African Journal of Urology (2017) **23**, 166–171

African Journal of Urology

Official journal of the Pan African Urological Surgeon's Association
web page of the journal

www.ees.elsevier.com/afju
www.sciencedirect.com

Infections and Inflammation
Original article

Antimicrobial susceptibility profile of community-acquired urinary tract infection in adults: A seven months prospective cross-sectional study in Dakar Town, Senegal☆

M.S. Barry[a,d,*], **B.A. Diallo**[b], **D. Kanté**[c], **I.S. Diallo**[d]

[a] *Medical Affairs Department, Sanofi West Africa, Senegal*
[b] *Department of Gynecology, University of Conakry, Guinea*
[c] *Department of Urology, University of Conakry, Guinea*
[d] *Institute of Infant Nutrition and Health (INSE), Guinea*

Received 26 May 2016; received in revised form 31 October 2016; accepted 30 November 2016
Available online 28 April 2017

KEYWORDS
Urinary tract infections;
Antibiotic susceptibility;
Community-acquired infections;
Developing country

Abstract
Introduction: With the increasing trend of antibiotic resistance, the management of urinary tract infection (UTI) is likely to become complicated, and there is a need for continuous surveillance of antibiotic susceptibility of uropathogens.
Objective: This study aimed to assess the current antimicrobial susceptibility pattern in the common uropathogens isolated from outpatients and hospitalized (<72 h).
Subjects and methods: This was a prospective observational study examining urinary isolates from patients aged ≥18 years. Urine samples were collected from 494 consecutive outpatient adults, clinically-suspected cases of urinary tract infections. Bacterial identification and antimicrobial susceptibility testing were carried out using the VITEK® 2 Compact kit of bioMérieux.
Results: The observed prevalence of UTI was (132/494) 26.7%, 95% CI [22.9%; 30.9%]. Among the 147 organisms isolated from 132 patients, more than 90% (133) were Gram-negative bacteria. Imipenem appeared as the most active drug, with less than 3% resistance of isolates. Amikacin and cefotaxim were in general active with susceptibility rate of 70% and 67% of isolates, respectively. However cefixim was the most active oral drug tested (61%). Trimethoprim/sulfamethoxazole, nalidixic acid and fluoroquinolons were the less active drug displaying a resistance rate of 73%, 69% and 60% respectively.

☆ This work is attributed to the Department of Urology at University of Conakry.

* Correspondence to: Sanofi—Afrique de l'Ouest, Immeuble EPI—43 Rue de Ziguinchor—PE 43, BP 3529 Dakar, Senegal.
E-mail addresses: mamadou-saidou.barry@sanofi.com, saidou_barry@hotmail.com (M.S. Barry), diallolarewel@yahoo.fr (B.A. Diallo), daoudak68@gmail.com (D. Kanté), diallopediatrie@yahoo.fr (I.S. Diallo).

Peer review under responsibility of Pan African Urological Surgeons' Association.

http://dx.doi.org/10.1016/j.afju.2016.11.005

Conclusion: Trimethoprim/sulfamethoxazole, nalidixic acid and fluoroquinolons should no longer be used as empirical treatments of UTI in Dakar. Alternatives must be recommended, such as cefixim the most active oral drugs available in this country.

Introduction

Urinary tract infection (UTI) is one of the most commonly encountered diseases by clinicians in developing countries, with an estimated annual global incidence of at least 150 million [1]. UTI refers to the presence of microbial pathogens within the urinary tract and can be asymptomatic or symptomatic [2]. Clinically, UTIs are categorized as uncomplicated or complicated. An uncomplicated UTI typically affects healthy individual who has no structural or neurological urinary tract abnormalities, and who is not pregnant or has not been catheterized [3]. All other UTIs are considered complicated.

Many different microorganisms can cause UTIs and the relative frequency of the pathogens varies depending upon age, sex, catheterization, and hospitalization, though the most common pathogens causing the simple ones in the community are *Escherichia coli* and other Enterobacteriacae [4].

