

# Opportunistic Infections and Associated Factors among HIV/AIDS Patients taking Ante-Retroviral Therapy Leku, Bona and Yirgalem Hospitals in Sidama Zone, Southern Ethiopia.

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## Research article

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# Abstract

## Background

Opportunistic infections are late complications of HIV infection is the depletion of the immune system. It is a major public health problem and high morbidity AIDS patients die of AIDS-related infections in developing countries like Ethiopia. Identification of opportunistic infections (OIs) is important to develop a specific intervention. Therefore, this study aimed to assess the burden and associated factors of opportunistic infections.

## Method

A facility-based cross-sectional study was conducted on 420 randomly selected HIV/AIDS patients taking anti-retroviral therapy. Data was collected from selected hospitals in Sidama Zone based on population proportion to size. Data was collected by a pre-tested questionnaire and a pre-tested checklist from the medical records of patients. Data entry and analyzed for descriptive and logistic regression models by SPSS v.23. The result declared as statistically significant at  $p < 0.05$ .

## Result

The magnitude of opportunistic infections was 39.6%. Major identified OIs was oral candidacies 23.2%, recurrent bacterial pneumonia 21.5%, Herpes zoster 6.3%, and Pulmonary Tuberculosis 6.0%.The magnitude of opportunistic associated with; older age [AOR=2.61, 95% CI: 1.30-5.23], No formal education [AOR=3.09, 95% CI: 1.11-8.60], monthly income below 1920 ETB [AOR=2.37, 95% CI: 1.43-3.94], initial CD4 count less than 200 cells/mm<sup>3</sup> [AOR=2.30, 95% CI:1.06-4.98), had no extra medicine additional to ART (prophylaxis) had [AOR= 8.79, 95% CI: 5.05-15.30], who interrupt ART medicines [AOR=2.16, 95% CI: 1.19- 3.91] and Khat chewing [AOR=5.52, 95% CI: 2.42-12.56] when compared to their counterparts.

## Conclusions

The overall magnitude of opportunistic infections was high when compared with other studies. Health officials and clinicians need to give attention to the strengthening of the provision if ART with prophylaxis on early-stage and adherence, implementation of the TB/HIV collaboration activity, and early initiation of ART to reduce opportunistic infections.

## Background

Human immune virus (HIV/AIDS), with which 36.7 million people were living and 2.1 million infected at the end of 2016, has been a major health problem throughout the world [1]. Around 36.7 million people worldwide are currently living with HIV, of which 52% reside in sub-Saharan Africa (SSA) [2]. It affected 1 in every 25 Adults (4.4%) is living with the deadly virus, account for nearly 70% of the global burden of HIV [3, 4]. Although the natural history of HIV inclines to be similar, the patterns of OIs that mainly

presented with different clinical manifestation regions to the region [5, 6]. CDC estimates that in 2015, 15% of the people with HIV in the United States were unaware or asymptomatic of their infections [7, 8]. The commonly reported opportunistic diseases in sub-Saharan Africa among HIV patients are Candidiasis, Pneumocystis carinii pneumonia (PCP), disseminated Mycobacterium avium complex (MAC) infection, Cryptococcus, Kaposi sarcoma, herpes zoster, and tuberculosis [9, 10].

The developing countries more suffer from bacterial and protozoal infections due to lack of resources [11, 12], HIV diagnosis, poor adherence to Anti-Retroviral Treatment (ART), drug resistance, poverty, poor nutrition, and high exposure to infectious agents [13]. The opportunistic infections may favor HIV replication and higher viral loads that lead to lower the quality of life of HIV infected persons, reduces patients' response to ART, increases stigma and limit one's ability to work, high medical care costs, and death [14, 15].

