Urinary tract infection among asymptomatic HIV patients in Benin City, Nigeria

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Accepted: 7 August 2009

ABSTRACT

The impact of human immunodeficiency virus (HIV) infection and CD4+ count on the prevalence of urinary tract infection (UTI) is studied to determine the prevalence of UTI among HIV and non-HIV subjects. Clean-catch midstream urine and venous blood was collected from 421 subjects comprising 317 HIV patients (89 men, 228 women) and 104 non-HIV subjects (48 men, 56 women). The HIV patients consisted of 101 highly active antiretroviral therapy (HAART)-naive subjects and 216 patients on HAART for three to six months. The HIV patients were asymptomatic and all subjects had no signs or symptom of UTI. Microbial isolates were identified in urine and susceptibility tests were performed. Only HIV patients on HAART had significantly higher prevalence of asymptomatic UTI compared with non-HIV subjects (27.78% *vs*. 17.31%, OR=1.8376, 95% confidence interval = 1.0198–3.3112, P=0.0411). Among both groups, CD4+ count <200 cells/μL was not associated with asymptomatic UTI. *Staphylococcus aureus* was the most common uropathogen (27.2%) and nitrofurantoin was the most active antibacterial agent. Most bacterial isolates were resistant to other antibacterial agents used (amoxicillin, amoxicillin-clavulanate, gentamicin, co-trimoxazole, tetracycline, nalidixic acid, ciprofloxacin and ofloxacin). Overall prevalence of asymptomatic UTI was 24.94%. HIV patients on HAART had a one- to three-fold higher risk of acquiring UTI. CD4+ count was not associated with asymptomatic UTI

KEY WORDS: CD4 lymphocyte count.
HIV.
Urinary tract infections.

Introduction

Acquired immunodeficiency syndrome (AIDS), caused by human immunodeficiency virus (HIV), is characterised by progressive damage to the immune system, resulting in the development of various opportunistic infections.[1] Among the opportunistic infections in HIV patients, research has focused on tuberculosis, sexually transmitted infections and malaria.[2–4] Available literature on urinary tract infection (UTI) and HIV/AIDS show conflicting reports. The areas of conflict include the impact of HIV on the incidence of UTI, aetiological agents and association with CD4+ count. While some authors report a higher frequency of UTI among HIV patients,[5,6] others report that HIV infection shows no significant impact on the incidence of UTI.[7,8]

In terms of aetiological agents of UTI among HIV-infected patients, *Escherichia coli*[5,7] and enterococci[6] have been reported as the predominant isolates. Also, HIV patients with a CD4+ count <200 cells/μL are reported by some authors to be at higher risk of UTI, while others report that CD4+ count is not associated with UTI.[8–10] To the authors' knowledge, there is no report on the incidence of UTI among HIV patients on highly active antiretroviral therapy (HAART).

This study aims to determine the prevalence of asymptomatic UTI among HIV patients and HIV-seronegative subjects, including the most common aetiological agents, as well as the effect of CD4+ count on the prevalence of UTI.

Materials and method

Study population

The study was carried out at the University of Benin Teaching Hospital, Benin City, Nigeria. A total of 421 subjects comprising 216 HIV patients on HAART for three to six months (59 men, 152 women), 101 HAART-naive HIV patients (25 men, 76 women) and 104 apparently healthy HIV-seronegative individuals (48 men, 56 women) took part. The HIV patients were out-patients and asymptomatic. Exclusion criteria included signs and symptoms of UTI, antibiotic usage within one week, and large fluid intake (less than one hour) before clinic attendance. Verbal informed consent was obtained from all subjects prior to specimen collection. Approval for the study was given by the Ethical Committee of the University of Benin Teaching Hospital, Benin City, Nigeria.

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Specimen collection and processing

Clean-catch midstream urine and 5 mL venous blood samples were collected from each patient. The urine specimens were collected into sterile universal containers with boric acid as preservative. The blood specimens were collected into EDTA and used for the CD4+ count.

