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Original Article **Open Access**

Resistance profiles of urinary *Escherichia coli* and *Klebsiella pneumoniae* isolates to antibiotics commonly prescribed for treatment of urinary tract infections at Monkole Hospital Center, Kinshasa, Democratic Republic of the Congo

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Abstract:

Background: The occurrence of urinary tract infection (UTI) caused by multi-drug resistant bacteria is increasing worldwide and has become a major public health concern that requires global attention. To promote better treatment outcome of UTI and raise awareness of antibiotic resistance in the Democratic Republic of the Congo (DRC), we investigated the antimicrobial resistance profile of bacterial pathogens frequently isolated from urine samples of inpatients and outpatients with symptoms of UTI at the Monkole Hospital Center (MHC), Kinshasa from June 2017 to May 2018.
Methodology: This was a retrospective review of results of uro-cultures of urine samples of both inpatients and outpatients who had clinical symptoms of UTI, over a period of one year at the MHC, Kinshasa, DRC. During this period, aerobic uro-cultures of urine were done on MacConkey agar (MAC) or Cystine-Lactose-Electrolyte-Deficient (CLED) agar media at 37ºC incubation for 24 hours. Identification of bacterial isolates on the culture media and antimicrobial susceptibility to sixteen selected antibiotics were done using the integral system enterobacteria and the Vitek® 2 automated system according to the manufacturer's instructions. The R-studio software was used for statistical analysis.
Results: Of the 2765 uro-cultures performed during the period of study, 809 (29.3%) were positive for bacteria with *Escherichia coli* being the most frequently isolated bacteria pathogens. There was no significant difference (p>0.05) in the resistance rates of both *E. coli* and *Klebsiella pneumoniae* to most of the antibiotics such as amoxicillin-clavulanic acid, piperacillin-tazobactam, amikacin, levofloxacin, norfloxacin, cefuroxime, cefotaxime, cefixime and cephalexin but resistance rates of *E. coli* compared to *K. pneumoniae* was significantly higher to cotrimoxazole (OR=2.06, p=0.0016), ofloxacin (OR=3.43, p=0.0019), ciprofloxacin (OR=1.624, p=0.044) and significantly lower to imipenem (OR=0.037, p=0.0046), nitrofurantoin (OR=0.292, p=0.0004) and fosfomycin (OR=0.311, p=0.0003). Both pathogens showed resistance rates of more than 50.0% to doxycycline, cefuroxime, cefixime and cephalexin but resistance rates of *K. pneumoniae* to ofloxacin and cotrimoxazole was less than 50.0%. The isolates were least resistant to imipenem, piperacillin-tazobactam and amikacin, with less than 13.0% resistance rate.
Conclusion: The findings of this study showed that *E. coli* is the most isolated bacterial uro-pathogen amongst patients with UTI at MHC Kinshasa, DRC, but both *E. coli* and *K. pneumoniae* were resistant to most commonly prescribed antibiotics used for treatment of UTI. Amikacin, piperacillin-tazobactam and imipenem demonstrated high *invitro* activity and should be prioritized for antimicrobial stewardship to prevent or delay emergence of resistance to them. To guarantee optimal treatment of UTI, regular pathogen surveillance and local antibiogram

reporting are required. Further studies are needed in DRC to assess the burden and factors driving antimicrobial resistance nationwide.

Keywords: urinary tract infection, bacteria; susceptibility; resistance; profile

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Profils de résistance des isolats urinaires d'*Escherichia coli* et de *Klebsiella pneumoniae* aux antibiotiques couramment prescrits pour le traitement des infections des voies urinaires au Centre Hospitalier Monkole, Kinshasa, République Démocratique du Congo

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Résumé:

