Asymptomatic Bacteriuria in Patients on Antiretroviral Drug Therapy in Calabar

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The prevalence of asymptomatic bacteriuria was carried out on 600 HIV Positive patients on antiretroviral drug therapy and 200 apparently healthy individuals (control subjects) in Calabar, Nigeria to determine the current status of asymptomatic bacteriuria among this category of patients. Urine samples were collected in sterile universal bottles and analyzed using standard laboratory diagnostic techniques and cultured using Lee and Williams technique. CD4 cell counts were also measured. The modified Kirby-Bauer sensitivity testing technique was used for antimicrobial testing of the isolates. Patients on antiretroviral therapy had 25.3% asymptomatic bacteriuria while control subjects had 13%. There was a statistically significant difference between the prevalence of infection in patients on antiretroviral therapy and the control subjects (p = 0.0013). Males had a higher prevalence than female subjects but there was no statistically significant difference between the occurrence of infection by gender (p = 0.66). The commonest urinary pathogens isolated amongst the test subjects were Staphylococcus aureus (87.2%) followed by Escherichia coli (84%) and Candida albicans (80.8%) while Candida albicans (19.2%) was the commonest isolated organism in control subjects followed by E. coli (16%) and S. aureus (12.8%). Subjects with CD4 count of less than 200x10^3 L^-1 showed the highest rate of asymptomatic bacteriuria of 92.3% among the test subjects while CD4 count >600x10^3 L^-1 had the highest rate of asymptomatic bacteriuria (35%) among the control subjects. Most of the isolates from patients on antiretroviral therapy were observed to be moderately or highly resistant to the commonly used antibiotics such as Chloramphenicol, Cotrimoxazole and Streptomycin but sensitive to Ciprofloxacin, Oxoflaxacin, Sparfloxacin and Rifampacin. This study has shown that patients on antiretroviral therapy are more prone to asymptomatic bacteriuria than normal healthy individuals and recommend the use of Ciprofloxacin or Rifampacin for the treatment of asymptomatic bacteriuria among this category of patients in our environment.

Key words: HIV seropositivity, prevalence, urinary tract infection, HIV treatment, calabar

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INTRODUCTION

People living with Human Immunodeficiency Virus (HIV) are likely to be more predisposed to urinary tract infections due to the suppression of their immunity and women in this category tend to get them more often due to the nature of their anatomy (Bakke and Digranes, 1991; Kayima et al., 1996; Kumamoto et al., 2002). With the advent of highly active antiretroviral therapy (HAART) which has shown to have an indirect (immune restoration) but long lasting preventive effect, this has improved considerably the health and life expectancy of people who are HIV positive (Spence et al., 1996). A study by Dworkin et al. (2001) has revealed antiretroviral drug administration to be an independent factor that contributed to a two-fold decrease in the incidence of bacterial infection such as pneumococcal disease.

Another approach by Paul et al. (1999) observed a two-fold decrease in the incidence of hospital admissions for HIV-infected patients on HAART. While in the contrary, Masliah et al. (2000) reported on the causes of death in HIV infected persons revealed a decrease in opportunistic infections but an increase in bacterial infections among patients on HAART. Men infected with HIV and presenting with a CD4 count of 200-10^4 L^-1 have shown an increased risk of acquiring bacteriuria (Hoepelman et al., 1992) while women with HIV or CD4 count below 0.2 x 10^5 L^-1 (or both) have a higher incidence of bacteriuria (Evan et al., 1995). Several reports have linked patients on antiretroviral with high prevalence rate of urinary tract infection (De Pinho et al., 1994; Bakke and Digranes, 1991; Delzell and Lefevre, 2000). A study at the London Royal Hospital, London revealed urinary tract infection to be more common in elderly patients compared to younger age patients with HIV infection (Evans et al., 1995) while another study by Ibadin et al. (2006) revealed HIV/AIDS to be a predisposing factor for increased incidence of urinary tract infection in the young.

A study from Chicago, United States revealed urinary tract infection in 10.2% of HIV positive patients and the most common etiologic agents were Staphylococcus aureus, Pseudomonas aeruginosa and Enterobacter cloacae. The implication of urinary tract infection associated with HIV is the increased cost of care for HIV/AIDS patients. Cotrimoxazole (Septin) is one of the drugs given to HIV/AIDS patients for opportunistic infections (Evan et al., 1995). This study was carried out to determine the prevalence of asymptomatic bacteriuria in patients on antiretroviral drug therapy in Calabar with a view to suggesting a new antibiotic regimen in the treatment of asymptomatic bacteriuria among HIV/AIDS patients on HAART in the study area.