A loopful (0.001 mL) of well-mixed urine was streaked on the surface of blood agar and a cystine lactose electrolyte deficient (CLED) medium (M6, Plasmatec Laboratories, UK). The plates were incubated aerobically at 37°C for 24 h, and

Table 1. Distribution of asymptomatic urinary tract infection by gender.

	Male		Female		Total	
	No. tested	No. infected (%)	No. tested	No. infected (%)	No. tested	No. infected (%)
Non-HIV subjects*	48	2 (4.17)	56	16 (28.57)#	104	18 (17. 31)
HIV patients, HAART-naive†,§	25	1 (4.00)	76	26 (34.21)#	101	27 (26.73)
Patients on HAART‡	64	5 (7.81)	152	55 (36.18)#	216	60 (27.78)
Total	137	7(5.11)	284	97 (34.15)	421	105 (24.94)

*Non-HIV *vs*. HIV: OR=1.8072 95%; CI=1.0274–3.1790; P=0.0381.

†HAART-naive *vs*. non-HIV: OR=1.7432; 95% CI= 0.8898–3.4153; P=0.1029.

‡On HAART *vs*. non-HIV: OR=1.8376; 95% CI=1.0198–3.3112; P=0.0411.

§On HAART *vs*. HAART-naive: P=0.8115.

#Male *vs*. female: $P<0.01$.

counts were expressed in colony forming units (cfu)/mL. A count of $\geq 10^5$ cfu/mL was considered significant to indicate UTI.

Each urine sample (10 mL) was centrifuged at 2000 x*g* for 5 min. The supernatant was discarded and a drop of the deposit was examined microscopically at high magnification for pus cells, red blood cells, epithelial cells, casts, crystals, yeast-like cells and *Trichomonas vaginalis*. The presence of pus cells (≥5 per high-power field) was considered significant to indicate infection. Urinary tract infection was diagnosed if the bacterial or pus cell count, or both, were significant in an individual. The isolates were identified by standard microbiological methods[11] and disc susceptibility tests for bacterial isolates were performed by an NCCLS method.[12]

The $CD4^+$ lymphocyte count was determined using flow cytometry (Partec, Germany) following the manufacturer's instructions.

Statistical analysis was performed using the χ^2 test and odds ratio (OR) analysis.

Results

Generally, there was a significant difference in the prevalence of asymptomatic UTI between HIV patients and non-HIV subjects (27.45% *vs*. 17.31%, respectively, P=0.038) and HIV infection was a risk factor for UTI (OR=1.8072, 95% confidence interval [CI]=1.027–3.179). When the prevalence of UTI in relation to HIV status (HAART-naïve or HAART) was compared with the prevalence in non-HIV subjects, only the prevalence among HIV patients on HAART was significantly different from controls (OR=1.8376, 95% CI=1.0198–3.3112, P=0.0411; Table 1). The female group showed significantly higher prevalence of asymptomatic UTI than the male group (Table 1).

Using a $CD4^+$ count of 200 cells/μL as a cut-off value, the prevalence of UTI among HIV patients did not differ significantly from those with a $CD4^+$ count ≥200 cells/μL (Table 2).

Staphylococcus aureus was the most predominant isolate, irrespective of HIV treatment status, with *E. coli* having the same prevalence (31.58%) among non-HIV subjects. *T. vaginalis* was seen only among HAART-naive HIV patients (Table 3). Table 4 shows the distribution of uropathogens by gender. With the exception of non-HIV subjects, male HAART-naive HIV patients and female HIV patients on HAART, *S. aureus* was the predominant isolate in both men and women. In female HIV patients on HAART, *Candida albicans* was the predominant isolate, while in male HAART-naive HIV patients and male non-HIV subjects, only one organism (coagulase-negative staphylococci) was recovered. In female non-HIV subjects, *E. coli* and *S. aureus* each showed a frequency of 33.33%.

Nitrofurantoin was the most active antibacterial agent, and tetracycline the least active. Susceptibility of bacterial isolates to any of the antibacterial agents was less than 70% (Table 5).

