Original Article

Opportunistic Infections and Associated Factors among HIV-Infected Adult Persons on Antiretroviral Therapy at Ruhengeri Referral Hospital, Rwanda: A cross-sectional study

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Abstract

Background

Human Immunodeficiency Virus (HIV) is among the highest health crises that humanity ever confronted and it causes progressive weakening of the immune system leading to opportunistic infections (OIs) or malignancies during the natural course of the disease.

This study aimed at assessing the prevalence and factors associated with the occurrence of OIs among adult PLWHIV on antiretroviral therapy (ART) at Ruhengeri referral hospital.

Methodology

A cross-sectional study was performed by reviewing records of HIV-positive adult (\geq 15 years) on ART enrolled at Ruhengeri referral hospital from 1st January 2007 to 31st December 2017. Opportunistic infections were reported based on clinical diagnosis and the prevalence of OIs was determined.

Results

The study reviewed records from 423 PLWHIV. Thirty-nine (9.2%) PLWHIV had been diagnosed with OIs; and frequent OIs were tuberculosis (20%), oral candidiasis, pneumonia and STI (15.6% each). The independent risk factors for developing OIs were being jobless (AOR = 5.03, 95% CI = 2.13, 32.99), spending more than five years on ART (AOR = 4.34, 95% CI = 1.12-16.78) and starting ART at WHO clinical stage III (AOR = 4.88, 95% CI = 1.65-16.78).

Conclusion

There is a need to strengthen the management of opportunistic infections despite the use of ART at Ruhengeri referral hospital.

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Background

Opportunistic infections (OIs) are infections that are more common and severe among PLWHIV because their immune systems are weakened. But nowadays OIs are less frequent among PLWHIV because of effective HIV treatment.[1] Globally, in 2020 there were 37.7 million [30.2 million–45.1 million] people living with HIV (PLWHIV), and among them 36.0 million [28.9 million–43.2 million] were adults (aged \geq 15 years).[2] Of the PLWHIV, 27.5 million [26.5 million-27.7 accessing million] were antiretroviral The estimated ART therapy.[2] global coverage increased from 7% in 2005 to 62% in 2018. Treatment scale-up declined deaths from AIDS-related illness from a peak of 1.7 million in 2004 to 770 000 in 2018. AIDS-related mortality declined by 42% from 2010 to 2017 in eastern and southern Africa,

reflecting the rapid pace of treatment scaleup in the region. In western and central Africa, declines were more modest (24% reduction).[3]

In Rwanda, there was an improvement of the quality of life for PLWHIV with a decrease in morbidity and mortality among PLWHIV in past years. Morbidity and mortality have greatly reduced by the high coverage of ART, early initiation of treatment that widens the eligibility criteria and improvement in diagnosis and treatment of opportunistic infections. According to the 2013 national estimates, annual deaths have reduced from 7300 in 2008 to 4500 in 2013 which represents a 38% reduction in 5 years.[4] Rwanda has also made impressive progress against the 90-90-90 targets, A remarkable improvement was also made bv the government of Rwanda against the 90-90-90 targets with 88% (198,000) of the 225,000 PLWHIV in the country diagnosed with HIV, 94% (187,000) of those diagnosed on ART in 2018, and 91% of those on ART (170,000) achieving viral suppression.[5] Despite all these efforts made by the country, there is no previous study that indicates the prevalence of OIs among PLWHIV on ART. The present study will provide information that is crucial for the planning of health services including the purchase of appropriate drugs and diagnostics. This study aimed to determine the prevalence of OIs and associated factors at Ruhengeri referral hospital, Rwanda.

Methods

Study design

A cross-sectional study was conducted to determine the prevalence and factors associated with OIs by reviewing records of adult PLWHIV (≥ 15 years) on ART enrolled at Ruhengeri Referral Hospital (RH) from 1st January 2007 to 31st December 2017.

Study area

Since 1999, Ruhengeri hospital became the RH for the Northern Province, but it continues to serve as a district hospital; serving 15 health centers with more than 374,000 populations from Musanze district. The hospital offers ART as one of the clinical services under internal medicine department. By July 2018, the service had around 1500 PLWHIV on ART, coming from Musanze district and neighboring districts.

