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Research Article

Prevalence of Opportunistic Infections in HIV-infected adult patients at Kenyatta National Hospital, Kenya

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Background: Opportunistic Infections (OIs) constitute the first manifestation of HIV infection, indicating significant immunodeficiency. OIs remain a leading cause of morbidity and mortality in HIV-infected persons. Since most of OIs are readily treatable and preventable, every effort should be made to facilitated their management. However, there is a need to establish local prevalence of OIs and evaluate their management. This would guide in prioritizing resource and support development of suitable management strategies.

Objective: The main objective of this study was to establish the prevalence of HIV-related OIs in adult patients.

Methodology: A hospital-based cross-sectional study conducted between July and August 2011 at Kenyatta National Hospital –Comprehensive Care Center (KNH-CCC). Adult patients who were HIV positive and attending outpatient clinic at KNH-CCC were included. Information was collected on patients' demographics, clinical characteristics and presence of new or active OIs. Data was analyzed using Statistical Package for social Sciences (SPSS) version 11.5.

Results: The prevalence of opportunistic infections was 14.1 % (95% CI: 10.7-18.5). Overall, the most commonly reported bacterial infection was pneumonia (6.4%) whereas pulmonary tuberculosis was reported in 3.6% of patients. Significant association was found between a patients' current OI status and WHO stage when HIV was diagnosed (AOR= 3.79 [95% CI = 1.43 – 10.03], P=0.007) and duration since HIV diagnosis (AOR 3.89 [95% CI= 1.58-9.59], P=0.003. 90% of patients were prescribed Co-trimoxazole as chemoprophylaxis agent.

Conclusion: There was a high prevalence of OIs among the HIV/AIDS patients at KNH-CCC. Bacterial Pneumonia and pulmonary tuberculosis were the most commonly observed OIs.

Keyword: Prevalence, Opportunistic-Infections, HIV, Patients.

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1. Introduction

Opportunistic infections (OIs) have been defined as infections that are more frequent, or more severe because of immunosuppression, were the main cause of morbidity and mortality in people living with HIV and AIDS (Walensky et al, 2006). However, the widespread uses of Highly Antiretroviral Therapy (HAART) and Chemoprophylaxis have had the most profound influence on reducing OI-related mortality (Walensky et al, 2006; Palella et al, 1998).

A review of incidence of HIV-related OIs between 1996 and 1998 in the United States, reported decreases in the incidence of *Pneumocystis carinii* pneumonia (PCP), esophageal candidiasis, and disseminated *Mycobacterium avium* complex (MAC) disease were more pronounced in 1995-1998, during which time highly active antiretroviral therapy (HAART) was introduced into medical care (Kaplan et al, 2000).

In Kuala Lumpur hospital, a retrospective review of 419 HIV/AIDS patients record showed that the prevalence of

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four major OIs were 48%, 13 %, 11% and 7 % for Tuberculosis, PCP, toxoplasmosis and cryptococcal meningitis respectively (Nissapatorn et al, 2003). Furthermore , the Indian study reported that parasitic infection were found in 35 % HIV infected patients and low CD_4 count was significantly associated with OIs (Kulkarni et al, 2009).

A cross- sectional study that was carried out in HIV-infected children at KNH-CCC estimated the prevalence of OIs to be 14.3 %. In addition, another cross –sectional study was carried out in Taita Tavet and Murang'a districts of Kenya, reported OIs prevalence of 3.3% and 4.1 % respectively (Mbatia, 2011). However, these few studies on the prevalence of OIs in Kenya have made it difficult to implement clinical strategies and program to prevent OIs consequences and decrease it cost of management. OIs consume a large share of healthcare budget and significantly impair HIV/AIDs patient's quality of life. Thus there is great interest in identifying and then remedying, predisposing factors that increase the risk of OIs.

2. Methodology

2.1 Study design

A hospital based cross-sectional review of HIV-infected adult patent's files to establish the prevalence and management of HIV/AIDS related opportunistic infections.

