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Research Article

Determinants of Opportunistic Disease among Patients Attending ART Clinic, in Western Oromia, Ethiopia

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ABSTRACT

Introduction: Human Immunodeficiency Virus (HIV), the causal agent for Acquired Immunodeficiency Syndrome (AIDS) is the world's greatest severe public health and development contest. Since the beginning of the epidemic, 38 million people are living with HIV/AIDS and 1.7 million people newly infected with HIV. Increased availability and accessibility of ART have essentially improved the survival rate, by lowering the incidence of OIs among people living with HIV/AIDS. The risk of developing Opportunistic infections in HIV patients depends on experience with potential pathogens, the virulence of pathogens, degree of host immunity, and the use of antimicrobial prophylaxis. In Ethiopia however remarkable decline of new infections (81%) for decades, since 2008 HIV incidence rate began to rise by 10% and the number of new infections diagnosed each year increased by 36% among all ages and doubled among adults. A limited study is describing the spectrum of opportunistic infection and associated factors in the study settings. Therefore, this study was aimed to determine the spectrum of opportunistic infections in the study area.

Methods: A facility-based retrospective cross-sectional study was employed from 2015-2019 G.C. The sample size was computed using the single population proportion formula. Accordingly, four hundred ninety-seven (497) medical records of study participants were reviewed. A simple random sampling technique was used to select the participants included in this study. Data were extracted from the ART follow-up database and medical records of the patients by using a standardized checklist, which was adopted from the Federal Ministry of Health HIV ART. The contents of the checklist include; socio-demographic characteristics and clinical information. Data had entered Epi data version 5.3.1 and analyzed using SPSS version 20. Bivariate analysis with a p-value <0.2 was done to see the association between outcome variables and independent variables. Variables with p<0.25 in bivariate analysis were entered for multiple logistic regressions. At 95% confidence interval, explanatory variables with P<0.05 in multiple logistic regression analysis were considered as a significant association.

Results: The study found that an overall prevalence of OIs was 62%. The finding of our study documented, from deferent HIV related OIs among patients on ART follow up at Nekemte Specialized Hospital ART clinic, the common types of OIs were; Pulmonary Tuberculosis (15.7%), Oral candidiasis (14.3%), Herpes Zoster (11.3%), Cryptococcus meningitides (5.9%), upper respiratory infection (5.8%, Persistent diarrhea (5.2%), and extra pulmonary tuberculosis (3.8%). The occurrence of OIs on adult PLHIV patients who were with baseline WHO stage of I was 53% lower as compared to those who were with advanced baseline WHO stage of II and more {AOR: 0.468, 95% CI (0.305-0.716). Moreover, Participants of Urban residents were 1.6 times more likely to develop OIs than those rural residents. Baseline WHO clinical staging and residence were identified as independent predictors of OIs among adult HIV-infected patients.

Conclusion: An overall prevalence of OIs was 62%. The prevalence of OIs is still high namely Pulmonary Tuberculosis, Oral candidiasis and Herpes Zoster are leading OIs among adult HIV-infected patients. Baseline

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WHO clinical staging and residence were identified as independent predictors of OIs among adult HIV infected patients.

Recommendations: Having skilled health professionals, early diagnosis of OIs among HIV infected patients, and having equipped laboratory diagnostic setup is mandatory to be able to deal with specific diagnoses and management of OIs. Further study is recommended to determine the relationship between residence and developing OIs among HIV patients on ART follow.

Keywords: Opportunistic infections; ART clinic; HIV infected patients; Ethiopia

Abbreviations: HIV: Human Immunodeficiency Virus; AIDS: Acquired Immune Deficiency Syndrome; ART: Highly Active Antiretroviral Therapy; OIs: Opportunistic Infections; PLWHIV: People Living with HIV; WHO: World Health Organization; USAIDS: United Nation Program on HIV/AIDS