Contexte: La survenue d'infections des voies urinaires (IVU) causées par des bactéries multirésistantes est en augmentation dans le monde et est devenue un problème majeur de santé publique qui nécessite une attention mondiale. Pour promouvoir de meilleurs résultats de traitement des infections urinaires et sensibiliser à la résistance aux antibiotiques en République démocratique du Congo (RDC), nous avons étudié le profil de résistance aux antimicrobiens des agents pathogènes bactériens fréquemment isolés à partir d'échantillons d'urine de patients hospitalisés et ambulatoires présentant des symptômes d'infection urinaire à l'hôpital de Monkole. (MHC), Kinshasa de juin 2017 à mai 2018.
Méthodologie: Il s'agissait d'une revue rétrospective des résultats d'urocultures d'échantillons d'urine de patients hospitalisés et ambulatoires qui présentaient des symptômes cliniques d'IU, sur une période d'un an au MHC, Kinshasa, RDC. Au cours de cette période, des urocultures aérobies d'urine ont été réalisées sur de la gélose MacConkey (MAC) ou de la gélose Cystine-Lactose-Electrolyte-Deficient (CLED) à 37°C d'incubation pendant 24 heures. L'identification des isolats bactériens sur les milieux de culture et la sensibilité antimicrobienne à seize antibiotiques sélectionnés ont été effectuées à l'aide du système intégral d'entérobactéries et du système automatisé Vitek® 2 conformément aux instructions du fabricant. Le logiciel R-studio a été utilisé pour l'analyse statistique.
Résultats: Sur les 2765 urocultures réalisées au cours de la période d'étude, 809 (29,3%) étaient positives pour les bactéries, *Escherichia coli* étant la bactérie pathogène la plus fréquemment isolée. Il n'y avait pas de différence significative (p>0,05) dans les taux de résistance d'*E. coli* et de *Klebsiella pneumoniae* à la plupart des antibiotiques tels que l'amoxicilline-acide clavulanique, la pipéracilline-tazobactam, l'amikacine, la lévofloxacine, la norfloxacine, la céfuroxime, la céfotaxime, la céfixime et céphalexine, mais les taux de résistance d'*E. coli* par rapport à *K. pneumoniae* étaient significativement plus élevés pour le cotrimoxazole (OR=2,06, p=0,0016), l'ofloxacine (OR=3,43, p=0,0019), la ciprofloxacine (OR=1,624, p=0,044) et significativement inférieur à l'imipénem (OR=0,037, p=0,0046), à la nitrofurantoïne (OR=0,292, p=0,0004) et à la fosfomycine (OR=0,311, p=0,0003). Les deux agents pathogènes ont montré des taux de résistance de plus de 50,0% à la doxycycline, au céfuroxime, au céfixime et à la céphalexine, mais les taux de résistance de *K. pneumoniae* à l'ofloxacine et au cotrimoxazole étaient inférieurs à 50,0%. Les isolats étaient les moins résistants à l'imipénème, à la pipéracilline-tazobactam et à l'amikacine, avec un taux de résistance inférieur à 13,0%.
Conclusion: Les résultats de cette étude ont montré qu'*E. coli* est l'uropathogène bactérien le plus isolé parmi les patients atteints d'infection urinaire au CMH de Kinshasa, en RDC, mais *E. coli* et *K. pneumoniae* étaient résistants aux antibiotiques les plus couramment prescrits utilisés pour le traitement des UTI. L'amikacine, la pipéracilline-tazobactam et l'imipénem ont démontré une activité in vitro élevée et devraient être prioritaires pour la gestion des antimicrobiens afin de prévenir ou de retarder l'émergence d'une résistance à ces derniers.

Pour garantir un traitement optimal des infections urinaires, une surveillance régulière des agents pathogènes et des rapports d'antibiogrammes locaux sont nécessaires. D'autres études sont nécessaires en RDC pour évaluer le fardeau et les facteurs à l'origine de la résistance aux antimicrobiens à l'échelle nationale.

Mots clés: infection urinaire; bactérie; susceptibilité; résistance; le profil

Introduction:

Urinary tract infections (UTIs) are one of the most common infectious diseases affecting approximately 150–250 million people worldwide every year (1). UTI refer to any type of urothelial inflammatory response that results from periurethral infection by one or several uropathogens usually residing in the gut (2). The periurethral infection can become invasive upon colonization of the urethra and pathogen migration to the bladder. The uropathogenic bacteria that invade the bladder can subsequently ascend to the kidneys and spread to the bloodstream to cause bacteraemia. Certain uropathogens such as *Escherichia coli* and *Pseudomonas aeruginosa* can also form biofilms leading to recurrent UTIs. Other serious complications include pyelonephritis with sepsis that can lead to renal damage and death (3).

Urinary tract infection profoundly affects the quality of life of affected individuals, who are predominantly females of all ages, infant boys, older men, and people with diabetes mellitus (3). It is estimated that 50% of females experience at least one UTI in their lifetime due to their short urethra that allows bacteria to easily reach the bladder from the anal region to cause ascending infection. This also applies to female children whose anus are usually wiped towards the genital area by most parents during body hygiene, which increase the risk of UTI in young girls (1). The urinary retention caused by uterine atony during pregnancy and at menopause may also contribute to bacterial proliferation in the urine (4). UTI result in considerable public health burdens, healthcare cost and societal costs such as time missed from work (3,5).