In Ethiopia, the adult HIV prevalence of Ethiopia was estimated to be 1.1% in 2015, and the second leading cause of death [16]. More than 90% of HIV/AIDS deaths are attributable to opportunistic infections and malignancies [11]. Even though nationally representative and comprehensive data regarding the magnitude of opportunistic infections lack in Ethiopia, some regional studies have shown the prevalence ranging from 19.7% to 48% [15, 17]. The prevalence of OIs among HIV patients on ART is still high namely; oral candidiasis 11.8%, followed by chronic diarrhea, 9.9% and tuberculosis 9.7% at Debre Markos referral hospital in Ethiopian [18]. Which associated with age, WHO stages of III and IV, chew khat, ART adherence, low level of hemoglobin, and recent weight [18]. Hence, it is very important to see the magnitude of opportunistic infections and its determinant factors to reduce the burden. This is important for researchers, clinicians, and health planners.

## Methods

### Study setting and study population

This study was conducted at Leku, Bona and Yirgalem Hospitals in the Sidama Zone in southern Ethiopia from February 01, 2019, up to May 01, 2019, which is one of the most densely populated areas in Ethiopia. Sidama Zone located about 275 kilometers away from Addis Ababa. Sidama has a variety of climatic conditions. Warm conditions cover 54% of the area. There are only three well-organized ART facilities at the hospital level. The source of populations were all HIV/AIDS patients who visited the ART clinic of the three hospitals in the Sidama zone. All HIV positive adults who had at least one month follow up on ART unit at selected hospitals within the study period was considered as the study population. All randomly selected HIV positive adults aged 18 years old and above and who can give informed consent were included in the study. While, All HIV-infected patients admitted to the intensive care unit, and seriously ill patients during the study period were excluded from the study.

### Sample size and sampling technique

The study was conducted on 420 calculated by a single population proportion formula by taking previously conducted prevalence of opportunistic infections in Debre Markos Referral Hospital, Northwest Ethiopia [18] and 10% possible non-response rate. The stratified sampling technique was used to recruit ART hospitals. The desired number of clients for each hospital was selected based on proportional sampling. Individual study participants were selected from each hospital were recruited by the random arrival of the ART unit.

## Data collection tools, and procedures

Data was collected by face to face interviews by using a pre-tested questionnaire; a pre-tested checklist done to collect information regarding OIs and patients' clinical records were reviewed. A pre-tested structured questionnaire was utilized to collect socio-demographic characteristics, clinical information, and other risk factors. The questionnaires were pretested and validated before two weeks in the study time in Dore Bafana primary hospital on 5% of HIV positive patients who attend ART clinic which was outside of the study area and necessary modifications were done based on the findings. Data collectors were five clinical nurses supervised by one BSC nurse supervisor and investigators. Training and practical demonstrations on interview techniques and document extraction procedures based on the checklist were given to data collectors for two consecutive days assessed for competency.

## Data quality control measures

Data collectors were trained and the questioners were pretested before the study time in similar settings which are not a part of the study area. After the data collection process, the data were checked for completeness and any incomplete or misfiled questionnaires filed again.

## Data Analysis

Data entry, cleaning, and analysis were done by SPSS V. 23. Descriptive analysis including frequency distribution and the percentage was made to determine the magnitude of the opportunistic infections, to describe socio-demographic and clinical characteristics. All factors with p-value <0.25 in the bivariate logistic regression analysis were a candidate to the multivariable model to control confounding effects. The Hosmer -Lemeshow goodness-of-fit statistic was used to assess whether the necessary assumptions for the application of multiple logistic regression are fulfilled. Odds ratios (OR) with 95% confidence intervals (CI) were calculated. Finally, p-value <0.05 declared a significant association.

## Terms and definitions

- Opportunistic infection: If the study participant diagnosed at least one or more opportunistic infections; any infections of bacteria, viruses, fungi, Parasitic or protozoa or multiple infections

reported on their medical record [7].

- Adverse effect: an unwanted effect caused by the administration of drugs. Onset may be sudden or developed over time.
- Current alcohol consumption: is defined as the use of alcohol at least once during the past 30 days before the survey.
- Khat chewing: is defined as the study participants who had chewed the leaves of Khat (*Catha edulis*) in the last 30 days.
- Cigarette smokers: is defined as individuals who had used smoke cigarettes form of tobacco in the last 30 days [19].