INTRODUCTION

Human Immunodeficiency Virus (HIV), the causal agent for Acquired Immunodeficiency Syndrome (AIDS) is the world's greatest severe public health and development contest [1]. As per a global joint estimate of the World Health Organization and United Nation Program on HIV/AIDS 2019, since the beginning of the epidemic, 76 million people have been infected with HIV and about 33 million people have died of HIV/AIDS, 38 million of people are living with HIV/AIDS; 1.7 million people newly infected with HIV in 2019 and 690,000 peoples died with HIV related diseases [2]. This epidemic remains a global public health challenge for 21 century [3], in the absence of a vaccine and curative therapy. Opportunistic infections (OIs) are defined as infections that occur more often or are more severe in people with weakened immune systems than in people with healthy immune systems because of immune suppression in HIV infected persons, and they are a major clinical manifestation of HIV patients [4]. Increased availability and accessibility of ART have essentially improved the survival rate, by lowering the incidence of Opportunistic infections among people living with HIV/AIDS [5]. In Ethiopia however remarkable decline of new infections (81%) for decades, 2008 HIV incidence rate began to rise by 10% and the number of new infections diagnosed each year increased by 36% among all ages and doubled among adults [6].

The risk of developing Opportunistic infections in HIV patients depends on experience with potential pathogens, the virulence of pathogens, degree of host immunity, and the use of antimicrobial prophylaxis [7]. Opportunistic infections (OIs) associated with HIV remain the single main cause of ill-health and death among HIV/AIDS patients in resource-poor settings. Therefore HIV-positive patients in resource-poor settings continue to suffer [8]. Evidence of studies conducted in different parts of Ethiopia had documented that, the incidence of OIs after HAART was increased in especially among hospitalized HIV-patients [9,10] and, reported the prevalence of OIs among HIV infected patients in the range of 33.3% in Addis Abeba to 88% in Dawro Zone Hospital [11-16]. Tuberculosis (TB), oral candidacies, Pneumocystis Carini Pneumonia (PCP), bacterial pneumonia, Herpes Zoster, Cryptococcus meningitides, Persistent diarrhea, Kaposi's sarcoma, and lymphoma are the most reported common opportunistic infections in HIV patients in Ethiopia, but major differences in the spectrum of OIs observed across the country [15,17,18].

Various literature suggested that, history of opportunistic infections, Hgb levels, WHO clinical staging, CD4 counts, taking past OI prophylaxis, ART drug adherence, monthly income, and occupation were identified as predictors of developing OIs among HIV infected patients [14-16,19,20]. However, methodological differences and variations of the duration of HART were observed across these studies. Timely specific diagnosis and consequent treatment to combat these infections are not only the concern for industrialized countries but also in the same way important to developing countries like Ethiopia. In Ethiopia, early diagnosis of OIs in HIV-infected patients is not an easy task, as there is a scarcity of laboratory diagnostic setup to be able to deal with a specific diagnosis of opportunistic infections. Therefore, the present study was planned to assess the prevalence, spectrum, and predictors of OIs among adult HIV-infected patients in this setup.

MATERIALS AND METHODS

Study setting

The study was conducted in Western, Oromia, Ethiopia. Oromia is one of the 10th regions in Ethiopia. Government hospitals in western Oromia provide preventive, curative, and rehabilitative services for populations of more than 3.5 million. Also, four governmental and one nongovernmental health center are serving the population of the town. ART service was initiated in 1998 G.C in the region. A total of 15400 adult patients were enrolled in ART starting from January 2015 to January 2019 G.C.

Study design and period

A facility-based retrospective cross-sectional study was conducted from January 2015 to January 2019 G.C.

Source population and study population

The source population was all adult patients who were on ART follow-up in Western, Oromia Region ART clinics. The study population was all adult patients who were selected by systematic sampling method from the source population and participated in the study during the study period.

Inclusion and exclusion criteria

Clinical records of all patients who were on ART follow-up and 18 years and above during the study period were included. However, Clinical records that do not have complete information relevant for the study were excluded from the study.

Sample size determination

The sample size was computed using the single population proportion formula shown below. Prevalence of opportunistic infections among adult patients on ART follow-up (P=48%) in Eastern Ethiopia was taken to determine sample size [13]. The margin of error (5%) and critical value at 95% confidence level were used. Ten percent (30%) contingency for incomplete data was considered. Finally, 498 adult patients on ART follow-up were included in this study.

