

**Original Article****Open Access****Prevalence of asymptomatic significant bacteriuria and antibiotic susceptibility pattern of bacterial isolates in HIV-infected patients in Ilorin, Nigeria**

*¹Bale, M. I., ¹Sinumvayo, J. P., ²Badmus, R. A., ³Babatunde, S. K., ⁴Aroyehun, A. B., and ¹Adeyemo, R. O.

¹Department of Microbiology and Parasitology, College of Medicine and Health Sciences, University of Rwanda, Republic of Rwanda

²Department of Microbiology Faculty of Pure and Applied Sciences, Kwara State University, Malete, Kwara State, Nigeria

³Department of Biological Sciences, Kola Daisi University, Ibadan, Nigeria

⁴Department of Clinical Nutrition, University of Aberdeen, King's College, Aberdeen, AB24 3FX, Scotland

*Correspondence to: muribaale@gmail.com; i.muritala@ur.ac.rw

Abstract:

Background: Urinary tract infection (UTI) is one of the most common type of infections worldwide, and this is usually preceded by asymptomatic significant bacteriuria (ASB). The emergence of antibiotic resistance in bacteria responsible for UTI makes this entity of public challenge, which has been fueled by human immunodeficiency virus (HIV) infection. This study determined the prevalence of ASB and antimicrobial susceptibility pattern of bacteria isolated from urine samples of selected HIV-infected patients in Ilorin, Nigeria.

Methodology: A cross-sectional study of 300 randomly selected HIV-positive patients from Sobi Specialist and Civil Service hospitals in Ilorin, Kwara State, Nigeria, was conducted from January to March 2019. Clean-catch midstream urine samples were aseptically collected from each selected participant, cultured on CLED and Blood agar plates, and incubated aerobically at 37°C for 24 hours. The bacterial growth on the culture plates were identified using standard microbiological techniques. The Kirby-Bauer disk diffusion method was used to determine the antibiotic sensitivity of the bacterial isolates against a panel of antibiotics.

Results: The overall prevalence of ASB among the participants was 22.3%. *Staphylococcus aureus* (41.8%, 28/67), *Escherichia coli* (25.4%, 17/67), and *Klebsiella pneumoniae* (17.9%, 12/67) were the predominant bacterial isolates. *Staphylococcus aureus* was resistant to amoxicillin-clavulanate (64.3%), ceftriaxone (53.6%), ciprofloxacin (64.3%), and nalidixic acid (71.4%); *E. coli* was also resistant to amoxicillin-clavulanate (70.6%), ceftriaxone (53.6%), ciprofloxacin (52.9%) and nalidixic acid (64.7%); and *K. pneumoniae* was moderately resistant to amoxicillin-clavulanate (50.0%) and resistant to ciprofloxacin (58.3%) and nalidixic acid (75.0%). Multidrug resistance (MDR) was observed in 40.8% of the isolates.

Conclusion: The isolation rate of high MDR bacteria highlights the growing challenge of ASB and UTIs that are becoming increasingly difficult to treat with available antibiotics. Health professionals should be aware of regional resistance pattern to consider in the current empirical antimicrobial therapy for ASB and UTIs among HIV-infected patients. Strategies to mitigate spread of resistance are urgently needed in the study area.

Keywords: antimicrobial resistance; asymptomatic significant bacteriuria; prevalence; HIV

Received Jun 18, 2023; Revised Jun 22, 2023; Accepted Jun 30, 2023

Copyright 2023 AJCEM Open Access. This article is licensed and distributed under the terms of the Creative Commons Attribution 4.0 International License , which permits unrestricted use, distribution and reproduction in any medium, provided credit is given to the original author(s) and the source. Editor-in-Chief: Prof. S. S. Taiwo

Prévalence de la bactériurie significative asymptomatique et schéma de sensibilité aux antibiotiques des isolats bactériens chez les patients infectés par le VIH à Ilorin, au Nigeria

*¹Bale, M. I., ¹Sinumvayo, J. P., ²Badmus, R. A., ³Babatunde, S. K., ⁴Aroyehun, A. B.,
et ¹Adeyemo, R. O.

¹Département de Microbiologie et de Parasitologie, Faculté de Médecine et des Sciences de la Santé,
Université du Rwanda, République du Rwanda

²Département de Microbiologie, Faculté des Sciences Pures et Appliquées, Université d'État de Kwara,
Malete, État de Kwara, Nigéria

³Département des Sciences Biologiques, Université de Kola Daisi, Ibadan, Nigéria

⁴Département de Nutrition Clinique, Université d'Aberdeen, le roi du Collège, Aberdeen, AB24 3FX, Écosse

*Correspondance à: muribaale@gmail.com; i.muritala@ur.ac.rw

Résumé:

Contexte: L'infection des voies urinaires (UTI) est l'un des types d'infections les plus courants dans le monde, et elle est généralement précédée d'une bactériurie significative asymptomatique (ASB). L'émergence de la résistance aux antibiotiques chez les bactéries responsables des infections urinaires fait de cette entité un défi public, qui a été alimenté par l'infection par le virus de l'immunodéficience humaine (VIH). Cette étude a déterminé la prévalence de l'ASB et le schéma de sensibilité aux antimicrobiens des bactéries isolées à partir d'échantillons d'urine de patients infectés par le VIH sélectionnés à Ilorin, au Nigeria.

