Effect of urinary tract infection on the prevalence of anaemia among HIV patients in Benin City, Nigeria

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Abstract
Objectives: To determine the prevalence of asymptomatic urinary tract infection (UTI) and anaemia among human immunodeficiency virus (HIV) and non-HIV subjects as well as the effect of asymptomatic UTI on the prevalence of anaemia.

Methods: Clean-catch midstream urine and venous blood specimens were collected from 421 subjects consisting of 216 HIV patients on highly active antiretroviral therapy (HAART), 101 HAART naive HIV patients and 104 apparently healthy non-HIV subjects. Urine specimens were processed to diagnose asymptomatic UTI, while the blood specimens were processed for haemoglobin (Hb) estimation. Anaemia was defined as Hb concentration <130g/L for males and <120g/L for females.

Results: HIV patients on HAART had significantly higher (p=0.046) prevalence of asymptomatic UTI compared with non-HIV subjects (27.8% vs 17.3%). HAART naive HIV patients had significantly higher prevalence of anaemia (79.2%) compared with those on HAART (44.4%) and non-HIV subjects (33.6%) (p<0.0001). The prevalence of anaemia was not significantly affected by asymptomatic UTI among the various groups of the study population (p>0.05).

Conclusions: An overall prevalence of 24.9% and 50.1% of asymptomatic UTI and anaemia respectively was recorded. Prevalence of asymptomatic UTI was higher among HIV patients on HAART while prevalence for anaemia was higher among HAART naive HIV patients. Asymptomatic UTI had no effect on the prevalence of anaemia in both HIV and non-HIV subjects.

Key words: HIV, urinary tract infection, anaemia, Nigeria


Introduction
Anaemia is the most commonly encountered haematological abnormality in human immunodeficiency virus (HIV) patients, occurs with increasing frequency and is a significant predictor of progression towards acquired immunodeficiency syndrome (AIDS) or death, with more than 70% of patients developing anaemia and requiring transfusion (1,2). Highly active antiretroviral therapy (HAART) entails treatment with a combination of two nucleoside reverse transcriptase inhibitors and a potent protease or non-nucleoside reverse transcriptase inhibitors, and is generally the gold standard for the management of HIV patients (2). HAART has been reported to increase the haemoglobin concentration and to reduce the prevalence of anaemia (2,3). However, among HIV patients on HAART, anaemia is still being reported (4,5).

The cause of anaemia in HIV patients is multi-factorial and includes infections, neoplasms, dietary deficiencies, blood loss, and medications (6). Urinary tract infection (UTI) is one of the infections observed among HIV patients, although reports on the impact of HIV on the prevalence of UTI are conflicting (7,8). Renal diseases have also been reported among HIV/AIDS patients (9). It is expected that renal damage in HIV patients will affect erythropoietin production and ultimately result in anaemia. To our knowledge, there are no published studies on the effect of UTI on the prevalence of anaemia among HIV patients. Hence this study set out to determine the prevalence of UTI and anaemia among HIV and non-HIV subjects as well as the effect of UTI on the prevalence of anaemia in both populations.

Methods
Study population
This study was carried out at the University of Benin Teaching Hospital, Benin City, Nigeria. A total 421 subjects were studied consisting of 317 HIV patients and 104 apparently healthy HIV sero-negative individuals. The HIV patients consisted of 216 patients on HAART for 3 – 6months and 101 HAART naive patients. The HIV patients were asymptomatic and all subjects had no sign or symptom of UTI and anaemia. Exclusion criteria include antibiotic usage within one week and large fluid in-take (in previous hour) before clinic attendance. The HAART regimen for HIV patients on HAART consisted of zidovudine, stavudine and nevirapine. Verbal informed consent was obtained from all subject before specimen collection. The study was approved by the Ethical Committee of the University of Benin Teaching Hospital.

Specimen collection and processing
Clean-catch mid-stream urine and 5 mL of venous blood was collected from each subject. Urine specimens were collected into a sterile screw-capped universal container containing a few crystals of boric acid as preservative. The blood specimens were collected in ethylene diamine tetra-acetic acid (EDTA) bottles.

A loopful (0.001mL) of well mixed un-centrifuged urine was streaked onto the surface of blood agar and cationic lactose electrolyte deficient (CLED) medium (M6: Plasmatec Laboratories, United Kingdom). The plates were incubated aerobically at 370C for 24 hours and counts were expressed in colony forming units (CFU) per mL. A count of ≥105 CFU/mL was considered to indicate asymptomatic UTI. Ten mL of each well-mixed urine sample was centrifuged at 2000g for 5mins. 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. Pus cells ≥5 per higher power field was considered to indicate infection.