Patients suffering from a symptomatic UTI are commonly treated with antibiotics. In the majority of community-acquired UTI, treatment decision is empiric, based on etiological microorganisms and available data reflecting antibiotic resistance, as indicated in certain recommended guidelines [5–7]. Considering the fact that resistance rates to antimicrobials commonly used in the treatment of UTI is increasing and susceptibility of microorganisms shows significant geographical variations [8], regular surveillance of resistance patterns at local level is necessary to guide clinicians in empiric treatment.

Two multicenter studies [9,10] conducted in Dakar city in 2001 and 2004–2006, respectively, showed dramatically high rates and increasing trend of resistance to the antibiotics frequently used in the community. Therefore, as the problem of antimicrobial resistance becomes more widespread, the management of UTI is likely to become complicated, and there is a need for continuous surveillance of antibiotic susceptibility of uropathogens.

In light of the above, the present study was undertaken to assess the current antimicrobial susceptibility pattern in the common uropathogens isolated from outpatients and hospitalized (<72 h) in Dakar Town.

Subjects and methods

This was a prospective observational study examining urinary isolates from patients aged ≥18 years.

Site and patient selection

From August 2012 to March 2013, outpatients were recruited from hospitals and clinics located in Dakar: hospital of Le Dantec, Mermoz Polyclinic, Pasteur clinic, SOS medical clinic, clinic of Madeleine, Fann Hock clinic, Cap clinic, and others general practitioners. This panel of health care settings was chosen to allow recruitment of patients coming from different social classes. An information letter was sent to many practitioners at different setting inviting them to participate to the study. Sixty-eight physicians gave their consent. The study included all patients having clinical evidence of UTI with symptoms presenting at the outpatient department of hospitals/clinics and those admitted for less than 72 h. All patients sampled gave consent to participate in the study.

Data collection and sample examination

A standard questionnaire was used to collect clinical and demographic data. Patient demographics information including age and gender was collected by physicians at the patient inclusion. Furthermore, physician collated information related to clinical variables, such as presence of urinary tract infection symptoms, use of antibiotics during the last 30 days and associated diseases. Fresh urine samples were collected at the Laboratoire Bio24. For admitted patients, urine sample was collected at the hospital site and immediately sent to the laboratory.

Urine samples of 10 mL were collected in a sterile container via the clean-catch midstream technique. Specimen was first examined macroscopically in order to evaluate general appearance including color and turbidity. Then, microscopic examination was done using the KOVA® cell for leukocyte and erythrocyte count, and the presence of bacteria, parasites, yeasts and crystals was assessed. Finally, culture for uropathogens isolation and count was performed in inoculating 10 μL of homogenized urines onto Chromogenic agar medium CPS3® BioMérieux and incubated at 37 °C for 18–24 h.

Depending on the number of colonies grown and with due clinical correlation as per recommendation, a specimen was considered positive for UTI if a single organism was cultured at a concentration of greater than 10^3 CFU/mL for the predominant uropathogens (i.e *E. coli*, *Staphylococcus saprophyticus*), >10^4 CFU/mL in case of the other common causes of UTI (i.e. other Enterobacteriaceae spp., *Enterococcus* spp., *Pseudomonas aeruginosa*), and >10^5 CFU/mL for the rare causes of UTI (i.e. *Streptococcus agalactiae, Acinetobacter baumanii*).

Bacterial identification and antimicrobial susceptibility testing were carried out using the VITEK 2 Compact® kit of BioMérieux. Testing was not performed for antibiotics to which organisms are known to be non-susceptible.

Data management and statistical analysis

Data were entered using CSPro version 5, and then transferred for analysis into Statistical Package for Social Science (SPSS)

Table 1 Demographic and clinical characteristics of all participants and from who pathogens were isolated, Dakar city.

	Number of patients screened (N = 494)	%	Number of patients with significant bacteriuria (N = 132)	%
Sex				
Male	375	75.9	102	77.3
Female	119	24.1	30	22.7
Age				
18–39 years	152	30.8	21	16.0
40–59 years	113	22.9	31	23.5
≥60 years	229	46.3	80	60.5
Duration of symptoms				
0–7 days	131	29.0	36	31
8–15 days	106	23.5	32	27.6
16–30 days	143	31.7	33	28.4
>30 days	71	15.7	15	12.9
Antibiotic use last 30 days				
Yes	86	18.0	23	23
No	391	82.0	77	77

program for Windows Version 19.0 (SPSS 19.0 Chicago Inc. III, USA). Susceptibility rate to antibiotics was analyzed for overall isolates, Gram-negative bacteria, and for *E. coli*.

