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Original Article

Distribution pattern and prevalence of opportunistic infections and their possible reciprocal effects among HIV patients, Burayu health centers, Ethiopia

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Abstract

Introduction: Opportunistic infections are a major public health problems in immuno-compromised individuals, particularly in HIV patients, and form a lethal combination, each speeding the progress of the other. The aim of this study was to assess the pattern and prevalence of opportunistic infections and their reciprocal effects among HIV patients attending the Burayu Health Centers.

Methodology: A health institution-based retrospective cross-sectional study was conducted on 1,448 HIV patients. All patients diagnosed with HIV and HIV-opportunistic co-infections with complete data were included. Logistic regression analysis was used to quantify the association of HIV-opportunistic co-infections and various socio-demographic and clinical variables.

Results: A total of 1,448 HIV- positive patients were reviewed and 572 (39.5%) were found to have opportunistic infections. The trend of HIV co-infection showed gradually decreased. Majority of HIV patients were found at a $CD4^+$ count < 200cells/mm^3.The rate of opportunistic infections increased with decreasing CD4 T-cell count. HIV-infected patients with a $CD4^+$ cell count of < 200 cells/mm^3 were found to be 44 times more likely to develop opportunistic infections. HIV-opportunistic co-infection was significantly associated with sex, marital status, ART drug adherence, residence, and educational status of the patients. The odds of co-infections in patients who were urban dwellers were 2 times higher than in those who lived in rural areas. Similarly, patients who were single were 3 times more likely to be infected with coinfections. Maleness was found to be protective from coinfection and it showed a reduction of 64%.

Conclusions: Opportunistic co-infections are more prevalent in HIV-infected patients with a $CD4^+$ cell count of < 200 cells/mm^3, poor drug adherence, and also associated with the occupation. So, regular examination and appropriate medication can reduce the prevalence of opportunistic co-infections.

Key words: co-infection; prevalence; opportunistic infections.

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Introduction

HIV epidemic remains one of the greatest global health challenges of the 21st century in the absence of an effective vaccine or curative therapy and making people susceptible to a variety of opportunistic infections (OIs) [1]. Opportunistic infections due to a weakened immune system cause significant morbidity and hospitalization that needs toxic and expensive therapies and often accelerates death in people with HIV infections. OIs lower the quality of life of HIV-infected persons, accelerate the rate of progression to full-blown AIDS, and reduce patients' response to antiretroviral treatment [2].

HIV promotes the progression of latent or recent infections of opportunistic infections to active disease and also increases the rate of occurrence. For instance, people living with HIV have an estimated 20-30 times higher risk of developing active TB than people without HIV infection [3]. Almost 80% of AIDS patients die from AIDS-related infections rather than HIV infection itself. Opportunistic infections (OIs) in HIV/AIDS patients may affect them in many ways. For instance, as reported by the Federal Ministry of Health, the presence of TB increases HIV replication, in an HIV-infected individual, which leads to increased viral load. This results in the rapid progression of HIV disease and also increases the occurrence of other OIs. The management of OIs and HIV co-infected individuals is challenging because of: pill burden, increase adverse effects, drug to drug interaction [4].

Severely immune-compromised HIV patients may develop a variety of opportunistic infections that have a significant impact on their well-being, quality of life, healthcare costs, and survival [5]. Both HIV and opportunistic infections like TB mostly affect the young and productive age group.

The introduction of antiretroviral therapy (ART) has reduced the incidence of OI among HIV-positive people who have received ART, however, people living with HIV in resource-poor communities have no access to ART. Prevention and treatment of OIs not only help HIV-positive people to live longer and healthier lives but also prevent tuberculosis and other transmissible OIs from spreading to others [1]

Antiretroviral treatment in people with HIV improves immunity and reduced the incidence of PCP and increased life expectancy in patients with pneumonia. However, PCP remains an important clinical problem, remaining a major opportunistic infection in individuals who do not respond to treatment, in those who do not adhere to the treatment and/or prophylaxis, HIV-positive individuals who have not been diagnosed, and in countries where the HIV carriers do not have access to effective antiretroviral treatment [5]. Quantifying the incidence and burden of these opportunistic infections is important for planning appropriate interventions and advocating for resources, as necessary. A great deal of uncertainty surrounds the global and regional OI estimates due to poorly resourced OI surveillance systems. These uncertainties need to be reduced to obtain relevant data, as they have an important role in improving our understanding of the burden of these infections. They are also crucial in helping to improve the design and implementation of OI interventions.