2.2 Study site

The present study was carried out at the Kenyatta National Hospital- comprehensive care center (KNH-CCC) between July and Aug 2011. KNH is the largest teaching and referral hospital in East Africa. Comprehensive Care Center is an out patients clinic that serves as primary care and public referral center for HIV/AIDS patients from all over Kenya.

Files were included in the study if the patients were HIV positive evidence by confirmatory result, adult defined by age of 18 years and above and attending outpatient clinic at KNH-CCC. Incomplete patient files (with missing pages) or files of patients previously included or files of patient with history of HIV exposure and tested HIV negative result were excluded from the study.

2.3 Study population

A total of 333 patient files were reviewed out of 1239 patients. 311 files were included in analysis and 22 files were eliminated form study because of failure to meet the inclusion criteria.

2.3 Sampling

Sample size for this study was calculated on the basis of the prevalence of 15%, at precision of 5 % and a 95 % level of confidence. The Fischer formula for determining the minimum sample size was used.

The files of patients seen by clinicians during the study period were obtained. The files were selected by simple random sampling and those meeting the inclusion criteria were reviewed for records of current opportunistic infections. The files were reviewed for any active or new OI recorded on that day of visit. OIs occurring on the previous visits and not active were not considered.

2.4 Data collection

The independent variable include patients' demographic characteristic such as age and sex.

The primary outcome of interest was proportion of HIV +ve adult patient who developed any of the following OIs: Bacterial infections (e.g. pulmonary tuberculosis, extraplumonary tuberculosis, bacterial pneumonia mycobacterium avium complex); fungal infections (e.g. oral candidiasis, esophageal candidiasis, *Pneumocystis jiroveci* pneumonia, cryptococcal neuralagia, hisotoplasmosis); viral infections (herpes infection, Hepatitis B virus, Hepatitis C virus infection, cytomegalovirus infections); related parasitic infections (e.g. cryptosporidiosis, toxoplasmic encephalitis); and related malignancy (e.g. Kaposi sarcoma, Non-Hodgkin's lymphoma).

The secondary outcome of interest were factors associated with OIs; these included CD_4 counts, viral load, World Health Organization stage of HIV, duration on HAART, clinical treatment failure and patient's social behavior such as alcohol , smoking and drug abuse and current opportunistic infection and their management.

2.5 Statistical analysis

Data were coded and entered into predesigned Microsoft Office Access 2003 and analyzed using Statistical Package for social Sciences (SPSS) version 11.5.

Descriptive statistics were computed to summarize the participant's social-demographic, medical history, factors predisposing HIV infected patients to develop OIs, current opportunistic infections and opportunistic infections management with regard to Kenya National guidelines. Categorical variables were summarized using frequency (%), while continuous variables were summarized using means.

Data were reported as mean +/- SD for continuous data, frequency (percentage) for categorical. The correlation between current opportunistic infections status and selected demographic characteristics and current OIs and patient medical history were assessed using logistic regression and all variables demonstrating an association at $P < 0.1$ during bivariate analysis were candidate for inclusion in multivariate analysis. Binary logistic regression 'backward conditional' method was used with removal at $P < 0.05$.

2.6 Ethical consideration

Institution approval to carry out the study was obtained from the Kenyatta National Hospital/University of Nairobi - Ethics and Research Committee (KNH/UON-ERC Ref No.: **KNH-ERC/A/161**). The review of patient files was done within KNH-CCC premises and data obtained was kept under lock and key or in pass worded computer. Data forms did not bear patients' name or clinic numbers'. Patients were only identified by study numbers.

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3. Results

From 15th July to 15th August 2011, a total of 311 files were reviewed for active Opportunistic infections present at the index visit. Demographic characteristics of the patients are summarized in **Table 1**. At the enrolment, the mean age of the patients was 41 ± (9SD) with rage of 21 and 74 years. The majority of participants 192 (58.8%) were female.

