

Prevalence of Opportunistic Infections and Associated Factors Among HIV-infected Patients on Antiretroviral Therapy in Eastern Zone of Tigray, Ethiopia:A Cross-sectional Study

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Abstract

Background: Opportunistic infections are diseases that cause infections in people whose immune systems are weakened. It is the most public health problem and the leading cause of morbidity and mortality of AIDS-related infections in developing countries. Identification of opportunistic infections is the core for developing a specific intervention. Despite this fact, information about the burden of opportunistic infections is lacking in the particular study. Therefore, this study aimed to assess the prevalence and associated factors of opportunistic infections among HIV-infected patients in Eastern zone of Tigray, northern Ethiopia.

Methods: An institutional-based cross-sectional study was done among HIV/AIDS patients taking antiretroviral therapy in Northern Ethiopia. A total of 394 study subjects was selected using a systematic random sampling method. Data was collected using a structured questionnaire. The collected data was entered and analyzed by SPSS version 22. Bivariate and multivariable logistic regression analysis with 95% confidence interval were used to find factors associated with opportunistic infections. The adjusted odds ratio was calculated to show the strength of the association. Variables with p-value of < 0.05 were considered statically significant.

Results: The mean age of the respondents was 41 (\pm 10). Of the study participants, about 52% (95% CI: 47.5-57.1) developed opportunistic infections. Being housewife occupation (AOR = 0.17; 95% CI: 0.07-0.46), CD4+ count < 200 cells/ μ l (AOR = 2.38; 95% CI: 1.3-4.67), poor adherence (AOR = 4; 95% CI: 1.95-8.2), and bedridden functional status (AOR = 13.9; 95% CI: 5.2-37) were independently associated with opportunistic infections.

Conclusion: This study stated the prevalence of opportunistic infections among HIV-infected patients is high. Being housewife occupation, poor ART adherence, low CD4+ count, and bedridden functional status were found to be associated with development of opportunistic infections. Therefore, health care providers must give continuous health education on primary prevention of opportunistic infections.

Introduction

Human Immunodeficiency Virus (HIV) pandemic is among the greatest health crises ever faced by humanity. Worldwide, 37.9 million people were living with HIV at the end of 2018 [1]. Sub-Saharan Africa carries the highest burden with an estimated 71% of the global total [1]. In Ethiopia, an estimated 715 404 people were living with HIV in 2015 and this increased to 722 248 in 2017 which was increased by 3748 infections from 2016 [2].

Opportunistic infections (OIs) are diseases that cause infections in people whose immune systems are weakened like in Human Immunodeficiency Virus Syndrome (HIV/AIDS) patients [3, 4]. Majority of the opportunistic infections often manifest at the end stage of the disease. These are the commonest leading causes of morbidity and mortality among people living with HIV/AIDS [5]. Greater than 90% of HIV/AIDS deaths contribute to opportunistic infections [6].

Morbidity and mortality in people living with HIV/AIDS are due to underlying immunosuppression, which leads to a life-threatening opportunistic infections during the natural course of the disease. Immune-compromised people living with HIV develops a number of OIs that have a significant burden on their quality of life, healthcare cost, well-being, and their survival [7, 8]. The development of OIs among people living with HIV depends on the degree of host immunity, virulence of the virus, and the use of antimicrobial prophylaxis [9]. Majority of the opportunistic infections among people living with HIV in Ethiopia are tuberculosis (21.23%), herpes zoster (11.2%), oral candidacies (9.5%), chronic diarrhea (3.6%), bacterial pneumonia (2%), central nervous system (CNS) toxoplasmosis (1.4%), and pneumocystis carini pneumonia (0.8%) [10].

HIV/AIDS-related opportunistic infections virtually cannot be cured except lifelong suppressive therapy after an acute infection. Therefore, primary prevention of such illness through prophylaxis is crucial [11]. Beside the presence of management and prevention modalities, OIs persisted to be the most challenge issues among HIV/AIDS patients [5, 12].

The provision of antiretroviral therapy (ART) decreases viral reproduction, increase the number of CD4+ lymphocytes counts and improve their function, re-establishing the defenses against the virus and improving the chance of survival [8, 13]. A study conducted in low and middle income countries indicated that there was a major reduction in OIs with ART use [14].

