

**ADDIS ABABA UNIVERSITY
COLLEGE OF HEALTH SCIENCES
SCHOOL OF NURSING AND MIDWIFERY**

**PREVALENCE OF OPPORTUNISTIC INFECTIONS AND
ASSOCIATED FACTORS AMONG ADULT HIV POSITIVE PATIENTS
ON THE NEW ANTI-RETROVIRAL TREATMENT PROTOCOL AT
THE HEALTH INSTITUTIONS OFFERING ART IN GEDEO ZONE,
SOUTHERN, ETHIOPIA, 2018.**

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**A RESEARCH THESIS SUBMITTED TO ADDIS ABABA UNIVERSITY
SCHOOL OF GRADUATE STUDIES, DEPARTMENT OF NURSING
AND MIDWIFERY IN PARTIAL FULFILLMENT OF THE
REQUIREMENTS FOR THE DEGREE OF MASTERS OF SCIENCE IN
ADULT HEALTH NURSING**

JUNE, 2018

ADDIS ABABA, ETHIOPIA

ADDIS ABABA UNIVERSITY
COLLEGE OF HEALTH SCIENCES
DEPARTMENT OF NURSING AND MIDWIFERY
MASTER OF SCIENCE RESEARCH PROJECT SUBMISSION FORM

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Duration of study	From April to Jun,2018
Study Area	Gedeo Zone All ART Offering Health Institutions, Southern Ethiopia (Dilla university referral hospital,cheffe,Wonago,Gedeb,Chelelekitu, Hroresa, Bule health center)
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ACKNOWLEDGEMENT

Above all, I thank the Almighty God. Next I would also like to thank Addis Ababa University, Collage of Health Sciences, Department of Nursing and Midwifery in general providing opportunity to develop this thesis and for its financial support in the accomplishment of this study. Also my heartfelt gratitude goes to advisors of research project work to Mr. Daniel Mengistu and my co- advisor Mr. Niguse Tadele from Addis Ababa University, Department of Nursing and Midwifery for their unfailing support, wisdom and guidance in each steps of the research project work. My acknowledgement extends to Dilla University for the training program sponsorship. And I would like to thank data collectors and study participants whose contribution was vital to go through the data collection work. Finally, I would like to thank my family and colleagues for their motivation, academic support, moral and spiritual support.

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LIST OF ABBREVIATIONS AND ACRONYMS

AAU	Addis Ababa University
AIDS	Acquired Immunodeficiency Syndrome
ART	Anti-Retroviral Therapy
BMI	Body Mass Index
CNS	Central Nervous System
FMOH	Federal Ministry of Health
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
INH	Isonicotinyl Hydrazide
OIs	Opportunistic Infections
PCP	Pneumocystis Carinii Pneumonia
PLWHA	People living with HIV/AIDS
SSA	Sub-Saharan Africa
TB	Tuberculosis
WHO	World Health Organization

ABSTRACT

Introduction: Opportunistic infections (OIs) are infections that are more frequent or more severe because of immune-suppression in HIV-infected persons, and they are the major clinical presentations of HIV patients. It accounts for more than 90% of HIV/AIDS death.

Objective: To assess the prevalence of Opportunistic infections and associated factors among adult HIV positive patients on the new antiretroviral treatment protocol at health institutions offering ART in Gedeo Zone, Southern, Ethiopia 2018.

Method: A Health facility-based cross-sectional study was carried among 266 HIV positive patients taking ART. The study was conducted in Gedeo Zone in all ART offering institutions. The data was entered in to EPI data version 4.2 and analyzed by using SPSS version 23. Bivariate analysis was performed to determine the association of each independent variable with the dependent variables (occurrence of OIs). A p-value <0.05 was considered statistically significant in this study.

Result: A total of 266 patients were included. The mean age of participants was 37.10 year with (SD±11.882). The Overall prevalence of OIs was found to be 38.7%. The most predominant OIs observed were oral candidiasis (10.5%), followed by pulmonary tuberculosis (9.8%) and Herpes zoster (5.6%). Baseline CD4 cell count, 200 cells/mm³ (AOR = 9.136; 95% CI =2.747, 30.386), baseline WHO clinical stage III/IV (AOR =2.717; 95% CI =14.20, 5.198), poor adherence (AOR=10.052; 95%CI=4.3062, 3.464), bedridden (AOR=3.266; 95% CI=1.637, 6.518), were found to have strong association with acquisition of OIs.