Méthodologie: Une étude transversale de 300 patients séropositifs sélectionnés au hasard dans les hôpitaux spécialisés et de la fonction publique de Sobi à Ilorin, dans l'État de Kwara, au Nigéria, a été menée de janvier à mars 2019. Participant, cultivé sur des plaques de CLED et de gélose au sang, et incubé en aérobiose à 37°C pendant 24 heures. La croissance bactérienne sur les plaques de culture a été identifiée en utilisant des techniques microbiologiques standard. La méthode de diffusion sur disque Kirby-Bauer a été utilisée pour déterminer la sensibilité aux antibiotiques des isolats bactériens par rapport à un panel d'antibiotiques.

Résultats: La prévalence globale de l'ASB parmi les participants était de 22,3 %. *Staphylococcus aureus* (41,8%, 28/67), *Escherichia coli* (25,4%, 17/67) et *Klebsiella pneumoniae* (17,9%, 12/67) étaient les isolats bactériens prédominants. *Staphylococcus aureus* était résistant à l'amoxicilline-acide clavulanique (64,3%), à la ceftriaxone (53,6%), à la ciprofloxacine (64,3%) et à l'acide nalidixique (71,4%); *E. coli* était également résistant à l'amoxicilline-acide clavulanique (70,6%), à la ceftriaxone (53,6%), à la ciprofloxacine (52,9%) et à l'acide nalidixique (64,7 %); et *K. pneumoniae* était modérément résistant à l'amoxicilline-acide clavulanique (50,0%) et résistant à la ciprofloxacine (58,3%) et à l'acide nalidixique (75,0%). La multirésistance (MDR) a été observée dans 40,8% des isolats.

Conclusion: Le taux d'isolement des bactéries MDR élevées met en évidence le défi croissant des ASB et des infections urinaires qui deviennent de plus en plus difficiles à traiter avec les antibiotiques disponibles. Les professionnels de la santé doivent être conscients du schéma de résistance régional à prendre en compte dans la thérapie antimicrobienne empirique actuelle pour l'ASB et les infections urinaires chez les patients infectés par le VIH. Des stratégies pour atténuer la propagation de la résistance sont nécessaires de toute urgence dans la zone d'étude.

Mots-clés: résistance antimicrobienne; bactériurie importante asymptomatique; prévalence; VIH

Introduction:

Globally, an estimated 38.4 million people are living with human immunodeficiency virus (HIV) with a high number of infected people (~25.6 million) in sub-Saharan Africa (1,2). Annually, an estimated 40.1 million people died from AIDS-related illnesses (3). In people living with HIV/AIDS (PLWHA), almost every part of the genitourinary system is affected with different diseases (4). HIV infects vital cells in the human immune system such as CD4⁺ (helper) T cells, macrophages and dendritic cells (5). HIV infection leads to low levels of CD4⁺ T cells through three main mechanisms; direct viral killing of infected cells, increased rate of apoptosis in infected cells, and killing of infected CD4⁺ T cells by CD8⁺ (cytotoxic) T-lymphocytes that recognize infected cells. When CD4⁺ cells count decline below a critical level, cell mediated immunity is lost and the body becomes progressively

more susceptible to opportunistic infections (6).

In man, the urinary tract is the second commonest site after the respiratory tract for bacterial infection (7). The urinary tract is an anatomical unit and infection of one part could generally spread to other parts (8). When the infection is localized at such single sites as the kidneys, it is referred to as pyelonephritis, to the urethra as urethritis or restricted to the bladder as cystitis and to the prostate as proctitis. It affects both old and young leading to a number of deaths either from acute infection or from chronic renal failure (9). Specific group of people are at increased risk of urinary tract infection. Vulnerable populations are women, especially during pregnancy, infants and elderly patients (10). Also, certain conditions may increase susceptibility to infections i. e. spinal cord injuries, urinary catheters, diabetes, multiple sclerosis, immunodeficiency and underlying urologic abnormalities (11). UTI is one of the most

common bacterial infections causing morbidity and hospitalization in HIV-infected individuals (12).

HIV disease is associated with a variety of renal syndromes in patients with low CD4⁺ cell counts associated with neurological complications which lead to urinary stasis and infection (13). Once the CD4⁺ count falls below 200 cells/mm³, the individual is at risk of a variety of opportunistic infections, from fungi, protozoa, viruses and bacteria. The most predominant causative organisms are encapsulated bacteria notably *Streptococcus pneumoniae* and *Haemophilus influenzae*, but non-typhoidal *Salmonella*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* have also been implicated (14). Among opportunistic infections, UTI accounts for approximately 60% of AIDS defining illnesses (7).

There are also reports of change in the resistance pattern over the last decade leading to serious therapeutic challenges (15). Since the distribution of these pathogens and their susceptibility to antibiotics varies regionally, and treatment for UTI is usually empirical, it is mandatory that there is an adequate knowledge of the epidemiological characteristics of the pathogens involved and their antibiotic susceptibility patterns. This will help to achieve good therapeutic outcomes and prevent the emergence of drug-resistant bacteria strains (16). This objective of this study is to determine the prevalence of ASB and the antimicrobial susceptibility pattern of bacteria isolated from urine samples of HIV-infected patients in selected HIV clinics in Ilorin, Nigeria.