However, about 75% of HIV-infected patients delayed ART initiation and had 33% pre-ART mortality rate because of HIV-related OIs [15]. Different studies done in Sub-Saharan Africa showed that still there is a high prevalence of OIs among HIV-infected patients taking ART [16, 17]. In Ethiopia, the burden of OIs increases from time to time alarmingly. The prevalence of OIs was 19.7% and 88.4% in 2012 and 2017 respectively [10, 18-22]. Also, different studies stated the factors associated with the development of OIs were age, gender, poor ART adherence, disease stage, habit of chat chewing, functional status, low CD4 level, hemoglobin level, weight, failure, and cross-resistance [13, 16, 17, 23].

For the strategies in HIV/AIDS-related morbidity and mortality to be reduced, identifying the prevalence of OIs play a significant role. Despite the fact different studies have been done on the prevalence of OIs among people living with HIV on ART in Ethiopia, however, majority of these studies were used only patients' clinical records to collect the data and important records of risk factors of OIs like adherence to AR, substance use, and prophylactic treatments was not studied [10, 16, 20, 22]. Besides, there are limitation of data on the prevalence of OIs and associated factors among HIV-infected patients in northern Ethiopia.

Therefore, this study aimed to assess the prevalence of OIs and associated factors among HIV/AIDS patients in Eastern Zone of Tigray, northern Ethiopia.

This study will be used to inform the policy makers and programmers to design appropriate care and control of opportunistic infections, to maintain a good quality of life and survival among people living with HIV/AIDS.

Methods And Materials

Study area, design, and period

The study was conducted in public health facilities of Eastern Zone, which is found in Tigray region, Ethiopia. Eastern Zone is located in the northern part of Ethiopia, which is 888 kilometers away from the capital City Addis Ababa. Based on the 2007 census conducted by a central static agency in Ethiopia, this Zone has a total population of 755,343 [24]. There are seven primaries and two general hospitals that provide ART services in Eastern Zone Tigray [25]. Out of these, three primaries and the two general hospitals were selected randomly. The study hospitals were Adigrat general hospital, Wukro general hospital, Atsbi primary hospital, Hawzen primary hospital, and Fatsi primary hospital. The study was an institution-based cross-sectional study conducted from April to May for two consecutive months in 2019.

Population

The source of the population was all HIV/AIDS patients in Eastern Zone that were enrolled for ART follow-up service. The study populations were people living with HIV/AIDS with an age of ≥ 18 years who were currently receiving ART. However, patients with edema like in congestive heart failure and ascites, and critically ill and/or patients with spinal deformity were excluded.

Sample size determination and sampling technique

The required sample size was determined using single population proportion formula taking 55.3% [20] prevalence of opportunistic infections among adults with HIV/AIDS on ART with 5% of margin error and 95% confidence interval (CI). By adding 4% of the non-response rate, the final sample size was determined as 394. There were a total of 3933 adult patients living with HIV who were enrolled in the follow-up in Eastern zone hospitals ART clinic.

From which, to select the required sample size the total sample size was proportionally allocated to the five public hospitals. Accordingly, the list of the patients were taken from the follow-up unit of the five public hospitals, and the sampling frame was developed. Then the first study subject was randomly selected from the sampling frame by using the lottery method and those participants were selected using a systematic sampling technique from the sampling frame.

Data collection instruments and procedures

Data were gathered using a structured and interviewer-administered questionnaire with the chart/document review. The questionnaire consisted of four parts. Part I: Sociodemographic characteristics. Part II: Lifestyle/behavioral characteristics such as alcohol consumption and smoking status. Part III: ART medication adherence. Part IV: Chart/document review used to extract information related to HIV related characteristics, including immunological status and clinical characteristics. According to the federal ministry of health, HIV ART follow-up guideline [26], HIV patients were expected to visit the ART follow-up clinic at least once a month. Data regarding the patient's demographic

information, clinical information (WHO, clinical staging), functional status (working, ambulatory, and bedridden) medical history, opportunistic infection diagnosis, adherence to ART, Isoniazid and/or cotrimoxazole prophylaxis use, CD4+ count and other laboratory results such as hemoglobin value, and any other treatment given and side effects would be registered in the standardized case report format.