Table 1: Demographic characteristic of the study Participants

Variable	N=311	%
Age in years		
18-24	6	1.9
25-34	76	24.4
35-44	133	42.8
45-55	75	24.1
> 55	21	6.8
Sex		
Male	128	41.2
Female	183	58.8
Marital status		
Single	73	23.5
Married	196	63.0
Divorced/Widowed	42	13.5
Education level		
</= Secondary	220	79.4
>Secondary	57	20.6
No response	34	
Occupation		
Unemployed	81	28.6
Employed	202	71.4
No response	28	

Assessment of patient's medical records reveals that 55.3% of patients had their HIV diagnosis more than 36 months prior to the study time (**Table 2**). After HIV diagnosis confirmation, approximately 84.2 % of patients initiated HAART instantly. At the beginning of therapy, 43.5% had CD4 cell count ≤ 200 cell/mm3. A high proportion of patients (35.1%) initiated HAART at WHO stage III with smaller proportioned (16.8%) being initiated at stage IV.

17.4% of patients had at least one of the three factors commonly associated with OIs. **Figure 1** shows distribution of participants by factors known to predispose HIV infected patients to OIs.

An analysis of current OIs showed that 4 participants (1.3%) had 2 types of infections while others 40 (12.9%) had only 1 type. This gave an overall prevalence of OIs of 14.1 % (95% CI: 10.7-18.75). The prevalence of current OIs was 20 % among patients taking Stavudine based regimen. 90% of patients were on Co-trimoxazole prophylaxis.

Table 2: Clinical characteristics of study participants

Variables	N=311	%
Duration since diagnosis in months		
0 - 12 months	64	20.6
13 - 24 months	37	11.9
25 - 36 months	38	12.2
>36 months	172	55.3
HAART started		
Yes	262	84.2
No	49	15.8
CD4 count (cells/mm3) when HAART started		
</= 200	131	43.5
>200	170	56.5
No response	10	
WHO stage when HIV was diagnosis		
I	73	25.6
II	64	22.5
III	100	35.1
IV	48	16.8
No response	26	
Duration being on HAART (Months)		
0 - 12 Months	47	15.1
13 - 24 Months	38	12.2
25 - 48 Months	70	22.5
>48 months	109	35.0
Not on HAART	47	15.1
Current HAART regimen base		
AZT based regimen	83	26.7
D4T based regimen	15	4.8
TDF based regimen	161	51.8
Other regimen	4	1.3
Not on HAART	48	15.4
Current WHO stage		
I	218	81.0
II	12	4.5
III	32	11.9
IV	7	2.6
No response	42	
Current CD4 count (cells/mm3)		
</= 200	54	21.8
>200	194	78.2
No response	63	

Opportunistic infections management compared to the Kenya National Manual for the management of HIV-related OIs and other condition. Over 29% of the OIs were managed according to the Kenya National guideline.

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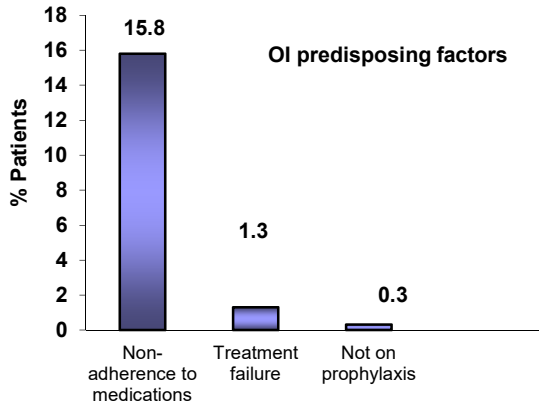

Figure 1: Distribution of patient by factors known to predispose HIV infected adult to develop OIs.

