

Population characteristics

Over a 3-year period, a total of 820 specimens were analysed. Of these, 96% of patients (783/822) were seen in the urology clinic rather than the ward. Some of the indications for urine sample collection included but were not limited to the following: recurrent UTI; preoperative urine microscopy; culture and sensitivity prior to endoscopic procedure within the urinary tract; urosepsis work-up; vesicoureteric reflux; evidence of pyuria; and presence of urine calculi. The median age of the group was 48.5 years (range 13 - 86 years). Seventy-five percent (613/820) of the total study population was male. Although there was no difference in the number of samples collected per year over the study period, there were significantly more people in the age categories 31 - 40 years and 41 - 50 years ($p=0.01$ in both categories) (Table 1).

Causative agents

The most common uropathogen identified was *E. coli* (383/820; 47%), followed by *Klebsiella spp.* (122/820; 15%). *Proteus* spp., *Providencia* spp. and *Morganella morganii* accounted for 6% (51/820) of the total isolates. Among the Gram-positive organisms, *Enterococcus* spp. accounted for 6% (51/820) of the total isolates, with *Enterococcus faecalis* accounting for >90% of these (47/51) (Fig. 1).

Trend of aetiological agents from 2021 to 2023

The two most common organisms were used for this analysis. Over the 3 years, there was an increase in the number of *Klebsiella* spp. identified from urine specimens of patients with cUTIs. However, this was not statistically significant (Table 2).

The antibiogram for *E. coli* and *Klebsiella* spp. is shown in Table 3. The overall susceptibility rates of *E. coli* were 100% for ertapenem and imipenem, 99.7% for meropenem, 93.3% for piperacillin-tazobactam, 90.1% for nitrofurantoin, 83.9% for amikacin, 79.5% for gentamicin, 67.2% for amoxicillin-clavulanic acid, 52.5% for ceftriaxone, 38.3% for cotrimoxazole and 20.6% for ciprofloxacin.

The overall susceptibility rates for *Klebsiella* spp. were 88.0% for meropenem, 86.3% for imipenem, 84.8% for ertapenem, 81.5% for amikacin, 62.8% for gentamicin, 62.1% for piperacillin-tazobactam, 49.2% for ciprofloxacin and cotrimoxazole, 47.9% for amoxicillin-clavulanic acid, 45.6% for ceftriaxone and 39.7% for nitrofurantoin.

E. coli was significantly associated with ciprofloxacin resistance compared with *Klebsiella* spp. ($p<0.001$). Almost all antimicrobials showed significantly greater resistance in *Klebsiella* spp. than *E. coli*. These were amoxicillin-clavulanic acid ($p<0.001$), piperacillin-tazobactam ($p<0.001$), nitrofurantoin ($p<0.001$), gentamicin ($p=0.04$) and the carbapenems ($p<0.001$). *E. coli* had a greater susceptibility to carbapenems (imipenem, meropenem and ertapenem) of >98%, as compared with *Klebsiella* spp. with a susceptibility of 84 - 88%.

Table 4 shows a total of 217 extended-spectrum beta-lactamase (ESBL) and 19 CRE isolates identified. The ESBL rates for both organisms were similar: 43% and 40%, respectively. However, a significantly higher proportion of *Klebsiella* spp. (15.3%) was CRE compared with *E. coli*.

Discussion

In this study, cUTI was studied over a 3-year period at a specialist urology service in Durban, SA. Significantly higher numbers of samples were received from male patients, and from patients aged between 31 and 40 years, and 41 and 50 years old. *E. coli* was the most common cause of cUTIs, followed by *Klebsiella* spp. High resistance rates were observed for ciprofloxacin, currently recommended as a treatment option for cUTI. This was significantly higher in *E. coli* compared with *Klebsiella spp.* However, lower resistance rates to nitrofurantoin, used for treating uncomplicated cystitis, were observed in *E. coli* compared with *Klebsiella* spp.

Our study found significantly more male than female patients over the 3-year period. This is in keeping with Italian and Romanian studies of urology outpatients.[16,17] However, many other studies report a predominance of females.[1,18] Due to the anatomical structure of the male genitalia, males are less susceptible to UTIs. The causes of UTI in males are multifactorial; however, further research is needed to identify the risk factors.