Antibiotics are currently the most recommended therapeutics for patients with UTI (5). These antimicrobials mostly belong to the classes of aminoglycoside, carbapenem, cephalosporin, penicillin and quinolone (6-8). However, antibiotic treatment of UTI is now challenged by the emergence and spread of multi-drug resistant (MDR) pathogens due to worldwide misuse of antibiotics (6-8). Limited access to quality, safe, efficacious, and affordable medical products also contribute to the emergence of antimicrobial resistance (AMR) in Democratic Republic of the Congo (DRC).

The mechanisms of resistance to antibiotics include inactivation of drug by microbial enzymes, enhanced drug efflux, limited uptake of drug, and alterations of the drug target (9). The presence of acquired plasmids encoding extended-spectrum β-lactamases (ESBLs) in some uropathogens such as *E. coli* and *K. pneumoniae* may also explain the rapid transmission of AMR pathogens in humans (3,10). Additionally, the emergence of class C β-lactamases (AmpC enzymes) and mobile-colistin-resistance (*mcr*) gene in certain bacterial strains is also associated with spread of multi-drug resistance (3,11).

These situations make the provision of appropriate antimicrobial therapies more challenging and the treatment of UTI more perplexing. This underlines the need for efficient strategies to promote better management of UTI, rational use of antibiotics and prevention of the emergence of MDR bacteria in our communities. Among these strategies, the determination of antibiotic sensitivity and resistance profiles of bacterial uropathogens is an affordable and easy way to constantly update the healthcare professionals about the status of antimicrobial susceptibility of urinary pathogens. The aim of this study therefore is to identify the most frequently encountered bacteria pathogens in urine samples of patients with clinical diagnosis of UTI at the Monkole Hospital Center, Kinshasa, DRC. In line with the World Health Organization (WHO) Global Action Plan (GAP) on AMR, the study also aimed to determine the resistance profile of these uropathogens to commonly used antibiotics as evidence for future guidance in UTI care in DRC.

Materials and method:

Study setting and population:

This study was conducted from June 1 2017 to May 31 2018 at the Monkole Hospital Center (MHC), a teaching hospital located in Mont-Ngafula, a township in Kinshasa Province in the western DRC. This healthcare facility is one of the health reference centers in Kinshasa, a city of more than 12 million inhabitants. The MHC provides medical care to approximately 100,000 people for both in-patient and outpatient annually. This study population consisted of both inpatients and outpatients with clinical suspicion of UTI.

Study design:

This study was a retrospective observational review of uro-cultures of patients with clinical symptoms and signs suggestive of UTI at MHC from June 2017 to May 2018.

Data were retrieved from the hospital registers on all patients with UTI irrespective of gender and age within the study period.

Ethical consideration:

The study was approved by the Medical and Directory Board of Monkole Health Center, Kinshasa, DRC. Data were carefully handled to avoid any link with the patient's identity to safeguard anonymity.

Specimen culture and bacteria identification:

During the period of study reviewed, urinary samples were aseptically collected in disposable sterile containers from both inpatients and outpatients including voided and catheter urine specimens. All the specimens were cultured within 30 minutes of collection in the biomedical laboratory of MHC on either MacConkey agar (MAC) or Cystine-Lactose-Electrolyte-Deficient (CLED) agar media (Becton Dickinson, Heidelberg, Germany). Urine samples were inoculated with calibrated platinum loop (0.01 ml) on the culture plates, and incubated aerobically at 37°C for 24 hours. Urine cultures with colonies count of ≥ 10^5 CFU/ml were considered indicative of UTI and were subjected to further analysis for bacterial pathogen identification.

For bacterial identification, colonies growing on culture plates were identified to species level using the integral system enterobacteria (Liofilchem, Roseto DA, Italy) and Vitek® 2 automated system (BioMérieux, Craponne, France) in line with manufacturer's instructions.

Antibiotic susceptibility test:

The antimicrobial susceptibility test was performed on each isolate using the integral system enterobacteria (Liofilchem, Roseto DA, Italy) and Vitek® 2 automated system (BioMérieux, Craponne, France) in line with the manufacturer's instructions. Sixteen antibiotics were used; imipenem, piperacillin-tazo bactam, amikacin, nitrofurantoin, fosfomycin, levofloxacin, amoxicillin-clavulanic acid, ciprofloxacin, cefotaxime, norfloxacin, ofloxacin, doxycycline, cotrimoxazole, cefuroxime, cefixime and cephalexin.