Discussion

Conflicting reports about the effect of HIV on UTI, prevalence of aetiological agents and effect of $CD4^+$ count are common.[5–10] Against this background, the present study focuses on determining the prevalence of UTI among asymptomatic HIV and non-HIV subjects, the most

Table 2. Effect of $CD4^+$ count on the prevalence of urinary tract infection among HIV patient.

	$CD4^+$ count <200 cells/μL		$CD4^+$ count >200 cells/μL	
	No. tested	No. infected (%)	No. tested	No. infected (%)
HAART-naive*	56	16 (28.57)	45	11 (24.44)
On HAART†	38	9 (23.68)	178	47 (26.40)

*OR=1.2364; 95% CI=0.5034–3.0213; P=0.6390.

†OR=0.865; 95% CI=0.3814–1.9616; P=0.7290.

Table 3. Prevalence of uropathogens.

		HIV patients		
	Non-HIV (%)	HAART-naive (%)	On HAART (%)	Total (%)
Escherichia coli	6 (31.58)	4 (12.90)	6 (9.38)	16 (14.04)
Klebsiella species	0 (0.00)	1 (3.23)	5 (7.81)	6 (5.26)
Proteus species	0 (0.00)	1 (3.23)	3 (4.69)	4 (3.51)
Staphylococcus aureus	6 (31.58)	8 (25.81)	17 (26.56)	31 (27.19)
Coagulase-negative staphylococci	4 (21.05)	5 (16.13)	10 (15.63)	19 (16.67)
Enterococcus faecalis	0 (0.00)	1 (3.23)	8 (12.50)	9 (7.89)
Candida albicans	3 (15.79)	7 (22.58)	15 (23.44)	25 (21.93)
Trichomonas vaginalis	0 (0.00)	4 (12.90)	0 (0.00)	4 (3.51)
Total	19 (16.67)	31 (27.19)	64 (56.14)	114

prevalent uropathogen and the effect of $CD4^+$ count on UTI prevalence.

In this study, HIV infection generally was a risk factor for UTI; however, the higher prevalence and risk factors observed among HIV patients were statistically significant only in HIV patients on HAART. The non-significant difference in the prevalence of UTI between HAART-naive HIV patients and their non-HIV counterparts has been reported.[7,8,13] Studies that show significant differences in the prevalence of UTI between HIV and non-HIV subjects used either AIDS patients[9,13] or HIV patients with symptoms of UTI.[5,9]

The prevalence of asymptomatic UTI in the present study, and in earlier work,[7,8] did not differ significantly between asymptomatic HAART-naive patients and their non-HIV counterparts. The reason for the significant difference in the prevalence of asymptomatic UTI between HIV patients on HAART and non-HIV subjects is not clear. It is possible that HAART interferes with urinary pH, a known factor in the prevention of UTI,[14] to predispose these HIV patients to UTI. However, verification of this will require further investigation.

The finding that women had a higher prevalence of asymptomatic UTI agrees with earlier studies.[15,16] Close proximity of the female urethral meatus to the anus, a shorter urethra, and sexual intercourse all have been reported as factors that influence this higher prevalence in women.[14,17]

It is generally accepted that $CD4^+$ count <200 cells/μL predisposes HIV patients to opportunistic infection.[18] The finding that $CD4^+$ count <200 cells/μL is not associated with asymptomatic UTI has been reported.[8] However, Evans *et al*.[9] report that UTI is significantly higher in HIV patients with $CD4^+$ count <200 cells/μL, which differs from the present study and may be attributed to the fact that AIDS patients were studied rather than asymptomatic HIV patients.