Conclusions and Recommendations: According to this finding, the prevalence of OI among HIV positive patients receiving ART was still high. CD4 cell count, advanced WHO stage, adherence, functional status, baseline BMI and khat chewing are predominantly mentioned factors associated with occurrence of OIs among HIV positive patients on ART. Therefore, interventions need to be design to promote early HIV testing and early enrollment HIV-infected individuals into ART services.

Keywords: Opportunistic infections, HIV patients, antiretroviral therapy, CD4, WHO clinical stage, Gedeo zone, Ethiopia

CHAPTER1: INTRODUCTION

1.1 Background

Human Immunodeficiency Virus (HIV) is a virus in the group of viruses called retroviruses. HIV destroys cells in the body, called CD4 T cells. CD4 T cells are a type of white blood cell (a lymphocyte) and were identified as the causative agent of Acquired Immune Deficiency Syndrome (AIDS). HIV infection is caused by one of two retroviruses, HIV-1 and HIV-2, resulting in wide range of clinical manifestations(1, 2).

Since the outbreak of HIV in 1981, it is estimated that over 30 million people worldwide have died due to AIDS of which more than 70% were from sub-Saharan (3). Ethiopia is not spared from this epidemic. The country is one of the three Sub-Saharan countries that have the highest number of HIV infected persons. The federal HIV/AIDS prevention and control office (HAPCO) in conjunction with international and local partners made single point estimate for adult HIV prevalence in Ethiopia. Accordingly the adult HIV infection prevalence was estimated at 2.1%(4).

The natural history of HIV disease may be indirectly affected by the occurrence of opportunistic diseases, because HIV viral load increases in patients with acute opportunistic diseases or the virus progressively destroy immune system of our body and finally lead Opportunistic infections(5). Also OIs leads to morbidity and mortality might grossly affect the health and quality of life of people infected with HIV. Survival in people infected with HIV has improved because of an increasingly powerful display of antiretroviral treatments(6, 7). Regarding the magnitude of opportunistic infections national representative and comprehensive data lacks in Ethiopia, some regional studies has shown the prevalence ranging from 17.7% to 48%(8).

OIs among HIV patients are attributed to many factors. According to the work of Mitiku and his colleagues, the risk for the advancement of OI in HIV patients depends on exposure to potential pathogens, virulence of the pathogens, the degree of host immunity, and the use of antimicrobial prophylaxis. Their result also showed significant association between OIs and CD4 counts, patient functional status at the beginning of ART, educational status and body weight (8). According to a study conducted in Nigeria duration of HIV diagnosis, duration of

HAART and adherence to HAART are significantly associated with OIs (6). Age and khat chewing were also shown to have significant association with OIs (7, 17, 25).

Antiretroviral therapy(ART):-Since 1995 ,antiretroviral therapy (ART) play great role in decreasing HIV related mortality and morbidity and as result increase quality of life as well as life expectance of HIV/AIDS patient(9-13). Additionally the advances in the introduction of antiretroviral therapy have reduced the HIV viral load, the occurrence of opportunistic infections (OIs), and death rates due to AIDS, especially in patients with increased CD4+ T cell counts.(10, 14-17). The issue of when to start ART was varying from time to time in different country. For example, USA, France and Brazil recommend that to start ART as patient is diagnosed with virus regardless of clinical and immunological stage. While several other countries recommended starting ART below a threshold of CD4 500/mm³ (18-20).

Currently the World Health Organization (WHO) 2015 treatment guidelines recommended ART initiation for all HIV-positive individuals to reduce the morbidity and mortality associated with HIV infection. ART is also recommended for individuals with HIV to prevent HIV transmission (21, 22). Ethiopia also currently adopted the new 2016 WHO guidelines, and developed a supplemental guide to implement Test and Start as of October 2017.This means that all HIV clients will start ART at the time of diagnosis, irrespective of theirCD4 count status(23).