Statistical analysis:

Statistical analysis of data was done using R studio. Data visualization was done with boxplot, interaction plot and ggline. Levene's test was used to assess homogeneity of variance and Shapiro-Wilk test to assess how close the data fit to a normal distribution. Two-way analysis of variance was used to test for significance of more than two means of continuous variables, and Pearson's Chi-squared test was used to compare the frequency of *E. coli* and *K. pneumoniae* and their antimicrobial resistance profiles in the analyzed samples. The significance level was $p<0.05$.

Results:

Results of data assessment:

The data assessment for linearity using Shapiro-Wilk test showed normally distributed population ($p>0.05$), and this was confirmed by the trend observed in the normal probability plot (Fig 1), in which almost all observations lie approximately on the straight line. The Levene's test for equality of variance of all observations confirmed that the variance is equal ($p>0.05$), hence the assumption check for the two-way ANOVA was met and the two-way ANOVA result is summarized in Table 1.

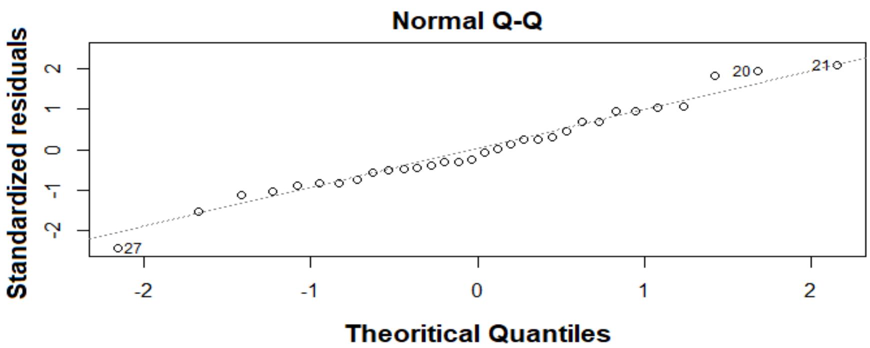

Fig 1: Normal probability plot

Table 1: Two-way analysis of variance

	Df	Sum Sq	Mean Sq	F value	p value
Antibiotic	1	13,970	13,970	188.633	$5.79\ e^{-14}$
Pathogen	1	1	1	0.017	0.896
Antibiotic: Pathogen	1	45	45	0.602	0.444
Residuals	28	2,074	74		

Frequency of bacterial pathogens in UTI:

During the 12-month study period, 2765 uro-cultures were reviewed and 809 (29.3%) were positive for significant bacterial pathogens with *E. coli* and *K. pneumoniae* the most prevalent (Table 2 and Fig 2). *Escherichia coli* was the single most frequently isolated bacterial pathogen (57.2%, n=463) followed by *K. pneumoniae* (14.8%, n=120) and other uropathogens (28.0%, n=226).

Of the total 809 isolates, 806 (99.6%) are Gram-negative bacteria belonging to 5 orders, 10 families, 18 genera and 35 species of bacteria (8 of which could not be identified to the exact species level) while 3 (0.4%) are Gram-positive belonging to 2 orders, 2 families, 2 genera and 3 species of bacteria (Table 2). The most frequently isolated species other than *E. coli* and *K. pneumoniae* are *Klebsiella oxytoca*, *Enterobacter cloacae, Citrobacter freundii, Serratia fonticola, Pseudomonas aeruginosa, Proteus mirabilis* and others, constituting 28% (n=226) of the uropathogens (Table 2).

Table 2: Frequency distribution of order, family, genera and species of bacterial uropathogens isolated from patients with urinary tract infection in Monkole Hospital Center, Kinshasa, Democratic Republic of the Congo