Understanding the predictors of HIV/opportunistic co-infections in the local context is critical for countries like Ethiopia to improve the health status of co-infected patients' co-management. The relative frequencies of specific OIs may vary in different countries and even in different areas within the same country like Ethiopia. The identification of OIs is very important for HIV and AIDS case management. The number of AIDS patients in Ethiopia increases from time to time whereas, limited information is available about the prevalence of OIs along with CD4 count in different parts of Ethiopia and the same is true in Burayu town. Assessing the distribution pattern and the prevalence of common OIs and reciprocal effects among the study population provided better information for health planners to adopt strategies to manage the impacts of OIs on the local people.

Methodology

Study area and Study population

The study was conducted in Burayu town administration which is found in the special zone of Oromia. Burayu has located 15 km to West Oromia from Addis Ababa on the main road of Ambo. Burayu town has six kebeles with a total area of 8,968.52 hectares. The population in Burayu town administration was 93,437. Among these, there were 45,784 males and 47,653 females. Burayu town has two public health centers, two health posts, and 111 private clinics (35 medium clinics, 36 primary clinics, 36 drug stores, and 4 pharmacies). Out of these health institutions, two public Burayu Health Centers were purposively selected for this study with the expectation that a greater number of HIV/AIDS patients visit the two health centers than the other health institutions. The study area is found between 8° 54'3" N - 9° 16' N latitudes and 38° - 38° 50' E longitudes.

Study design

Research design is the blueprint for fulfilling the research objective and answering research questions. It is a master plan specifying the methods and procedures for collecting and analyzing the needed information. The present study was descriptive (concerned with determining the frequency with which an event occurs) and explanatory (concerned with determining the cause-and-effect relationship). Moreover, the study utilized a cross-sectional approach, i.e., all relevant data was collected at a single point in time. This is a retrospective study where data from the past seven years (2013-2019) was utilized. The study included all records of individuals registered in the log book from 2013-2019 and diagnosed with HIV infection and HIV-opportunistic co-infections.

Sampling procedure

Health Centers with high patient inflow were selected to obtain sufficient data. The target population was defined as all patients with HIV during the seven years period. The study sample included all patients that visited the Health Center with HIV and HIV/opportunistic co-infections between 2013 and 2019 (for 7 years).

Methods of data collection

Relevant data were collected by using a checklist, which was adopted from the health center's clinical record format for monitoring HIV/AIDS patients on ART. The data collection was carried out typically by secondary data source from a pre-recorded document of the patients' registration book and patient clinical card in the Health centers and appropriate information about characteristics of the outpatients for the last seven years (2004 to 2010) were collected.

Data analysis

Data were entered into a data entry file using SPSS software Version 20 and were analyzed. Results were presented via frequency and percentages with tables. To assess the significance of the association between HIV-opportunistic co-infections and various socio-demographic and clinical variables, logistic regression was used. A p value < 0.05 was considered to be significant.

Table 1. Socio-demographic and clinical characteristics of the HIV-positive patients at Burayu Health Centers from 2013-2019 (N = 1448).

Characteristics	n (%) *
Sex	
Male	579 (40.0)
Female	869 (60.0)
Age (years)	
≤ 15	168 (11.6)
15 – 30	530 (36.6)
31 – 45	518 (35.8)
Above 45	232 (16.0)
Residence	
Urban	1028 (71.0)
Rural	420 (29.0)
Nutritional status	
Normal	869 (60.0)
Moderate	463 (32.0)
Severe	119 (8.0)
ART adherence	
Good	912 (63.0)
Fair	449 (31.0)
Poor	87 (6.0)
WHO clinical stage	
Who stage1	463 (32.0)
Who stage 2	472 (32.6)
Who stage 3	488 (33.7)
Who stage 4	52 (3.6)
CD4 cell count	
< 200 cell/mm^3	488 (33.7)
200 – 500 cell/mm^3	588 (40.6)
Above 500 cell/mm^3	372 (25.7)
Educational status	
No formal education	405 (28.0)
Primary education	420 (29.0)
Secondary education	405 (28.0)
Tertiary	217 (15.0)
Marital Status	
Single	652 (45.0)
Married	449 (31.0)
Separated/Divorced	159 (11.0)
Widowed/widower	188 (13.0)
Occupation	
Government Employee	159 (11.1)
Private Employee	562 (38.8)
Unemployed	494 (34.1)
Students	233 (16.1)

