

# Multi Drug Resistant Uropathogens in HIV: Are They A Threat to Community?

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## Abstract

**Introduction:** Untreated Urinary tract infections accounts for 7-60% of opportunistic infections in immunocompromised hosts. Asymptomatic bacteriuria is one among the important causes of opportunistic infections in HIV seropositive. Urinary tract infections became quite alarming as isolated uropathogens exhibits high percentage resistance to almost all antibiotics. Limited data is available from India on the frequency of asymptomatic bacteriuria in HIV seropositive.

**Aims & Objectives:** The present study was taken up to know the prevalence of asymptomatic urinary tract infections among HIV patients.

**Materials & Methods:** 200 HIV seropositive patients without any complaints of urinary symptoms were included in the study. Patients with urinary tract abnormalities, diabetes mellitus, pregnancy etc. were excluded from the study. Patient's history of antibiotics & anti retroviral treatment intake was noted. Urine samples were processed by standard protocols. Antibiotic susceptibility testing was performed using Kirby-Bauer's disk diffusion method. CD4 counts were done using FACS Calibur.

**Results:** Among 200 HIV patients in the study, 100 patients were on antiretroviral treatment. Out of 200 urine samples, 60 (30%) samples showed significant growth. 40 patients with significant bacteriuria were on antiretroviral treatment. Out of 60 samples, 48 (80%) isolates were bacteria & 12 (20%) were identified as Candida species. Commonest bacterial isolates were Staphylococcus aureus 34 (56.66%), Enterococcus species 09 (15%), Escherichia coli 03 (5%). Isolates showing resistance to three or more than three categories of antibiotics were considered as multi drug resistant bacteria. 28 bacterial isolates were showing multi drug resistance. 15 (44.11%) of Staphylococcus aureus were methicillin resistant.

**Discussion:** Higher prevalence of resistant uropathogens in HIV patients is a definitive threat. The early identification of multi drug resistant uropathogens in these patients and their proper treatment will help in patient betterment & also avoids the spread of these bacteria to the community.

**Conclusion:** Routine urine screening of HIV seropositive might help in the early detection of multi drug resistant uropathogens.

**Keywords:** Asymptomatic bacteriuria, HIV, Multidrug resistant uropathogens

## INTRODUCTION

The Acquired Immunodeficiency Syndrome (AIDS) caused by Human Immunodeficiency Virus (HIV) is the most important public health problem. Though HIV infections made delayed into India, its spread has been very rapid and at present, India has the distinction of having the largest number of people living with HIV in the world.<sup>1</sup> Urinary tract infection (UTIs) is one of the significant illnesses

that cause burden on national exchequer. It is not only common nosocomial infection but an important source of morbidity in community as well.<sup>2</sup> Urinary infections are one of the most common bacterial infections and the cause of morbidity and hospitalization in HIV positive individuals.<sup>3</sup> HIV disease is associated with a variety of renal syndromes. In patients with low CD4 counts, bladderareflexia and hyporeflexia are common neurologic complications, which lead to urinary stasis and ultimately infection.<sup>4,5</sup>

However, prevalence of data on the frequency of UTIs in HIV infected patients is limited & is not updated. Urinary tract infections accounts for a significant proportion of patient's daily hospital visits in HIV patients.<sup>6</sup> Asymptomatic bacteriuria (ASB) is isolation of a specified quantitative count of bacteria in an appropriately collected urine specimen obtained from a person without symptoms or signs referable to urinary infection.<sup>7,8</sup> Untreated UTI accounting for 7-60% of opportunistic infections could be a source for ascending urinary tract infection and septicemia in immunocompromised hosts.<sup>4</sup>

UTI accounts for a large proportion of anti-bacterial drug consumption.<sup>3</sup> Resistance to commonly prescribed antibiotics for UTI is an expanding global problem both in developed as well as developing countries.<sup>8</sup> Due to widespread and injudicious use of antibiotics at community level, we are encountered with more resistance patterns to common antibiotics.<sup>2</sup> UTI became quite alarming as isolated uropathogens exhibits high percentage resistance to almost all antibiotics.<sup>9</sup> These multidrug resistant (MDR) pathogens are relentlessly multiplying in HIV patients & thus become an important circulating source of infection in the community.