Study proposal was approved by the National Committee of Ethics of the Ministry of Health and Social Action, Senegal.

Results

Demographic and clinical characteristics of registered patients in this study are presented in Table 1. Pathogens were isolated from 132 of the 494 adults who submitted urine samples, which represent an observed UTI prevalence rate of 26.7%, 95% CI [22.9%; 30.9%]. According to age (mean 61 ± 18), patients with significant bacteriuria were classified in three categories: 18–39 years (16%), 40–59 years (23.5%) and ≥60 years (60.5%). Fifteen (11.3%) patients presented a co-infection and therefore 147 microbial isolates were found.

Patient was considered having clinically UTI, if investigators noted one or more of the following symptoms: dysuria, pollakiuria/polyuria, nocturia, urinary urgency, present or increased incontinence, Haematuria, turbid urine and fever with flank pain. Urinary infection symptoms were reported for 451 (91%) participants and data were missing for 43 patients. The duration of the symptoms was ≤15 days for more than half (52.5%) of patients, and 71 (15.7%) subjects presented infection symptoms since at least 30 days. Among patients with significant bacteriuria, twenty three (23%) of them had use antibiotic therapy during the past 30 days. Of these patients, 102 (77.3%) were male and 30 (22.7%) were females.

Of the 147 organisms isolated, more than 90% (133 isolates) were Gram-negative bacteria (Table 2). *E. coli* (50.3%), *Klebsiella* (14.3%), *P. aeruginosa* (9.5%) and *Enterobacter cloacae* (6.8%) were the predominant (>80%) isolates associated with UTI, while Gram-positive organisms constituted 9.5% of isolates.

Overall susceptibility of isolates is summarized in Table 3. With less than 3% of isolates' resistance, imipenem appeared as the most active drug. Trimethoprim/sulfamethoxazole (TMP–SMX), nalidixic acid and fluoroquinolones (ciprofloxacin, ofloxacin) displayed a resistance rate exceeding 60%. The third generation of cephalosporin (cefixim, cefotaxim) and amikacin was globally active, with susceptibility rate as high as 60%. Among Gram-negative isolates, imipenem against appeared the most active agent with susceptibility rate of 98% of isolated bacteria. Amikacin, cefotaxim and cefixim were also active. However, susceptibility rate of isolates to TMP–SMX, and fluoroquinolones was very low. Similar figure of susceptibility to antibiotics was observed for *E. coli* strains, except with nitrofurantoin drug which showed a resistance rate less than 20%.

Table 2 Distribution of uropathogens isolated from community-acquired infection, Dakar city.

	Number of isolates	%
Gram-negative bacilli		
Escherichia coli	**74**	**50.3**
Klebsiella (*pneumoniae, oxytoca*)	21	14.3
Pseudomonas (*aeruginosa*, sp.)	14	9.5
Enterobacter cloacae	10	6.8
Providencia (*rettgeri, stuartti*)	5	3.4
Morganella morganii	4	2.7
Acinetobacter baumanii	2	1.4
Proteus vulgaris	1	.7
Burkholderia cepacia	1	.7
Shigella dysenteria	1	.7
Gram-positive cocci		
Enterococcus (*faecalis, faecium*)	8	5.4
Staphilococcus (*saprophiticus, homonis,* sp.)	4	2.7
Aerococcus viridams	2	1.4
Total	147	100.0

Discussion

This study aimed to assess susceptibility profile of isolated bacteria from adult urinary tract infections. Of the 494 adults enrolled in this study, pathogens were isolated from 132 (26,7%) patients with 147 isolates. Gram-negative bacteria represented the majority of isolates

Table 3 Susceptibility profile of pathogens isolated from community-acquired urinary tract infections to various antibiotics drugs.