$N=(Z1-A/2)2Pq$

Sampling procedure and technique

Ethiopia has ten regional states and Oromia regional state is the largest region having more than one-third of the total population of the country. The western Oromia region was purposefully selected for the study. There are fifteen functional government hospitals currently providing ART in the western Oromia region. A total of 15400 patients were enrolled on HIV starting from January 2015 to January 2019 G.CRandom sampling technique was used to select 3 hospitals Then, using simple random sampling technique; a computer-based random number generating using the patient's registry as the sampling frame, a total number of 498 patients were selected to be included in the study. Data of 2015-2019 was considered and any incidence of OIS and co-morbidities was collected both from a patient chart and history sheet.

Operational D definition

Development of OIS: infections caused secondary to HIV infection.

Adherence level: Is the degree to which patients accept the treatment process.

Adherence: is defined as good if adherence is >95% (<2 doses of 30 doses or <3 doses of 60 dose is missed); poor if adherence is between 85 and 94% (3–5 doses of 30 doses or 3-9 dose of 60 doses is missed). Adherence was measured by pills count.

Data collection tools and techniques

Data were extracted from the ART follow-up database and medical records of the patients by using a standardized checklist, which was adapted from the Federal Ministry of Health HIV ART, follow-up guideline [21]. The contents of the checklist include socio-demographic characteristics (age, sex, marital status, residence, ethnicity, religion, and employment and Educational status) and clinical information (CD4 level, WHO stage, Adherence, weight, co-morbidities). Data extraction was performed by a trained health professional that had experience in ART clinic service. A total of 3 individuals two BSc nurses and 1 Health officer were involved in data extraction. Data were retrieved from the hospital's ART registry document which is a standard format for sending comprised data to the health monitoring information system.

Data quality assurance

Two days of rigorous and extensive training with the final version of the questionnaires were given to each data collector and supervisor before the pre-test. Collected data was checked by supervisors before being sent to the data entrée on daily basis. We pre-tested the questionnaires on 10% of the sampled pregnant women of Nekemte health center, that were not included in the main study, and modification was done based on the pre-test observations. The supervisors kept the alleyway of the field procedures and checked the completed questionnaires daily to approve the accuracy of data collected, and the research team managed the overall work of data collection. To ensure the quality of data, the selected individual's medical record was evaluated for completeness and all the needed information was checked. To avoid bias, Patient clinical records with redundant, incomplete, or missing information were omitted.

Data processing and analysis

Data were double entered using EPiData version 3.1 software. Data were cleaned, coded, and checked for missing and outliers, for further analysis exported to SPSS version 25 statistical software. The outcome variable was dichotomized as the development of OIS=1(Present) and development of OIS=0 (Absent). Bivariate analysis and multivariable analyses were done to see the association between each independent variable and outcome variables using binary logistic regression. The assumptions for binary logistic regression were cheeked. The goodness of fit was checked by Hosmer-Lemeshow statistic and omnibus tests. All variables with $p<0.25$ in the Bivariate analyses were included in the final model of multivariable analysis to control all possible confounders. Multico-linearity test was carried out to see the correlation between independent variables by using the standard error and collinearity statistics (variance inflation factors >10 and standard error >2 were considered as suggestive of the existence of multi co-linearity). The direction and strength of statistical association were measured by an odds ratio with 95% CI. Adjusted odds ratio along with 95% CI was estimated to identify factors associated with animal development of OIS. Correlation between independent variables was checked using the Pearson Correlation Coefficient. P-value<0.2 was used as a cut-off point to select variables for the final model. Backward elimination was used, and P-value<0.05 was considered statistically significant.

Ethics considerations

All methods of this study were carried out in accordance with the Declaration of Helsinki-Ethical principle for medical research involving human subjects. An ethical approval letter was obtained from Oromia Regional Health Bureau, Ethiopia before the commencement of data collection. Then an official letter was written to respective hospitals for permission. The hospital's management and staff of ART clinic were requested for permission of entry using an official letter and the hospital granted permission for data collection. The patients' names were not collected. All data extracted from the patient's registry were kept strictly confidential. Since secondary data was used, consent was waived by hospital management and staff of the ART clinic. Informed consent was not sought for the present study because we have already used the secondary data after permission was obtained from hospitals. The HIV infected, the result of the study was communicated to respective any beneficiary bodies.