A review of patients' Current OIs was analyzed as presented in **Table 3**. The most commonly reported bacterial infection was pneumonia (6.4%), whereas pulmonary tuberculosis by 3.6 % of the participants. Among fungal infections, oral candidiasis (0.6%) and fungal skin infection (0.6 %) had the highest frequency of occurrence as reported by the participants.

Table 3: Current opportunistic infections

Variable	N= 311	%
Related bacterial infections		
Pulmonary TB	12	3.6
Pneumonia bacterial	20	6.4
None	280	90.0
Related fungal infections		
Oral Candidiasis	2	0.6
Esophageal Candidiasis	1	0.3
Pneumocystic jiroveci Pneumonia	1	0.3
Fungal skin Infection	2	0.6
None	305	98.1
Related Viral Infection		
Herpes infection (HSV and HZV)	2	0.6
Hepatitis C virus infection	1	0.3
None	308	99.0
Related parasitic infection		
Worms	1	0.3
None	310	99.7
Related Malignancy		
Kaposi sarcoma	2	0.6
Invasive carcinoma, cervix	1	0.3
None	308	99.0
Other opportunistic infection		
Wasting syndrome	1	0.3
Diarrhea	3	1.0
None	307	98.7

Multivariable regression was performed to identify independent predictor(s) of current state of opportunistic infection among adult patients diagnosed with HIV. Four factors associated with current opportunistic infections status at P<0.1 during bivariate analysis were considered for multivariate analysis. These include; (1) Duration since HIV diagnosis (months), (2) WHO clinical stage of disease when HIV was diagnosed, (3) Duration being on HAART (months) and (4) Current CD4 count. After fitting all the four factors together, variance of opportunistic infection due to duration being on HAART (months) and current WHO clinical stage was less than the variance of opportunistic infection due to duration since HIV diagnosis (months) and WHO clinical stage when HIV was diagnosed, there by rendering the two factors (Duration being on HAART (months) and Current WHO disease stage) statistically insignificant and therefore removing them from the model. Duration since HIV diagnosis (months) and WHO clinical stage when HIV was diagnosed were therefore retained in the final model.

Adjusting for duration since HIV diagnosis (months), WHO clinical staging of disease III or IV was significantly associated with current opportunistic infection (AOR= 3.79 [95% CI = 1.43 – 10.03], P=0.007). A patient in stage III or IV when HIV was diagnosed has 3.79-folds risk of having opportunistic infection compared to one in stage I.

Similarly, adjusting for WHO clinical stage of disease when HIV was diagnosed, less than or equal to 12 months duration since diagnosis was significantly associated with current opportunistic infection (AOR= 3.89 [95% CI = 1.58 – 9.59], P=0.003). A patient with less than or equal to 12 months duration since HIV diagnosis has 3.89-folds risk of having opportunistic infection compared to one with more than 36 months.

4. Discussion

The present study was designed to establish the prevalence of OIs in HIV infected patient at Kenyatta National Hospital- Comprehensive care Center. The prevalence of OIs was found to be 14.1% (95% CI: 10.7-18.5). Our finding is almost similar to the cross-sectional study carried out in children infected with HIV at KNH which estimated the prevalence of OIs in children to be 14.3 % (Mutua, 2008). However, it expected that there should be a reduction in OIs prevalence among HIV-infected adults following initiation of antiretroviral therapy and chemoprophylaxis (Detels et al, 2001; Kaplan et al, 2000; Mocroft et al, 2003).

The finding of this study is higher than the findings of cross-sectional study that was carried out in Murang'a and Taita Taveta, which estimated the prevalence of OIs to be 4.1% and 3.3% respectively (Mbatia, 2011). This difference may be attributed to geographical and population density variation between Nairobi, Murang'a and Taita Taveta. Or because: KNH being a referral hospital may have received more seriously ill patients than the district hospital.

Bacterial pneumonia was the most frequent opportunistic infection (6.4%). However, retrospective review of cohort of HIV infected patients in Lebanon showed that cerebral toxoplasmosis is the most frequent

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OI reported by 21%, followed by fungal infections with 17% (Gebo et al, 2005).