	All isolates				Gram-negative isolates				*Escherichia coli* strains			
	Number of isolates	Susceptible	Intermediate	Resistant	Number of isolates	Susceptible	Intermediate	Resistant	Number of isolates	Susceptible	Intermediate	Resistant
Amoxicillin/clavulanic acid	117	41%	9%	50%	116	41%	9%	49%	74	51%	9%	39%
Cefixim	102	61%	1%	38%	101	60%	1%	39%	60	75%	2%	23%
Cefotaxim	113	67%	4%	29%	113	67%	4%	29%	71	82%	1%	17%
Imipenem	142	97%	1%	2%	132	98%	1%	1%	74	100%	0%	0%
Amikacin	132	70%	20%	9%	131	70%	21%	9%	74	74%	23%	3%
Nalidixic acide	116	31%	0%	69%	116	31%	0%	69%	74	35%	0%	65%
Ciprofloxacin	139	39%	1%	60%	130	37%	2%	62%	73	45%	1%	53%
Ofloxacin	119	38%	2%	61%	118	37%	2%	61%	74	43%	3%	54%
Nitrofurantoin	116	48%	16%	36%	116	48%	16%	36%	73	74%	7%	19%
Trimethoprim/sulfamethoxazole	134	25%	1%	73%	121	23%	2%	75%	70	21%	1%	77%

(>90%). Globally, bacterial pathogens isolated were susceptible to four of the ten antimicrobial tested: imipenem, amikacin, cefotaxim and cefixim. Imipenem was the most active agent among isolates, whereas, TMP–SMX, nalidixic acid and fluoroquinolones were the most inactive antimicrobial.

The majority of patients with significant bacteriuria were male (77.3%). This observation is uncorrelated with known distribution of UTIs in relation with sex, with higher occurrence among females [1], because women are mostly vulnerable due to their anatomy and reproductive physiology [11]. The predominance of males in this study was expected, as majority of included patients were recruited from urology services, where consultations for suspected UTI are less frequent among women.

The findings of this study confirmed the predominance of Gram-negative bacteria in the epidemiology of urinary tract infections [3], particularly *E. coli* which seemed the major etiological pathogen accounting for more than health of uropathogens isolated. However, the frequency of *E. coli* is likely decreasing in Dakar as its proportion failed between 2001 and 2006, from 77% to 54%, respectively [9,10], and to finally reach 50% in this study.

Antibiotics are usually used to treat patients suffering from a symptomatic UTI. The most common antimicrobial agents used include β-lactams, TMP–SMX, and fluoroquinolones. Nevertheless, these treatments can result in long-term alteration of the normal microbiota of the vagina and gastrointestinal tract and in the development of multidrug-resistant microorganisms [11,12]. Overall susceptibility data indicate that the first line drugs exhibited low susceptibility rate. In general, TMP–SMX, nitrofurantoin, nalidixic acide, fluoroquinolones and amoxicillin-clavulanic acid were the most inactive drugs as they showed a susceptibility rate less than 50%. The figure remained the same with regard to disaggregated susceptibility analysis (Gram-negative bacteria and *E. coli*), except for nitrofurantoin which was effective against *E. coli* strains with susceptibility rate of 74%.

This finding is consistent with that reported in other African studies [13,14], and an increasing resistance to fluoroquinolones and TMP–SMX has been noted internationally [8]. In clinical practice in West African countries, physicians often start antibiotic therapy with inexpensive and well known broad-spectrum agents, such as ciprofloxacin and TMP–SMX, and this could explain why they displayed high level of resistance. The International clinical practice guidelines [6] suggest that when resistance rate is known to exceed 20%, TMP–SMX should not be used empirically for treatment of uncomplicated cystitis in women.

The most active drug among uropathogens isolated in this study was imipenem, the only antibacterial that exhibited 97% susceptibility rate of all urine isolates and 100% of *E. coli* strains. Despite the fact that the majority of isolates were highly sensitive to imipenem, this drug should not nevertheless be recommended for empirical treatment due to its high purchase price and its route of administration (only injectable form existed).