Study population and sampling

This study targeted PLWHIV enrolled at Ruhengeri RH from 1st January 2007 to 31st December 2017. We included in the study, PLWHIV who were aged 15 years old and above. The PLWHIV who were not in ART and aged below 15 years were excluded from the study. Given that the prevalence of OIs among PLWHIV on ARV is unknown in Rwanda, the study used 48% as a proxy of the prevalence of OIs among PLWHIV on ART to determine the sample size, which was recently reported by Ethiopia, a country with almost similar health care setting as Rwanda.[6] An inflation rate of 10% was added to the sample to account for possible missing data from PLWHIV files. Then, a sample of 423 participants was considered for this study. A systematic random sampling technique was used to obtain the required sample from 862 files. A case was considered as OI based on clinical diagnosis, since no laboratory examinations had been recorded for all PLWHIV.

Data collection and statistical analysis

Data were extracted using Excel sheet; then. analyzed using STATA, version 15.0(StataCorp). Descriptive analysis was performed to calculate frequencies and summary statistics (mean, standard deviation, and percentage) to describe socio-demographic clinical the and characteristics of the study participants. Bivariate analysis with binary logistic regression was performed to determine the relationship between the study variables and the outcome (OIs coded into two categories: Having OI or Not having OI). Then, all significant variables from the bivariate analysis were put into a full logistic regression models for the multivariate analysis to determine the risk factors associated with OIs.

Crude and adjusted odds ratios (CORs and AORs), with 95% confidence intervals (CIs), were used to describe the strength of the association between the study variables. The association was set to be significant at p-value ≤ 0.05 .

Ethical considerations

This study was ethically approved by Institutional Review Board of University of Rwanda, College of Medicine and Health Sciences, with Approval Notice No 383/ CMHS IRB/2018. Ruhengeri RH provided authorization for data collection. The staff working in the ART service at Ruhengeri RH were trained about the methodology of the study before being involved in data extraction. During data extraction, individual information leading to easy identification was not captured, and PLWHIV files were only accessed by ART service providers. Data were stored in password protected computers and only accessed by the main researcher.

Results

Prevalence of opportunistic infections Out of 423 PLWHIV, 39 had diagnosed OIs, representing an overall prevalence of 9.2%. The most prevalent OIs were tuberculosis (20% of all OIs), followed by oral candidiasis, pneumonia and STI with 15.6% each (Table 1).

Table 1. Prevalence of opportunistic infections among adult PLWHIV on ART at
Ruhengeri Referral Hospital from 2007-2017

Category	Frequency	Percentage (%)	
Have OI	39	9.2	
Do not have OI	384	90.8	
Diagnosed OIs (n=39)			
Tuberculosis	9	20.0	
Oral candidiasis	7	15.6	
Pneumonia	7	15.6	
STI	7	15.6	
Hepatitis B	2	4.4	
Non bloody diarrhea	2	4.4	
Onycomycoces	2	4.4	
Cutaneous mycoses	1	2.2	
Infectious dermatitis	1	2.2	
Kaposi's sarcoma	1	2.2	
Oro-pharyngeal candi- diasis	1	2.2	
Parotiditis	1	2.2	
Rheumatoid arthritis	1	2.2	
Skin lesion	1	2.2	
Suppurative adenitis	1	2.2	
Vaginal candidiasis	1	2.2	

PLWHIV = people living with HIV; ART = antiretroviral therapy.

Statistical relationship between characteristics of people living with HIV on antiretroviral therapy and opportunistic infections at Ruhengeri Referral Hospital

The majority of the PLWHIV were aged 45-54 years (33.8%), female (64.1%), living in urban area (85.6%), married (42.8%), farmers (54.6%) and had primary educational level (57.2%). Pre-ART had been provided to almost all participants (97.6%) and by December 2017, 75.7% of the participants had spent more than five years on ART. At ART initiation, most of participants were at WHO clinical stage 1 (40.2%). The majority had CD4 counts varying between 200 and 499 (61.2%) and almost all of them were at first line regimen (92.2%) (Table 2).