Materials and method:

Study setting and participants:

This study was carried out in the HIV clinics of Sobi Specialist and Civil Service hospitals in Ilorin, the capital city of Kwara State, Nigeria, over a period of 3 months (January to March 2019). The laboratory aspect of the study was conducted at the department of microbiology, University of Ilorin Teaching Hospital, and the department of microbiology, Kwara State University, Malet.

A total of 300 HIV-infected individuals receiving HIV care were consecutively recruited over the period of the study, and the sample size was calculated using a formula as previously described (17).

Ethical consideration:

Ethical approval was obtained from the Ethics Review Committees of the Ministry of Health, Ilorin, and Kwara State University Ethics Committee. Written informed consent was obta-

ined from the participants before inclusion in the study.

Data and sample collection:

Appropriately labeled universal sample bottle was given to each participant for collection of clean catch midstream urine specimen following explanation of the procedure for such collection. The samples were immediately transported to the department of microbiology, University of Ilorin Teaching Hospital for analysis.

Demographic and clinical information were obtained from each patient including the age and gender, history of UTI, antibiotic use, and history of opportunistic infections. Participants whose urine sample yielded growth were requested to provide another early morning clean-catch mid-stream urine sample for confirmation.

Microscopic examination and culture of urine:

Each urine sample was well mixed and centrifuged at 3200 rpm for 5 mins. The supernatant was decanted and a drop of the sediment was placed on a sterile glass slide and covered with a cover slip and was viewed under 10x and 40x objective lens to observe for white blood cells, red blood cells, casts, crystals, epithelial cells, and ova of parasites.

Each urine sample was shaken to allow for homogeneity. Using a standard sterile wire loop (calibrated to deliver 0.001ml of urine), a loopful of the urine was aseptically inoculated onto Blood and Cystine Lactose Electrolyte Deficient (CLED) agar plates. The plates were incubated aerobically at 37°C for 24 hours, and examined macroscopically and microscopically for bacterial growth (18).

Significant bacteriuria was determined on the culture plate when there was $\geq 10^5$ colony forming units per milliliter (19). Colonies of urine culture with significant bacteriuria were Gram stained and bacteria identified by conventional biochemical tests (20).

Antimicrobial susceptibility testing (AST):

Using the modified Kirby-Bauer disk diffusion test, 3 to 5 pure colonies of the isolates to be tested were selected, and emulsified in sterile saline solution, thoroughly mixed to prepare bacterial inoculum that was standardized by matching the turbidity of the inoculum with 0.5 McFarland standard. A sterile swab stick was dipped into the inoculum and gently squeezed against the inside of the tube in order to remove excess fluid in the swab. The swab was used to inoculate sterile Mueller-Hinton (MH) agar plate, which was left to dry for about 5 mins. A sterile forcep was then used to place the antimicrobial-

impregnated disks on the surface of the agar plate, which was incubated at 37°C for 24 hours.

The diameter of zone of inhibition of the isolate to each antibiotic was measured with a calibrated ruler, and results interpreted as sensitive or resistant according to the Clinical and Laboratory Standards Institute (CLSI) guideline (21). The following antibiotic discs (Oxoid, UK) were used; amoxicillin-clavulanate (30µg), gentamicin (10µg), ciprofloxacin (5 µg), nalidixic acid (30µg), ceftazidime (30µg), ceftriaxone (30 µg), nitrofurantoin (100µg), imipenem (10 µg), ceftioxin (30µg) and clindamycin (2µg).

Detection of ESBL in Gram-negative bacteria isolates:

Gram-negative bacterial isolates presumptively identified as ESBL-producing in the AST (ceftazidime zone diameter of inhibition < 22 mm or ceftriaxone zone < 25 mm) were confirmed as ESBL-producing by the double disk synergy test (21). The inoculum was prepared and agar plates inoculated as done for the AST. Ceftazidime (30µg) and ceftriaxone (30µg) discs were placed on either side of amoxicillin-clavulanic acid (20/10µg) 15 mm apart. ESBL-positive strains showed an expansion of the zone of inhibition of either cephalosporin toward the amoxicillin-clavulanate disk, giving a dumbbell shape (22).

Detection of methicillin resistance in *Staphylococcus aureus* isolates:

Mueller-Hinton agar plates were inoculated with *S. aureus* isolates as done for routine AST. Cefoxitin 30µg disks were applied and the plates were incubated at 37°C for full 24 hours. An isolate was considered to be an MRSA strain if the cefoxitin inhibition zone diameter was ≤ 21 mm (21).

Statistical analysis of data

Data were described in frequency and percentages. The Pearson Chi-square test was used to determine association of ASB with gender and age group of participants. P value < 0.05 was considered statistically significant at 95% confidence interval.

Results:

Three hundred HIV-positive individuals were enrolled into the study, with age range of 0-80 years, with female predominance (262, 87.3%). The CD4 counts of the participants ranged from 58 to 1082 cells/mm³ (Table 1). Table 2 shows the results of culture of the urine samples, with samples from 67 (22.3%) individuals yielding significant bacteriuria, while 233

(77.7%) samples had either no growth or no significant growth, and 51 (17.0%) samples had mixed bacterial growth.