## Results

A total of 420 HIV positive adults were enrolled in the study in the ART clinic of the selected three hospitals, 414 participants were interviewed yielding a response rate of 98.57%. The average age of the participants aged 18–55 years, with the mean ( $\pm$ SD) age of 30.69 ( $\pm$ 7.350). More than half of the studied participants 234 (56.5%) were female and 171 (41.3%) in the age category of 25 - 34 years old. The majority of 259 (62.6%) were married and 264(63.8%) were living with their families. Regarding educational status, 25 (6.0%) have no formal education, 102 (24.6%) had a primary school, and 287 (69.3%) had high school and above education. The working status of the participants 278 (67.1%) was actively working. The monthly income of the households, 223 (53.9%) earned between 300 - 1920 ETB, and 191 (46.1%) earned more than 1920 ETB (Table 1).

## Environmental and Behavioral related characteristics

The majority of 273 (65.9%) were living in the cemented floor house. Most of 401 (96.9%) had a latrine, among this 395 (95.4%) were shared with their family and neighbors. More than half of 287 (69.8%) used Garbage can or sac to disposer refuse. The main source of drinking water was 398 (96.1%) pipe water. Regarding behavioral related factors, 27 (6.5%) were used any tobacco products, among this 14 (3.4%) were current cigarette smokers. The prevalence of Khat chewing was 48 (11.6%). Regarding alcohol consumption, 71 (17.1%) were ever drunk alcohol, 63 (15.2%) were drinking alcohol in the last 30 days (Table 2).

## Health care system and Clinical Setting related factors

However, more than half of the participants 263 (63.5%) had doubts about health care providers. The majority of 376 (90.8%) knew the importance of adherence to ART. Mainly, 352 (85.0%) were believe that using ART improves life and lives longer, 408 (98.6%) were agree that ART can prevent OIs and AIDS (S1).

# Patient health condition related factors

Eighty-three (20.0%) of the study participants had a history of side effects on ART drugs and 202 (48.8%) were taken extra drugs additional to ART drugs (S1). Nearly half of, 206 (49.8%) were on WHO clinical stage I, while 83 (20.0%) and 31 (7.5%) were on WHO clinical stage III and IV, respectively (Fig. 1).

## The magnitude of Opportunistic Infections

The overall magnitude of opportunistic infections was 39.6%, [95% CI: 35.0 - 44.4] were found to be infected by one or more opportunistic infections among HIV/AIDS Patients taking ART at Selected Hospitals in Sidama Zone, Southern Ethiopia. Major identified opportunistic infections were oral candidacies 96 (23.2%), recurrent bacterial pneumonia 89 (21.5%), Herpes zoster 26 (6.3%), Pulmonary Tuberculosis 25 (6.0%), Extrapulmonary TB. 24 (5.8%), and Crypto-coca meningitis 9 (2.2%) (Fig. 2).

## Associated Factors for Opportunistic Infections

In the multivariate analysis age of respondents, household monthly income, initial CD4 count, education, had no extra medicine additional to ART (prophylaxis), taking ART medicines properly, and Khat chewing remained as the determinant of opportunistic infections. This study result shows that advancing in the age had about 2.6 times more exposed to develop OIs [AOR = 2.61, 95% CI: 1.30–5.23], as compared with younger age. No formal education had [AOR = 3.09, 95% CI: 1.11–8.60], Household monthly income below 1920 ETB had [AOR = 2.37, 95% CI: 1.43–3.94], had more exposed to OIs as to their counterparts. Initial CD4 count less than 200 cells/mm<sup>3</sup> had [AOR = 2.30, 95% CI: 1.06–4.98], The study participants who had no extra medicine additional to ART (prophylaxis) [AOR = 8.79, 95% CI: 5.05–15.30], interrupt ART medicines had [AOR = 2.16, 95% CI: 1.19- 3.91] and Khat chewing [AOR = 5.52, 95% CI: 2.42–12.56] were more exposed to OIs when compared to their counterparts (Table 3).