The study assessed the statistical association of each study variable with the outcome (having or not having OIs). During the bivariate binary logistic regression, age between 35-44 years was found to protect PLWHIV from developing OIs compared to age below 25 years (COR = 0.28; 95% CI = 0.10, 0.82; p = 0.02).

Jobless PLWHIV were five times more likely to develop OIs compared to farmers [COR = 5.01; 95% CI = 1.74, 14.79, p = 0.003]. The risks of developing OIs among PLWHIV on ART at Ruhengeri referral hospital was not statistically significantly different among gender, marital status, educational level and residence (Table 2).

Considering clinical characteristics, adherence to ART above 95% was negatively associated with development of OIs (COR =0.32; 95% CI = 0.14; 0.74; p = 0.007). Those who had spent more than five years on ART were four times at risk of having OIs compared to those who had spent less than 5 years (COR = 4.2; 95% CI = 1.27, 14.02; p = 0.02). Those who started ART at WHO clinical stage 2 and 3 were 3 and 5 times respectively more at risk of having OIs compared to those who started ART at WHO clinical stage 1, i.e., WHO clinical stage II, (OR =3.01; 95% CI =1.11, 8.15; p = 0.03) and WHO clinical stage 3 (OR =5.4; 95% CI = 2.07, 14.1; p = 0.001)] (Table 2).

Characteristics	Total (%)	Do not have OI	Have OI	COR (95%Cl)	P-Value
	N = 423	Frequency (%)	Frequency (%)	-	
Gender		·			
Female	271 (64.1)	249 (91.9)	22 (8.1)	1	
Male	152 (33.9)	135 (88.8)	17 (11.9)	1.43 (0.73,2.78)	0.30
Marital status					
Divorced	39 (9.2)	37 (94.9)	2 (5.1)	1	
Married	181 (42.8)	170 (93.2)	11 (6.1)	1.20 (0.25,5.63)	0.82
Single	104 (24.6)	86 (82.3)	18 (17.3)	3.87 (0.85,17.54)	0.08
Widower	99 (23.4)	91 (91.2)	8 (8.1)	1.63 (0.33,8.02)	0.55
Age group (in yea	.rs)				
15-24	35 (8.3)	28 (80)	7 (20)	1	
25-34	48 (11.3)	41 (85.4)	7 (14.6)	0.68 (0.22,2.16)	0.52
35-44	137 (32.4)	128 (93.4)	9 (6.6)	0.28 (0.10,0.82)	0.02
45- 54	143 (33.8)	131 (91.6)	12 (8.4)	0.37 (0.13,1.01)	0.05
55-64	53 (12.5)	50 (94.3)	3 (5.7)	0.24 (0.06,1.00)	0.05
Over 65	7 (1.6)	6 (85.7)	1 (14.3)	0.67 (0.07,6.47) crude odds ratio; ART = a	0.73

Table 2. Distribution of the individual characteristics of PLWHIV on ART and their statistical relationship with OIs at Ruhengeri referral hospital