Order	Family	Genus	Species	Frequency
Gram negative				
Enterobacterales	Enterobacteriaceae	Escherichia	*Escherichia coli*	463 (57.2)
		Klebsiella	*Klebsiella pneumoniae*	120 (14.8)
			Klebsiella oxytoca	24 (3.0)
		Enterobacter	*Enterobacter cloacae*	43 (5.3)
			Enterobacter aerogenes	12 (1.5)
			Enterobacter hafnia	11 (1.4)
		Citrobacter	*Citrobacter* spp	39 (4.8)
			Citrobacter freundii	4 (0.5)
			Citrobacter koseri	1 (0.1)
		Arizona	*Arizona* spp	30 (3.7)
		Salmonella	*Salmonella* spp	1 (0.1)
		Raoultella	*Raoultnella ornithinolytica*	3 (0.4)
	Yersinaceae	Serratia	*Serratia fonticola*	4 (0.5)
			Serratia liquefaciens	4 (0.5)
			Serratia spp	9 (1.1)
			Serratia odorifera	1 (0.1)
			Serratia rubidaea	1 (0.1)
	Morganellaceae	Morganella	*Morganella morganii*	1 (0.1)
		Proteus	*Proteus mirabilis*	6 (0.7)
			Proteus vulgaris	2 (0.3)
		Providencia	*Providencia rettgeri*	2 (0.2)
			Providencia stuartii	1 (0.1)
	Hafniaceae	Edwardsiella	*Edwardsiella* spp	2 (0.3)
	Erwiniaceae	Pantoea	*Pantoea* spp	1 (0.1)
Pseudomonadales	Pseudomonadaceae	Pseudomonas	*Pseudomonas aeruginosa*	5 (0.6)
			Pseudomonas spp	3 (0.4)
			Pseudomonas oryzihabitans	2 (0.2)
			Pseudomonas paucimobilis	2 (0.2)
			Pseudomonas luteola	1 (0.1)
			Pseudomonas putida	1 (0.1)
	Moraxellaceae	Acinetobacter	*Acinetobacter baumannii*	3 (0.4)
			Acinetobacter lwoffii	1 (0.1)
Sphingomonadales	Sphinomonadaceae	Sphingomonas	*Sphingomonas paucimobilis*	2 (0.3)
Aeromonadales	Aeromonadaceae	Aeromonas	*Aeromonas* spp	1 (0.1)
Neisseriales	Neisseriaceae	Chromobacterium	*Chromobacterium violaceum*	1 (0.1)
Gram positive				
Bacillales	Staphylococcaceae	Staphylococcus	*Staphylococcus cohnii*	1 (0.1)
			Staphylococcus saprophyticus	1 (0.1)
Actinomycetales	Micrococcaceae	Kocuria	*Kocuria kristinae*	1 (0.1)
Total				**809 (100)**

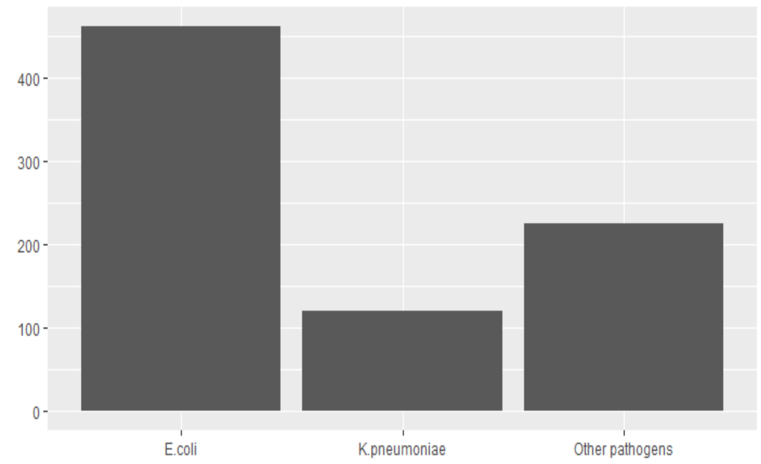

Fig 2: Frequency of isolation of bacterial pathogens from urine of patients with suspected urinary tract infection in Monkole Health Center, Kinshasa, DRC.

Resistance profiles of *E. coli* and *K. pneumoniae* isolates:

The resistance profile showed that both pathogens exhibited highest resistance to cephalexin while *E. coli* exhibited least resistance to imipenem (0%) and *K. pneumoniae* to piperacillin-tazobactam (5.1%) as shown Fig 3a, Fig 3b, Fig 4 and Table 3. Both *E. coli* and *K. pneumoniae* had similar trend in resistance rates (p>0.05) to most of the antibiotics; piperacillin-tazobactam, amikacin, levofloxacin, norfloxacin, amoxicillin-clavulanic acid, cefotaxime, cefuroxime, cefixime, cephalexin and doxycycline (Fig 3b, Table 3).

By bivariate analysis however, the resistance rates of *E. coli* compared to *K. pneumoniae* were significantly higher to cotrimoxazole (OR=2.060, p=0.002), ofloxacin (OR=3.427, p=0.0019), ciprofloxacin (OR= 1.624, p=0.0442), and significantly lower to imipenem (OR=0.03704, p=0.0049), nitrofurantoin (OR=0.2930, p=0.0004) and fosfomycin (OR=0.3112, p=0.0003) (Table 3).