Staphylococcus aureus was the most frequently isolated bacteria (41.8%, 28/67), followed by *Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Pseudomonas aeruginosa* and coagulase negative staphylococci CoNS), accounting for 25.4% (17/67), 17.9% (12/67), 7.5% (5/67), 4.5% (3/67) and 2.9% (2/67) respectively (Fig 1).

Table 3 shows the frequency distribution of ASB among the participants with respect to age group and gender. There was no significant association between ASB and age group of the participants ($p=0.9632$). Although, ASB prevalence was higher among the female participants (23.3%) compared to the male participants (15.8%), the difference was not statistically significant ($p=0.4077$).

Table 4 shows the AST pattern of the isolates. *Staphylococcus aureus* was resistant to amoxicillin-clavulanate (64.3%), ceftriaxone (53.6%), ciprofloxacin (64.3%), and nalidixic acid (71.4%); *E. coli* was also resistant to amoxicillin-clavulanate (70.6%), ceftriaxone (53.6%), ciprofloxacin (52.9%), and nalidixic acid (64.7%); *K. pneumoniae* was moderately resistant to amoxicillin-clavulanate (50.0%), and resistant to ciprofloxacin (58.3%) and nalidixic acid (75.0%); *K. oxytoca* was resistant to amoxicillin-clavulanate (80.0%), gentamicin (60.0%), ciprofloxacin (60.0%) and nalidixic acid (80.0%); *P. aeruginosa* was resistant to gentamicin (100.0%), ciprofloxacin (66.7%), and nalidixic acid (100%); while coagulase negative staphylococci were resistant to nalidixic acid (100.0%) and moderately resistant to nitrofurantoin (50.0%) and ciprofloxacin (50.0%).

Discussion:

In this study, the prevalence of ASB was 22.3%. The observation of the relatively high prevalence of ASB in this study may require the need for laboratory investigation as a criterion for the commencement of treatment in HIV-infected patients. Our finding is in agreement with a study conducted in Osogbo, Nigeria which reported a prevalence of 23.5% (23), but higher than the rates of 11.9% reported in Gondar (24) and 10.7% in Jimma (4) Ethiopia, while the rate is lower than those reported from studies conducted in Ebonyi State, Nigeria with 93.8% (25), and in Tamil Nadu India, with 77.5% (26). The disparity in rates might be attributed to differences in sample size (small sample size might overestimate the proportion), geographical variation, and socioeconomic conditions.

The prevalence of ASB in our study participants appears to be much higher than those reported in other parts of the country and globally as most studies report prevalence of 3-15 % (27,28). Only a few studies such as those by Ojoo et al., (29) have reported relatively high prevalence as ours. Another study in this environment also reported a high prevalence of 18% among HIV-infected pregnant women (30). compared with HIV-negative population within the same region, it appears that the prevalence of

ASB is similar to what was obtained in our study population. A community-based study on HIV-negative individuals in the same region also reported a prevalence of 22.6%, which is comparable to our prevalence of 22.3% (31). Similar findings were also reported by Gugino et al., (32) and Widmer et al., (28) as they did not find any difference in the prevalence of ASB between their study population of HIV-positive women and HIV-negative controls.

Table 1: Age group and gender distribution of HIV-infected study participants attending selected HIV clinics in Ilorin, Nigeria

Gender	Male (%)	Female (%)	Total (%)
Age group (years)			
0-10	1 (0.3)	3 (1.0)	4 (1.3)
11-20	1 (0.3)	4 (1.3)	5 (1.7)
21-30	3 (1.0)	44 (14.7)	47 (15.7)
31-40	8 (2.7)	95 (31.7)	103 (34.3)
41-50	12 (4.0)	68 (22.7)	80 (26.7)
51-60	8 (2.7)	38 (12.7)	46 (15.3)
61-70	4 (1.3)	9 (3.0)	13 (4.3)
71-80	1 (0.3)	1 (0.3)	2 (0.7)
Total	38 (12.7)	262 (87.3)	300 (100.0)
CD4+ count (/mm³)			
<200	8 (2.7)	86 (28.7)	94 (31.3)
200-500	18 (6.0)	120 (40.0)	138 (46.0)
>500	12 (4.0)	56 (18.7)	68 (22.7)
Total	38 (12.7)	262 (87.3)	300 (100.0)

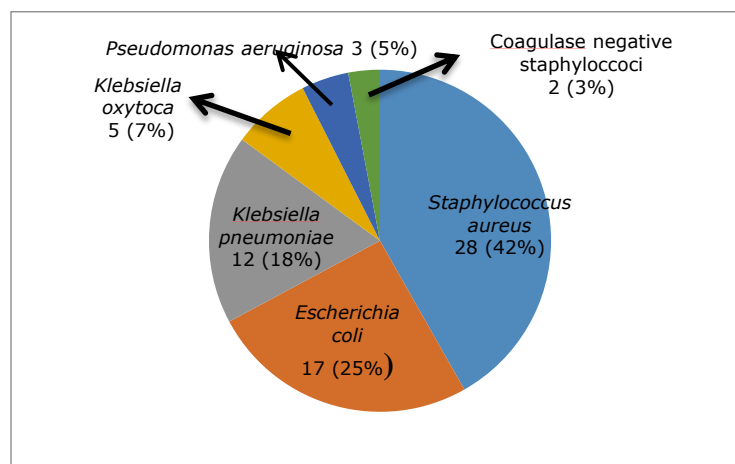


Fig 1: Frequency distribution of isolated bacteria from HIV-infected study participants attending selected HIV clinics Ilorin, Nigeria