Anthropometric measurement was carried out to determine the nutritional status of the study participants' by using Body Mass Index (BMI). The weight of the study subjects was measured using a beam balance to the nearest 0.1 Kg and measuring range up to 160 Kg. Weight was measured with light clothing and no shoes. Calibration was performed before weighing each participant by setting it to zero. Weighing scale also checked against a standard weight for its accuracy on a daily basis. The height of the participants was measured using a vertical height scale standing upright in the middle of the board and recorded to the nearest 0.5 cm. Study participants were asked to take off their shoes, stand erect, and look straight in the horizontal plane. The occiput, shoulder, buttocks, and heels touched measuring board and height was recorded to the nearest 0.01cm [27].

Then BMI was computed by dividing weight in kg by the square of the height in meters (kg/m²). Accordingly, the study participants were classified as undernourished (underweight) if their BMI was less than 18.5kg/m². To maintain consistency, the questionnaire was first prepared in English then translated to the local language (Tigrigna) and was back-translated to English by professional translators. Then, data were collected through face to face interview and document review. Five individuals who have completed their BSc in nursing education from a recognized University were recruited as data collectors. Two days training was given to the data collectors on the objectives of the study, how to keep confidentiality of information, the contents of the questionnaire. On the days of data collection, the principal investigator and another two senior BSc nurse who have experience in data collection were supervised the data collection process by checking consistency and completeness of the questionnaire and given appropriate support during the data collection process.

Data processing and analysis

The collected data were entered and analyzed using SPSS version 22. Both bivariate and multivariable logistic regression analysis were used to assess the between each independent variable and dependent variable. Variables with p-value < 0.25 significance level in the bivariate logistic regression was taken to multivariable logistic regression. Then, p-value < 0.05 in multivariable logistic was used to declare statically significance. The odds ratio was estimated at 95% CI to show the strength of association. Finally, text and tables were used to describe the results.

Definition of variables

Opportunistic infections: Were defined as in accordance with the list of opportunistic diseases stated in the Ethiopian National guideline for comprehensive HIV care, treatment, and prevention [28]

Medication adherence was assessed using Morisky medication adherence score to ART medications having eight questions each with yes = 1 and no = 0, good adherence if they score 7–8, and poor adherence if they score ≤ 6 [29]

Alcoholic - a person who drinks 10.5 units of alcohol and above per week [30]

Results

Socio-demographic characteristics of respondents

A total of 394 HIV positive patients were included. Of those, 249 (63.2%) of the patients were females. The mean age (\pm SD) of the respondents was 41 (\pm 10). Concerning the occupation of the study population, 139 (35.3%) of the respondents were farmers. Regarding educational level, nearly half (49.2%) were not able to read and write (Table 1).

Clinical, behavioral, and nutritional status characteristics of respondents

The clinical condition of the participants indicated that about 205 (52%) had an opportunistic infections. Majority of the respondents; 260 (66%) were in WHO clinical stage I. Of the total respondents, 55 (14%) did not use isoniazid preventive therapy (IPT) prophylaxis. Concerning the level of CD4+ count and functional status, about 149 (37.8%) and 62 (15.7%) had CD4+ level < 200 cells/ μ l and bedridden respectively. Moreover, about 328 (83.2%) of participants had poor adherence to the ART medication (Table 2).

Bivariate and multivariable logistic regression for factors associated with opportunistic infections among ART initiated HIV/AIDS patients

In this study, both bivariate and multivariable logistic regression analysis were computed. In the bivariate logistic regression, gender, age, educational level, occupation, medication adherence, IPT and co-trimoxazole prophylaxis, CD4+ count, WHO clinical staging, duration with HIV, and functional status were among the factors identified as candidate variables for multivariable logistic regression analysis. Out of those, only four variables were significantly associated with OIs when data were employed with multivariable logistic regression analysis. Therefore, participants with housewife occupation (AOR = 0.17; 95% CI: 0.07-0.46), poor adherence to ART (AOR = 4; 95% CI: 1.95-8.2), CD4+ count < 200 cells/ μ l (AOR = 2.38; 95% CI: 1.3-4.67), and bedridden functional status (AOR = 13.9; 95% CI: 5.2-37) were more likely to be infected with opportunistic infections (Table 3).