*The percentage is calculated from the total examined for the respective characteristic.

Results

Socio-demographic and clinical characteristics of the study participants

A total of 1,448 HIV-positive patients were reviewed of which 869 (60%) were females and 579 (40%) were males. The mean age of the study participants was 29.79 years. HIV infection was highest in the age range 15-30 years (530, 36.6%) followed by 518 (35.8%) and 232 (16%) in the age groups 31-45 years and > 45 years, respectively. The lowest prevalence rate of 168 (11.6%) was observed in the age group less than 15 years.

A majority of the HIV patients (1028, 71%) were urban residents while 420 (29%) resided in rural areas indicating that the incidence of HIV was higher in urban areas than in rural areas. The majority of participants with HIV were at a normal nutritional status 869 (60%) with good ART adherence 912 (63%) (Table 1). Many of the study participants (488, 33.7%) were at WHO clinical stage III, about 472 (32.6%) were at WHO clinical stage II, and the remaining 463 (32%) and 52 (3.6%) were at WHO clinical stage I and IV, respectively. Regarding their CD4 count, about 521 (36%) of participants had a CD4 count between 200-500 cells/mm^3, 536 (37%) were < 200 cells/mm^3, and 391 (27%) greater than 500 cells/mm^3 (Table 1). Regarding their marital status, the majority of the study participants were never married (single) (652, 45%), and about 449 (31%) of the participant was married. In terms of occupation, 562 (38.8%) of the participants were privately employed while 494 (34.1%) were unemployed (Table 1).

Prevalence of Opportunistic Infections among HIV infected patients

Due to the unavailability of data for other opportunistic infections, data was only collected from 2013-2019 from two Burayu Health Centers. Out of

Table 2. Prevalence of opportunistic infection among HIV/AIDS patients at Burayu Health Centers from 2013-2019 (n = 1448).

Opportunistic infection	n (%) *
Tuberculosis (TB)	348 (24)
Oral candidasis	275 (19)
Bacterial pneumonia	152 (10.5)
Chronic diarrhea > one month	101 (7)
Cryptosporidiosis	119 (8.2)
Herpes zoster	175 (12.1)
Upper respiratory tract infections	119 (8.2)
Extra pulmonary tuberculosis	67 (4.6)
Esophageal candidiasis	61 (4.2)
Others	32 (2.2)

*The percentage is calculated from the total examined for the respective characteristic, Others (*Herpes simplex*, PGL, *Pneumocystis carinii*, Pneumonia, Toxoplasmosis).

Table 3. Trends of HIV and HIV-opportunistic co-infection among HIV Patients at Burayu health centers between 2013 and 2019.

Year	HIV Positive	HIV/Opportunistic co-infection N (%) *
2005	264	116 (20.3%)
2006	242	94 (16.4%)
2007	234	85 (14.8.%)
2008	202	75 (13.1%)
2009	217	70 (12.2%)
2010	153	71 (12.4%)
2011	136	61 (10.7%)

*The percentage is calculated from the total examined for the respective characteristic.

1448 HIV patients, 572 OIs were observed from 448 patients during the study period. The overall prevalence of OIs among the study participants was 39.5% (572/1448). Among these, 328 (22.65%) patients had only one opportunistic infection during the study period. The most common types of OIs among HIV patients in ART in the study area from 2013-2019 were: TB 348 (24%), oral-candidiasis 275 (19%), Herpes zoster 143 (12.1%), and bacterial pneumonia 152 (10.5%) (Table 2).