1.2 Statement of the Problem

According to the WHO global report of 2015, the number of people living with HIV/AIDS has increased from 33.3 million in 2010 to 36.7 million including 2.1 million newly infected people. Among this Sub-Saharan African countries share 69% of global HIV burden. Ethiopia, being one of the Sub-Saharan African countries, was found to have more than 691 thousand people (~1.1%) living with HIV/AIDS (5). Despite the advanced Antiretroviral therapy that has led to reduction in HIV viral load, OIs and death rate of AIDS, OIs is still a major cause of hospitalization and death among HIV patients on ART (10) and together with HIV/AIDS related malignancies, it accounts for more than 90% of HIV/AIDS death (5, 24). National representative and comprehensive data regarding the magnitude of opportunistic infections lacks in Ethiopia, some regional studies has shown the prevalence ranging from 17.7% to 48% (8).

Therefore, identifying the prevalence of OIs is crucial step in reducing morbidity and mortality associated with HIV/AIDS (4). Currently there is a change on the WHO ART initiation protocol. Unlike the previous ART initiation protocols, the new protocol of WHO (2015) recommends rapid ART initiation (within seven days from the day of HIV diagnosis) to all people living with HIV following a confirmed HIV diagnosis and clinical assessment regardless of CD4 cell count and WHO clinical staging (25-28). In our country the new treatment protocol was put in to application since November 2016, a month after it is launched by WHO.

Even though, a numerous pioneering studies have investigated to assess prevalence of opportunistic infections and associated factors among HIV positive patients those started ART by using the previous WHO ART initiation protocol; particularly studies conducted in Wolaita Sodo and Addis Ababa public hospitals were not considered factors that contribute to the development of the OIs (8). Furthermore, in addition to being conducted on HIV positive patients those start ART according previously developed WHO ART initiation protocol, the results of the studies were varying from region to region. With regard to the newly developed WHO ART guideline, however; few studies have been carried on HIV positive patients on the new WHO ART initiation protocol in Ethiopia in general and particularly in Gedeo zone to assess the prevalence and associated factor of opportunistic

infections. Therefore, the purpose of this study is to assess the prevalence and associated factors of opportunistic infections among adult HIV patients on the new antiretroviral treatment protocol in Gedeo Zone All ART offering Health Institutions.

1.3 Significance of the Study

As indicated in the literature the global burden of HIV/AIDS is increasing from time to time and the degree of morbidity and mortality is increasing in both developed and developing countries. Opportunistic infection is an important factor that is responsible for increasing morbidity and mortality among HIV patients and together with HIV/AIDS related malignancies accounts for more than 90% of HIV/AIDS death. The type of opportunistic infection affecting people living with HIV/AIDS varies from region to region.

The finding of this study may benefit to the regional and zonal education, health policy makers and managers to intend appropriate policies, plans and intervention programs for the minimization of opportunistic infections among HIV positive patients on ART.

The result of this study may be beneficial for HIV/AIDS care providers to aware the prevalence and contributing factors of opportunistic infections among people living with HIV positive patient on ART, in order to provide better patient safety and care, for the particular region, as well as the study area, so as to design better strategies to prevent the development of opportunistic infections among HIV patients. It will be creating awareness for the health institution, NGOs and the society as a whole to understand about OIs and action to be taken to prevent morbidity and mortality due to opportunistic infection. It also benefits study population for early screening and better care. Finally, the outcome of this finding will also provide good insight for newly developed WHO guidelines.

The results of this study will be serve as a reference, baseline and guide for other researcher who wants to study about prevalence of opportunistic infections and associated factors among HIV positive patients who had started ART based on the new antiretroviral treatment protocol.

CHAPTER 2: LITERATURE REVIEW

2.1 HIV/AIDS

Infection with Human Immunodeficiency Virus (HIV) leads to progressive immune destruction as a result of persistent viral replication which predisposes to opportunistic infection (OIs) and malignancies(6, 26).The report of Global Burden of Disease indicated that globally, 38.8 million people were living with human immunodeficiency virus (HIV), 2.5 million new HIV infections, and 1.2 million HIV/AIDS (acquired immunodeficiency syndrome) deaths in 2015(29). Sub-Saharan Africa (SSA) contributed 76% (29 million) of the total HIV infected people, 76% (1.9 million) of the total new HIV infections, and 75% (0.9 million) of the total HIV/AIDS deaths. While the same researcher forwarded that in Ethiopia, there were 768,040 HIV-infected people, 39,140 new HIV infections, and 28,650 HIV/AIDS deaths in 2015(29).