Discussion

This study is focused on assessing the prevalence of opportunistic infections and associated factors among HIV-infected patients after the initiation of ART. The current study found that about 52% (95% CI: 47.5-57.1) of HIV/AIDS patients had one or more opportunistic infections. This result is consistent with

other institutional-based studies conducted in Ethiopia such as Lemlem Karl hospital (55.3%) [20], Hiwot Fana Hospital (48%) [10]. But, it is higher than studies done in Gondar and Addis Ababa 19.7% and 33.6% respectively [18, 21]. However, this finding is lower than a study conducted in Dawro Zone hospital (88.4%) [19]. This different result among different studies could be explained by the discrepancy in health care awareness of the population and variation in the degree of host immunity. Also, it could be due to methodological difference in selecting participants or due to sample size variation.

Concerning the factors associated with opportunistic infections, respondents whose occupation housewife were 83% times less likely to develop opportunistic infections [AOR = 0.17; 95% CI: 0.07-0.46]. Moreover, people living with HIV with CD4+ count less than 200 cells/ μ l were 2.38 times more likely develop opportunistic infections when we compared those patients with CD4+ count more than 500 cells/ μ l (AOR = 2.38; 95% CI: 1.3-4.67). Other studies showed similar associations [16, 19, 31]. This finding sounds true since CD4+ cells play a central role in the activation of both cellular as well as humoral immune response to fight against infections. Therefore, individuals with low CD4+ cells have poor immunity and they are highly susceptible to develop opportunistic infections.

Moreover, medication adherence currently showed a significant association with opportunistic infections. The present study indicated that participants who had poor adherence to ART medication were found 4 times more likely to be suffering from opportunistic infections compared to those who have good adherence to ART medication (AOR = 4; 95% CI ((1.95-8.2). This result is also in agreement with other studies conducted in developing countries [16, 31, 32]. This could be because proper medication adherence to ART will suppress viral replication and would increase the level of CD4+ count that intern reduce susceptibility of new opportunistic infections.

In addition, functional status of patients was strongly associated with increased morbidity with opportunistic disease. Patients who were in bedridden functional status at baseline were 13.9 times at high risk of developing opportunistic infections compared to those with working functional status (AOR = 13.9; 95% CI: 5.2-37). This might be suggests as participants who were bedridden might be immune-compromised and predisposed to any opportunistic infections or this might be explained by lack or limited mobility of HIV-infected patients who may start to lose interest in eating because they cannot get enough stimulation on a regular basis and unable to care for themselves.

Limitation Of The Study

The limitation of this study is related to the cross-sectional nature of the study, which could not accurately show the cause and effect relationship between factors and outcome of interest. There may have been recalled bias and social desirability bias since some of the variables such as medication adherence and substance use (alcohol and smoking status) of the study participants were based on self-reports.

Conclusion

This study stated the prevalence of OIs among HIV-infected patients on ART is still high.

Being housewife occupation, poor ART adherence, low CD4+ count, and bedridden functional status were found to be associated with the development of OIs. Therefore, for people living with HIV who are on ART, health care providers must give continuous health education on primary prevention/screening of OIs, adherence to medications, public awareness, and community mobilization. Also, the continuous assessment of patients for signs and symptoms of OIs after starting ART, particularly among patients that have risk factors mentioned in this paper will lead to an earlier OIs diagnosis and ultimately to reduce morbidity. Additionally, strong epidemiologic studies evaluating the reasons for the high level of OIs among HIV-infected patients are recommended.

List Of Abbreviations

AIDS-Acquired immune Deficiency Syndrome; AOR-Adjusted Odds Ratio; ART- Antiretroviral Therapy; BMI- Body Mass Index; HIV- Human immunodeficiency Virus; IPT- Isoniazid preventive therapy; OIs- Opportunistic Infections; WHO- World Health Organization; COR-Crude Odds Ratio, CI-Confidence Interval; SPSS- Statistical Package for Social Science.