E. coli was the most common uropathogen identified in this study, followed by *Klebsiella* spp. A systematic review of UTIs in sub-Saharan Africa found a similar prevalence of *E. coli* UTIs.[19] In India, a retrospective study conducted in a urology hospital showed similar rates of 55% and 18.8% for *E. coli* and *Klebsiella* spp., respectively.[10] In another study, *E. coli* and *Klebsiella* spp. were

Table 1. Patient location and demographic details (2021 - 2023) (*N*=820)

Characteristic	2021, *n* (%)*	2022, *n* (%)*	2023, *n* (%)*	*p*-value†
Total analysed, *n*‡	247	309	264	0.02
Location				
Urology clinic§	236 (95.5)	291 (93.9)	259 (97.7)	0.06
Urology ward§	11 (4.5)	19 (6.1)	6 (2.3)	0.08
Age, years				
Total, *n*‡	239	306	263	0.01
Median (IQR)¶	63 (47 - 72)	62 (50 - 71)	57 (42 - 69)	<0.001
0 - 20§	5 (2.1)	7 (2.3)	5 (1.9)	0.95
21 - 30§	22 (9.2)	19 (6.2)	12 (4.6)	0.11
31 - 40§	23 (9.6)	27 (8.8)	43 (16.3)	0.01
41 - 50§	19 (7.9)	28 (9.2)	42 (16.0)	0.01
51 - 60§	42 (17.6)	56 (18.3)	52 (19.8)	0.81
61 - 70§	60 (25.1)	82 (26.8)	45 (17.1)	0.02
>70§	68 (28.5)	87 (28.4)	64 (24.3)	0.47
Gender				
Total, *n*‡	246	308	263	0.02
Male§	186 (75.6)	232 (75.3)	195 (74.1)	0.92
Female§	60 (24.4)	76 (24.7)	68 (25.9)	0.92
p-value‖	<0.001	<0.001	<0.001	

IQR = interquartile range.
Missing data removed. $P<0.05$ considered significant.
*Unless otherwise indicated.
†Comparison between the years for the urology clinic.
‡X^2 goodness-of-fit with Yates correction.
§*Z*-column proportional test.
¶Kruskal-Wallis equality-of-populations rank test.
‖Male v. female.

