Pattern of opportunistic infections in HIV Patients who fail first line antiretroviral therapy in Jos, Nigeria

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Abstract

Background: Opportunistic infections (OIs) are an important cause of morbidity and mortality in persons living with human immuno-deficiency virus (HIV) infection and may be an indication of failure of antiretroviral therapy (ART).
Methods: This descriptive cross-sectional study was carried out at a large HIV clinic of the Jos University Teaching Hospital (JUTH), North-central Nigeria. Hundred patients were randomly selected from a sample frame of 320 patients on antiretroviral therapy of at least 6 months who failed ART.
Results: Fifty-nine (59%) were females. The mean age of the patients was 41 ± 9 years. The median duration on ART was 7.5months IQR (6-17) and the median CD4 cell count was 139 cell/ml^3 IQR (69-245). The prevalence of OIs was 26% with the following frequencies: oral/ vaginal candidiasis 39%, chronic diarrhoea 26%, dermatitis 23% and pulmonary tuberculosis 13%. Neither age, sex, ART default, hepatitis co-infection, baseline CD4 count, nor CD4 count at the time of virological failure was associated with OIs.
Conclusion: Oral/vaginal candidiasis, diarrhoeal diseases, and tuberculosis are common opportunistic infections in HIV patients who fail first line antiretroviral therapy. No risk factor was associated with virological failure in this cohort of patients.

Keywords: Opportunistic infections, HIV, antiretroviral therapy.

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Introduction

Opportunistic infections (OIs) are important cause of morbidity and mortality in persons living with human immuno-deficiency virus (HIV) infection and may be an indicator of failure of antiretroviral therapy (ART) for those on therapy.[1] HIV patients are at risk of developing infectious complications more than immuno-competent persons.[1] With a population of 160 million people and HIV prevalence of 4.1%, Nigeria accounts for 10% of the world's HIV burden.[2,3]

The burden of OIs in Nigeria is therefore expected to be high. Opportunistic infections will continue to lead to significant morbidity and mortality in patients who fail ART. Antiretroviral therapy is cardinal in reducing morbidity and mortality related to HIV infection. It is important both in preventing OIs and in the resolution or improvement of some OIs.[4] Based on the Recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association/Infectious Diseases Society of America when Ois occur in the setting of ART failure drug resistance testing should be done, antiretroviral drug regimen modified and OIs appropriately treated.[5] Most cases of opportunistic infections in patients on ART occur after virological failure. Opportunistic infections may also occur in patients with virological suppression due to immune reconstitution inflammatory syndrome.[6] There is paucity of data on the pattern of OIs among Nigerians failing first line ART. We undertook this study to describe the pattern of OIs among patients who failed first line ART at a teaching hospital in north-central Nigeria.

Materials and Methods

This descriptive cross-sectional study was carried out at the HIV clinic of the Jos University Teaching Hospital (JUTH), North-central Nigeria. The study was conducted between July and December, 2010. One hundred patients were randomly selected using computerised generated random numbers from sample frame of 320 patients on antiretroviral therapy who had failed first line ART based on persistently elevated viral load (VL) >1000copies/ml for at least 6 months. The first line antiretroviral drug regimen comprised of three drug combination: Two nucleoside analogues zidovudine, stavudine or tenofovir with emtricitabine/lamivudine and non-nucleoside analogue either nevirapine or efavirenz. The data collected included demographics, HIV/ hepatitis B and/or C co-infection, presence of

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opportunistic infections at the time of virological failure, baseline CD4 counts and CD4 counts at the time of virological failure. Diagnosis of oral/vaginal candidiasis, dermatitis and chronic diarrhoea were done clinically. Pulmonary tuberculosis was defined based on presence of cough > two weeks with or without fever, weight loss, night sweats or haemoptysis and demonstration of acid fast bacilli (AFB) in two or more sputum samples and/or chest X-ray features compatible with tuberculosis. CD4 count was determined using flow cytometry (count bit Y-R 1004 Partec Muster Germany) and HIV Viral load quantification was done using Polymerase Chain Reaction (PCR) technology with Roche Ampliclor HIV-1 Monitor® Test version1.5.