Declarations

Ethics approval and consent to participate

Ethical clearance was obtained from Adigrat university research and community service directorate office. A letter of support was also issued from the Tigray Regional Health Office to each respective health institution. Besides, information about the study was provided and written informed consent was obtained from study participants to confirm their willingness for participation.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interest

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Authors' contributions

TH: Has initiated the idea, carried out the study and provided the final version. HH: Critically revised the paper and has contributed to the pre-test of the tool. KG: Recruit data collectors and participates in

reviewing the design. HT: Participate in analysis. BT: participate in writing the manuscript.

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Tables

Table1: Socio-demographic characteristics of HIV infected patients in Eastern Zone Tigray, Ethiopia, 2019

Variables	Category	Frequency	Percentage
Gender	Male	145	36.8
	Female	249	63.2
Age	18-24	23	5.8
	25-34	64	16.2
	>35	307	77.9
Marital status	Married	126	32
	Single	81	20.6
	Divorced	106	26.9
	Widowed	81	20.6
Level of education	Can't read and write	194	49.2
	Can read and Write	80	20.3
	Primary school	69	17.5
	Secondary school	36	9.1
	Diploma and above	15	3.8
Occupation	Farmer	139	35.3
	Housewife	44	11.2
	Governmental employee	35	8.9
	Daily worker	49	12.4
	Merchant	37	9.4
	No work	83	21.1
	Other	7	1.8
Religion	Orthodox	381	96.7
	Muslim	6	1.5
	Catholic	6	1.5
	Other	1	0.3
Ethnicity	Tigray	392	99.5
	Amhara	2	0.5
Residence	Urban	207	52.5

	Rural	187	47.5
Average monthly income	<1920	293	74.4
	>1920	101	25.6

Table 2: Clinical, behavioral, and nutritional status of HIV infected patients in Eastern zone of Tigray, Ethiopia, 2019

Variables	Category	Frequency	percentage
Khat chewing status	No	384	97.5
	Yes	10	2.5
History of smoking	No	380	96.4
	Yes	14	3.6
Alcohol consumption	No	327	83
	Yes	67	17
Undernutrition	Yes	169	42.9
	No	225	57.1
Weight in Kg	<60 Kg	360	91.4
	>60 Kg	34	8.6
Medication adherence	poor	328	83.2
	Good	66	16.8
Functional status	Working	255	64.7
	Ambulatory	77	19.5
	Bedridden	62	15.7
Opportunistic infection	No	189	48
	Yes	205	52
CD4+ count (cells/ μ l)	<200	149	37.8
	200-349	86	21.8
	350-499	62	15.7
	>500	97	24.6
Level of Hemoglobin	<10	42	10.7
	>10	352	89.3
WHO clinical stage	Stage I	260	66
	Stage II	37	9.4
	Stage III	78	19.8
	Stage IV	19	4.8
IPT prophylaxis	No	55	14

	Yes	339	86
Co-tromoxazole Prophylaxis	No	72	18.3
	Yes	322	81.7
Duration of HIV/AIDS	<2 years	13	3.3
	2 -5 years	60	15.2
	>5 years	321	81.5

Table 3: Bivariate and multivariable analysis of factors associated with opportunistic infections in Eastern Zone, Tigray, Ethiopia, 2019