S. aureus was reported as the most prevalent isolate in a recent study of diabetes mellitus (DM) and non-DM patients in the authors' hospital.[17] This may indicate a changing pattern in the local prevalence of uropathogens. *S. aureus* is part of the normal flora of the female perineum and vulva. Staphylococci are also part of the vaginal flora, and manipulations that alter the vaginal flora, such as insertion of a contraceptive device – a known risk factor for UTI – can result in opportunistic UTI with this organism.[17]

The reason why *T. vaginalis* was seen only among HAART-naive HIV patients is unclear, although sexually transmitted infection increases the susceptibly to acquire and transmit HIV infection.[3]

The *in vitro* antibacterial susceptibility results indicate high resistance to most of the antibacterial agents available. This may be due to the fact that most clinicians treat patients without recourse to laboratory guidance.[19] Nitrofurantoin was the most active agent but it is bacteriostatic in action and there is a need to evaluate its effectiveness in HIV patients.

The authors are aware that many workers do not

Table 4. Distribution of uropathogens by gender.

	Non-HIV subjects		HAART-naive patients		Patients on HAART	
	Male (%)	Female (%)	Male (%)	Female (%)	Male (%)	Female (%)
Escherichia coli	0 (0.00)	6 (33.33)	0 (0.00)	4 (13.33)	0 (0.00)	6 (10. 17)
Klebsiella species	0 (0.00)	0 (0.00)	0 (0.00)	1 (3.33)	0 (0.00)	5 (8.47)
Proteus species	0 (0.00)	0 (0.00)	0 (0.00)	1 (3.33)	0 (0.00)	3 (5.08)
Staphylococcus aureus	0 (0.00)	6 (33.33)	0 (0.00)	8 (26.67)	4 (80.00)	13 (22.03)
Coagulase-negative staphylococci	1 (100)	3 (16.67)	1 (100)	4 (13.33)	0 (0.00)	10 (16.95)
Enterococcus faecalis	0 (0.00)	0 (0.00)	0 (0.00)	1 (3.33)	0 (0.00)	8 (13.56)
Candida albicans	0 (0.00)	3 (16.67)	0 (0.00)	7 (23.33)	1 (20.00)	14 (23.73)
Trichomonas vaginalis	0 (0.00	0 (0.00)	0 (0.00)	4 (13.33)	0 (0.00)	0 (0.00)

Table 5. Susceptibility profiles of bacterial isolates.

Antibacterial agent (μg/disc)	Organism					
	Escherichia coli (*n*=16)	*Klebsiella* spp. (*n*=6)	*Proteus* spp. (*n*=4)	*Staphylococcus aureus* (*n*=31)	CONS (*n*=19)	*Enterococcus faecalis* (*n*=9)
Amoxicillin (30)	1 (6.25)	1 (16.67)	1 (25.00)	10 (32.25)	6 (31.58)	4 (44.44)
Amoxicillin/clavulanate (30)	6 (6.25)	1 (16.67)	2 (50.00)	11 (35.48)	5 (26.32)	4 (44.44)
Gentamicin (10)	3 (18.75)	0 (0.00)	1 (25.00)	5 (16.13)	5 (26.32)	4 (44.44)
Co-trimoxazole (25)	1 (6.25)	1 (16.67)	0 (0.00)	1 (3.23)	1 (5.26)	0 (0.00)
Tetracycline (25)	0 (0.00)	0 (0.00)	0 (0.00)	1 (3.23)	0 (0.00)	1 (11.11)
Nitrofuratoin (300)	9 (56.25)	1 (16.67)	2 (50.00)	16 (51.61)	12 (63.16)	6 (66.67)
Nalidixic acid (30	3 (18.75)	0 (0.00)	0 (0.00)	ND	ND	ND
Ciprofloxacin (5)	6 (37.50)	2 (33.33)	2 (50.00)	10 (32.25)	8 (42.11)	5 (55.56)
Ofloxacin (5)	6 (37.50)	0 (0.00)	1 (25.00)	5 (16.13)	6 (31.58)	3 (33.33)

CONS=coagulase-negative staphylococci; ND=not done.

recommend the treatment of asymptomatic UTI based mainly on the presence of significant bacteriuria. Thus, the present study also used the presence of pus cells as an indicator of active infection. The prescription of antibiotics without laboratory guidance is rife in the Nigerian setting, and the susceptibility results presented here may serve as a guide for empirical treatment. □

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