Our data showed that pulmonary tuberculosis and diarrhea were the second leading OIs with a prevalence of 3.6% and 1.0% respectively. This finding is contrary to the finding of Kuala Lumpur hospital based study that estimated prevalence of tuberculosis to be 48% (Kaplan et al, 2000). However, Kuala Lumpur hospital based study was a retrospective of HIV-infected cohort from 1994 to 2011.

In South Africa, one out of six patients (16%) who had no symptoms of tuberculosis at the time of diagnosis screening actually had positive sputum culture for TB (Wood et al, 2007). Even adding chest X-ray, clinician may still miss many cases (Greenberg et al, 1994). Furthermore, tuberculosis diagnosis requires several days before definite and objective diagnosis is confirmed. Therefore, there is possibility that some tuberculosis cases may have been missed during the study period or referred to TB clinic. However, our finding is more than 3 folds the finding of WHO Global surveillance and monitoring project which reported the rate of TB-HIV co- infection exceed 1 per 100 population in some areas in Sub-Saharan Africa (WHO, 2011).

Kaposi sarcoma (KS) was among the commonly reported OIs by 0.6% of patients. However, observation cohort of HIV–infected adult with AIDS associated KS in South Africa estimated the prevalence of KS to be 3.6% (Chu et al, 2010). This difference may explained by the variation of study design.

The study found that there was significant association between study population's current OIs and WHO stage when HIV was diagnosed (P=0.007). There was high proportion of OI among participants in WHO stage III or IV of the disease (20.3%) compared to those in stage I(9 .6%). The proportion of OI among participants in stage II (6.3%) is less than those in stage I. A patients in stage III or IV was 3.7 [95% CI: 1.43-10.03] times more likely to develop OI compared to one in stage I.

These findings support the fact that majorities of patients are unaware of their HIV infection and seek medical care when OIs become initial indictor of their disease (Jones et al, 1999; Perbost et al, 2005; Croda et al, 2006). Hence a lot of efforts are needed to enhance and encourage early detection of asymptomatic HIV-infected patients and providing them with timely antiretroviral therapy and appropriate chemoprophylaxis against specific OIs, would decrease morbidity, mortality and improve the quality of life of HIV-infected patients in the country.

Similarly, adjusting for WHO clinical stage when HIV was diagnosed, less than or equal to 12 months duration since HIV diagnosis was significantly associated with current OI (AOR = 3.89 [95% CI: 1.58-9.59], P= 0.003).

Out 0f the 44 patients with at least one opportunistic infection, 29.5% were not managed according to the Kenya National Manual for the Management of HIV-related OIs and other conditions. OIs have been the principle cause of morbidity and mortality in people living with HIV and AIDS (Walensky et al, 2006). However, in the early 1990's, the use of HAART, chemoprophylaxis and better strategy for management of OIs contributed to improve quality of life and survival by reducing OIs related mortality (Palella et al, 1998; Walensky et al, 2006). Hence a lot of effort is needed to reinforce adherence of health care providers to National Manual for management of HIV-related OIs and other conditions, which is the better strategy to improve quality of life and survival.

5. Conclusion

The overall prevalence of opportunistic infections was 14.1%. Bacterial Pneumonia and pulmonary tuberculosis were the most commonly observed opportunistic infections during the study period. Co-trimoxazole chemoprophylaxis was used by more than 90% of the patients, indicating a high adherence by the health workers to the national OIs prophylaxis recommendations. However, more than 29% of opportunistic infections were not managed according to the Kenya National Manual for the management of OIs and related Conditions.

These findings support the recent WHO recommendations to start ART earlier before profound immune destruction occurs. Adherence of health care providers to Kenya National Guideline in management of OIs should be reinforced.

Conflict of Interest Declaration

This research was solely sponsored by Sudan People's Liberation Army (SPLA) Medical Corps. The Funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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