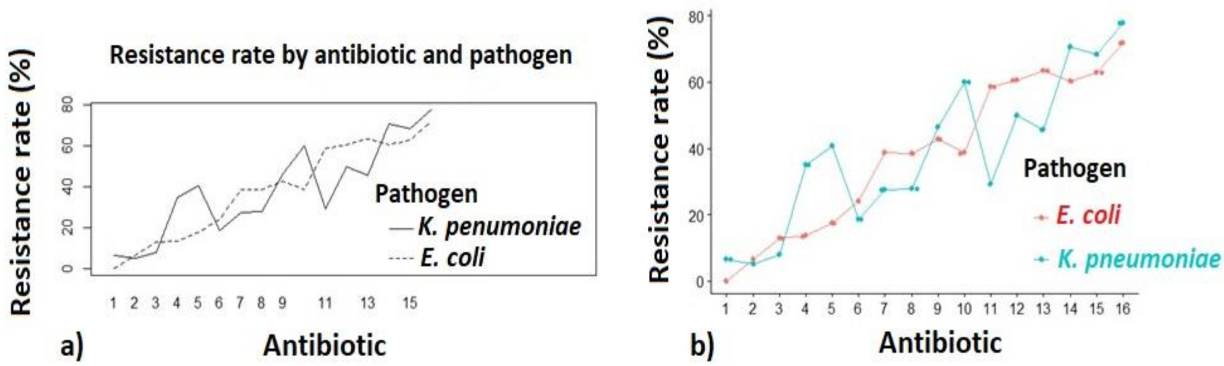

Fig 3. Interaction plot (a) and line plot (b) for resistance rate by antibiotic and pathogen. Antibiotics are codified from 1 to 16 as shown in Table 2.

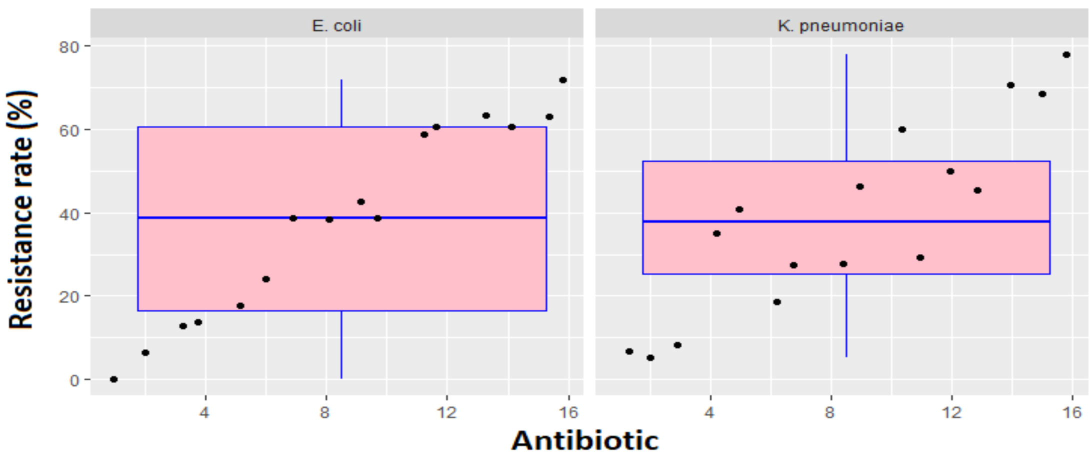

Fig 4: Boxplot distribution of resistance rate of *E. coli* and *K. pneumoniae* to antibiotics

Table 3: Comparative frequency of resistance of urinary *Escherichia coli* and *Klebsiella pneumoniae* isolates to sixteen selected antibiotics routinely used in Monkole Hospital Center, Kinshasa, Democratic Republic of the Congo