Most of the times for treating UTI, empirical therapy is used till culture and susceptibility patterns are available.<sup>8</sup> It is necessary to have a good knowledge of the etiological agents, their epidemiological characteristics and antibacterial susceptibility profiles.<sup>3</sup> Unfortunately nearly all available current data on uropathogens are derived mostly from female patients. Uropathogens causing UTI in different age groups of male patients and their antibiotic susceptibility are scarcely available one.<sup>9</sup>

As limited data is available from India on the frequency of ASB/UTIs in HIV seropositive and comparison of these infections between pre-antiretroviral treatment (ART) and ART patients, the present study aimed to assess its occurrence by screening and culture methods. However there is paucity of literature on the role of the virus in predisposition to infections of the urinary tract.<sup>4</sup> By its nature, the HIV predisposes to multi system/organ infection. It can thus be hypothesized that the incidence of UTI in individuals with HIV/AIDS would be increased in comparison to non-infected individuals.<sup>10</sup> Early diagnosis and apt treatment are the identified imperative factors for their elimination and there by avoid associated urosepsis plus renal scarring risk.<sup>9</sup>

So this study was taken up to know the prevalence of urinary tract infections and their antibiotic susceptibility pattern in asymptomatic individuals of HIV/AIDS patients.

## MATERIALS & METHODS

This prospective study was carried out at the department of Microbiology, Mysore Medical College & Research institute, Mysore from July 2013 to December 2013.

200 HIV seropositive patients attending integrated counseling and testing centre (ICTC) antiretroviral treatment (ART) Centre were included in the study. 100 patients who were taking ART & 100 patients who were not on ART (non-ART) without any urinary symptoms were taken for the study. Patients with urinary tract abnormalities, diabetes mellitus, pregnancy etc. were excluded from the study.

Urine samples were collected from patients after counseling. Detailed history of antibiotics intake and history of ART drugs was taken. CD4 counts of these patients were done using BD-FACS Calibur.

Midstream urine samples were collected from the patients in sterile containers. Samples were processed within 30 min of collection. Microscopy and culture were done as per the standard protocols. Isolates grown were identified using standard biochemical reactions.<sup>11</sup> Antibiotic susceptibility testing was performed using Kirby-Bauer's disk diffusion test as per CLSI guidelines. Antibiotics used for the isolates were Ampicillin-30 µg, Cotrimaxazole-1.25/23.75 µg, Erythromycin-15 µg, Clindamycin-2 µg, Nitrofurantoin-300 µg, Ciprofloxacin-5 µg, Norfloxacin-10 µg, Cefoxitin-30 µg, Linezolid-30 µg, Vancomycin-30 µg, Gentamycin-10 µg, Imipenem-10 µg, Ceftazidime-30 µg, Cefotaxime-30 µg, Amoxyclavulanic acid-30 µg.<sup>12</sup> Isolates showing resistance to three or more than three categories of antibiotics were considered as MDR bacteria.<sup>13</sup>

## RESULTS

A total of 200 urine samples were collected from 200 HIV seropositive patients. The age of the population studied ranged between 8-70 years. The mean age was 33 years. 33 (55%) patients with asymptomatic bacteriuria were females & 27 (45%) were males (Table 1). Out of 200 urine samples, 60 (30%) samples showed significant growth. Among them 48 isolates were bacteria and 12 were identified as Candida species. 20 (58.82%) of Staphylococcus aureus were showing multidrug resistance (Table 2).

Out of 60 infected patients, 23 of them had CD4 counts <350, 23 had HIV-TB co-infection and 15 of them were on ART (Table 3).

