Original Article

Pattern of comorbidities among highly active anti-retroviral therapy-naive HIV-infected adult Nigerian patients at initial diagnosis

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Abstract

Background: Comorbidities associated with HIV infection may have profound impact on the future clinical outcomes of infected patients. This study was carried out to assess the prevalence and types of comorbidities in newly diagnosed, highly active anti-retroviral therapy (HAART)-naïve adult HIV patients.

Methods: A retrospective study of 501 consecutive newly diagnosed, HAART-naïve HIV-infected patients was carried out between April 2014 and September 2015 at the University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria. Demographic characteristics, clinical data and comorbid disease condition at initial presentation were retrieved from the hospital records of study patients. Summary statistics was used to present discrete variables. Medians were calculated for continuous variables (age and CD_4 counts). Kruskal–Wallis test was used to compare the medians across the different groups, and the Dunn's post's test was used to compare medians between two groups.

Results: One hundred and sixty-one (32.1%) of 501 study patients were identified with comorbid conditions, of which 6 patients had more than one comorbid condition, indicating polypathology. The prevalence of comorbid conditions observed include renal disease (14.4%), hypertension (6.2%), tuberculosis (3.4%), oral thrush (2.4%), malaria (1.6%), urinary tract infection (2.2%), hepatitis-B (1%), diabetes mellitus (0.6%), while oesophageal candidiasis, herpes zoster, hepatitis-C and toxoplasmosis were 0.2% each. Comorbidities of infective origin were found predominantly in patients with WHO clinical class 3 and 4, corresponding with declining CD_4 cell counts. Renal disease was present in all four clinical stages of HIV.

Conclusion: Renal disease was the most prevalent comorbidity. Comorbidities of infective origin were found almost exclusively in patients with WHO clinical class 3 and 4. Findings highlight the need for detailed evaluation at initial presentation, prior to treatment initiation.

Keywords: Adult patients, comorbidity, highly active anti-retroviral therapy-naïve, HIV, polypathology

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Received: 05.09.2016, **Accepted:** 14.09.2016

Access this article online	
Quick Response Code:	Website: www.phmj.org
	DOI: 10.4103/0795-3038.204716

How to cite this article: Oko-Jaja RI, Awopeju A. Pattern of comorbidities among highly active anti-retroviral therapy-naive HIV-infected adult Nigerian patients at initial diagnosis. Port Harcourt Med J 2017;11:34-7.

INTRODUCTION

HIV infection is a complex multifactorial disease with a large disease burden, especially in resource-constrained settings such as Sub-Saharan Africa. Its impact is multisectorial and constitutes major health, social and economic challenges. Comorbidities in HIV infection may be infective or non-infective, HIV-related or non-HIV-related and may arise as consequences of immunosuppression, or the state of chronic inflammation and immune activation, which may inflict injury on multiple organs leading to progressive and disseminated organ damage and ageing.[1-3] These comorbidities often include infections and infestations (bacterial, viral, fungal mycobacterial and protozoal), metabolic states, malignancies, anaemia, hepatitis, renal disease, high blood pressure, heart disease and diabetes, among others.[4-6] Comorbidities in HIV infection may cause further decline in health status arising from long-term toxicity in the infected individuals even when on highly active anti-retroviral therapy (HAART).[2,4,5]

It has, therefore, become necessary for physicians to undertake thorough evaluation of HIV-infected patients at the earliest possible stage of contact with the health-care system to determine the presence and severity of these comorbid states, to optimise patient care and treatment outcomes. This study was carried out to assess the comorbid conditions in adult patients with HIV infection at the point of first presentation and diagnosis in the University of Port Harcourt Teaching Hospital (UPTH), Port Harcourt, Nigeria.

METHODS

Study subjects

This was a retrospective study of 501 adult Nigerian patients who were diagnosed with HIV infection and subsequently commenced on combination HAART for the first time at the study site (UPTH, Port Harcourt, Nigeria) between April 2014 and June 2015. Patients were not previously diagnosed with HIV and were, therefore, ART-naïve. Comorbid conditions included disease conditions found in study patients at initial diagnosis of HIV at the study site. The ethical approval was obtained from the Research and Ethics Committee of the UPTH.

Data collection

Demographic and clinical data and results of laboratory investigations which included basic haematologic indices, CD_4 cell count, serum urea, creatinine, electrolytes, liver enzymes and blood glucose estimates and comorbid disease condition(s) at presentation were retrieved from the hospital records of study patients. The patients were divided into different groups of clinical stages of disease as described by the WHO.[7] Renal function was determined by calculating the glomerular filtration rate, using the simplified modification of diet in renal disease formula as described by Cooper *et al.*[8]

Statistical analysis

The Graphpad Prism software version 6 (Graphpad, San Diego, USA) was used to analyse the data. Summary statistics was used to present data on categorical variables such as comorbidity, sex, marital status and disease stage. Medians were calculated for continuous variables (age and CD_4 cell counts). Kruskal–Wallis test was used to compare the medians across the different groups, and the Dunn's post's test was used to compare medians between two groups. $P \leq 0.05$ was considered statistically significant.