Statistical analysis

Statistical analysis was done using Epi Info™ 7.1.3. Uniformly distributed continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were expressed as proportions. Non-uniformly distributed continuous data were reported as median with inter-quartile range. Chi-square test was used to compare categorical variables. Univariate and multivariate analyses were done to determine factors associated with Ois.

Ethical consideration

The study was approved by the Human Research Ethics Committee of the Jos University Teaching Hospital. Informed consent was obtained from the subjects before enrolment into the study. Data was kept secure and anonymity maintained. Patients with OIs were treated with appropriate drugs.

Results

Characteristics of the patients

The subjects had a slight preponderance of females (59%) with a mean age of the patients was 41 ± 9 years. The median duration on ART was 7.5months IQR (6-17) and the median CD4 cell count was 139 cell/ml^3 IQR (69-245). The predominant age groups of the study population were 25-34 and 35-44 years, which accounted for 37% and 36% respectively, of the study population.

Pattern and risk factors of opportunistic infections

The prevalence of OIs was 26%. Figure 1 shows that candidiasis (39%), chronic diarrhoea (26%), dermatitis (23%), pulmonary tuberculosis (13%) were the commonest OIs. Table 1 shows the results of univariate and multivariate analyses of the associations of OIs. Neither age, sex, ART default, hepatitis co-infection, baseline CD4 count nor CD4 count at the time of virological failure were associated with OIs.

Table 1. Characteristics of HIV patients who fail first line antiretroviral therapy in Jos

Characteristics	Value N=100 N (%)
Mean age (SD)	41±9 years
Females	59 (59%)
Married	51(51%)
Median CD4 cou nt(IQR), cells/mm ^{3}	139 (69-245)
Median duration on ART, months	7.5 (6-17)
WHO Stage	
Stage 1	21 (21%)
Stage 2	54 (54%)
Stage 3	21 (21%)
Stage 4	4 (4%)

Table 2. Showing factors associated with occurrence of opportunistic infections on univariate and multivariate analysis

Variables	Univariate OR (95% CI)	Multivariate AOR (95% CI)
Age: (yrs), ≤40/>40	0.62 (0.25-1.58)	0.99 (0.31-3.17)
Sex: Male/female	0.55 (0.21-1.43)	0.56 (0.17-1.84)
HIV/Hepatitis co - infection: Yes/No	0.57 (0.17-1.86)	0.76 (0.20-2.90)
Treatment default: Yes/No	1.18 (0.43-3.23)	1.41 (0.46-4.37)
Baseline CD4 count: <350/>350 cells/mm^3.	0.95 (0.09-9.52)	6.07 (0.18-204.36)
Cd4 count at time of virological failure: <350/>350 cells/mm^3	0.71 (0.14-3.57)	0.62 (0.06-6.18)

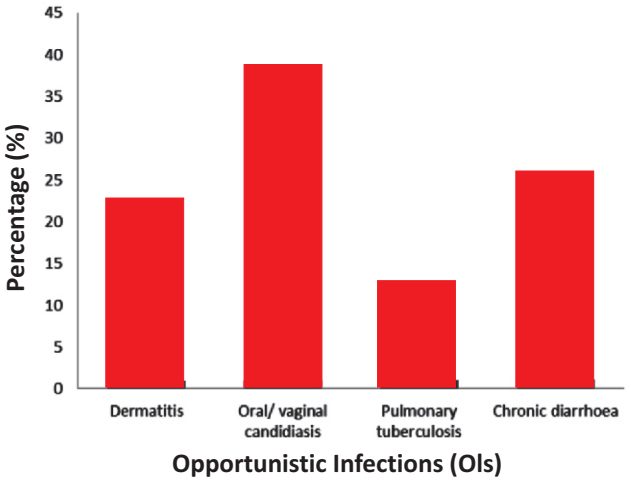

Figure 1. Opportunistic infections in HIV patients who fail first line antiretroviral therapy in Jos, Nigeria

Discussion

We studied the demographic variables prevalence and pattern of OIs in people living with HIV patients who fail first line antiretroviral therapy in Jos. The prevalence of OIs in this study was 26% this is fairly higher than 22.4% among patients predominantly on HAART in South East Nigeria but much lower than 68.6% among pre-HAART cohorts in Ilorin. [7,8] This is due to the virological failure of our cohort. This suggests that opportunistic infections generally are lower even on a failing regimen than those who are not on ART.