**Table 1: Distribution of cases of asymptomatic bacteriuria among non-ART/ART patients**

Gender	No of cases with ASB	Pre ART	On ART
Male	27	12	15
Female	33	08	25
Total	60	20	40

**Table 2: Percentage of multidrug resistant bacteria (MDR) among different bacterial isolates**

Type of Isolate	No of cases	MDR cases
S. aureus	34	20
Enterococcus spp	09	05
Escherichia coli	03	02
CONS	01	00
Acinetobacterspp	01	01
Candida spp	12	00
Total cases	60	28

CONS-Coagulase negative Staphylococcus, S. aureus-Staphylococcus aureus

**Table 3: Asymptomatic bacteriuria patients in relation with CD4 count**

CD4 count	No of cases examined	No of cases with ASB
<50	10	03
50 to 200	27	15
201-350	30	05
>350	133	25
Total	200	48

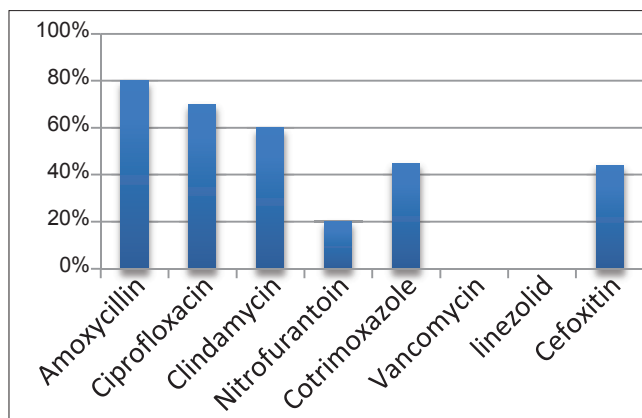
Fifteen (44.11%) isolates of Staphylococcus were MRSA. Graphs 1 and 2 showing antibiotic resistance of Staphylococcus aureus & Enterococcus species.

## DISCUSSION

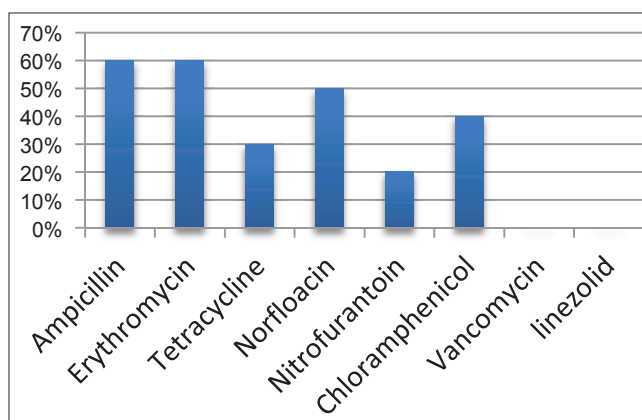
More than 40 million people are living with HIV and to this pool additional 14,000 people are estimated to be added everyday.<sup>6</sup> Opportunistic infections are the cause of high morbidity and mortality in HIV/AIDS patients. Prompt and accurate diagnosis and management of opportunistic infections will not only prolong the life of an HIV infected individual but also improve the quality of life.<sup>4</sup> There has been concern about the prevalence of UTIs amongst HIV infected patients in recent times, thus we investigated the occurrence and antibiogram of uropathogens among pre-ART & ART HIV seropositive individuals.

In our study out of 200 HIV positive cases, 48 (24%) showed significant bacteriuria that correlates with the other studies.<sup>14,15</sup>

More than 90 % of UTIs are due to enteric Gram positive and Gram negative bacteria including Staphylococcus



**Graph 1: Percentage of antibiotic resistance of Staphylococcus aureus isolates**



**Graph 2: Percentage of antibiotic resistance of Enterococcus Species**

aureus, Escherichia coli, Pseudomonas aeruginosa, Proteus mirabilis and Klebsiella pneumoniae.<sup>6</sup> In our study most of the infections were caused by Staphylococcus aureus 34/60 (56.66%), Enterococcus 09/60 (15%), Escherichia coli 03/60 (5%) cases (Table 2). Candiduria was seen in 12/60 (20%) cases. This observation correlates to the results of another study where Staphylococcus was the most common uropathogen.<sup>14</sup> These are in contrast to the observations of various studies that have reported E. coli, Klebsiella, Pseudomonas and Enterococcus as the most common urinary isolates.<sup>16-18</sup> Another study from Bangalore has reported E. coli 5/12 (41.7%) followed by Staphylococcus aureus 3/12 (25%), Pseudomonas aeruginosa 2/12(16.7%), Klebsiella pneumoniae 1/12 (8.3%), Coagulase negative Staphylococcus 1/12 (8.3%).<sup>7</sup> The changing pattern of etiology in various geographical regions & susceptibility pattern should be taken into consideration before initiating treatment for UTI in AIDS patients.

