

Prevalence and Associated Risk Factors of Opportunistic Infections among Anti-Retro Viral Treatment Naïve HIV/AIDS Infected Patients

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Abstract

Background: Opportunistic infections (OIs) continue to cause substantial morbidity on patients with HIV infection and contribute to mortality. The aim of this study was to assess the prevalence and risk factors of OIs among Anti-Retro viral treatment (ART) naïve HIV/AIDS patients.

Methods: Institutional based cross-sectional study was designed to assess the prevalence and risk factors of OIs among ART naïve HIV/AIDS patients. This study was conducted among 418 study participant. Data was collected by reviewing the cards' of the patients for OIs at a baseline and by interviewing the participants for socio-demographic variables. The data was entered into Epi data version 3.1 and transferred to SPSS version 20 software package for analysis.

Result: Out of 418 study participants 219 (52.4%) of them had OIs. The most common OIs were Tuberculosis (TB) (13.2%), followed by Recurrent Upper Respiratory tract infection (URTI) (8%) and Herpes Zoster (7.2%). Risk factors identified were advanced World Health Organization (WHO) stage (stage III and IV) (Adjusted odds Ratio (AOR)=3.84 95% CI=1.9, 7.73), <200 CD4 count at a baseline (AOR=2.2 95% CI=1.22, 4.06) and a primary and secondary school attended study participant (AOR=2.04 95% CI 1.10, 3.78) (AOR=2.53 95% CI 1.27, 5.03), respectively. Besides this, mean difference of CD4 count at a baseline showed that there was a significant difference between advanced WHO stages and stage I and II (t=3.158 p=0.002) and also it was significant between gender (t=-2.9 p=0.004).

Conclusion: The prevalence of OIs were 52.4% which seems low relative to previous studies conducted among the ART naïve HIV/AIDS infected population; the commonest OI was TB, followed by a recurrent URTI and Herpes Zoster. Need a continuous awareness for healthcare providers in order to improve decisions regarding prophylaxis, early screening and appropriate diagnosis and management of OIs among HIV/AIDS infected patients.

Keywords: Opportunistic infections (OIs); Anti-retro viral treatment (ART) naïve; HIV/AIDS patients

Background

Opportunistic infections (OIs) are defined as infections that are more frequent or more severe because of immunosuppressant in HIV-infected persons and the principal cause of morbidity and mortality in this population [1]. The risk for the development of OIs in HIV patients depends on exposure to potential pathogens, virulence of the pathogens, the degree of host immunity and the use of antimicrobial prophylaxis [2].

Clinical observations in HIV-positive patients show increased plasma HIV viral load (VL) during opportunistic illnesses (OIs) suggesting active HIV replication in response to OIs. Besides independently it increases the risk of death, occurrence of OIs may also increase the risk of HIV transmission through their effects on HIV RNA VL [3].

Opportunistic infections continue to cause substantial morbidity in patients with HIV infection and contribute to mortality. With the advent of more potent antiretroviral therapy, the risk of opportunistic diseases can clearly be lowered. Improved immune function and specific prophylaxis together can lessen the risk of opportunistic diseases and improve survival in advanced HIV disease [4].

The most common opportunistic diseases in HIV patients are *Candida esophagitis*, *Pneumocystis carinii pneumonia* (PCP), disseminated *Mycobacterium avium* complex (MAC) infection, cytomegalovirus (CMV), Cryptococcus, kaposi sarcoma, herpes zoster and tuberculosis [2]. Opportunistic diseases cause substantial morbidity,

result in hospitalization, necessitate toxic and expensive therapies and shorten the survival of people with HIV infection. Virtually all HIV-related mortality is preceded by opportunistic disease, whether or not it meets the case definition for AIDS [4].

It is important to recognize that the relationship between OIs and HIV infection is bi-directional. HIV causes the immune-suppression that allows opportunistic pathogens to cause disease in HIV-infected persons. Opportunistic infections, as well as other co-infections that may be common in HIV-infected persons, such as sexually transmitted infections (STIs), can adversely affect the natural history of HIV infection by causing reversible increases in circulating viral load that could accelerate HIV progression and increase transmission of HIV [1].

To reduce the burden of OIs appropriate interventions should be implemented to promote and enable HIV positive individuals to enter into ART programs as early as possible [5]. The magnitude of OIs may

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vary in different countries and even in different areas within the same country. Identifying the common types OIs at specific area will help in implementing the preventive measures against those infections. There was no study conducted to reveal the burden and risk factors for OIs among HIV-infected naïve to ART in study area, so that the study aimed to assess the prevalence and risk factors of OIs among ART naïve HIV/AIDS patients.