## Discussions

This facility-based cross-sectional study revealed that the magnitude of opportunistic infections was 39.6%, [95% CI: 35.0 - 44.4] were found to be infected by one or more opportunistic infections among HIV/AIDS Patients taking ART at Selected Hospitals in Sidama Zone, Southern Ethiopia. Major identified opportunistic infections were Oral candidacies 23.2%, recurrent bacterial pneumonia 21.5%, Herpes zoster 6.3%, and Pulmonary Tuberculosis 6.0%. This study result was consistent with the study findings in Wolaita Zone, Southern Ethiopia 45.3% [11] and Uganda 43% [9]. This result higher when compared to eastern Ethiopia 20.2% had any form of tuberculosis, oral candidiasis, herpes zoster [15], 22.4% Nigeria [20], 19.7% Northern Ethiopia [21]. While, it was slightly lower when compared with 61.7% Nigeria [22], 47.6% Taiwan [23], and 48% eastern Ethiopia [15]. The discrepancy might be due to differences in geographical areas of study participants, high exposure to infectious agents, social-economic status, drug resistance, immunity and nutrition, may affect the magnitude of OIs.

This study result revealed that advancing in the age was more exposes to OIs as compared with younger age. Similar to the United States [24], and Northwest Ethiopia [25]. The possible reason maybe, when they grow older the patients' immune get decreased due to the increased number of viral load and other factors predispose to OIs. In addition to that, the study participants who had no formal education exposes to OIs more when compared with high and above education. This finding was also similar to Debre Markos Referral Hospital, Northwest Ethiopia [25], and eastern Ethiopia [15]. This may due to a lack of health-related information about prevention, early symptoms and health benefits. Low household monthly income was more exposed to OIs than to their counterparts. This finding is consistent with Bangladesh [26], and the Lao People's Democratic Republic (PDR) [27]. This might due to household income directly related to the nutritional status and sanitation status of the individuals.

Initial CD4 count less than 200 cells/mm<sup>3</sup> was more exposed to OIs as compared with higher CD4 count. This study finding agrees with eastern Ethiopia [15], and the Amhara region, Ethiopia [28]. This might due to the low body defense mechanism favored the OIs. The study participants who interrupt ART medicines and who had no extra medicine additional to ART (prophylaxis) had high odds of to develop OIs. This study finding consistent with eastern Ethiopia [15], and Dessie hospital ART clinic, Northeast Ethiopia [29]. This might due to OIs could be prevented by using extra drugs additional to ART drugs or prophylaxis.

This study result showed that Khat chewing was more exposed to OIs. Similarly reported in Northwest Ethiopia [25], and eastern Ethiopia [15]. The possible reason may be, chewing Khat causes malnutrition due to poor appetite and it affects health-seeking behavior by temporary relief.

This study result shows there was a high prevalence of OIs. This may due to there is an endemic intestinal parasite in the area which exposes the patient to daily activities or this could be a sign of resistance/ treatment failure that needs to be further investigated. Which related to occurred irrespective of the income status, chewing Khat, interrupt ART medicines and who had no extra medicine additional to ART (prophylaxis), low educational status and due to poor level of health-seeking behavior of the study participants. These study findings recommend for more consideration on different strategies to address early detection for better prevention, evaluation, and management. Future research should explore more by triangulating with qualitative study for factors with OIs to design targeted interventions.

This study has potential limitations as the study is cross-sectional in design; it neither represents the seasonal variation of nutritional outcomes nor establishes a causal relationship. In addition to this, the odds ratios of the cross-sectional study did not show the strength of an association.