Trends of HIV and HIV/Opportunistic Co-infection

As indicated in Table 3, the incidence of HIV-positive patients, between 2013 and 2019, was 264 in 2013, 242 in 2014, 234 in 2015, 202 in 2016, 217 in 2017, 153 in 2018, and 136 in 2019. Between 2013 and 2019 HIV prevalence showed a fluctuating trend. As shown in Table 3, 116 (20.3%) in 2013, 94 (16.4%) in 2014, 85 (14.8%) in 2015, 75 (13.1%) in 2016, 70 (12.2%) in 2017, 71 (12.4%) in 2018, and 61 (10.7%) in 2019. The trend of opportunistic-HIV co-infection showed gradually decreased.

Association between CD4 cell count and HIV-Opportunistic co-infections

In a total of 1448 HIV-positive patients, 572 (39.5%) were found to have opportunistic infections. Of these, 431 (29.8%) HIV patients had a $CD4^+$ count below 200 cells/mm^3 and had opportunistic infections. In HIV patients with $CD4^+$ cell counts between 200 and 500 cells/mm^3, 102 (7%) had opportunistic infections. Meanwhile, 39 (2.69%) of HIV patients with $CD4^+$ counts above 500 cells/ mm^3 had opportunistic infections.

Majority of HIV patients were found at a $CD4^+$ count < 200 cells/mm^3. The rate of opportunistic infections increased with decreasing CD4 T-cell count. Therefore, the current study showed that HIV-infected patients with $CD4^+$ cell count of < 200 cells/mm^3 were found to be 44 times more likely to develop opportunistic infections compared to those with CD4+ counts of above 200 cells/mm^3 (OR = 43.9, 95% CI, 31.6-61.0, $p < 0.0001$). HIV patients who had a CD4 cell count above 200 cells/mm^3 were found to be safe from opportunistic infections. For instance, HIV patients who had CD4 cell count 200-500 cells/mm^3 were 83% times less likely of contracting an opportunistic infection than those with a $CD4^+$ cell count of < 200 cells/mm^3. Similarly, HIV patients who had a CD4 cell count above 500 cells/mm^3 were 89% times less likely to develop an opportunistic infection than those with a $CD4^+$ cell count of < 200 cells/mm^3 (Table 4).

HIV-Opportunistic co-infections and associated factors among HIV patients

Univariate logistic regression analysis was conducted to identify the associated factors for the occurrence of opportunistic infections among HIV patients taking ART as described in Table 5. HIV-opportunistic co-infection was significantly associated with sex, marital status, ART drug adherence, residence, and educational status of the patients. The odds of co-infections in patients who were urban dwellers were 2 times higher than in those who lived in

Table 4. HIV-opportunistic co-infections in relation to CD4+ cell count in two Burayu Health Center between 2013 and 2019 (N = 1448).

CD4 cell count		HIV/Opportunistic co-infection		OR (95% CI)	*p* value
		Co-infected N (%) *	Not co-infected N (%) *		
< 200 cell/mm^3	Yes	431 (88.3%)	57 (11.7%)	43.9 (31.6-61.0)	< 0.0001
	No	141 (14.7%)	819 (85.3%)	1.00	
200 - 500 cell/mm^3	Yes	102 (17.3%)	486 (82.7%)	0.17 (0.13-0.22)	< 0.0001
	No	470 (54.7%)	390 (45.3%)	1.00	
Above 500 cell/mm^3	Yes	39 (10.5%)	333 (89.5%)	0.11 (0.08-0.16)	< 0.0001
	No	533 (49.5%)	543 (50.5)	1.00	

*The percentage is calculated from the total examined for the respective characteristic.

rural areas. Similarly, single patients were 3 times more likely to be infected with co-infections. Moreover, patients who were illiterate were 5 times more likely to have co-infections. Maleness was found to be a protective factor from co-infection with 64% fewer opportunistic infections as compared to females (Table 5).