MATERIALS AND METHODS

Study area: This study was carried out between August, 2007 and September, 2008 in Calabar the capital city of Cross River State, Nigeria. The current prevalence of HIV in the Cross River State is 10% (WHO, 2007). The University of Calabar Teaching Hospital (UCTH) and the General Hospital (GH), Calabar provide tertiary and secondary health care needs of the people including HIV/AIDS care and support. However, there are about eighteen private clinics that provide supportive health care to patients.

Subjects and consent: A total of 600 unselcted HIV-positive subjects aged 5 to 69 years who were currently on HAART at the 2 of the free HIV treatment centres in Calabar metropolis and 200 apparently healthy control subjects were investigated. Approvals were sought and obtained from the management of the free-HIV treatment centres. Informed consent was also sought and obtained verbally from the patient (or patient’s relations for those below 18 years) before inclusion in the study. The unharminful nature and advantage of the research was also explained to each patient or their relation.

Collection of samples: Patients after due counseling were enrolled consecutively for the study. Patients were screened for HIV-1 and HIV-2 using Trinity Biotech capillus HIV-1/HIV-2 agglutination assay test-kit manufactured by Trinity Biotech PLC at Jamestown, USA and Bray, Ireland and SD Bioline HIV -1/2 3.0 test-kit manufactured by standard diagnostic INC Kyonggi-do, Korea. Sterile universal bottles were issued to each subject for the collection of clean catch mid-stream urine specimen. The age, sex and hospital form numbers were recorded on the specimen bottles.

Questionnaire administration: Questionnaires were also administered on each of the subjects for the following information; prior history of UTI, antibiotic usage, sex, marital status, date of starting antiretroviral drugs therapy, duration of treatment, CD4 count and history of any opportunistic infections.

Processing of urine samples: Each urine specimen was cultured onto Cysteine Lactose Electrolyte Deficient (CLED) agar and blood agar using (Leigh and Williams, 1964). Specimens were also examined both macroscopically and microscopically. Gram stain and standard biochemical tests were used to identify the organisms. The media used included Sabouraud agar, serum and corn meal agar for identification of Candida.
**Results**

Of the 800 subjects examined, 600 were patients on HAART while 200 were apparently healthy individuals (control subjects) residing in the same study area where this investigation was carried out. Out of the 600 test subjects, 152 (25.3%) had asymptomatic bacteriuria while 26 (13%) control subjects had asymptomatic bacteriuria. Table 1 shows the distribution of asymptomatic bacteriuria among subjects examined. The highest rate of asymptomatic bacteriuria in test (40%) and control subjects (18.8%) were in age groups 11-20 and 41-50 years, respectively. The lowest prevalence of infection in test subjects (0%) occurred in age group 1-10 while that of the control subjects occurred in the age groups 1-10 and >50 years, respectively. The rate of infection in test subjects who were 50 years and above was less. There was a statistically significant difference between the occurrence of infection in the test subjects and in the control subjects ($\chi^2 = 6.14; df = 1; p = 0.013$). The distribution of asymptomatic bacteriuria among subjects examined by gender is shown on Table 2. The highest prevalence of asymptomatic bacteriuria occurred in males (28.6%) while females had 23.8%. There was no statistically significant difference between the occurrence of infection in males and females ($\chi^2 = 0.189; df = 1; p = 0.663$). Table 3 shows the distribution of organisms isolated among test and control subjects examined. Amongst the test subjects Staphylococcus aureus had the highest frequency (87.2%), followed by Escherichia coli (84%) and Candida sp., (80.8%). The distribution of infection by $CD_4$ count of the subjects examined is shown on Table 4. The highest prevalence of infection occurred among test subjects with $CD_4$ count range 1-200 (92.3%) while the lowest occurred in the ranges 401-600, 601-800, 801-1,000 (9%). In the control subjects the highest prevalence of infection occurred in the $CD_4$ count range 600 and above (35%) while the lowest occurred in the range 1-200 and >100 (9%). There was a statistically significant difference between occurrences of infection and level of $CD_4$ count.
There was a strong positive correlation between occurrence of infection and level of CD4 count ($r = 0.9$).