The pattern of OIs were as follows: candidiasis (39%), chronic diarrhoea (26%), dermatitis (23%), pulmonary tuberculosis (13%). Other studies in Africa also found candidiasis, tuberculosis, chronic diarrhoea and dermatitis as the leading OIs.[7-10] The commonest OI in our study was candidiasis (39%). This is higher than other studies in Nigeria and other resource constraint countries where prevalence was between 5% and 27.2%.[7,9,11-13] These studies were done among ART naïve and those on HAART but not in patients with virological failure. This suggests that candidiasis may predict virological failure. This is corroborated by other studies that found candidiasis as a predictor of antiretroviral therapy failure.[14,15] We found 26% patients with chronic diarrhoea this is understandably lower than an earlier study done among ART naïve patients where frequency of 32% was found.[16] This may be due concomitant ART and cotrimoxazole therapy which prevents diarrhoeal diseases. Other studies in sub-Saharan Africa found frequencies between 1.5 and 3.3% in patients on antiretroviral therapy.[7,10] Dermatitis was found in 23% of our patients this is higher than an earlier study that found frequency of 16% in ART naïve patients.[16] However, much lower frequency was found in patients on ART of 5.6%.

Tuberculosis unarguably is an important opportunistic infection causing considerable morbidity and mortality in HIV infected patients. The risk of developing tuberculosis among people living with HIV is estimated to be between 12-20 times higher than among persons without HIV infection.[17] Globally, tuberculosis is the major cause of death accounts for 1 in 3 deaths in HIV infected patients.[18,19] In our study despite virological failure the frequency of tuberculosis was 13%, this frequency is much lower compared to an earlier study done in the same setting but among patients presenting late who were not on ART, tuberculosis frequency was 61.8%.[9] This may suggests that failing ART regimen is better than no ART in morbidity associated with tuberculosis. However, similar study done in South-eastern Nigeria found a lower frequency of tuberculosis of 7.7%. [11] Their observed lower frequency is probably because their patients had not yet failed antiretroviral therapy.

We did not find baseline CD4 cell count <350 cell/ml^3, poor adherence to ART, current CD4 cell count <350 cell/ml^3, HIV hepatitis B/C co-infection and male gender to be independently associated with occurrence of OIs in patients who fail first line ART. Our finding suggests that in HIV cohorts that have virological failure, the virological failure may be the most important risk factor. This is corroborated by other studies that found viral load as an independent predictor of opportunistic infections. [20,21] The main challenge in viral load monitoring is its high cost in resource constraint countries. Low cost point of care viral load testing methods such as the ultrasensitive p24 assay, the reverse transcriptase (RT) assay and in-house reverse transcription quantitative polymerase chain reaction (RT-qPCR) would be invaluable in resource constraint countries[22] . Onwuba and colleagues[23] in their study among HIV cohorts in Nigeria also demonstrated unreliability of CD4 count in predicting the occurrence of OIs. However, the EuroSIDA and Swiss HIV cohort study found CD4 count to be significantly associated with occurrence of OIs.[24,25] These studies did not take into account the quality of CD4 cells which has been found to show inter-individual and intra-individual variability in absolute CD4 counts thus limiting its clinical usefulness.[26]

This study had certain limitations. The use of regularity of drug pick-ups was used as a measure of adherence; this may not actually mean that subjects were actually taking their medication. Diagnosis of oral/vaginal candidiasis, dermatitis and chronic diarrhoea were done clinically. Additionally, diagnosis of pneumocystis Pneumonia, CMV and sepsis were not elaborately pursued as such it may underestimate the prevalence of these Ois.

Conclusion

This study demonstrated that a quarter of patients on a failing ART regimen have OIs with oral/vaginal candidiasis, diarrhoeal diseases, dermatitis and tuberculosis being the most common. Therefore patients on ART presenting with these opportunistic infections should be evaluated for possible antiretroviral failure. Chemoprophylaxis against these common OIs may be considered in patients with virological failure.

Conflict of Interest

None declared in this work.

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