RESULTS

Socio-demographic characteristics

A total of four hundred ninety-seven study adult HIV/AIDS patients' ART records were looked over in this study. The mean age of the respondents was 33 (SD+8) years and ranged from 25-41 years. Nearly half 247(49.7%) of the study participants were in an age interval of 26-37 years. Of the total respondents' majority, 312(62.8%) of them were females and, 308(62%) were living in an urban area. Regarding marital status, more than half of the study participants, 311(62.6%) were married and 186(37.4%) of them were single. Among the participants, 242(48.7%) were orthodox religion followers and, 178(35.8%) had attended primary education. Concerning the educational status, most of the participants, 293(58.8%) were unemployed (Table 1).

Clinical characteristics of PLWH

As noted in Table 2, the majority of the study participants had good adherence 476(95.8%) and 303(61%) of the patients had developed an opportunistic infection. Regarding the current status of the patients' majority of them, 420 (85%) were in the WHO stage (Table 2).

Table 1: Socio-demographic characteristics of the study participants (N=497) at Western Oromia ART clinic, Ethiopia, 2020.

Characteristics	Frequency Number (N)	Percentage (%)
Age category		
18-25	104	20.9
26-35	245	49.3
36-45	105	21.1
46-55	43	8.7
Sex		
Male	185	37.2
Female	312	62.8
Residence	52.5	52.5
Urban	308	62
Rural	189	38
Marital status		
Married	311	62.6
Single	186	37.4
Religion		
Orthodox	242	48.7
Protestant	205	41.3
Muslim	50	10
Educational status		
Primary	178	35.8
Secondary	141	28.4
College and above	84	16.9
No formal education	94	18.9
Occupation		
Employed	144	29
Unemployed	290	58.8
Others	63	12.2

Table 2: Clinical characteristics of PLWH among clients attending ART clinic (N=497) at Western Oromia, Ethiopia, 2020.

Characteristic (N=497)	Number	Percentage (%)	95% CI	
			Lower	Upper
Adherence				
Good	476	95.8	95.8	97.6
Poor	21	4.2	2.4	6
Development opportunistic disease				
Yes	303	61	56.1	65.2
No	194	39	34.8	43.91
Current CD4 Status				
243.4	103	20.7	17.3	24.6
243.5-417.4	126	25.4	20	29.3
417.5-609.4	130	26.2	21.5	28.9
>=609.5	138	27.8	24.2	32.1

WHO staging	Baseline WHO		Current WHO		
	N	%	N	%	
Stage 1	127	25.6	420	85	Stage 1 CI=(81.8-88.1)
Stage 2	370	74.4	74	15	>=2stage2=(11.9-18.2)

Prevalence and spectrum of opportunistic disease among PLHIV on ART

Among 497 study participants, 310 had diagnoses of opportunistic infections (OIs), yielding an over prevalence of 62% (310/497). From these, 215(79%) of the HIV-infected patients had only one opportunistic infection. Whereas, 45(17%) and 11(4%) of patients had two and three opportunistic infections respectively (Table 3). The most, common type of opportunistic infections among VIV infected patient's attending ART clinic in the current study was, pulmonary tuberculosis 78(15.7%), followed by Oral candidiasis 71(14.3%), Herpes Zoster 56(11.3%), Cryptococcus meningitides was 29(5.9%), upper respiratory infection 28(5.8%, Persistent diarrhea 27(5.2%), and extra pulmonary tuberculosis 17(3.8%) (Table 4).

Factors associated with the development of opportunistic

Multiple binary logistic regression analysis was run, considering those variables p-value<0.25. Factors associated with the occurrence of OIs among adult HIV-infected patients who were on ART were assessed in the current study. Accordingly, baseline WHO clinical staging and residence were identified as independent predictors of OIs among adult HIV-infected patients. The occurrence of opportunistic infection on adult PLHIV patients who were with baseline WHO stage of I was 53% lower as compared to those who were with advanced baseline WHO stage of II and more {AOR: 0.468, 95% CI (0.305-0.716). Moreover, participants of Urban residents were 1.6 times more likely to develop opportunistic infections than those rural residents (Table 5).

Table 3: Number Opportunistic infection (OIs) among adult PLWH at Western Oromia ART clinic, Ethiopia, 2020.