Characteristics	Total (%)	Do not have OI	Have OI	_ COR (95%Cl)	P-Value
	N = 423	Frequency (%)	Frequency (%)	_	
Educational level					
None	86 (20.3)	80 (93)	6 (7)	1	
Primary	242 (57.2)	222 (91.7)	20 (8.3)	1.20 (0.46,3.10)	0.71
Secondary	86 (20.3)	74 (86.1)	12 (13.9)	2.16 (0.77,6.05)	0.14
University	9 (2.1)	8 (88.9)	1 (11.1)	1.67 (0.18,15.63)	0.66
Residence					
Rural	61 (14.4)	56 (91.8)	5 (8.2)	1	
Urban	362 (85.6)	328 (90.6)	34 (9.4)	1.16 (0.43,3.09)	0.77
Occupation					
Farmer	231 (54.6)	213 (92.2)	18 (7.8)	1	
Jobless	20 (4.7)	14 (70)	6 (30)	5.07 (1.74,14.79)	0.003
Paid employee	78 (18.4)	76 (97.4)	2 (2.6)	0.31 (0.07,1.37)	0.12
Self employed	69 (16.3)	61 (88.4)	8 (11.6)	1.55 (0.64,3.74)	0.33
Student	25 (5.9)	20 (80)	5 (20)	2.96 (0.99,8.81)	0.05
Adherence to ART					
<95%	43 (10.2)	34 (79.1)	9 (20.1)	1	
>95%	379 (89.8)	349 (92.1)	30 (7.9)	0.32 (0.14,0.74)	0.007
ART period in years					
< 5	103 (24.3)	100 (97.1)	3 (2.9)	1	
> 5	320 (75.7)	284 (88.7)	36 (11.3)	4.2 (1.27,14.02)	0.02
WHO clinical at ART	initiation				
Stage 1	170 (40.2)	164 (96.8)	6 (3.5)	1	
Stage 2	131 (30.9)	118 (90.1)	13 (9.9)	3.01 (1.11,8.15)	0.03
Stage 3	109 (25.8)	91 (83.5)	(<i>)</i>	5.4 (2.07,14.1)	0.001
Stage 4	13 (3.1)	11 (84.6)	2 (15.4)	5.0 (0.89,27.55)	0.07
CD4 count at ART in					
>500	43 (10.2)	38 (88.4)	5(11.6)	1	
200-499	259 (61.2)	239 (92.3)	20 (7.7)	0.63 (0.22,1.79)	0.39
<200	121 (28.6)	107 (88.4)	14 (11.6)	0.99 (0.33,2.94)	0.99
ART Regimen line					
First	390 (92.2)	353 (90.5)	37 (9.5)	1	
Second	32 (7.6)	30 (93.7)	2 (6.3)	0.64 (0.14,2.77)	0.55
Third	1 (0.2)	1 (100)	-	-	
Pre-ART provided					
No	10 (2.4)	9 (90)	1 (10)	1	
Yes	413 (97.6)	375 (90.8)	38 (9.2)	0.91 (0.11,7.39)	0.93

Table 2. Distribution of the individual characteristics of PLWHIV on ART and their statistical relationship with OIs at Ruhengeri referral hospital

PLWHIV = people living with HIV; OIs = opportunistic infections; COR = crude odds ratio; ART = antiretroviral therapy.

Risk factors of opportunistic infections among people living with HIV on antiretroviral therapy at Ruhengeri referral hospital

In order to determine the independent variables that were statistically associated with OIs in the bivariate analysis, a multivariable logistic regression was performed, and adjusted odds ratio (AOR), 95% CI and p-values are reported. Within that model, jobless PLWHIV were five times more likely to have OIs (AOR = 5.03; 95% CI = 2.13, 32.99) compared to farmers.

The PLWHIV who had spent more than five years on ART were 4.34 times more likely to have OIs (AOR = 4.34, 95% CI = 1.12-16.78) compared to those who had spent less than 5 years. Those who started ART at WHO clinical Stage 2 and Stage 3 were 2.94 times (AOR = 2.94; 95% CI = 0.99, 8.73) and 4.88 times (AOR = 4.88; 95% CI = 1.65, 14.40) respectively more likely to have OIs compared to those who started ART at WHO clinical stage 1 (Table 3).

Table 3. Multivariate analysis for risk factors of OIs among PLWHIV on ART at Ruhengeri RH

Characteristics	AOR (95%Cl)	P-Value	
Age group (years)			
15-24		1	
25-34	1.68 (0.30,9.55)	0.56	
35-44	1.17 (0.19,7.01)	0.87	
45- 54	1.50 (0.25,8.88)	0.65	
Over 55	1.22 (0.16,9.01)	0.85	
Adherence to ART			
<95%		1	
>95%	0.42 (0.16,1.14)	0.09	
Occupation			
Farmer		1	
Jobless	5.03 (2.13,32.99)	0.002	
Paid employee	0.27 (0.06,1.25)	0.09	
Self employed	2.22 (0.86,6.04)	0.12	
Student	2.16 (0.36,12.94)	0.40	
Period since ART initia	tion in years		
< 5 years		1	
> 5 years	4.34 (1.12,16.78)	0.03	
WHO clinical stage at A	RT initiation		
Stage 1		1	
Stage 2	2.94 (0.99,8.73)	0.05	
Stage 3	4.88 (1.65,14.40)	0.004	
Stage 4	4.23 (0.56,31.95)	0.16	