Methods

This study was conducted at Hiwot Fana University Specialized University Hospital (HFSUH) from February 2016 to March 2017 among HIV/AIDS infected patient started ART in less than two years. The study specifically conducted in ART clinic, the hospital is university hospital, Haramaya University found in Eastern Ethiopia.

A cross-sectional study was conducted to assess the prevalence and risky factors of OIs before the beginning of first ART regimen in a population of patients on treatment from less than two years. Some Important data regarding IOs developing before treatment were collected at baseline or reviewed from recorded data while socio-demographic variables were collected by interviewing the participant. Simple random sampling method was used and sample size was calculated using single proportion formula. Since there was no study conducted on OI among ART naïve in the study area proportion 0.5 was used, based on these facts final sample size was 422 (after adding 10% contingency). Data was collected by a trained Nurse who has been working in ART clinic. Structured questionnaires were used to assess prevalence and risk factors of OIs and to collect socio-demographic and risk factors variables among ART naïve HIV/AIDS patients.

For data analysis completed questionnaires were edited, coded, cleaned for consistency, and entered into Epi data 3.1 software. The Data was exported to SPSS version 20 for analysis. Binary and Multivariable logistic regression was used to look whether the OIs had association with different risky factors. The association between OI and predictor variables (risky factor) was first analyzed in the binary logistic regression model. Then predictor variables were retained and entered to the multivariable logistic regression analysis. A p-value<0.05 was considered as a cut off point for a predictor to be significantly associated with the outcome.

For keeping data quality training (Orientation) was given for data collectors and two individual were entered the data (double entry) to computer to minimize the error during data entry.

Results

Socio-demographic variables

Of 422 participants initially included into the study, 4 of them were excluded due to incomplete data, the final study participants were 418. The mean age of the study participants were 37 (standard deviation \pm 12.4 years) in years, with range 2 to 75 years. Urban community consists more than 95% of study population and 67% were population with less than 40 years old (productive age group). More than 66%, 43% and 67% were female, attended primary education and orthodox Christian followers, respectively (Table 1).

Prevalence of OI at baseline (naïve to ART)

From 418 study participants 219 (52.4%) of them had a OIs. Most of the participants, 204 (93.2%) had only a single OI. The most common OIs among HIV/AIDS patients at baseline was TB (13.2%), followed by Recurrent URTI (8%) and Herpes Zoster (7.2%) (Table 2).

Characteristics	Frequency	Percent
Residence		
Urban	379	95.7
Rural	17	4.3
Age		
<40 years	284	67.9
\geq 40 years	134	32.1
Sex		
Male	141	33.5
Female	277	66.3
Education		
No Education	75	17.9
Primary	182	43.5
Secondary	102	24.4
Tertiary	52	12.4
Marital Status		
Single	46	57
Divorced	26	29
Widowed	40	43
Married	86	91
Religion		
Orthodox	282	67.5
Muslim	103	24.6
Protestant	22	5.3
Other	5	1.2
Income		
Poor	158	37.8
Average	208	49.8
Better	20	4.8

Table 1: Socio-demographic variable among HIV/AIDS patient during baseline at HFSUH from February 2016 to March 2017.

Name of OI	Frequency	Percent (%)
Tuberculosis	55	13.2
Recurrent Upper Respiratory Tract Infection	35	8
Herpes Zoster	30	7.2
Minor Mucocutaneous	16	3.8
Oral candidiasis	14	3.3
Chronic Diarrhea (>1 month)	12	2.9
Pneumonia	9	2.2
Sexually Transmitted Infection (STI)	8	1.9
Urinary Tract Infection (UTI)	6	1.4

Table 2: Prevalence of OI among HIV/AIDS patient during baseline at HFSUH from February 2016 to March 2017.

Factors associated with OIs among HIV patients at baseline

With this study, participants with advanced WHO stage (III and IV) were almost four times more likely affected by different OIs than WHO stage I and II (AOR=3.84 95% CI=1.9, 7.73); individual who had CD4 count <200 at baseline were 2.2 times more likely infected by OIs than those had CD4 count >350 at baseline (AOR=2.295% CI=1.22, 4.06) and participants who attended primary and secondary school were 2.04 and 2.53 times more likely affected by OIs than non-educated participant(AOR=2.04 95% CI 1.10, 3.78) (AOR=2.53 95% CI 1.27, 5.03), respectively. By binary logistic regression participants with more than 40 years old were more likely affected with OIs (COR=1.67 95% CI 1.1, 2.54), but it wasn't significant by multivariable logistic regression (Table 3).