S/N	Opportunistic infections (OIs)	Frequency (N)	Percentage (%)
1	One Opportunistic infection (OIs)	215	79
2	Two Opportunistic infection (OIs)	45	17
3	Three Opportunistic infection (OIs)	11	4
4	Total	310	100

Table 4: Prevalence of Opportunistic infection (OIs) among adult PLWH at Western Oromia ART clinic, Ethiopia, 2020.

S/N	Opportunistic Infection (OIs)	Frequency (N)	Percentage (%)
1	pulmonary tuberculosis	78	15.7
2	Oral candidiasis	71	14.3
3	Herpes Zoster	57	11.3
4	Cryptococcus meningitides	30	5.9
5	Upper respiratory infection	29	5.8
6	Persistent diarrhea	26	5.2
7	Extra pulmonary tuberculosis	19	3.8

Table 5: Multiple logistic regression analysis for selected variables with the occurrence of Opportunistic Infections among adult PLWH at Western Oromia ART clinics, Ethiopia, 2020.

Characteristic N=497	Development of OIS		Crude OR with(95% CI)	Adjusted OR (95% CI)
	Present	Absent		
Adherence				
Good	288	188	0.613(0.234-1.607)	0.555(0.200-1.55)
Poor	15	6	1	1
Current CD4 status				
<243.4	78	47	1.159(0.697-1.929)	1.235(0.712-2.140)
243.5-417.4	77	46	1.169(0.701-1.950)	1.332(0.774-2.294)
417.4-609.4	74	50	1.034 (0.623-1.716)	1.104 (0.651-1.874)
4	4	4	4	4

DISCUSSION

The current study assessed the prevalence and predictors of opportunistic infection among adult patients who were on ART follow-up in Western Oromia hospitals, ART clinics. The study found that an overall prevalence of opportunistic infections was 62%. This finding is comparably higher than the prevalence of HIV related opportunistic infections reported in different studies conducted in Addis Ababa (33.3%), North West Ethiopia (33.3%), Eastern Ethiopia (48%), Southern Zone Tigray (55.3%), and Eastern Zone of Tigray (52%) [12-16], Nevertheless comparably lower than of the studies in conducted in Dawro Zone Hospital (88%) and Kenya (78.8%) [11,22]. The reason for variation across studies might be due to the difference in duration of follow-up, the difference in CD4 level, and the degree of host immunity of study subjects. The current study followed study participants for five years.

Evidence of studies conducted indifferent parts of Ethiopia noted that opportunistic infections are common among HIV-infected people. The finding of our study documented, from deferent HIV related OIs among patients on ART follow up at Nekemte Specialized Hospital ART clinic, the common types of OIs were; Pulmonary Tuberculosis (15.7%), Oral candidiasis (14.3%), Herpes Zoster (11.3%), Cryptococcus meningitides (5.9%), upper respiratory infection (5.8%, Persistent diarrhea (5.2%), and extra pulmonary tuberculosis (3.8%). Pulmonary Tuberculosis was the most common leading OI among HIV-infected people in this study area. Similarly, in a study conducted in Dawro Zone hospital, pulmonary tuberculosis (18%) was observed as the most common OI among patients on ART follow-up during the study period (11). However, the result is comparably lower than the finding of a study conducted in Southern Zone Tigray (16). In the current study Oral candidiasis was observed as the second leading OI; on contrary, it was documented as the first common type of OI in a study conducted in Debra Marko's Referral Hospital (11.8%), Southern Zone Tigray (11%), Uganda (34.6%) and India (49%) [8,12,16,23] and, third in Dawro Zone (15.6%) [11]. The reason for this variation might be explained by deference in quality of laboratory diagnosis in most of the country, the difference in Geographical area of study participants, and methodological deference in selecting study participants. Herpes Zoster was acknowledged as the third common type of OI in this study setup. The prevalence of Herpes Zoster in the current study is comparably consistent with the finding of a study conducted in Eastern Ethiopia (11.2%) [13] and Southern Zone Tigray(10.8%,) [16], in the contrary study of Eastern Ethiopia and Southern Zone Tigray had observed as the second common type of OIs.