Table 2: Frequency of bacteria growth from urine of HIV-infected study participants attending selected HIV clinics in Ilorin, Nigeria

Results of culture growth	Frequency of growth	Percentage
Significant growth	67	22.3
No significant growth	57	19.0
Mixed growth	51	17.0
No growth	125	41.7
Total	300	100.0

Table 3: Association of ASB with gender and age group in HIV-infected participants attending selected HIV clinics in Ilorin, Nigeria

Demographic Characteristics	Significant bacteriuria			χ^2	OR (95% CI)	p value
	Yes (%) [67 (22.3)]	No (%) [233 (77.7)]	Total (n=300)			
Age group (years)						
0-20	2 (22.2)	7 (77.8)	9	0.2828	NA	0.9632
21-40	32 (21.3)	118 (78.7)	150			
41-60	29 (23.0)	97 (77.9)	126			
61-80	4 (26.7)	11 (73.3)	15			
Gender						
Male	6 (15.8)	32 (84.2)	38	0.6856	0.6178 (0.2467-1.547)	0.4077
Female	61 (23.3)	201 (76.7)	262			

χ^2 = Chi square; OR = Odd ratio; CI= Confidence interval; NA=Not applicable

The usual trend in ASB is for the prevalence to be higher in the female population (23), and our study also reported similar finding. We found the prevalence of asymptomatic bacteriuria to be higher in the females than males in keeping with reported trend, which is attributed to the proximity of the urethra to the anus and its short length (33). We, however could not establish statistically significant association ($p=0.4077$) and therefore cannot conclude on such association in this group of HIV-infected individuals.

In the present study, the highest prevalence of ASB was recorded in the age group 61-80 years (26.7%) followed by age group 41-60 years (23.0%), age group 0-20 years (22.2%) and age group 21-40 years (21.3%). However, the association of ASB with age group was not statistically significant ($p=0.9632$). The ASB rate of 21.3% recorded in the age 21-40 years in our study is lower compared to the ASB rate of 53.9% reported in a slightly comparable age group 20-29 years in Irrua, Nigeria (34), but higher than 12.7% in the age group 18-26 years in Gondar Ethiopia (24).

Our study did not show significant difference in the ASB rate in the younger and older age groups in spite of the established fact that ASB rate tend to be higher in the younger age group in relation to the increased sexual activity of this age group, which is a recognized predisposition to bacteriuria and UTI (35). However, several studies have also reported that older age groups, especially the elderly, are also at risk of significant bacteriuria (31,35,36).

UTIs appear to be multifactorial in patients with HIV infections as CD4⁺ level declines (37), and many research studies have reported this (38,39,40,41). This implies that the more immune compromised the patient is, the higher the risk of UTI and possibly to other opportunistic infections. The declining CD4⁺ count makes it easier for bacterial pathogens to adhere to the urinary epithelium (27). Ezechi et al., (30) in their study on the risk factors for ASB in HIV-infected pregnant women also reported similar findings. Furthermore, they found high viral load, low haemoglobin, and previous UTI to be associated with ASB. However, we did not explore these parameters in our study.

Table 4: Antibiotic susceptibility of isolated bacteria from HIV-infected participants attending HIV clinics of selected Hospitals in Ilorin, Nigeria

Organisms	Antibiotics Patterns (%)								
	AMC	CN	CIP	NA	CAZ	CRO	F	IPM	FOX
<i>Staphylococcus aureus</i> (n=28)	S 10 (35.7)	15 (53.6)	10 (35.7)	8 (28.6)	NT	13 (46.4)	15 (53.6)	NT	20 (71.4)
	R 18 (64.3)	13 (46.4)	18 (64.3)	20 (71.4)	NT	15 (53.6)	13 (46.4)	NT	8 (28.6)
<i>Escherichia coli</i> (n=17)	S 5 (29.4)	13 (76.5)	8 (47.1)	6 (35.3)	14 (82.4)	14 (82.4)	12 (70.6)	NT	NT
	R 12 (70.6)	4 (23.5)	9 (52.9)	11 (64.7)	3 (17.6)	3 (17.6)	5 (29.4)	NT	NT
<i>Klebsiella Pneumoniae</i> (n=12)	S 7 (58.3)	6 (50.0)	5 (41.7)	3 (25.0)	7 (58.3)	7 (58.3)	10 (83.3)	NT	NT
	R 5 (41.7)	6 (50.0)	7 (58.3)	9 (75.0)	5 (41.7)	5 (41.7)	2 (16.7)	NT	NT
<i>Klebsiella oxytoca</i> (n=5)	S 1 (20.0)	2 (40.0)	2 (40.0)	1 (20.0)	3 (60.0)	3 (60.0)	5 (100)	NT	NT
	R 4 (80.0)	3 (60.0)	3 (60.0)	4 (80.0)	2 (40.0)	2 (40.0)	0	NT	NT
<i>Pseudomonas aeruginosa</i> (n=3)	S 2 (66.7)	1 (33.3)	0	0	2 (66.7)	3 (100)	3 (100)	3 (100)	NT
	R 1 (33.3)	2 (66.7)	3 (100)	3 (100)	1 (33.3)	0	0	0	NT
Coagulase negative staphylococci (n=2)	S 2 (100)	2 (100)	1 (50.0)	0	NT	2 (100)	1 (50.0)	NT	2 (100)
	R 0	0	1 (50.0)	2 (100)	NT	0	1 (50.0)	NT	0