Discussion

This study aimed to determine the prevalence and risk factors associated with occurrence of OIs among PLWHIV on ART at Ruhengeri RH. The overall prevalence of OIs was 9.2%. This prevalence is quite low compared to the rest of the countries in the region, namely in Ethiopia, where it stands at 39.6% in selected public hospitals in Sidima National Regional State; [7] 33.6% in Addis Ababa, [8] 88.4% in Dawro Zone hospital [9] and 52% in Eastern Zone of Tigray.[10] The OIs prevalence remains higher in many other countries, such as in South-West Nigeria (Ibadan) with 46.6% among newly enrolled PLWHIV aged 50 years or above, [11] and 78.8% among older adults in Kenya.[12] This lower prevalence in Rwanda when compared with similar countries results from efforts made by the Rwanda Biomedical Center and other agencies in the management of PLWHIV in different angles of their life including medical, psychosocial and nutritional care as per the national guidelines; with rigorous mentorship from the national level, the HIV/ AIDS and STIs.[13]

The commonest OIs were tuberculosis accounting for 20% (n = 39), oral candidiasis, pneumonia and STI accounting for 15.6% each. These common OIs PLWHIV are similar to those documented among PLWHIV receiving ART in other settings, namely in Kenyatta National Hospital in Nairobi, Kenya,[12] in Port Harcourt, Nigeria,[14] and in urban Ugandan cohort.[15] Tuberculosis remains one of the top OIs in many health care settings, with devastating effect on CD4+T cell counts, such as in Sichuan, China.[16]

This study found that being jobless was statistically associated with having OIs among PLWHIV on ART at Ruhengeri RH. If being jobless can be related to one's economic status, a study conducted on factors influencing the quality of life among PLWHIV in coastal South India showed that people with higher socioeconomic status among others, had shown better scores across all the domains of quality of life.[17]

Apart from that, there is no other study that found being jobless as a risk factor to developing OIs.

Spending more than five years on ART was found to be a risk factor to developing OIs. Findings from other studies show rather a decline in risk to developing OIs as the time spent on ART increases, such as in an urban Ugandan cohort [15] and at Ayder Referral Hospital, Mekelle, Ethiopia.[18] Starting ART at clinical stage 3 was identified by this study as a risk factor to developing OIs. Similar findings were observed in a study conducted in Southern zone Tigray, Ethiopia,[10] and at Debre Markos referral hospital, Northwest Ethiopia among HIV-infected children on ART.[19]

In our study, bivariate analysis shows that good adherence to ART protects PLWHIV from developing OIs, which corroborates other studies whereby poor adherence remains quite a negative factor.[7,9,20] According to multivariable analysis in this study, age had no effect on developing OIs, unlike in other studies conducted among PLWHIV on ART in Southern Ethiopia, whereby, OIs were found to be associated with being aged 35 years or above.[7] Another study on epidemiology of OIs in HIV-infected PLWHIV on ART in Cameroon showed that being aged 50 years or above was associated with the occurrence of OI.[21]

Like any other retrospective work, this study suffers from an information loss as some PLWHIV clinical records and laboratory investigations results could not be accessed due to record archiving problems. However, the revised and validated records showed a few associated factors that can trigger the health care providers' mind towards improving the management of HV-infected PLWHIV on ART in Ruhengeri RH and similar settings.

Conclusion

The findings of this study show that OIs among PLWHIV on ART are at a prevalence of 9.2% in Ruhengeri RH. The commonest OIs were tuberculosis accounting for 20%, oral candidiasis, pneumonia and STI accounting for 15.6% each. The factors associated to the occurrence of OIs are being jobless, starting ART in clinical stage 3 and spending more than five years on ART.

These findings show a need to make more effort in the follow up of PLWHIV and management of OIs in addition to ART provision.

We suggest also conducting a prospective cohort study in the same setting to better assess the risk factors for OIs while having all required data.

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Author contributions

II, and JN conceptualized the study, designed the methods data analysis and drafted the manuscript. AN and CMCS contributed to the data analysis and the general review of the manuscript. II collected and analyzed the data. All authors provided final approval of the manuscript for its publication

Conflict of interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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