This study assessed the level of ART adherence among adult HIV patients who were on ART in Nekemte Specialized Hospital. The level of adherence identified here was 95%, which is consistent with the suggested level of ART treatment adherence. In the current suggestion, at least 95% of ART adherence level is needed to overwhelm viral replication, show clinical improvement, and better CD4 count [24]. Despite, the level of adherence is in agreement with recommended level; the result of the current level of adherence was comparably higher than the documented finding of a study conducted in Eastern Ethiopia (85%) [20] and Goba hospital (90.8%) [25] and lower than finding of a study conducted in Nigeria(98.7%) [17]. The reason for the variation could be due to the duration of HART. Here in this study, the study participants have been on ART for a longer duration, and commonly those who were taking the drug/s for a longer period attain skills in what way to compact with difficulties hampering them not to adhere. Further, the context of Socio-Demographic variations might explain the observed difference.

Factors associated with the occurrence of OIs among adult HIV patients who were on ART were as well assessed. Concerning factors associated with the occurrence of OIs, baseline WHO clinical staging and residence were identified as independent predictors of OIs according to the result of the current study. The occurrence of opportunistic infection on adult PLHIV patients who were with baseline WHO stage of I was 53% lower as compared to those who were with advanced baseline WHO stage of II and more. Thus participants with advanced baseline WHO stage of II was 47% more likely risky to develop OIs as compared to those with WHO stage of I. The finding is in agreement with the other four studies conducted in different parts of Ethiopia (Eastern Ethiopia, Gonder, Addis Ababa, and Debre Marcos [12-16,18]. The study conducted in Eastern Ethiopia reported that participants with advanced WHO stage of III was four times more likely to develop OIs than those with WHO stage of I. similarly, a study conducted in Gonder documented that, WHO clinical stage of III HIV infected patients was nine times more likely to develop OIs than those with WHO clinical stage of I. The finding of Study conducted in Debre Marcos noted that, WHO stage of III HIV infected were five times more likely to develop OIs than those with WHO stage of I. likewise, Study conducted in Addis Ababa reported that, HIV infected patients with WHO clinical stage of III was two times more likely to develop OIs than those with WHO clinical stage of I. Comparable conclusions were appreciated in studies conducted in different countries [19,22,23,26].

Moreover, the Odd of the occurrence of opportunistic infection on adult PLHIV patients who were urban residents was 1.6 times higher as compared to those who were rural residents. Participants of Urban residents were 1.6 times more likely to develop opportunistic infections than those rural residents. However, studies conducted in deferent in different countries found no association of residence with developing opportunistic infection [12-13,19,26]. Thus limited evidence was generated on the association of residence and developing OIs among HIV-infected people. Therefore, further study is recommended to determine the relationship between residence and developing opportunistic infections among HIV patients on ART follow-up.

The retrospective nature of the study makes some variables less explanatory and the cause-effect of relationships cannot be measured. Finally, since we used secondary data some variables were not documented well and many OIs were supposed diagnosis may be stated a likely limitation of the current study.

CONCLUSION

An overall prevalence of opportunistic infections was 62%. The prevalence of opportunistic infections is still high namely Pulmonary Tuberculosis, Oral candidiasis and Herpes Zoster are leading OIs among adult HIV-infected patients. Baseline WHO clinical staging and residence were identified as independent predictors of OIs among adult HIV infected patients. Having skilled health professionals, early diagnosis of OIs among HIV infected patients, and having equipped laboratory diagnostic setup is mandatory to be able to deal with specific diagnoses and management of opportunistic infections. Further study is recommended to determine the relationship between residence and developing opportunistic infections among HIV patients on ART follow.

DECLARATIONS

Not applicable

AVAILABILITY OF DATA AND MATERIALS

The minimal data set used to reach the conclusions is available within the manuscript. Moreover, additional data required can be obtained from the corresponding author on a reasonable request.

COMPETING INTERESTS

The authors declare no conflicts of interest in this work.

AUTHORS' CONTRIBUTIONS

All authors were involved in the conception, design of the study, and statistical analysis and result interpretation. MBF drafted the manuscript which was reviewed for intellectual content by DJA and HFG. All authors read and approved the final version for submission and agreed to be accountable for all aspects of the article.

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