S/N	Antibiotic name	Percentage (number) Resistance to *Escherichia coli*	Percentage (number) Resistance to *Klebsiella pneumoniae*	x^2	COR (95% CI)	P value
1	Imipenem	0 (0/172)	6.6 (4/61)	7.918	0.03704 (0.00196-0699)	0.0049*
2	Piperacillin-Tazobactam	6.5 (26/402)	5.1 (5/99)	0.849	0.787 (0.345-1.795)	0.7707
3	Amikacin	13 (55/422)	8.1 (8/99)	1.414	1.705 (0.7842-3.706	0.2345
4	Nitrofurantoin	13.6 (25/184)	34.9 (22/63)	12.51	0.2930 (0.1502-0.5715	0.0004*
5	Fosfomycin	17.6 (49/278)	40.7 (22/54)	13.02	0.3112 (0.1667-0.5812)	0.0003*
6	Levofloxacin	24.2 (79/327)	18.7 (14/75)	0.749	1.389 (0.7364-2.616)	0.3868
7	Amoxicillin-Clavulanic acid	38.8 (59/152)	27.5 (14/51)	1.677	1.677 (0.8357-3.364)	0.1954
8	Ciprofloxacin	38.4 (168/437)	27.8 (30/108)	3.811	1.624 (1.022-2.580)	0.0442*
9	Cefotaxime	42.7 (194/454)	46.4 (52/112)	0.361	0.8609 (0.5683-1.304)	0.5482
10	Norfloxacin	38.6 (17/44)	60 (12/20)	1.744	0.4198 (0.1424-1.238)	0.1867
11	Ofloxacin	58.6 (78/133)	29.3 (12/41)	9.688	3.427 (1.609-7.301)	0.0019*
12	Doxycycline	60.5 (23/38)	50 (6/12)	0.095	1.533 (0.4156-5.658)	0.7576
13	Cotrimoxazole	63.3 (274/433)	45.5 (46/101)	10.00	2.060 (0.1330-3.192)	0.0016*
14	Cefuroxime	60.4 (32/53)	70.6 (12/17)	0.221	0.6349 (0.1951-2.066)	0.6385
15	Cefixime	63 (34/54)	68.4 (13/19)	0.022	0.7846 (0.2575-2.391)	0.8817
16	Cephalexin	71.8 (28/39)	77.8 (14/18)	0.235	0.7273 (0.1958-2.701)	0.8782

Numbers in brackets indicate the proportion of resistant isolates to total number of isolates tested per antibiotic; x^2=Chi square, COR=Crude Odd Ratio; CI=Confidence Interval; S/N = serial number of antibiotics; * = statistically significant at $p<0.05$

Discussion:

This study reports *E. coli* prevalence of 57.3% among bacterial pathogens isolated from patients with clinical UTI during the one-year period of study (June 2017 and May 2018) at Monkole Health Center in Kinshasa, Democratic Republic of the Congo. *Escherichia coli* is a commensal bacterium of the human intestinal microbiota, which is highly frequent in faecal samples, as reported recently in a study conducted among Congolese students (12). Due to the anatomic proximity of the anal zone to the genito-urinary area in humans, poor hygiene may justify the high incidence of *E. coli* in UTI as this bacterium can easily colonize the urinary tract and predispose to UTI (13).

The prevalence of *E. coli* in our study is comparable to the 58.5% reported in North Kivu province in the eastern part of DRC, and to the prevalence reported in previous studies from different countries worldwide (10, 14-19). However, a few studies have reported different rates where *E. coli* accounted for less than 20% of UTI cases (20,21). These differences suggest the existence of remarkable variability in the prevalence of uropathogens from one place to another. On the other hand, the prevalence of 14.8% reported for *K. pneumoniae* is within the range of 13-18% reported from studies conducted in the province of Kivu, DRC as well as from other countries such as Algeria, Bangladesh, Equatorial Guinea and Morocco (14,16,22,23), but higher than 2-9% rate reported from studies conducted in Honduras, Nigeria, China and Oman (10,15,17,24,25). Also, the prevalence of rare uropathogens in our study (~28%) agrees with the findings of a study conducted in Central Europe between 2011 and 2019 (14).

The urinary *E. coli* and *K. pneumoniae* isolates in our study showed high resistance to most of the first and second line oral and parenteral antibiotics such as cotrimoxazole, ofloxacin, ciprofloxacin, levofloxacin, amoxicillin-clavulanate and cefuroxime commonly used in Kinshasa, confirming the existence and challenges of AMR in bacterial uropathogens in DRC. Levofloxacin and nitrofurantoin remain the drug of choice among oral antibiotics, and have been advocated as first-line treatment of UTI in Kinshasa in line with international guidelines, yet the average resistance rate of *E. coli* and *K. pneumoniae* to both antibiotics in our study is over 20%, which is a warning sign of emerging resistance to them (26,27). Although norfloxacin and ofloxacin are recognized in several countries as effective fluoroquinolones against bacterial uropathogens, resistance rates in the present study varies from 30 to 60% for both *E. coli* and *K. pneumoniae,* which indicates that these antibiotics may not be effective in treatment of UTI in DRC.

The high resistance profile to antibiotics observed in this study can be accounted for by the overuse of these antibiotics leading to long-term exposure of both *E. coli* and *K. pneumoniae* to these antibiotics in Kinshasa. Indeed, most healthcare practitioners often prescribe one of these drugs for treatment of UTI, and sometimes without laboratory evidence of antibiotic susceptibility testing on these isolates. In addition to this, self-medication is a driving factor as this practice is associated with inappropriate use of antibiotics. Therefore, there is a need to reinforce control measures for antibiotic use and protect available antimicrobials from misuse in order prevent or delay emergence of resistance to them. This is the case for antibiotics such as imipenem, piperacillin-tazobactam and amikacin which can be proposed as second-line antibiotics for treatment of UTIs in Kinshasa, in line with the World Health Organization AWaRe categorization of antimicrobials (28). The observed low resistance rate of both pathogens to these antibiotics may be explained by the fact that they are not commonly prescribed in Kinshasa owing to their limited availability in open market.