Antimicrobial sensitivity pattern of isolates from test and control subjects is shown on Table 5. Most of the isolates showed multidrug resistance among the test subjects. *Escherichia coli* was highly sensitive to Ciprofloxacin 84 (100%) and Augmentin 84 (100%) and lowest sensitivity was in Streptococcus 0 (0%) and chloramphenicol 0(0%). *Staphylococcus aureus* was highly sensitive to Ciprofloxacin 68 (100%) and Augmentin 68 (100%) and least sensitive to Gentamicin 64 (94.1%), Amoxicillin 64 (94%), doxycycline 60 (88.2%), Oxacillin 60 (88.2%), Augmentin 52 (76.4%).

**DISCUSSION**

This study was an attempt to evaluate the prevalence of asymptomatic bacteriuria among HIV positive individuals on antiretroviral drug therapy. Patients on antiretroviral drug therapy had prevalence rate of 25.3% which is in consonance with the findings of Schowald *et al.* (1999) in United States of America who had 25% asymptomatic bacteriuria among patients on antiretroviral drug therapy. This prevalence rate is higher than that of Ibadin *et al.* (2006) and Delzell and Lefevre (2000), who reported 6.3 and 7% in Benin City and United States of America, respectively. The low infection rate obtained among subjects aged 50 years and above could be due to the fact that subjects in these age-group adhere to antibiotic principles, have declining sexual activity due to change in priority and so less risk of exposure to UTI and less likelihood of bacteriuria. Also, it may probably be as a result of sampling error whereby fewer numbers of people fall within this age group and above as compared to the larger number that clustered around the age group of 21 to 40 years. It may also be due to self medication among that age group.

Men had a higher prevalence (28.6%) than women (23.8%) even though it was not statistically significant. This is higher than that of Lipsky (1989), who reported 0.9% among homosexual men on antiretroviral therapy in London. The 23.8% prevalence rate in women is higher than that of Spence *et al.* (1996), who reported 15.9% and they also observed asymptomatic bacteriuria to be found in significant number in HIV infected women irrespective of their immune status. *Escherichia coli* (84%) and *Staphylococcus aureus* (87.2%) were the most common organisms isolated. This was higher than that of Ibadin *et al.* (2006), who had 50%
of Escherichia coli and 10% of Staphylococcus aureus among adolescents and young adults on Antiretroviral therapy in Benin City, Nigeria. This disagrees with the findings of Hooton et al. (2000) and Smith et al. (1995) who had E. coli as the most common organism isolated.

The distribution of infection according to CD4 count showed that subjects in the test group with CD4 count in the range of 1-200 had the highest level of significant bacteriuria (92.3%). This agrees with the work of Hoepelman et al. (1992), who had 30% significant bacteriuria in CD4 count <200×10^6 L⁻¹ in men with HIV-1 on antiretroviral therapy. The lower level of immunity of those with low CD4⁻ could account for this. About a third of the control subjects with CD4 count of 600 and above had asymptomatic bacteriuria. This disagrees with the expectation of lower infection due to high CD4 count. This could be due to subjects with normal CD4 count having a higher tendency to sexual activity which is a predisposing factor. Of particular importance is the in vitro sensitivity pattern of the strains of bacteria isolated in the study area. Wide spread sensitivity of isolates to antibiotics were observed with mostly the Quinolones like Ciprofloxacin, Clenoxacin, Sparfloxacin and Ofloxacin; while Augmentin showed appreciable sensitivity pattern to the isolates. In particular the isolates of E. coli and S. aureus in the test and control subjects were highly sensitive (100%) to Ciprofloxacin and Refoxacin. This sensitivity pattern can be compared to that of Manfredi et al. (2001), who had complete resistance to Ampicillin, Gentamicin and Cefoperazone but sensitive to Quinolones, Piperacillin and Ceftazidime. This study has established a higher prevalence of asymptomatic bacteriuria (25.3%) among patients on antiretroviral drug therapy compared to normal healthy individuals (13%). It has also shown a statistically significant difference in the prevalence of significant bacteriuria between individuals on antiretroviral drug therapy and relatively healthy individual. The marked resistance by bacteria to the commonly used antibiotics may be due to drug abuse. This study has demonstrated a significant level of asymptomatic bacteriuria among patients on HAART and so this population should be screened for this potential problem as part of their routine HIV care. It is therefore, recommended that the use of quinolones like ciprofloxacin or refoxacin in the treatment regimen of asymptomatic bacteriuria among HIV AIDS patients on HAART be encouraged in this environment. This finding also emphasizes the need to check widespread abuse of antibiotics which probably has led to resistance by bacteria to the commonly used antibiotics in the study area.

REFERENCES