CD4 count mean difference at baseline for OI affected and some risk factors

CD4 count mean difference were done to check whether there was a difference with CD4 count at baseline with different risk factors among OI infected participants and those free from OI. Mean difference of CD4 count was significantly different when the individual

Variables	OI		COR (95% CI)	AOR (95% CI)
	No	Yes		
Sex				
Male	63	77	1.16 (0.77, 1.75)	0.83 (0.5, 1.37)
Female	135	142	1	
Age				
<40 years	146	138	1	1.39 (0.87, 2.24)
≥40 years	52	82	1.67 (1.1, 2.54)*	
Weight				
<60 kg	111	128	1.09 (0.74, 1.61)	0.97 (0.65, 1.57)
≥60 kg	87	92	1	
Marital Status				
Single	46	57	1.17 (0.72, 1.93)	1.00 (0.58, 1.74)
Divorced	26	29	1.17 (0.58, 1.93)	0.91 (0.49, 2.02)
Widowed	40	43	1.02 (0.60, 1.71)	0.99 (0.48, 1.72)
Married	86	91	1	
Residence				
Urban	182	197	1.98 (0.72, 5.48)	1.44 (0.5, 4.12)
Rural	11	6	1	
Education				
No Education	43	32	1	
Primary	82	100	1.64 (0.95, 2.28)	2.04 (1.10, 3.78)*
Secondary	39	63	2.17 (1.18, 3.98)*	2.53 (1.27, 5.03)**
Tertiary	28	24	1.15 (0.57, 2.35)	1.36 (0.62, 3.00)
Khat Chewing				
Yes	34	52	1.49 (0.92, 2.42)	1.53 (0.88, 2.67)
No	162	166	1	
Baseline WHO stage				
Stage I&II	186	164	1	
Stage III&IV	12	52	4.9 (2.54, 9.5)***	3.84 (1.9, 7.73)***
Baseline CD4				
<200	82	118	2.16 (1.27, 3.66)**	2.2 (1.22, 4.06)*
200-350	68	70	1.54 (0.88, 2.9)	1.6 (0.86, 3.02)
>350	48	32	1	

* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$

Table 3: Binary and multivariable logistic regression between OI at baseline and other risk factors at HFSUH from February 2016 to March 2017.

Variable	Mean (SD)	t-value	Mean difference	95% CI of mean difference
OI				
No	255 (153.3)	3.158*	46.45	17.54-75.36
Yes	208 (147)			
Sex				
Female	245.67 (152.6)	-2.9*	-45.1	-75.8 - -14.4
Male	200.53 (146.7)			
Age				
<40 years	237 (154.7)	1.4	22.6	-8.6-53.9
≥40 years	215 (144.7)			
Weight				
<60 kg	230.53 (152.7)	0.15	0.218	-29.3-19.1229.74
≥60 kg	230.32 (150.92)			
Chew Khat				
Yes	226 (145.61)	-0.345	-6.357	-42.6-29.9
No	232.39 (153.86)			
WHO stage				
I and II	239.41 (149.97)	3.14*	63.68	23.8-103.56
III and IV	175.73 (145)			

* $p < 0.05$

Table 4: CD4 count mean difference at baseline for OI and other variables at HFSUH from February 2016 to March 2017.

were affected by OIs compared with the patients who were free from OI ($t=3.158$ $p=0.002$), besides this there was significant different between WHO stage I and II and III and IV ($t=3.14$ $p=0.002$). Finally the CD4

count mean difference between female and male was also significant ($t=-2.9$ $p=0.004$) (Table 4).

Discussion

The intention of this study was to assess the magnitude of OIs and risk factors among ART naïve HIV/AIDS patients in HFSUH. Majority of the study participants were female (66.3%) and less than 40 years age (67.9%) (Table 1), this finding was consistent with a study from North Ethiopia and South Africa [5,6]. This is because those populations are biologically and socially more vulnerable and sexually more active compared to the other age groups (the older) to HIV infection, respectively. Females had more mean CD4 count (\pm standard deviation) than male at a baseline 245.67 (152.6) and 200.53 (146.7), respectively. CD4 count mean difference between female and male was also significant ($t=-2.9$ $p=0.004$) (Table 4). This finding was also consistent with the study conducted in North Ethiopia and India which revealed female HIV patients had higher mean CD4 cell counts than male ($p < 0.002$) before ART was initiated [6,7].

Prevalence of OIs among ART naïve HIV/AIDS patients

This study revealed that prevalence of OIs among ART naïve HIV/AIDS patients was 52.4%. This prevalence was lower than the finding from North Ethiopia, 88.9% at baseline [5]. This was because nowadays most of HIV/AIDS patients start ART at early stage than previous. But it was higher than studies conducted among patients on ART [2,8,9] this variation comes due to the population variation as it's known OIs occur more in HAART naïve compared to the HAART sensitized [10]. The most common OIs among ART naïve HIV/AIDS patients was TB (13.2%), which was lower than the study conducted among naïve to ART 34.5% at Felege Hiwot Hospital, Ethiopia [5]. However comparable with studies carried out in Debre Markos and Harar, Ethiopia which revealed 9.7% and 18% prevalence among HIV patients on ART respectively, although the study subject was different [2,8]. The more prevalent OI next to TB was Recurrent URTI (8%); this finding was again consistent with study carried out in India 6.35% [11]. But it was uncommon or not prevalent by other studies.