AMC- augmentin, CN- gentamicin, CIP- ciprofloxacin, NA- nalidixic acid, CAZ- ceftazidime, CRO – ceftriaxone, F – nitrofurantoin, IPM – imipenem, FOX –cefoxitin, S – sensitive, R – resistant, NT – not tested

Staphylococcus aureus was the most predominant causative agent of ASB in the present study accounting for 41.8% of the uropathogens. A similar finding was reported from in Ebonyi State, Nigeria (25), and in Tamil Nadu, India (26), but contrasted the findings from Gondar (24) and Jimma (4) in Ethiopia, and in a tertiary care hospital in India (42), where *E. coli* was the mostly commonly isolated uropathogen, with frequency of 56.1%, 54.3% and 41.7% respectively. The variation in the type of bacteria isolates might be due to differences in sample size of studies, specimen collection techniques, sample processing methods, and personal and environmental hygiene factors (38).

Antimicrobial resistance is a major clinical challenge in treating infections caused by different bacterial pathogens and has increased over the years. In the present study, there was high resistance rates to some commonly used antibiotics, especially nalidixic acid, amoxicillin-clavulanate (augmentin), ciprofloxacin, and moderate resistance to gentamicin and ceftriaxone. This is to somewhat comparable with the study reports from Gondar (24) and Jimma (4) in Ethiopia. The resistance to the antibiotics may be due to the fact that some of these drugs are used for prophylaxis against opportunistic infections associated with HIV (43). The variations in the reports of resistance from the studies may

be due to the differences in the distribution of resistant strains across the different settings.

Multidrug resistance has serious implications on the health outcome of HIV-infected patients (44,45). It is quite alarming to note that almost 40.8% of the isolates in this study were resistant to two or more antimicrobials. This is similar to a report of 46.0% by Dadi et al., (46) in Hiwot Fana Ethiopia, but higher compared to 28.0% reported in Mysore India by Murugesh et al., (45), and lower than the 95.0% reported in Gondar Ethiopia (24). The high resistance rate to the most commonly prescribed antibiotics in our study might be due to easy availability of these drugs in the community and their cheap costs, which make them subject to misuse (47). It could also be due to the use of antibiotics for other non-human purposes such as in livestock rearing and animal husbandry activities, which may be accelerating the growth of resistance (25,46).

The strength of our descriptive study is that it evaluated urine samples for pathogenic bacteria and highlighted the emergence of antimicrobial resistance that provides precise scientific data needed to develop strategy for the appropriate treatment, prevention, and control of UTI. However, we did not attempt to identify other causative agents (anaerobic bacteria, viruses, and fungi) that would have made a signi-

ficant contribution to the true prevalence of ASB in HIV-positive patients in our setting.

Conclusion:

In conclusion, the prevalence of ASB in HIV-infected persons in this study is relatively higher than some previous findings and common pathogens such as *S. aureus*, *E. coli*, and *K. pneumoniae* are the major agents of ASB. The isolation of high MDR bacteria highlights the growing challenge of UTIs, that is becoming increasingly difficult to treat with available antibiotics. Future studies need to focus on exploring a range of causative pathogens and the mechanisms of antimicrobial resistance.

Contributions of authors:

BMI designed the research and perform data analysis; SJP performed data analysis; BRA carried out the data collection and analysis; BSK reviewed the manuscript; AAB prepared the tables and figures. All authors reviewed the results and approved the final version of the manuscript.

Source of funding:

Authors received no external funding

Conflict of interest:

Authors declared no conflict of interest

References:

- Obeagu, E. I., Godfred, Y. S., Amekpor, F., Ofodile, A. C., Edoho, S. H., and Ahamefula, C. Prevention of new cases of human immunodeficiency virus: pragmatic approaches of saving life in developing countries. *Madonna University Journal of Medicine and Health Sciences*. 2022; 2 (3): 128-134.
- Sewale, Y., Afenigus, A. D., Haile, D., and Shiferaw, W. S. Magnitude of hypertension and associated factors among human immunodeficiency virus positive adults receiving anti-retroviral therapy at Debre Markos Referral Hospital, North-west, Ethiopia. *HIV/AIDS-Research and Palliative Care*. 2020: 629-637.
- Abuto, W. Survival and predictors of mortality among HIV positive adult patients on highly active antiretroviral therapy in public hospitals of Kambata Tambaro Zone, Southern Ethiopia: a retrospective cohort study. *HIV/AIDS Res Palliative Care*. 2021: 271-281.
- Debalke, S., Cheneke, W., Tassew, H., and Awol, M. Urinary tract infection among antiretroviral therapy users and non-users in Jimma University Specialized Hospital, Jimma, Ethiopia. *Int J Microbiol*. 2014; 6
- Cunningham, A. L., Donaghy, H., Hama, A. N., Kim, M., and Turville, S. G. Manipulation of dendritic cell function by viruses. *Curr Opin Microbiol*. 2010; 113: 524 - 529.
- Kemajou, T. S., Ajugwo, A. O., Oshoma, C. E., and Enabulele, O. I. Antibiotic Resistance of Bacterial Isolates from HIV Positive Patients with Urinary Tract Infection (UTI) in Port Harcourt, Nigeria. *J AIDS Clin Res*. 2016; 7: 594.
- Ani, O. C., Onwe, C. S., and Nnabugwu, C. C. Evaluation of female residents for urinary tract infections, Onicha Local Government Area, Ebonyi State, Nigeria. *Nig J Parasitol*. 2015; 36(1): 50-54.
- Ramstedt, M., Ribeiro, I. A., Bujdakova, H., Mergulhão, F. J., Jordao, L., Thomsen, P., and Sjollem, J. Evaluating efficacy of antimicrobial and antifouling materials for urinary tract medical devices: Challenges and recommendations. *Macromol Biosci*. 2019; 19 (5): 1800384.
- Katz, A. R. Urinary tract infections and acupuncture. *Am Med J Publ Health*. 2003; 9: 702-723.
- Ovalle, A., and Levancini, M. Urinary tract infections in pregnancy. *Curr Opin Urol*. 2001; 11 (1): 55-59.
- Foxman, B. Epidemiology of urinary tract infection: incidence, morbidity, and economic costs. *Dis Mon*. 2003; 49 (2): 53-70.
- Iweriabor, B. C., Obi, C. L., and Akenyemi, O. Uropathogens isolated from HIV-infected patients from Limpopo Province, South Africa. *Afr J Biotechnol*. 2012; 11: 1059810604.
- Samje, M., Yongwa, O., Enekegbe, A. M., and Njaya, S. Prevalence and antibiotic susceptibility pattern of bacteriuria among HIV-seropositive patients attending the Bamenda Regional Hospital, Cameroon. *Afr Health Sci*. 2020; 20(3): 1045-1052
- Hidron, A. I., Kempker, R., Moanna, A., and Rimland, D. Methicillin-resistant *Staphylococcus aureus* in HIV-infected patients. *Infect Drug Resist*. 2010; 3: 73-86.
- Gajdács, M. Increasing relevance of Gram-positive cocci in urinary tract infections: a 10-year analysis of their prevalence and resistance trends. *Sci Rep*. 2020; 10 (1): 1-11.
- Timothy, O. O., Olusesan, F. J., Adesola, B. O., Temitayo, A. A., David, F. O., and Ige, O. O. Antibiotic resistance pattern of bacterial isolates from cases of urinary tract infections among hospitalized and out-patients at a tertiary health facility in South Western Nigeria. *Ann Trop Med Publ Health*.
- Schlesselman, J. J. Sample size requirements in cohort and case-control studies of disease. *Am J Epidemiol*. 1974; 99 (6): 381-384. <https://doi.org/10.1093/oxfordjournals.aje.a121625>
- Cheesbrough, M. *Microbiology tests: District Laboratory practices in tropical countries*. Volume 2. Cambridge University Press, UK. 2006: 35-70.
- Bale, M. I., Babatunde, S. K., and Awe, S. Prevalence of methicillin resistant *Staphylococcus aureus* bacteriuria among pregnant women attending secondary health hospitals in Ilorin, Nigeria. *J Adv Microbiol*. 2021; 21 (9): 50-57.
- Fawole, M. O., and Oso, B. A. Characterization of Bacteria. In *Laboratory Manual of Microbiology*. Spectrum Books Limited, Nigeria. 2004; 22-33.
- Clinical and Laboratory Standards Institute (CLSI). *Performance Standards for Antimicrobial Susceptibility Testing*. 27th M100. Clinical and Laboratory Standards Institute; PA, USA. 2017
- Bradford, P. A. Extended Spectrum β Lactamases in the 21st century: Characterization, Epidemiology and Detection of This Important Resistance Threat. *Clin Microbiol Rev*. 2001; 14: 933-951.
- Olowe, O., Ojo-Johnson, B., Makanjuola, O., Olowe, R., and Mabayoje, V. Detection of bacteriuria among human immunodeficiency virus seropositive individuals in Osogbo, south-western Nigeria. *Euro*