## Conclusions

This study result shows there was a high prevalence of opportunistic infection among HIV/AIDS patients taking anti-retroviral therapy. This indicates that the threatening burden of opportunistic infections couldn't be averted by only the provision of anti-retroviral therapy. The most common opportunistic infections were of oral candidiasis, herpes zoster, and tuberculosis (pulmonary and extrapulmonary).

Older age of respondent, household monthly income, initial CD4 count, advancing WHO clinical staging, had no formal education, had no extra medicine additional to ART (prophylaxis), participants who interrupt ART medicines, and Khat chewing were found determinant factors for opportunistic infections when compared to their counterparts.

## **Declarations**

## **Abbreviations**

ART = Ante-retroviral therapy, CD4 = Cell with CD-4 marker, ETB = Ethiopian birr, OIs = Opportunistic infections, SPSS = Statistical Package for Social Science, STD = Sexually transmitted disease, TB = Tuberculosis, WHO = World Health Organization

## **Ethics approval and consent to participate**

Ethical clearance was obtained from Hawassa university college of medicine and health sciences ethical review committee, support letter was also requested from the Sidama zone health bureau. All participants informed well about purpose, risk and benefit, and confidentiality. Participation was fully voluntary and written informed consent (verbal consent for who cannot read and write respondent) was obtained from each participant. The patients' medical records were reviewed anonymously, and all information obtained from medical records was kept confidential.

## **Consent for publication**

Not applicable.

## **Availability of data and materials**

There is no remaining data and materials, all information is clearly presented in the main manuscript.

## **Competing interests**

The authors declare that they have no conflict of interests.

## **Funding**

No funding was obtained.

# Authors' contributions

DW wrote the proposal, participated in data collection, analyzed the data and drafted the paper and manuscript writing. FB approved the proposal with some revisions, participated in data collection, analysis. authors read and approved the final manuscript.

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## Tables

Table 1: Socio-demographic characteristics of the study participants among HIV/AIDS Patients taking ART at Selected Hospitals in Sidama Zone, Southern Ethiopia, 2019.

Category	No. (%)
Age of Respondents	
18 -24 years	89 (21.5)
25 - 34 years	171 (41.3)
35 or above years	154 (37.2)
Sex of respondents	
Male	180 (43.5)
Female	234 (56.5)
Marital status	
Married	259 (62.6)
Unmarried	54 (13.0)
Divorced	50 (12.1)
Separated	14 (3.4)
Widowed	37 (8.9)
Education status	
No formal education	25 (6.0)
Elementary School	102 (24.6)
High School	254 (61.4)
Diploma and Above	33 (8.0)
Working situation	
Working actively	278 (67.1)
Unemployed	121 (29.2)
Pensioner	15 (3.6)
Live with	
My family	264 (63.8)
Live alone	77 (18.6)
My parents	54 (13.0)
Unstable	16 (3.9)
No answer	3 (0.7)
Household income in Ethiopian Birr	
300 - 1920	223 (53.9)
> 1920	191 (46.1)

*NB: Working actively (government, NGO, Private and self employed), Income: based on (HCE, 2016) Exchange rate 1 USD to 29.3673ETB*

Table 2: Environmental and Behavioral related characteristics among HIV/AIDS Patients taking ART at Selected Hospitals in Sidama Zone, Southern Ethiopia, 2019.