In this study, amikacin displayed a good susceptibility rate among pathogens species isolated, with a resistance rate less than 10% of all Gram negative bacteria (3% for *E. coli*), and this observation is consistent with results reported in other countries [14–16]. In addition, amikacin have been shown to be effective (up to 94.1%)

against the extended-spectrum beta-lactamase (ESBL)-producing Gram-negative bacteria [16]. However, this drug is only commercialized in injectable form, which limits its usage empirically in the treatment of uncomplicated UTIs. Moreover, cefotaxim also exhibited a good affectivity against isolates (67% of all isolates and 82% of *E. coli* strains), but the resistance rate of Gram-negative bacteria was as higher as 29%, suggesting that this injectable drug could not be recommended as first line therapeutic for community-acquired UTIs.

Finally, the most effective oral antimicrobial agent tested in this study was cefixim, which displayed sensitivity up to 61% and 75% against all isolates and *E. coli* strains, respectively. Yet, nevertheless, more than 20% of *E. coli* strains, the most common pathogen isolated, were resistant to cefixim. Despite this resistance level, this antibiotic however appeared as the only suitable empirical treatment option for adults with community-acquired UTIs.

In view of the study results one might be tempted to think that combination therapy could be another treatment option. However, combination therapies are recommended [6,17,18] for nosocomial or catheter-related UTI, complicated UTI and management of multidrug resistance. On the other hand, multidrug resistance of uropathogens species isolated in this study was not evaluated, implying that future studies are needed in order to recommend more appropriate alterative treatment regimen. Furthermore, empirical treatment must be based on both antibiogram and patient specific characteristics [17], while this study failed to analyze susceptibility profile of isolates taking into account the severity of the infection and vulnerability of the patients such as underlying diseases.

Results of this study should be interpreted with caution. Despite the number of contributing sites (hospital and clinics), the majority of patients came from urology services, and consequently participants are older and often presented comorbidity. Therefore, breaking down susceptibility patterns for the whole Dakar city may not accurately represent these patterns. Nevertheless, the observed overall resistance rates of isolates are likely still relevant, as resistance of uropathogens is known to vary geographically [19,20]. Moreover, sub-groups analysis according to patient characteristics and severity of the infection were not performed, and thus, results of this study are unlikely to be generalized to every adult patient presenting with UTI.

In general practice, urine sample of patients with UTI are not routinely tested, and susceptibility testing is recommended only in cases of treatment failure or suspected complications [3–21]. Consequently, in the absence of more accurate local antimicrobial susceptibility pattern, the results of this study could serve as a valuable source for antibacterial drugs prescription in empirical treatment of UTI.

Conclusion

This study highlights the need for routine surveillance and monitoring studies to provide physicians with knowledge about the most effective empirical treatment of UTI. Globally, there was a high prevalence of bacterial pathogens with high resistance rate to commonly used antibiotics. The findings of the study suggested that TMP–SMX, nalidixic acid and fluoroquinolons should no longer be used as empirical treatments of UTI in Dakar. Imipenem and amikacin were the most active antibacterial among isolates. However, for empirical treatment of UTI, cefixim was the most active oral drug tested in this study and must be recommended as the first line of choice in this population.

Authors' contribution

MSB and BAD: conception of the study design; MSB and DK: data management and statistical analysis; MSB, BAD and DK: writing the first draft of the manuscript; ISD: reviewing the manuscript. All authors read and approved the manuscript.

Conflict of interests

The study was supported by Sanofi West Africa. MSB is an employee of Sanofi as Medical advisor. All other authors declare that they have no competing interests.

Source of funding

Sanofi West Africa.

Acknowledgments

The study was entirely sponsored by Sanofi West Africa. We thank the steering committee members, notably Dr. Tidiane Siby, Dr. Edgard Macondo, Dr. Papa Alassane Diaw and Dr. Rose Marie Diop Diouf. We appreciate the collaboration received from participating physicians who ensured inclusion of patients. We are grateful to Dr. Cheikh Tidiane Ndao for coordinating and monitoring the study implementation.