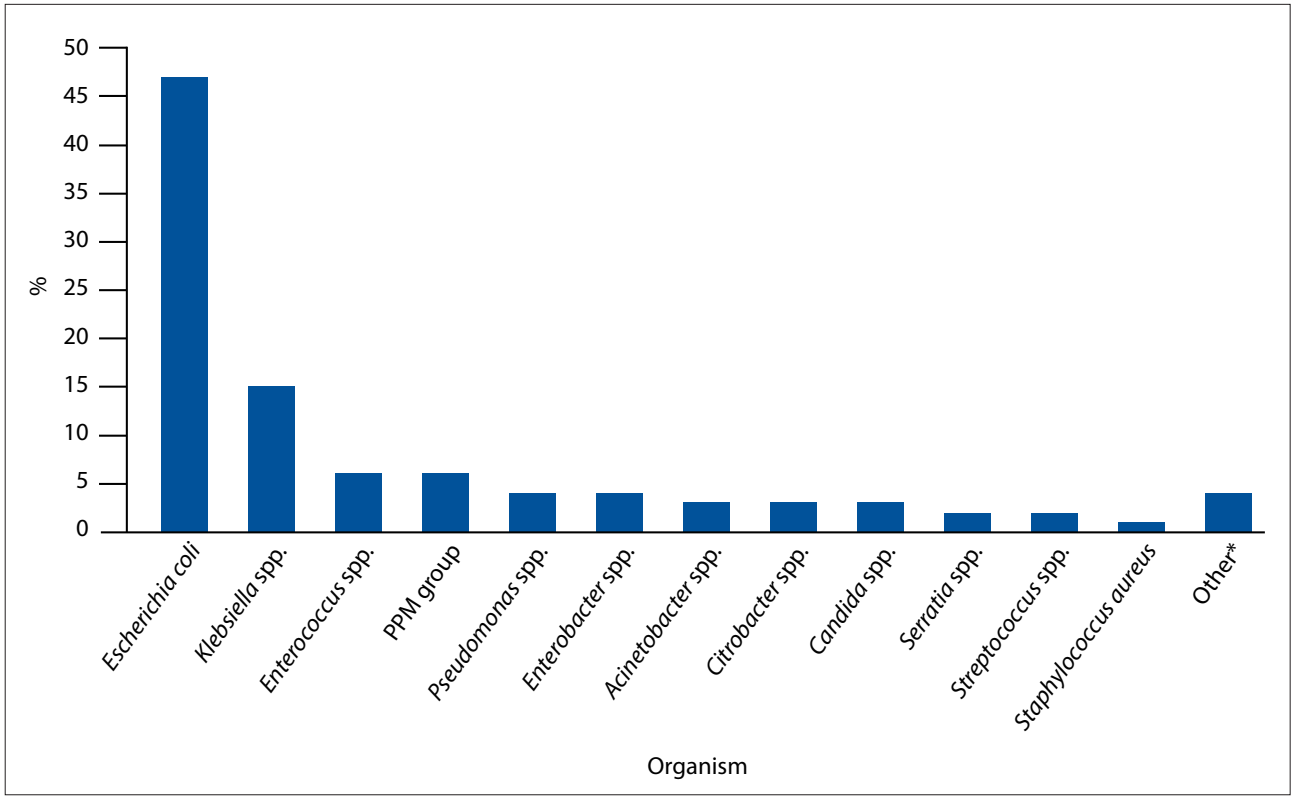

Fig. 1. Distribution of organisms from urinary specimens of patients with complicated urinary tract infections, 2021 - 2023. (PPM = Proteus *spp.,* Providencia *spp.,* Morganella morganii.*) *Other included:* Stenotrophomonas maltophilia, Raoultella *spp.,* Achromobacter xylosoxidans, Aeromonas *spp.,* Alcaligenes faecalis, Chryseobacterium indologenes, Kluyvera cryocrescens, Pandoraea *spp.,* Ralstonia insidiosa *and* Staphylococcus *spp. Only 2 isolates were* Staphylococcus saprophyticus.

isolated in ~50% and 27% of cases, respectively.[1] A study on bacterial uropathogens conducted in a SA tertiary hospital highlighted similar findings, with *E. coli* at 53% followed by *Klebsiella* spp. at 14%.[7]

Enterococcus is the leading Gram-positive bacterial uropathogen seen in the literature.[8,20] Compared with a local study, our study had twice as many enterococcal infections.[7] The difference in prevalence of *Enterococcus* spp. contributing to UTIs can be attributed to gender, clinical characteristics, biofilm formation and other virulence factors.[8]

Our study demonstrated an alarming rate of ciprofloxacin-resistant *E. coli* isolates. A study conducted in Spain demonstrated lower rates of fluoroquinolone resistance of 37.2% in patients with complicated community-acquired UTIs.[20] Other studies have shown higher resistance rates for ciprofloxacin of 50%, while an Indian study showed similar resistance of 70% in *E. coli*.[10,20] The recommendation is that if fluoroquinolone resistance exceeds 10%, then it should not be used empirically for community-acquired cUTIs.[21]

Over the 3-year period, 15% of *Klebsiella* spp. were carbapenem-resistant. This was slightly higher than the findings in two other studies, one conducted in Lebanon[22] and the other in Romania,[17] with carbapenem resistance rates of 6.6% and 12%, respectively. Furthermore, an epidemiological study in south-west Nigeria showed that 20.8% of uropathogens were carbapenem-resistant, which is similar to our study.[23]

Increasing antimicrobial resistance (AMR) results in limited antimicrobial options available for treatment. The National Institute for Communicable Diseases in SA has released their latest surveillance report for AMR; however, this only includes uncomplicated community-acquired uropathogens. There is a gap in local surveillance data conducted on AMR in patients with cUTIs. The present study highlights the need to consider revision of current treatment protocols, particularly in patients with urological problems, owing to the high rates of fluoroquinolone resistance seen in our setting (KwaZulu-Natal Province, SA). In a specialised urological clinic or ward that services patients with cUTIs, fluoroquinolones will need to be used with caution, and close follow-up of susceptibility results is essential. Gentamicin may still be a good option for inpatient use, as is currently recommended, because only 20% resistance was seen in *E. coli*. Approximately 40% of *E. coli* and *Klebsiella* spp. were resistant to 3rd-generation cephalosporins, therefore these should also be used with careful follow-up of susceptibility data. Low resistance rates were noted with nitrofurantoin, and this drug may be a consideration, noting the limitations of its utility. Piperacillin-tazobactam susceptibility was high among *E. coli* isolates. This may be a reasonable intravenous alternative for inpatients with ESBL-producing *E. coli*, as it is a carbapenem-sparing option that may reduce the prevalence of CRE.[24,25]

Table 2. Trend of *E. coli* and *Klebsiella* spp. from 2021 to 2023

Year	*E. coli* (*n*=385), *n* (%)	Klebsiella spp. (*n*=122), *n* (%)	*p*-value*
2021†	117 (30.4)	32 (26.2)	0.44
2022†	138 (35.8)	39 (32.0)	0.50
2023†	130 (33.8)	51 (41.8)	0.13
p-value‡	0.42	0.10	

E. coli = *Escherichia coli*.
*Overall *p*-value comparing *E. coli* v. *Klebsiella* spp. from 2021 to 2023.
†Calculated using the *z*-column proportional test.
‡X^2 goodness-of-fit with Yates correction.