2.2 Prevalence of opportunistic infections

Opportunistic infections are late complications of HIV infection for the most part in patients with less than 200 CD4+ T-cells per micro liter. The causative agents are opportunistic organisms such as pneumocystis carnie pneumonia, mycobacterium complex and cytomegalovirus (CMV) that cause illnesses in compromised immune systems. The common bacterial, fungal and protozoon parasites are also severe in HIV/ AIDS patients(24, 30).

People with human immunodeficiency virus (HIV) are vulnerable to opportunistic infections (OIs) because they take advantage of the opportunity offered by a weakened immune system. Since the beginning of the HIV epidemic, OIs have been recognized, as common complications of HIV infection and which mostly manifest at advanced stage of HIV/AIDS, are the leading causes of morbidity and mortality despite the existence of prevention and treatment modalities. (26, 31). According to Nurilign and Getachew, the prevalence of OIs among HIV patients on ART is still high in different countries, which requires several protective activities or strategies from the ministry of health (MOH), hospitals, health professionals and patients(31). Even though nationally representative and comprehensive data regarding the magnitude of opportunistic infections lacks in Ethiopia, some regional studies has shown the prevalence ranging from 17.7% to 48%(8).

According to Ethiopian Federal Ministry of Health, Oropharyngeal candidiasis and tuberculosis(TB) are identified as the commonest OIs, in Ethiopia the co-infection rate of TB is 20-50%, followed by disease of central nervous system (CNS), sepsis, pneumocystis carnie pneumonia(PCP), bacterial pneumonia. Kaposi's sarcoma and lymphoma were reported as 8.4% and 3% respectively. They also stated additional milder infections such as Herpes zoster and other skin infection occur in early World Health Organization Clinical stages (Stage I&II), Whereas serious, life- threatening infection such as CNS toxoplasmosis in Ethiopia, general prevalence is about 80% in the adult population and cryptococcal meningitis occur in later WHO clinical stages (stage III and IV) with severe immunity suppression that means among patients with a CD4+ T lymphocyte count <50 cells/mm³. But some life-threatening infections, such as pneumonia and TB, may occur in early as well as in later WHO clinical stages(32).

A descriptive case series study was carried out from October 2013 to February 2014 in India showed that the highest rate of OIs among HIV patients in ART in this study area were tuberculosis 50% of all opportunistic infections, followed by 49% candidiasis,16% Pneumocystosis,15% parasitic diarrhea and 9%Cryptococcal infection (2).

A descriptive and analytical cross-sectional study among 339 adult HIV-infected patients receiving Highly Active Antiretroviral Therapy (HAART) for a median duration of 3 years at the Federal Medical Centre, Owerri, Nigeria was conducted and the result of their study showed that a total of 96 OIs were observed from the study. From these 76 patients had diagnosed OIs giving an overall prevalence of 22.4%. Among this 55 (16.2%) patients had single OI, 20 (5.9%) had dual OIs while 1 (0.3%) had triple OIs. The highest rate of OIs among HIV patients in ART in this study area were Candidiasis 29%,Dermatitis19%, Chronic diarrhea5%, Sepsis 5%, Bacterial pneumonia 3%, Cryptococcal meningitis 2%, Genital herpes simplex 2%, Genital warts 2%, Herpes Zoster 2% and Kaposi's sarcoma1%(6).

A cross sectional study design was conducted in Debre Markos referral hospital among 423 HIV patients captivating ART from 5 to 7years. A total of 181 OIs were observed from the study participants during the study period. The total prevalence of OIs among the study

participants were 42.8%. The highest rate of OIs among HIV patients in ART in this study area were oral candidiasis 50(11.8%), followed by chronic diarrhea for greater than 1 month 42(9.9%), tuberculosis 41(9.7%), Esophageal candidiasis 19(4.5%), severe bacterial pneumonia 13(3.1%), Pneumocystic carnie pneumonia 12(2.8%), Cryptococcus meningitis 2(0.5%), and septicemia 2(0.5%)(31).

A hospital-based retrospective study was conducted in Hiwot Fana Specialized University Hospital, Eastern Ethiopia among 358 HIV-infected adult patients on ART from April to June 2014. There were a total of 185 OIs diagnosed in the 172 patients and the overall prevalence of OIs among HIV/AIDS patients on ART was 48%. The highest prevalent rates of OIs observed were tuberculosis (TB) (21.23%), followed by Herpes zoster (11.2%) and oral candidiasis (9.5%)(8).