- J Microbiol Immunol. 2015; 5 (1): 126-130.
24. Alemu, A., Dagne, M., Alem, M., and Gizachew, M. Uropathogenic bacterial isolates and their antimicrobial susceptibility patterns among HIV/AIDS patients attending Gondar University Specialized Hospital, Gondar, Northwest Ethiopia. *J Microbiol Res Rev.* 2013; 1(4): 42-51.
 25. Ifeanyi-chukwu, I., Emmanuel, N., and Chika, E. Frequency and antibiogram of uropathogens isolated from urine samples of HIV infected patients on antiretroviral therapy. *Am J Biosci.* 2013; 1 (3): 50-53.
 26. Xavier, T. F., Auxilia, A., and Kannan, M. Isolation and characterization of UTI pathogens from HIV positive patients of Karur District, Tamil Nadu, India. *Int J Curr Microbiol Appl Sci.* 2015; 558-563
 27. De-Pinho, A. M., Lopes, G. S., Ramos-Filho, C. F., et al. M. Urinary tract infection in men with AIDS. *Genitourin Med.* 1994; 70: 30-34.
 28. Widmer, T. A., Theron, G., and Grove, D. Prevalence and risks of asymptomatic bacteriuria among HIV-positive pregnant women. *South Afr J Epidemiol. Infect.* 2010; 25 (1): 28-32.
 29. Ojoo, J., Paul, J., Batchelor, B., et al. Bacteriuria in a cohort of predominantly HIV-1 seropositive female commercial sex workers in Nairobi, Kenya. *J Infect.* 1996; 33: 33-37
 30. Ezechi, O. C., Gab-Okafor, C. V., Oladele, D. O., et al. Prevalence and risk factors of asymptomatic bacteriuria among pregnant Nigerians infected with HIV. *J Matern-Fetal Neonat Med.* 2013; 26 (4): 402-406
 31. Olowe, O. A., Makanjuola, O. B., Olabiyi, K. O., Akinwusi, P. O., Alebiosu, C. O., and Isawumi, M. A. Asymptomatic bacteriuria among elderly and middle-aged rural community-dwellers in South-Western Nigeria. *Infect. Drug Res.* 2013; 6: 55-58
 32. Gugino, L., Russo, T., Wactawski-Wende, J., Good-nough, S. L., Tristram, D. A., and Mylotte, J. Asymptomatic bacteriuria in human immunodeficiency (HIV)-infected women. *Prim Care Update Ob Gyns.* 1998; 5 (4): 146
 33. Iduoriyekemwen, N. J., Sadoh, W. E., and Sadoh, A. E. Asymptomatic bacteriuria in HIV positive Nigerian children. *J Med Biomed Res.* 2012; 11 (1): 88-94.
 34. Samuel, S., Salami, T., Adewuyi, G., Babatope, E., and Ekozien, M. Prevalence of urinary tract infections among a cohort of HIV positive patients accessing care in a rural health centre in Nigeria. *J Microbiol Biotechnol Res Scholars.* 2012; 2 (4): 507-510.
 35. Hermann, V., Palma, P., Geo, M. S., and Lima, R. S. Urinary tract infections: pathogenesis and related conditions. *Int Urogynecol J.* 2002; 13: 210-213
 36. Ariathianto, Y. Asymptomatic bacteriuria – prevalence in the elderly population. *Aust Fam Physician* 2011; 40, 805-809
 37. Omeregie, R., and Eghafona, N. Urinary tract infection among asymptomatic HIV patients in Benin City, Nigeria. *Br J Biomed Sci.* 2009; 66 (4): 190-193.
 38. Adebayo, A., and Salman, A. "Prevalence and predictors of asymptomatic bacteriuria in HIV positive pregnant women. *J Med Med Sci Res.* 2014; 3 (5): 48-54.
 39. Akinbami, A., Bode-Shojobi, I., and Ajibola, S. Prevalence of asymptomatic bacteriuria in HIV infected patients in a Tertiary Hospital in Lagos, Nigeria. *World J AIDS.* 2013; 3 (2): 105-110.
 40. Fenta, G., Legese, M., and Weldearegay, G. Bacteriuria and their antibiotic susceptibility patterns among people living with HIV attending Tikuran Bessa specialized and Zewditu memorial hospital ART clinics, Addis Ababa, Ethiopia. *J Bacteriol Parasitol.* 2016; 7 (5): 1-7.
 41. Skrzat-Klapaczynska, A., Matlosz, B., and Bednarska, A. Factors associated with urinary tract infections among HIV-1 infected patients. *PLoS One.* 2018; 13 (1): 2-18.
 42. Banu, A., and Jyothi, R. Asymptomatic bacteriuria in HIV-positive individuals in a tertiary care hospital. *J HIV Human Reprod.* 2013; 1 (2): 54.
 43. Lyamuya, E., Moyo, S., Komba, E., M., and Haule, M. Prevalence, antimicrobial resistance and associated risk factors for bacteriuria in diabetic women in Dar Es Salaam, Tanzania. *Afr J Microbiol Res.* 2011; 5 (6): 683-689.
 44. Rashmi, K., Ravikumar, K., Nimitha, J., and Bhagyashree, H. Asymptomatic bacteriuria in HIV/AIDS patients: occurrence and risk associated with low CD4 counts. *J Evol Med Dental Sci.* 2013; 2 (19): 3358-3366.
 45. Muruges, K., Deepa, S., Ravindranath, C., and Venkatesha, D. Multidrug resistant uropathogens in HIV: are they a threat to community? *Int J Sci Study.* 2014; 2 (3): 38-42.
 46. Dadi, M., Senthilkumar, B., and Berhanu, S. Prevalence, Antimicrobial Susceptibility Pattern of Bacterial Isolates, and Associated Factors of Urinary Tract Infections among HIV-Positive Patients at Hiwot Fana Specialized University Hospital, Eastern Ethiopia. *Canadian J Infect Dis Med Microbiol.* 2019; 19: 8.
 47. Eyasu, M., Kassahun, K., Yilikal, A., Yewondwossen, T., and Alemayehu, K. Food Medicine and Healthcare Administration and Control Authority of Ethiopia, Addis Ababa, Ethiopia, 3rd edition. 2014