References

[1] Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. Urinary tract infections: epidemiology, mechanisms of infection and treatment options. Nat Rev Microbiol 2015;13(5):269–84.
[2] Foxman B. The epidemiology of urinary tract infection. Nat Rev Urol 2010;7(12):653–60.
[3] Stapleton AE. Urinary tract infection pathogenesis: host factors. Infect Dis Clin North Am 2014;28(1):149–59.
[4] Kumar MS, Ghosh S, Nayak S, Das AP. Recent advances in biosensor based diagnosis of urinary tract infection. Biosens Bioelectron 2016;80:497–510.
[5] Scottish Intercollegiate Guidelines Network (SIGN). Management of suspected bacterial urinary tract infection in adults. Edinburgh: SIGN; 2012. SIGN publication no. 88. Available at: http://www.sign.ac.uk. [Accessed February 2016].
[6] Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis 2011;52(5):e103–20.
[7] Société de Pathologie Infectieuse de Langue Française (SPILF). Recommandations de bonne pratique: Diagnostic et antibiothérapie des infections urinaires bactériennes communautaires de l'adulte. SPILF; 2015. Available at: http://www.infectiologie.com.
[8] Schito GC, Naber KG, Botto H, Palou J, Mazzei T, Gualco L, et al. The ARESC study: an international survey on the antimicrobial resistance of pathogens involved in uncomplicated urinary tract infections. Int J Antimicrob Agents 2009;34(5):407–13.

[9] Dromigny JA, Ndoye B, Macondo EA, Nabeth P, Siby T, Perrier-Gros-Claude JD. Increasing, prevalence of antimicrobial resistance among Enterobacteriaceae uropathogens in Dakar, Senegal: a multicenter study. Diagn Microbiol Infect Dis 2003;47(4):595–600.

[10] Sire JM, Nabeth P, Perrier-Gros-Claude JD, Bahsoun I, Siby T, Macondo EA, et al. Antimicrobial resistance in outpatient *Escherichia coli* urinary isolates in Dakar, Senegal. J Infect Dev Ctries 2007;1(3):263–8.

[11] Foxman B. Urinary tract infection syndromes: occurrence, recurrence, bacteriology, risk factors, and disease burden. Infect Dis Clin North Am 2014;28(1):1–13.

[12] Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. BMJ 2010;340:c2096.

[13] Akoachere JF, Yvonne S, Akum NH, Seraphine EN. Etiologic profile and antimicrobial susceptibility of community-acquired urinary tract infection in two Cameroonian towns. BMC Res Notes 2012;5:219.

[14] Mohammed MA, Alnour TM, Shakurfo OM, Aburass MM. Prevalence and antimicrobial resistance pattern of bacterial strains isolated from patients with urinary tract infection in Messalata Central Hospital, Libya. Asian Pac J Trop Med 2016;9(8):771–6.

[15] Gupta S, Kapur S, Padmavathi D. Comparative prevalence of antimicrobial resistance in community-acquired urinary tract infection cases from representative States of northern and southern India. J Clin Diagn Res 2014;8(9):DC09–12.

[16] Cho YH, Jung SI, Chung HS, Yu HS, Hwang EC, Kim SO, et al. Antimicrobial susceptibilities of extended-spectrum beta-lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae* in health care-associated urinary tract infection: focus on susceptibility to fosfomycin. Int Urol Nephrol 2015;47(7):1059–66.

[17] Hsueh PR, Hoban DJ, Carmeli Y, Chen SY, Desikan S, Alejandria M, et al. Consensus review of the epidemiology and appropriate antimicrobial therapy of complicated urinary tract infections in Asia-Pacific region. J Infect 2011;63(2):114–23.

[18] Grabe M, Bartoletti R, Bjerklund-Johansen TE, Cai T, Çek M, Köves B, et al. Guidelines on urological infections: urological infections—limited update. Eur Assoc Urol 2015;V2:237–57 Available at: http://uroweb.org/guideline/urological-infections/?type=archive.

[19] Erb A, Stürmer T, Marre R, Brenner H. Prevalence of antibiotic resistance in *Escherichia coli*: overview of geographical, temporal, and methodological variations. Eur J Clin Microbiol Infect Dis 2007;26(2):83–90.

[20] Boyle DP, Zembower TR. Epidemiology and management of emerging drug-resistant Gram-negative bacteria: extended-spectrum β-lactamases and beyond. Urol Clin North Am 2015;42(4):493–505.

[21] Ministère de la Santé, et de la Prévention. Recommandations nationales pour le bon usage des antibiotiques: Livret 2 Antibiothérapie des infections communautaires de l'adulte et de l'enfant. Version 2010. 1st edition.