Facility based cross-sectional study was conducted to describe the prevalence of OIs and socio demographic factors associated for occurrence of OIs in Addis Ababa public hospital from January to end of February 2011. Out of the 566 clinical records assessed for the presence of OIs, the overall prevalence of OIs was 17.7%. Among this oral candidiasis 329 (58.1%), herpes zoster 198(35%) and pulmonary TB 166 (29.3 %,) were found out to be the predominant OIs observed in the order given. When the frequencies for both pulmonary and extra pulmonary TB 94(16.6%) were combined the prevalence for TB of all forms was 260 (45.9%) making it the second predominant OI in the study subjects. OIs like toxoplasmosis of the CNS 40(7.1%), PCP 28(4.9%) cryptococcal meningitis 21(3.7%) and cryptosporidiosis with diarrhea 20(3.5%), made up 100 (17.7 %) of the total cases of the OIs observed(30).

A cross sectional study was conducted on 360 adult HIV-infected patients attending antiretroviral therapy clinic Gondar University Hospital from February 2012-April 2012. The overall prevalence of OIs was (19.7%). The highest prevalent rates of OIs observed were tuberculosis (TB) (9.72%), followed by oral candidiasis(5%), diarrhea (3.3%), skin fungal infection(1.67%), pneumonia(1.38%) and other(1.67%)(33).

2.3 Factors associated with opportunistic infections

Factors associated with occurrence of OIs among HIV patients taking ART were also assessed in different countries at different time. Accordingly the risk for the advancement of OIs in

HIV patients depends on exposure to potential pathogens, virulence of the pathogens, the degree of host immunity, and the use of antimicrobial prophylaxis(8).

2.3.1. Socio-demographic factors

A study conducted in India found that the median CD4 count in HIV-infected male patients was significantly lower than in female patients, males were nearly three times more likely to be at an advanced stage of immune-suppression (characterized by CD4 counts of $<200/\text{mm}^3$) as compared to females (51% and 19%, respectively), the median viral load in males was 109 622 RNA copies/ml and was significantly higher than that in females (20614 RNA copies/ml)(34). A retrospective cross-sectional study conducted in Brazil showed that an educational level of less than eight years of education was observed in 51.6% ($n=361$) of the cases, and 91.4% ($n=640$) of the individuals resided in urban areas(10).

The study conducted in Nigeria showed that the risk of having OIs is did not significantly differ according to gender, place of residence and marital status(6). The study conduct in Eastern Ethiopia showed that the prevalence of OIs among males (48.7%) and females (47.8%) was comparable. The highest prevalence of OIs was found in those individuals in the age group of 30–39 years old (52.0%), with secondary school educational level (57.4%), rural dwellers (52.5%)(8). The study conducted in Northwest Ethiopia show that age less than 40 years old were 0.47 times less likely to acquire OI than patients at older ages, educational status of primary education was preventive compared to non-educated patients(31). The study conducted in Gondar University Hospital, Northwest Ethiopia reported the prevalence of OIs was comparable among males (21.5%) and females (18.5%), highest prevalence of OIs was depicted among age group 55 and above as far as marital status is concerned single and divorced study subjects depicted higher prevalence. Almost similar prevalence of OIs was observed among different educational levels(33)

2.3.2 Clinical factors

The study conducted in India showed that Patients with a baseline CD4 count $<200/\text{mm}^3$ were almost six times more likely to develop OIs compared to those with CD4 counts of $>350/\text{mm}^3$ (34). The other study conducted in India also forwarded that advanced WHO clinical stage (III & IV) at baseline to be independent clinical risk factors for the incidence of OIs. This could be because of lower immunity as WHO staging is higher that further

predispose for OIs. They also stated that majority of Patients start the treatment at their advanced stage of AIDS that will be difficult to overturn the stage easily with treatment(35). Study conducted in Nigeria showed that Occurrence of OIs had a significant positive association with duration of HIV diagnosis <3 years, duration of HAART <36 months ,HAART non-adherence, WHO clinical stage 3-4, CD4 cell count < 200 cells/mm³,BMI <25kg/m² and hemoglobin <10 g/dl(6).The study conducted in Eastern Ethiopia showed that WHO clinical stages III and IV were more likely develop OIs compared to those participants at WHO clinical stages I.As well as the study also imply that the patient with CD4 cell counts of <200 cells/mm³were more likely develop OIs than their counterparts with higher CD4 cell counts. Also the highest prevalence of OIs was found with body weight <60 kg (8).