Our findings should provide reliable information to assist practitioners who usually treat UTI empirically. Nevertheless, it should be noted that empirical antibiotic therapy based on epidemiological data does not always consider variations in susceptibility that may occur temporally and locally (or even regionally). This situation may lead to the emergence of MDR bacteria. Consequently, it will be important to emphasize antimicrobial therapy based on susceptibility patterns of pathogens. In this way, it will be possible to streamline the use of antibiotics and guarantee that they are as effective as possible in treatment of UTIs by using only molecules that demonstrate good results in susceptibility tests, thereby reducing the over exposure of bacteria to other antibiotics. Our findings should also set the stage for the establishment of a public health database for antimicrobial resistance surveillance as well as for the implementation of local policies for the rational use of antibiotics in DRC. Indeed, it is of great importance for hospitals and institutional care to know and update their local resistance profiles to antibiotics since empirical antibiotic therapy is based on epidemiological data. This strategy may reduce the medical costs as well as the morbidity and mortality rates caused by UTI. On the other hand, epidemiological databases may serve as a referential tool ensuring effective implementation of the policy adopted for UTIs management. They also make possible the identification of new points of intervention for controlling antimicrobial resistance.

In line with the above and considering the temporal and geographic variations in antimicrobial susceptibility, further investigations are needed nationwide to tackle the emergence and spread of antimicrobial resistance in DRC. In this context, public and professional education coupled with general awareness programs on the importance of good personal hygiene and environmental sanitation are of interest. Moreover, the promotion and evaluation of medical and veterinary practice guidelines constitute critical issues to tackle antimicrobial resistance. Excessive use of antibiotics in animal health and production has been identified among the driving forces of antimicrobial resistance (29,30). Therefore, in the context of "One Health", good antimicrobial stewardship at the hospital, in the animal sector as well as at the community level is crucial to slow down the emergence of antibiotic resistance.

In addition, curbing the spread of antibiotic-resistant pathogens in Kinshasa will also entail dealing with the promotion of affordable healthcare as well as fighting against substandard and counterfeit drugs.

We acknowledged some limitations of this study. For instance, the antimicrobial susceptibility testing of the uropathogens was simultaneously performed on both inpatients and outpatients, which makes it impossible to determine the susceptibility rates of bacteria to antibiotics in each group of patients. Moreover, the lack of distinction between community and hospital-acquired infections did not allow further investigations of the risk factors that may influence drug management and preventive measures. Being a retrospective review, there is the limitation of data accessibility and completeness, which did not allow us to include data beyond 2018 in the analysis. Therefore, future studies should focus on addressing these limitations and conducting cross-sectional or prospective cohort studies that can generate complete data.

Conclusion:

Our study showed that *E. coli* is the most frequent bacterial uropathogen isolated from patients with clinically suspected UTI at MHC, Kinshasa, DRC. We also observed that both *E. coli* and *K. pneumoniae* exhibited high resistance rates to the first and second-line antibiotics such as cotrimoxazole, levofloxacin, ofloxacin, ciprofloxacin, cefuroxime and cefotaxime used in DRC. Amikacin, piperacillin-tazobactam and imipenem were the most effective antibiotics with the pathogen demonstrating least resistance to them .

To guarantee optimal therapy of UTI, regular surveillance of AMR pathogens and generation of periodic antibiogram are required to guide empirical therapy. Further studies are needed to determine the national prevalence of nosocomial and community-acquired UTI and the antimicrobial resistance profiles of uropathogens. There is a dire need to develop the DRC national action plan to tackle AMR, which should be implemented following the "One Health' approach.

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Contributions of authors:

GKM was involved in study conceptualization, investigation, methodology, data collection, data analysis, resource provision, validation, visualization, writing the first manuscript draft, review and editing; FNL was involved in formal analysis, investigation, methodology, resource provision, validation, review and editing; OKK was involved in investigation, methodology, review and editing; JMIL was involved in investigation, methodology, review and editing; LMT was involved study conceptualization, formal analysis, methodology, project administration, validation, review and editing; PBM was involved in study conceptualization, formal analysis, resource provision, supervision, validation, review and editing, and fund acquisition.

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Conflict of interest:

Authors declare no conflict of interest

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