Discussion

As indicated in the present study, the trend of opportunistic-HIV co-infection showed a gradually decreased, which is similar to the study done by Amare [6]. This might be due to the intensive delivery of INH prophylaxis to prevent opportunistic infection of TB as soon as they detect HIV positive. The other possible explanation may be due to the improved availability of antiretroviral therapy (ART), improvement in general patient care as well as better diagnostic and therapeutic management of AIDS-related disease [7]. This could also be due to the current strategic plan of the ministry of health in Ethiopia, which expands health facilities across the country and increased awareness of the community through health education on the prevention and control of HIV.

HIV infection was higher in the 15-30 years age range (36.6%), followed by 35.8% and 16.0% in the age group 31-45 years and > 45 years respectively. The lowest prevalence rate was observed in the age group less than 15 years (11.6%). Burayu is a developing town with a lot of new investments. A large number of labor migrants were moving from the surrounding districts (woredas) to the town in search of job opportunities who were the most sexually active young age groups and with more HIV infections. This finding is similar to a study done in Ethiopia [7,8]. People within this age group are sexually active and may have more than one sexual partner which might contribute to the increase in HIV infection.

In this study, HIV infection was higher in females (60%) than in males (40%). The gender difference in HIV prevalence obtained in this study is similar to a study done by Sintayehu *et al* [9] in South Ethiopia and a study done by Knbs and Macro [10] in Kenya. According to the 2011 EDHS, the adult prevalence was almost twice as high among females compared to males. The burden and distribution of HIV-opportunistic co-infection respective of the prevalence level by age showed that the greatest burden of co-infection was among those in the 15-30 years age-group 236 (41.3%), followed by those 31-45 years of age, 205 (35.8%) while the least was among those less than 15 years of age, (57 %). This finding is supported by a similar study conducted in India[11], Nigeria [12], and Dire Dawa [7]. This is a sexually active age group in which both opportunistic and HIV prevail most.

Almost all opportunistic infections among HIV cases were found at a $CD4^+$ count < 200 cells/mm^3. The rate of opportunistic infections increased with decreasing CD4 T-cell count among HIV-infected individuals. The highest infection rate 431/572 was at

Table 5. Univariate analysis for factors associated with HIV-Opportunistic co-infections among HIV patients attending two Burayu Health Centers from 2013-2019 (N = 1448).

Characteristics	HIV-Opportunistic co-infection		COR (95% CI)	*p* value
	Co-infected N (%) *	Not-co-infected N (%) *		
Sex				
Male	149	430	0.36 (0.29-0.45)	< 0.0001
Female	423	446	1.00	
Age (years)				
< 15	57	111	23.5 (3.2-174)	0.000
15 – 30	236	294	1.4 (0.85-2.2)	0.19
31 – 45	205	313	0.04 (0.03-0.06)	0.000
Above 45	74	158	1.00	
Residence				
Urban	458	570	2.1 (1.6-2.7)	<0.0001
Rural	114	306	1.00	
ART adherence				
Good	61	801	1.00	
Fair	377	72	0.32 (0.16-0.62)	0.001
Poor	134	3	2.21 (1.12-4.37)	0.022
Educational status				
Illiterate	272	131	5.1 (4.0-6.6)	< 0.0001
Literate	300	745	1.00	
Marital Status				
Single	470	529	3.02 (2.34-3.89)	< 0.0001
Married	102	347	1.00	

*The percentage is calculated from the total examined for the respective characteristic.

$CD4^+$ T cell counts of < 200 cell/mm^3. There is a possibility that clinical disease can occur at any $CD4^+$ T-cell, the present study showed that HIV-positive individuals develop the disease at a significantly lower $CD4^+$ T-cell count. The effect of HIV on the immune system is monitored by measuring the $CD4^+$ T-lymphocyte count in the blood [13]. HIV infection leads to low levels of $CD4^+$ counts making the body more susceptible to OIs. When the CD4+ T-cell counts decline below a critical level of 200 cells/ mm^3, the cell-mediated immunity declines and OI's appear [14]. This finding is in accordance with other studies from Gondor, Ethiopia, which report that HIV-infected patients with $CD4^+$ counts < 200 cells/mm^3 were more likely to develop OIs compared to the reference group of patients with $CD4^+$ count > 350 cells/mm^3 [15]. Similar findings were observed in a study conducted by Mala and Oberoi [14], they screened the HIV seropositive patients for OI in relation to their $CD4^+$ counts in a tertiary care hospital in North India. Among 80 HIV patients, 38 (47.5%) patients were positive for OIs. Among these positive patients presenting with OI's, a majority (13.6%) had a $CD4^+$ count of < 200 cells/μL, and there was a strong association between the two parameters [14]. This is due to HIV attacks and destroyed T- helper cells. As the immune system becomes increasingly damaged by HIV, it becomes susceptible to opportunistic infection [16]. The effect of HIV on the immune system is monitored by measuring the $CD4^+$ T-lymphocyte (helper T-cell) count in the blood. As $CD4^+$ T-cell count decreased, the prevalence of OIs increased.