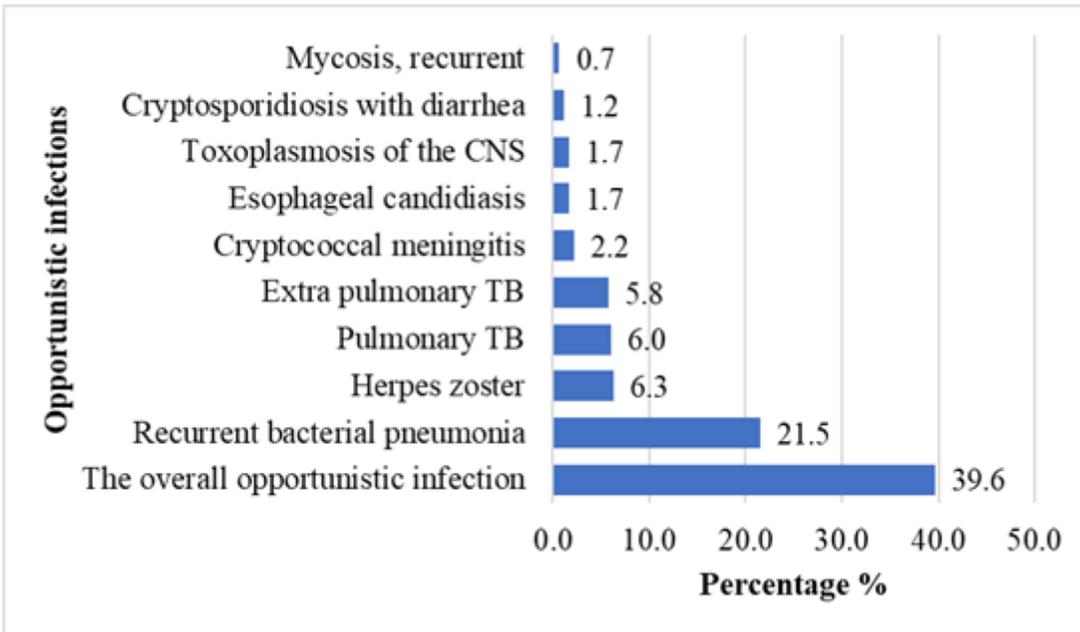
<b>Variable Category</b>	<b>No. (%)</b>
Floor of living house	
Mud	89 (21.5)
Cement	273 (65.9)
Wood	40 (9.7)
Others	12 (2.9)
Latrine available	
Yes	401 (96.9)
No	13 (3.1)
Ownership of the latrine	
Private Owned	19 (4.6)
Shared with neighbors	395 (95.4)
Source of water for drink	
Pipe	398 (96.1)
Others	12 (4.9)
Living with domestic animals and pets	
Yes	108 (26.1)
No	306 (73.9)
Use any tobacco products	
Yes	27 (6.5)
No	387 (93.5)
Smoke cigarettes in last 30 days	
Yes	14 (3.4)
Never	400 (96.6)
Ever drunk alcohol	
Yes	71 (17.1)
No	343 (82.9)
Currently drinking	
Yes	63 (15.2)
No	351 (84.8)
Khat chewing	
Yes	48 (11.6)
No	366 (88.4)

Table 3: Bivariable and multivariable logistic regression analysis for opportunistic infections among on ART patients at selected hospitals in Sidama Zone, Southern Ethiopia, 2019.