Study limitations

Our study is limited to urology patients who may have a different antimicrobial susceptibility profile to other patients with cUTI, and results cannot be generalised to other categories of patients. This study was conducted at only one study site, and organisms may have variable resistance patterns geographically. Owing to the retrospective nature of the study, some antimicrobial data were missing. In addition, clinical and prior antimicrobial data were not available, which would have added more value.

Conclusion

Complicated UTIs pose a significant burden on healthcare owing to increasing AMR, with the added challenge of limited antimicrobial options available. Our study demonstrated increased resistance to ciprofloxacin and 3rd-generation cephalosporins, the currently recommended antimicrobials for the treatment of cUTIs. Apart from the high ESBL prevalence among the uropathogens detected in this study, the CRE prevalence of 15% in *Klebsiella* spp. is of great concern. Enhanced surveillance and appropriate empirical antimicrobial therapy based on local microbiological data are essential. In light of the increase in resistance patterns to commonly used antimicrobials, we advocate revision of local antimicrobial guidelines for cUTIs.

Table 3. Antibiograms of *Escherichia* coli v. *Klebsiella* spp.

	E. coli				*Klebsiella spp.*				
Antimicrobial	Total, *n*	S (%)	I (%)	R (%)	Total, *n*	S (%)	I (%)	R (%)	*p*-value*
Amoxicillin-clavulanic acid	379	255 (67.2)	77 (20.3)	47 (12.4)	121	58 (47.9)	22 (18.2)	41 (33.9)	<0.001
Piperacillin-tazobactam	368	344 (93.3)	13 (3.5)	11 (3.0)	116	72 (62.1)	10 (8.6)	34 (29.3)	<0.001
Ciprofloxacin	383	79 (20.6)	0	304 (79.4)	122	60 (49.2)	0	62 (50.8)	<0.001
Nitrofurantoin	381	344 (90.1)	20 (5.2)	17 (4.5)	121	48 (39.7)	34 (28.1)	39 (32.2)	<0.001
Cotrimoxazole	379	145 (38.3)	0	234 (61.7)	122	60 (49.2)	0	62 (50.8)	0.043
Cefotaxime/ceftriaxone	356	187 (52.5)	8 (2.2)	161 (45.2)	114	52 (45.6)	1 (0.9)	61 (53.5)	0.233
Gentamicin	380	302 (79.5)	1 (0.2)	77 (20.3)	121	76 (62.8)	6 (5.0)	39 (32.2)	<0.001
Amikacin	366	307 (83.9)	57 (15.6)	2 (0.5)	119	97 (81.5)	12 (10.1)	10 (8.4)	<0.001
Ertapenem	350	350 (100)	0	0	112	95 (84.8)	4 (3.6)	13 (11.6)	<0.001
Meropenem	361	360 (99.7)	0	1 (0.3)	117	103 (88.0)	0	14 (12.0)	<0.001
Imipenem	361	360 (100)	0	0	117	101 (86.3)	3 (2.6)	13 (11.1)	<0.001

S = sensitive; I = intermediate; R = resistant.
**P*-values recalculated using a 2 × 3 Pearson χ^2 test.
Fallback: if I=0 in both species (structural zero), collapse to 2×2 (S v. I+R) and apply χ^2 or Fisher's exact test.

Table 4. ESBL v. CRE strains of *E. coli* v. *Klebsiella* spp. in complicated urinary tract infections

Resistance pattern	*E. coli* (*n*=383), *n* (%)	*Klebsiella spp.* (*n*=117), *n* (%)*	*p*-value†
ESBL	170 (43.3)	47 (40.2)	0.49
CRE	1 (0.2)	18 (15.3)	<0.001
p-value‡	<0.001	<0.001	

ESBL = extended-spectrum beta-lactamase; CRE = carbapenem-resistant *Enterobacterales; E. coli* = *Escherichia coli.*
*Missing data.
†*E. coli* v. *Klebsiella* spp.
‡ESBL v. CRE within each species.

Data availability. Data are available from the author on request.
Declaration. None.
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