In this study, marital status was significantly associated with opportunistic infection. Unmarried (single) HIV patients showed high HIV-opportunistic co-infection, 47/572(82.2%). Married, 102/72(17.8%) HIV patients were less likely to develop an opportunistic infection which is comparable with reports in the Amhara region [17]. It might be explained as unmarried (single) persons are younger than a married person and have a different lifestyle, especially males, who often migrate to towns in search of jobs. Based on the place of residence of patients, a slightly high prevalence of HIV-opportunistic co-infection was observed in urban areas than rural areas (458/572 versus 114/572%). This is because of overcrowding, poverty, and high prevalence of HIV infection.

The education level of the data reviewed showed; most HIV-opportunistic co-infection occurred in uneducated patients. Regarding the occupation of patients, co-infection was higher among unemployed individuals. This high prevalence rate might be due to the poor (low) standard of living in the study area and its attendance with no education which is associated with poor knowledge of opportunistic infection and HIV, risk of infection, and distribution and access to health care [18].

The other clinical risk factor that has a significant association with the occurrence of opportunistic infection was ART drug adherence. Adherence to treatment is a determining factor in improving the quality of life of patients and the treatment success; however, it is one of the biggest challenges for AIDS patients [19]. People with good ART adherence were less likely to develop an opportunistic infection as compared with patients with poor ART adherence. From different OIs in HIV patients, the common types of OIs among HIV patients on ART in the current study area were pulmonary tuberculosis (24%; 348/1448), oral candidacies (19%; 275/1448) and herpes zoster (12.1%;175/1448). Similar findings were also observed in other studies [20-22]. This might be because their diagnosis is relatively easy to from patients than other OIs. However, it is higher than similar studies carried out in Ethiopia in Gondor and Debre Markos, which is documented 19.7% and 33% prevalence respectively [15,23]. This difference might be due to variations in the degree of host immunity, exposure to pathogens, and methodology difference in selecting study subjects.

The other OI that is found in the study area is Cryptosporidiosis. The prevalence of Cryptosporidiosis in this investigation was 8.2%, which was higher compared with a study conducted in ART centers in Addis Ababa and Wolaita Southern Ethiopia was reported at 3.5% [22] and 2.5% [21]. But the prevalence of Cryptosporidiosis was low when compared with other studies conducted previously in India 30.1% [24], South Ethiopia 34.3% [25], and Wolaita Ethiopia 14.2% [26]. This variation in the prevalence of Cryptosporidiosis among HIV/AIDS patients might be due to exposure to food and water contaminated with *Cryptosporidium* oocyst, and the immune status of HIV/AIDS patients. The incidence of diarrhea in the present study (7%) was higher compared with the studies in Eastern Ethiopia (3.6%) [20]. However, the prevalence was lower than in the study conducted in India (29.6%) [27]. Factors like poor sanitary practices and the unavailability of safe drinking water might be responsible for these variations.

Conclusions

The finding suggests that HIV-opportunistic co-infection was present more among males, age range from 15-30 years, single, private and unemployed

individuals, uneducated, WHO clinical stage III and IV, CD4 cell count < 200cells/mm^3, urban, and poor ART drug adherence. This calls for focusing on an intervention strategy for the early diagnosis and treatment of opportunistic infections and early ART treatment of all persons with HIV/AIDS for better treatment outcomes and to reduce transmission.

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