RESULTS

Table 1 shows the basic demographic and clinical characteristics of the 501 patients in the study. Median age of the patients was 34 years (range: 18–74 years). Females were 322 (64.3%) and males were 179 (35.7%). Fifty-five (11.0%) of the study patients were in WHO clinical stage 1 of HIV infection, 76 (15.2%) were in clinical stage 2, 151 (30.1%) were in clinical stage 3 and 219 (43.7%) were in clinical stage 4. Two hundred and fifty-five (44.9%) of the patients were married, 145 (28.9%)

Table 1: Sociodemographic and clinical data of patients (*n*=501)

Variables	Frequency (*n*%)
Age in years (median, IQR)	34 (29-42)
Gender (%)	
Male	179 (35.7)
Female	322 (64.3)
Marital status (%)	
Single	145 (28.9)
Married	225 (44.9)
Divorced	11 (2.2)
Separated	6 (1.2)
Widower/widow	20 (4.0)
Undisclosed	94 (18.8)
Clinical stage (%)	
Stage 1	55 (11.0)
Stage 2	76 (15.2)
Stage 3	151 (30.1)
Stage 4	219 (43.7)
Comorbidity (%)	
Renal disease	63 (12.6)
Hypertension	31 (6.2)
Tuberculosis	17 (3.4)
Oral thrush	12 (2.4)
UTI	11 (2.2)
Malaria	8 (1.6)
Hepatitis B	7 (1.4)
Diabetes mellitus	5 (1.0)
Oesophageal candidiasis	3 (0.6)
Herpes zoster	1 (0.2)
Hepatitis C	1 (0.2)
Toxoplasmosis	1 (0.2)
None	340 (67.9)

IQR: Interquartile range, UTI: Urinary tract infection

were single, 11 (2.2%) were divorced, 6 (1.2%) were separated, 20 (4.0%) were widowed, while 94 (18.8%) did not disclose their marital status.

One hundred and sixty-nine comorbid conditions were found in 161 (32.1%) of the 501 study patients; 14 of these comorbid conditions were identified on 6 (1.2%) patients as polypathology (or concurrent presence of 2 or more comorbidities in one patient) as shown in Table 2. No comorbid condition was found in 340 patients (67.9%). The distribution of comorbid conditions is shown in Table 1. There was no stroke, cardiac failure or any solid or haematological malignancies in the study patients.

Table 3 shows age, CD_4 cell count and comorbid conditions of the study patients according to the (WHO) HIV clinical staging at presentation. The median age of patients in clinical stage 1 was 30 years, with median CD_4 count of 623 cells/μL (IQR, 563–728); comorbid conditions in this clinical stage included hepatitis-B, hepatitis-C and urinary tract infection (UTI; $n = 1$ each). The median age of patients in clinical stage 2 was 31 years, with median CD_4 count of 412 cells/μL (interquartile range [IQR], 373–438); however, no comorbid conditions were found among patients in this clinical stage. On the other hand, patients in clinical stage 3 had a median age of 35 years and median CD_4 count of 271 cells/μL (IQR, 219–308); comorbid conditions among patients in this stage included tuberculosis ($n = 16$), oral thrush ($n = 12$), hepatitis-B ($n = 4$), UTI ($n = 4$) and diabetes mellitus ($n = 3$). In clinical stage 4, patients had a median age of 35 years, a median CD_4 count of 99 cells/μL (IQR, 47–148), while associated comorbid conditions included systemic hypertension ($n = 31$), UTI ($n = 6$), oesophageal candidiasis ($n = 3$), hepatitis-B ($n = 2$), diabetes mellitus ($n = 2$), tuberculosis ($n = 1$) and toxoplasmosis ($n = 1$). There was no significant difference ($P > 0.05$) in the age distribution of the patients in the different clinical stages. However, there were significant differences ($P < 0.05$) in CD_4 cell count between the different clinical stages.