Blood samples were analysed for haemoglobin with a Sysmex KX – 21 haematology analyzer (Sysmex Corporation, Kobe, Japan).
Table 1. Prevalence of asymptomatic urinary tract infection and anaemia

<table>
<thead>
<tr>
<th></th>
<th>Non-HIV (n = 104)</th>
<th>HAART naive (n = 101)</th>
<th>On HAART (n = 216)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UTI</td>
<td>18 (17.3%)</td>
<td>27 (26.7%)</td>
<td>60 (27.8%)*</td>
</tr>
<tr>
<td>Anaemia</td>
<td>35 (33.7%)</td>
<td>80 (79.2%)+,#</td>
<td>96 (44.4%)</td>
</tr>
</tbody>
</table>

Figures in parenthesis are percentages
* On HAART vs non—HIV: p = 0.046
+ HAART naÔve vs Non-HIV: p<0.0001
# HAART naive vs On HAART: p < 0.0001

Table 2. Effect of urinary tract infection on prevalence of anaemia.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Number Tested</th>
<th>Number with anaemia (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-HIV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>with UT</td>
<td>18</td>
<td>9 (50.0%)</td>
</tr>
<tr>
<td>without UTI</td>
<td>86</td>
<td>26 (30.2%)</td>
</tr>
<tr>
<td>HAART naive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>with UT</td>
<td>27</td>
<td>24 (88.9%)+,#</td>
</tr>
<tr>
<td>without UTI</td>
<td>74</td>
<td>56 (75.7%)</td>
</tr>
<tr>
<td>On HAART</td>
<td></td>
<td></td>
</tr>
<tr>
<td>with UT</td>
<td>60</td>
<td>26 (43.3%)</td>
</tr>
<tr>
<td>without UTI</td>
<td>156</td>
<td>70 (44.9%)</td>
</tr>
</tbody>
</table>

+ HAART naive vs non-HIV: P = 0.0061
# HAART naive vs on HAART: p < 0.0001

Anaemia was defined according to WHO criteria (10). For males this was a haemoglobin concentration of less than 130g/L, for females less than 120g/L.

Statistical Analysis
Data was analysed using Chi (X2) square test or Fisher’s exact test using the statistical software INSTAT. Statistical significance was set at the p 0.05 level.

Results
Only HIV patients on HAART had a significantly higher prevalence of UTI compared with their non-HIV counterparts (27.8% vs 17.3% respectively; p=0.046). As shown in Table 1 the prevalence of anaemia was significantly higher among HAART naive HIV patients compared with those on HAART and non-HIV subjects.

The prevalence of anaemia in all study subjects was not significantly affected by asymptomatic UTI. However, as shown in Table 2, the prevalence of anaemia among HAART naive HIV patients with UTI was significantly higher than those of non-HAART and non-HIV subjects.

Discussion
Against the background of infection (of which UTI is one) being one of the causes of anaemia among HIV patients (6), this study focused on determining the prevalence of asymptomatic UTI and anaemia among HIV and non-HIV subjects as well as the effect of UTI on the prevalence of anaemia in the study population.

In our study, only HIV patients on HAART had significantly higher prevalence of asymptomatic UTI compared with non-HIV subject. It is known that the antibacterial property of human urine lies in its low pH, high urine urea concentration and osmolality (11). It has been reported that some anti-retrovirals used in the HAART regimen results in crystalluria, nephrolithiasis, decreased glomerular filtration rate and decreased urine osmolality (12). This may affect the antibacterial properly of urine and may explain our results.

The prevalence of asymptomatic UTI among HAART naive HIV patients was higher than that for non-HIV subjects, though failing to reach statistical significance. This finding is in agreement with earlier reports (7). Reports that showed higher prevalence of UTI either studied AIDS patients, or HIV patients with symptoms of UTI (8,13).

The prevalence of anaemia among HAART naive HIV patients was significantly higher than non-HIV subjects and HIV patients on HAART. The finding that apparently healthy individuals (even those without UTI) had anaemia agrees with an earlier report and a worsening economy was suggested as a possible reason (14). Bone marrow suppression, especially the erythroid lines, have been reported among other mechanisms as the cause of anaemia among HIV patients (2,6). With HIV patients on HAART, inclusion of zidovudine in the HAART regimen and production of antibodies against HAART agents have also been reported as possible mechanisms (4,6,14). Zidovudine is among the HAART agents used by HIV patients in this study.

The presence of asymptomatic UTI did not affect the prevalence of anaemia in both HIV and non-HIV subjects. A broad spectrum of renal diseases had been reported in patients with HIV/AIDS (9). It is expected that renal damage in HIV patients will affect erythropoietin production and ultimately result in anaemia. This was not observed in this study and may be due to the fact that our patients were asymptomatic and as such may not have developed renal complications. An assessment of renal function of
such patients is needed to confirm this. The higher prevalence of anaemia among HAART naive HIV patients with UTI in comparison to other populations in this study is therefore not due to UTI, but to HIV infection itself. HAART naive HIV patients should be placed on HAART, preferably a regimen without zidovudine, to reduce the prevalence of anaemia and improve the quality of life of HIV patients (2).

In conclusion, an overall prevalence of asymptomatic UTI and anaemia of 24.9% and 50.1% respectively was observed in this study. The prevalence of asymptomatic UTI was higher among HIV patients on HAART, while the prevalence of anaemia was higher among their HAART naive counterparts. Asymptomatic UTI had no effect on the prevalence of anaemia.

Acknowledgement
We thank the Management of the University of Benin Teaching Hospital for permission to carry out this study.

References

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