Opportunistic infections				
Variables	No	Yes	COR (95% CI)	AOR (95% CI)
	Nº (%)	Nº (%)		
Gender				
Male	54(28.6%)	91(44.4)	1.99(1.31-3.03)	1.01(0.55-1.98)
Female	135(71.4)	114(55.6)	1	1
Age				
18-24	14(7.4)	9(4.4)	1	1
25-34	37(19.6)	27(13.2)	1.14(0.43-3)	0.66(0.17-2.57)
>35	138(73)	169(82.4)	1.9(0.8-4.5)	0.85(0.24-2.99)
Educational level				
Cannot read and write	104(55)	90(43.9)	0.43(0.14-1.31)	0.71(0.14-3.66)
Can read and write	44(23.3)	36(17.6)	0.41(0.13-1.31)	0.45(0.09-2.33)
Primary school	23(12.2)	46(22.4)	1(0.31-3.27)	0.87(0.17-4.39)
Secondary school	13(6.9)	23(11.2)	0.88(0.25-3.15)	1.4(0.25-7.42)
Diploma and above	5(2.6)	10(4.9)	1	1
Occupation				
Farmer	64(33.9)	75(36.6)	1	1
Housewife	33(17.5)	11(5.4)	0.28(0.13-0.91)	0.17(0.07-0.46)*
Governmental employee	12(6.3)	23(11.2)	1.64(-0.76-3.55)	0.66(0.2-2.13)
Daily worker	27(14.3)	22(10.7)	0.69(0.36-1.33)	0.38(0.16-0.95)*
Merchant	14(7.4)	23(11.2)	1.4(0.66-2.95)	0.98(0.36-2.64)
No work	36(19)	47(22.9)	1.11(0.64-1.93)	0.74(0.36-1.53)
Other	3(1.6)	4(2.0)	1.14(0.25-5.27)	0.39(0.05-3.32)
Khat chewing history				
No	188(99.5)	196(95.6)	1	1
Yes	1(0.5)	9(4.4)	8.6(1.1-68)	4.6(0.18-115)
Smoking history				

No	187(98.9)	193(94.1)	1	1
Yes	2(1.1)	12(5.9)	5.8(1.28-26.33)	2.3(0.18-29)
Alcohol consumption				
Not drinker	165(87.3) 162(79)		1	1
Drinker	24(12.7)	43(21)	1.83(1.1-3.15)	0.98(0.44-2.2)
Medication adherence				
Poor	146(77.2)	182(88.8)	2.33(1.34-4.04)	4(1.95-8.2)*
Good	43(22.8)	23(11.2)	1	1
Functional status				
Working	163(86.2)	92(44.9)	1	1
Ambulatory	19(10.1)	58(28.3)	5.41(3.03-9.64)	6.5(3.2-13.6)
Bedridden	7(3.7)	55(26.8)	13.9(6.09-31.83)	13.9(5.2-37)
CD4+ cells/μl counts				
< 200	51(27)	98(47.8)	2.98(1.76-5.07)	2.38(1.3-4.67)*
200-349	40(21.2)	46(22.4)	1.78(0.99-3.22)	1.37(0.67-2.8)
350-499	39(20.6)	23(11.2)	0.92(0.48-1.77)	0.81(0.37-1.76)
>500	59(31.2)	38(18.5)	1	1
WHO Clinical staging				
Stage I	120(63.5)	140(68.3)	1	1
Stage II	13(6.9)	24(11.7)	1.58(0.77-3.24)	0.66(0.25-1.77)
Stage III	43(22.8)	35(17.1)	0.69(0.42-1.16)	0.8(0.39-1.61)
Stage IV	13(6.9)	6(2.9)	0.39(0.15-1.07)	0.25(0.07-0.88)
IPT prophylaxis				
No	19(10.1)	36(17.6)	1.9(1.05-3.46)	0.9(0.4-1.97)
Yes	170(89.9)	169(82.4)	1	1
Co-trimoxazole				
No	29(15.3)	43(21)	1.5(0.87-2.46)	1.4(0.68-2.75)
Yes	160(84.7)	162(79)	1	1

Hg level				
<10 mg/dl	13(6.9)	29(14.1)	2.23(1.12-4.43)	0.53(0.21-1.37)
>10 mg/dl	176(93.1)	176(85.9)	1	1
Duration of HIV/AIDS				
< 2 years	8(4.2)	5(2.4)	1	1
2 -5 years	40(21.2)	20(9.8)	0.8(0.23-2.76)	1.1(0.25-5)
>5 years	141(74.6)	180(87.8)	2.04(0.65-6.38)	2.7(0.66-11.2)
Weight in Kg				
<60 Kg	176(93.1)	184(89.8)	0.65(0.31-1.33)	0.5(0.2-1.3)
>60 Kg	13(6.9)	21(10.2)	1	1

N.B: 1- Reference category, *- Variables that showed significant association at p - value ≤ 0.05

Supplementary Files

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