Candida is a much known successful opportunistic pathogen in HIV people. If at all, candida is the cause for UTIs, there is a definitive chance for it to establish systemic infection.

People living with HIV are likely to be more predisposed to UTI due to the suppression of their immunity and women in this category tend to get UTI more often due to the nature of their anatomy.<sup>19</sup> The bacteriuria was significantly more in females than males i.e. 33/60 (55%) cases in our study (Table 1). This follows the trend in normal healthy individuals where females are at higher risk of being infected with UTI. However this finding is in contrast with the studies that have reported a lower prevalence rate in female.<sup>14,20</sup> Whether anatomical considerations affect the incidence of UTIs in HIV patients or multiple factors operate like sexually active age, behavioral abnormalities and prevalence of HIV in both sexes or exclusion of pregnant females in our study.

In our study among 48 patients with asymptomatic bacteriuria, 34 were on ART and 14 were non-ART (Table 1). Asymptomatic bacteriuria was more among the patients who were on ART than non-ART, probably that lower CD4 counts in ART patients predicts the lower immune status with higher chances of opportunistic infections like asymptomatic bacteriuria.

Among 48 isolates, 28 were shown to be MDR of which 16 were found to be resistant to Co-trimoxazole (Table 2). Fifteen (44.11%) isolates of *Staphylococcus aureus* were MRSA (Graph 1). The emergence of antibiotic resistance in the management of urinary tract infections is a serious public health problem particularly in the developing world where apart from high level of poverty, ignorance and poor hygiene practices, there is also a high prevalence of fake and spurious drugs of questionable quality in circulation.<sup>19</sup> Out of 48 infected patients, 23 of them had CD4 counts <350 (Table 3), 23 had HIV-TB co-infection and 15 of them were on ART at the time of urine examination, which again adds to the burden of antimicrobial resistance. It is observed that the patients with immunosuppression have a very high chance of developing bacteriuria. The patients who are on Cotrimoxazole prophylaxis with asymptomatic bacteriuria or UTI should not receive Cotrimoxazole, as they are most likely to be resistant. Co-trimoxazole prophylaxis did not have significant effect in prevention of ASB. Also it becomes necessary that antibiotic resistance pattern should be known before any treatment, which avoids unnecessary antibiotics.

An immunocompromised status like HIV is a hotspot for MDR pathogens to multiply relentlessly and become source of infection to other healthy population.

UTI in HIV-positive patients tends to recur, requiring longer treatment and it is suggested that treatment should be culture-specific.<sup>21</sup> Diverse studies across the globe have reported the incidence of asymptomatic bacteriuria in HIV

patients as 3.1%-to the maximum of 26% compared to an average prevalence of 0.04% in healthy population.<sup>4</sup> It would have been useful to investigate more aggressively with better history taking and physical examination of HIV patients. We have considered significant bacteriuria ( $10^5$  Cfu/ml) for our study. With the immunocompromised status of HIV patients, a lower colony counts cannot be ignored. So the actual prevalence of infection will be definitely more and has to be considered.

HIV positive patients are liable to acquire opportunistic infections. But with the advent of highly active antiretroviral therapy (HAART) which has shown to have an indirect immune restoration but long lasting preventive effect.<sup>19</sup> Early initiation of ART helps in immune reconstitution and possible reduction of viral load. This has improved considerably the health and life expectancy of people who are HIV seropositive. An attempt to diagnose UTI/ASB early will surely help the patient to avoid complications.

## CONCLUSION

Routine urine examination for UTI could be considered for HIV patients on ART. The present study suggested that the early initiation of ART might help the patient to maintain the immune status which in turn help in preventing the opportunistic infections. The identification of MDR pathogens in these patients and their proper treatment will help in patient betterment & also avoids the spread of these MDR bacteria to the community.

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