Table 2: Pattern of polypathology in six study patients

Comorbidities	Prevalence (%)
TB, malaria and renal dysfunction	2 (1.2)
Hypertension, UTI	2 (1.2)
TB and oesophageal candidiasis	1 (0.6)
Malaria and hypertension	1 (0.6)

TB: Tuberculosis, UTI: Urinary tract infection

Table 3: Distribution of CD_4 cell count and comorbidities in clinical stages of presentation

Clinical stage	Age (median, IQR)**	CD4 (median, IQR)*	Comorbidities
Stage 1	30 (26.0-42.5)	632 (563-728)	HCV (*n*=1) HBsAg (*n*=1) UTI (*n*=1)
Stage 2	31 (27.0-41.5)	412 (373-438)	Nil
Stage 3	35 (30-44)	271 (219-308)	UTI (*n*=4) DM (*n*=3) HBsAg (*n*=5) PTB (*n*=16) Oral thrush (*n*=12) Malaria (*n*=6)
Stage 4	35 (30-42)	99 (47-148)	HBP (*n*=31) DM (*n*=2) HBsAg (*n*=2) Tuberculosis (*n*=1) Toxoplasmosis (*n*=1) Oesophageal candida (*n*=3) UTI (*n*=6) Malaria (*n*=2)

*CD_4 cell counts between the different groups are statistically significant ($P<0.05$), **Difference between the age distribution of the different groups is not statistically significant ($P>0.05$). UTI: Urinary tract infection, IQR: Interquartile range, HCV: Hepatitis C virus, HBsAg: Hepatitis B surface antigen, DM: Diabetes mellitus, PTB: Pulmonary tuberculosis, HBP: High blood pressure

DISCUSSION

In this study of HAART-naïve HIV-infected adult Nigerian patients at their first presentation leading to diagnosis (and subsequent treatment with HAART), comorbidity was prevalent. Thirty-two per cent of these patients were found with comorbidities. This finding is higher than those of Guaraldi *et al.*[1] and Denue *et al.*[2] who reported comorbidity prevalence of <20% in similar ART-naïve HIV-infected adult patients. The most prevalent comorbidity in this study was renal disease, observed in 14.4% of the study population. This is in contradistinction to the report of Denue *et al.*[2] which showed a chronic renal disease prevalence of 1.2% in HIV-infected adults in northeastern region of Nigeria. Renal disease may derive from direct viral injury to the kidney, and/or indirect effects attributable to chronic persistent systemic inflammation, collagen deposition and accelerated or premature organ ageing.[9] Other possible causes of renal disease may include multiple drug use to treat undiagnosed intermittent febrile illnesses, abuse of nonsteroidal anti-inflammatory drugs, use of traditional herbal remedies or chronic glomerulonephritis.[2]

The comorbidities are classifiable into two broad groups – infective and noninfective. Infective comorbidities may be a direct consequence of HIV-related immunodeficiency. On the other hand, noninfective comorbidities may be due to the premature ageing process sequel to chronic persistent systemic inflammation, reduced vascular endothelial reactivity and increased endovascular hypercoagulability in HIV-infection.[6,10-12]

The noninfective comorbidities comprised renal disease, hypertension and type 2 diabetes and constituted a majority (108/169, 63.9%) of all comorbidities found in the study.

Infective comorbidities included pulmonary tuberculosis, oral candidiasis, UTI, malaria, hepatitis B, oesophageal candidiasis, varicella zoster, toxoplasmosis and hepatitis C, which collectively constituted a minority (37.5%) appeared to cluster in those patients in clinical stages 3 and 4 with lower CD_4 cell counts. The presence of hepatitis B and C is difficult to interprete in these patients, but they are known to share same routes of transmission as HIV. Except for renal disease whose prevalence was very high, each disease prevalence was below its current local national figure, suggesting a complex mix of factors in determining comorbidities in treatment-naïve patients at initial presentation.[2]

According to WHO clinical stage of HIV infection, a large majority (73.8%) of this study population were within stages 3 and 4. A first presentation and disease diagnosis at clinical stages 3 and 4 represents late presentation to care. Factors predisposing to late presentation or delay in seeking care in this setting may include poverty, ignorance of availability of medical care, logistic problems including cost of transportation from place of residence to hospital, superstition, traditional beliefs, fear of stigmatisation and health-seeking habits of individuals or groups.[13-17] It has been reported that most individuals may not seek medical care in established health institutions early in their disease, especially in developing countries.[11]

A median age of 34 years was observed among the study patients reflecting that our study population was young, in agreement with reports of other studies.[9,10] HIV is known to mostly afflict the young, sexually active segments of populations in all regions globally. A higher female:male ratio (of 1.7:1) in this study was in agreement with reports of other studies[10,11] but may also be partly accounted for the well-known more positive health-seeking behaviours of the female gender, compared to their male counterparts.

This study had a number of limitations. It was a retrospective, single-centre study. Case file records often showed incomplete entries for some study patients and laboratory investigations were not extensive.

CONCLUSION

In this study, most (67.9%) of the study patients were without comorbid conditions. Renal disease was the most common comorbidity, followed by hypertension and tuberculosis. Infective comorbidities were found almost exclusively in the advancing stages of HIV disease (WHO clinical stages 3 and 4). Frequency of polypathology was low. Findings highlight need for detailed evaluation at initial presentation prior to treatment initiation, to optimise clinical outcomes. A larger, prospective multicentre study is advised.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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