	Opportunistic infection		COR (95% CI)	AOR (95% CI)	P-Value
	Yes	No			
	No. (%)	No. (%)			
<b>Age</b>					
18 -24 years	20 (22.5)	69 (77.5)	1	1	
25 - 34 years	66 (38.6)	105 (61.4)	2.17(1.21, 3.89)	1.45(0.73, 2.99)	0.286
35 or above years	78 (50.6)	76 (49.4)	3.54(1.96, 6.39)	2.61(1.30, 5.23)	0.007*
<b>Education status of respondents</b>					
No formal education	15 (60.0)	10 (40.0)	2.76(1.20, 6.37)	3.09(1.11, 8.60)	0.031*
Elementary School	48 (47.1)	54 (52.9)	1.64(1.04, 2.59)	1.20(0.69, 2.09)	0.522
High School and Above	101 (35.2)	186 (64.8)	1	1	
<b>Average monthly income</b>					
< 1920 ETB	107 (48.0)	116 (52.0)	2.17(1.44, 3.26)	2.37(1.43, 3.94)	0.001*
1920 and above	57 (29.8)	134 (70.2)	1	1	
<b>Initial CD4 count</b>					
< 200 cells/mm <sup>3</sup>	26 (54.2)	22 (45.8)	2.58(1.41, 4.71)	2.30(1.06, 4.98)	0.035*
≥ 200 cells/mm <sup>3</sup>	138 (37.7)	228 (62.3)	1	1	
<b>Take extra medicine additional to ART (prophylaxis)</b>					
Yes	25 (13.8)	156 (86.2)	1	1	
No	139 (59.7)	94 (40.3)	9.23(5.62, 15.16)	8.79(5.05, 15.30)	<0.001*
<b>Taking ART medicines properly</b>					
Yes	115 (34.5)	218 (65.5)	1	1	
No	49 (60.5)	32 (39.5)	2.90(1.76, 4.78)	2.16(1.19, 3.91)	0.011*
<b>Smoke cigarettes in last 30 days</b>					
No	155 (38.8)	245 (61.3)	1	1	
Yes	9 (64.3)	5 (35.7)	2.85(0.94, 8.65)	1.08(0.22, 5.27)	0.926
<b>Khat chewing</b>					
No	131 (36.0)	233 (64.0)	1	1	
Yes	33 (66.0)	17 (34.0)	3.45(1.85, 6.44)	5.52(2.42, 12.56)	<0.001*

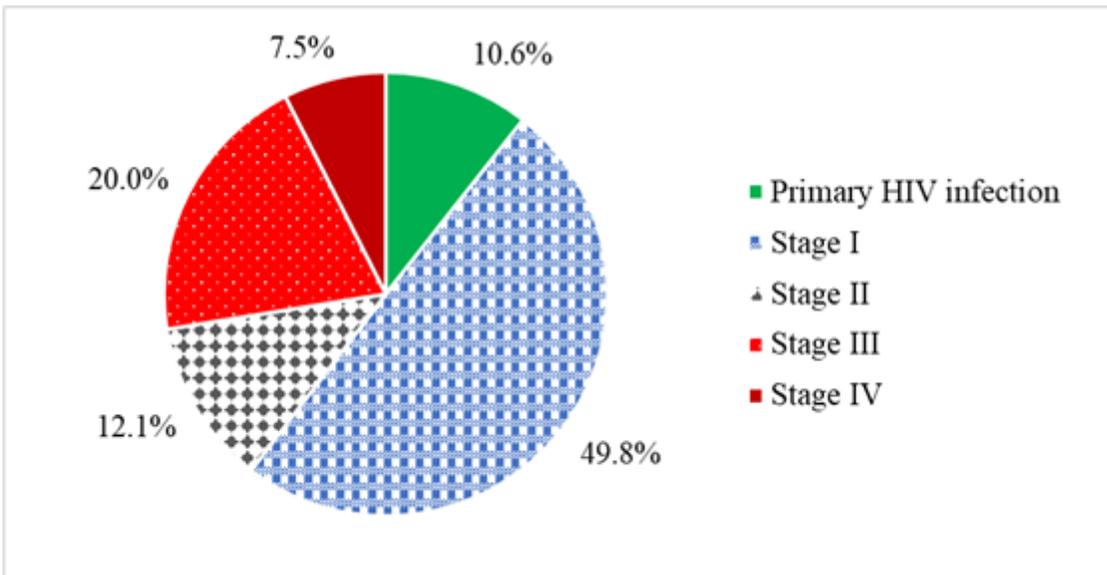
**NB:** \* statistically significant on multivariate analysis p-value (<0.05), **COR:** crude odds ratio, **AOR:** adjusted odds ratio, **CI:** confidence interval, **1:** reference.

## Figures



**Figure 1**

Magnitude of opportunistic infections among HIV/AIDS on ART at Selected Hospitals in Sidama Zone, Southern Ethiopia 2019 (n=414).



**Figure 2**

WHO clinical staging among HIV/AIDS on ART at Selected Hospitals in Sidama Zone, Southern Ethiopia 2019 (n=414).

## Supplementary Files

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