The third prevalent OI was Herpes Zoster (7.2%), which was lower than study carried out among naïve to ART 30.7% at Felege Hiwot Hospital, Ethiopia [5]. The finding was comparable with study conducted in Harar, Ethiopia 10.6% among patients on ART [8], but higher than study from Nigeria and India 0.6% and 3.75%, respectively [9,12]. Generally relative to studies conducted among naïve to ART, the prevalence of OIs found by this study was lower. This was because currently most HIV-positive patients were enrolled in ART program at medium (<350) CD4 cells levels. Besides those commonest OIs and others listed on Table 2 were also prevalent among HIV patients in both naïve and ART started patents according to different studies [2,5,7,12].

The risk factors for OIs among ART naïve HIV/AIDS patients

This study identified study participant with advanced WHO stage (III and IV) were almost four times more likely developed different OIs than WHO stage I and II (AOR=3.84 95% CI=1.9, 7.73); which was in concordant with other studies from Nigeria (OR=9.48, 95% CI=5.37-17.05, $p < 0.0001$) [7], northwest Ethiopia (AOR=4.76, 95% CI=2.16, 10.47) [2], India (OR=24.04, 95% CI=5.5-105.01; $p=0.00$) [12] and Harar, Ethiopia (that revealed participants with advanced WHO stages III and IV were four and three times more likely to develop OIs than those with a WHO stage of I, respectively) [8]. Those findings indicated advanced WHO clinical stage of the disease were significantly associated with OIs among HIV/AIDS patients. Mean difference of

CD4 count was also significantly different between WHO stage I and II and III and IV ($t=3.14$ $p=0.002$) (Table 4).

Individual who had CD4 count <200 cell/mm³ at baseline were 2.2 times more likely develops OIs than those who had CD4 count >350 at baseline (AOR=2.2 95% CI=1.22, 4.06). This finding was in line with other studies conducted in Harar, Ethiopia (AOR=1.645 95% CI=2.187, 3.983) [8], Nigeria (OR=3.76, 95% CI=2.14-6.65, $p<0.0001$) [7], India (OR=2.61, 95% CI=1.32-5.16; $p=0.00$) [12] and Peru, India (which revealed the chances of developing OIs increased with decreasing CD4 counts and incidence rates of OIs were six times higher in patients with CD4 counts below 200/mm³ as compared to others) [11]. Therefore OIs correlated with lower CD4 cell counts at baseline or poor immune system among HIV/AIDS patients. Besides this, this study have revealed that mean difference of CD4 count was significantly different when the individuals who were developed OIs compared to those who were free from OIs ($t=3.158$ $p=0.002$) (Table 4).

Participant who attended primary and secondary school were 2.04 and 2.53 times more likely affected by OIs than non-educated participant (AOR=2.04 95% CI 1.10, 3.78) (AOR=2.53 95% CI 1.27, 5.03), respectively. This finding was inconsistent with the study conducted in Ethiopia which revealed the majority of ART-naïve HIV patients were from low levels of education and with minimum monthly income [5].

Limitations of the Study

The study was cross sectional and the OIs was collected by reviewing data at baseline, so if it was prospective data, follow up study, it was more preferable because we may miss variable or OIs among participants.

Conclusion and Recommendation

The prevalence of OIs among ART naïve HIV patients was 52.4%, which seems low relative to previous studies conducted among ART naïve HIV infected population. The commonest OI was TB, followed by recurrent URTI and Herpes Zoster. Opportunistic infections had associated with low CD4 (<200 cells/mm³), Advanced WHO clinical stage (III and IV) and educational status of study participant. To intervene OIs need a continuous awareness for healthcare providers, in order to improve decisions regarding prophylaxis, early screening and appropriate diagnosis and management of OIs among HIV-infected individuals.

Ethical Clearance

Ethical clearance for the study was obtained from institutional research Ethics review committee of Haramaya University. Prior to

interviewing for socio-demographic variable, verbal informed consent was obtained from the participants.

Author Contribution

FU designed the study, participated in data collection, analysis, interpretation, and write-up, drafted the manuscript, and revised the manuscript. AA participated in analysis, interpretation and write-up, drafted the manuscript, and revised the manuscript. ZA Participated on drafting the manuscript, interpretation and revised the manuscript. All authors read and approved the final manuscript.

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