The study conducted in northwest showed that patients at baseline WHO stages III&IV were at high risk of OI development, good ART adherence was preventive for OIs occurrence, and patients with a base line CD4 count of less than 200 cells/mm³ were almost double risk of OIs development than their counter parts with higher CD4 count at baseline patients with recent hemoglobin level of ≥ 10 g/dl were less likely to develop OI after ART started and patients with recent weight of <60 kg were at higher risk of developing OIs than their counter parts with > 60 kg(31). The study conducted in Gondar University Hospital, Northwest Ethiopia reported, World Health Organization clinical stage VI and III showed highest prevalence while least prevalence was observed among clinical stage I patients(33).

2.3.3. OIs prophylaxis

The study conducted in Eastern Ethiopia showed that participants who were not on co-trimoxazole and INH prophylaxis were more likely develop OIs compared to their counterparts who were on co-trimoxazole prophylaxis(8). The study conducted in Gondar University Hospital, Northwest Ethiopia reported, Prevalence of OIs was higher among patients who were not on co-trimoxazole prophylaxis compared to their counter parts who were on co-trimoxazole prophylaxis(33).

2.3.4. Functional status

The study conducted in Eastern Ethiopia showed that Participants who were bedridden and ambulatory were more likely to develop OIs compared to patients at work during initiation of ART(8).

2.3.5. Personal habits

The other study conducted in India forwarded that People who use khat along with ART medications are at risk to develop OIs than those who don't use Khat(35). study conducted in resource limited setting in Nigeria also found alcohol consumption and smoking to have no association with occurrence of OIs among HIV patients taking ART(6). The study conducted in Northwest Ethiopia showed that Patients who used to chew Khat was found to be at risk for OIs occurrence. Alcohol use and cigarette smoking were not found to be associated with occurrence of OIs among HIV patients taking ART (31).

2.4 Antiretroviral Therapy (ART)

Antiretroviral therapy has been shown to decrease viral replication, increase CD4+ T-cell count, decrease the frequency of opportunistic infections, improve quality of life and prolong life expectancy of HIV infected patients(27, 28, 36).The time of ART initiation for HIV positive patient according to WHO was revised from time to time. WHO first published guidelines on the use of antiretroviral therapy (ART) for HIV infection among adults and adolescents in 2002, and on the use of ARV drugs to prevent mother-to-child HIV transmission in 2004(25) .

According to WHO guideline, ART initiation time regarding CD4 cell revised and changed time to time. The 2006 WHO guideline recommends <200 cells/mm³, the 2009 WHO guideline revised stated that Start antiretroviral treatment in all patients with HIV who have CD4 count <350 cells/mm³irrespective of clinical symptoms, the 2013 Guidelines recommends that national HIV programmes provide ART to all people with a confirmed HIV diagnosis with a CD4 count of 500 cells/mm³or less, giving priority to initiating ART among those with severe/advanced HIV disease.

Currently According to WHO 2016 Rapid ART initiation should be offered to all people living with HIV following a confirmed HIV diagnosis and clinical assessment regardless of CD4 cell count and WHO clinical staging(25-27, 37).Ethiopia has adopted the new 2016 WHO guidelines, and developed a supplemental guide to implement Test and Start as of October 2017.This means that all HIV clients will start ART at the time of diagnosis, irrespective of theirCD4 count status(23).

Globally the introduction of antiretroviral therapy (ART) in 1996 significantly reduced HIV-related deaths (29, 38, 39). The global ART coverage in 2015 was low (40.6%), with North Africa and Middle East having the lowest coverage (19%) (29, 38). The coverage of ART varies between high-income and low-income country. High-income countries had the highest coverage (67%), and Sub-Saharan Africa (SSA) had coverage of about 42% (29). The ART coverage in Ethiopia in 2015 was (52%) (29, 38)

2.5. Conceptual frame work

This conceptual framework is developed after extensive literature review to show factors associated with opportunistic infections.

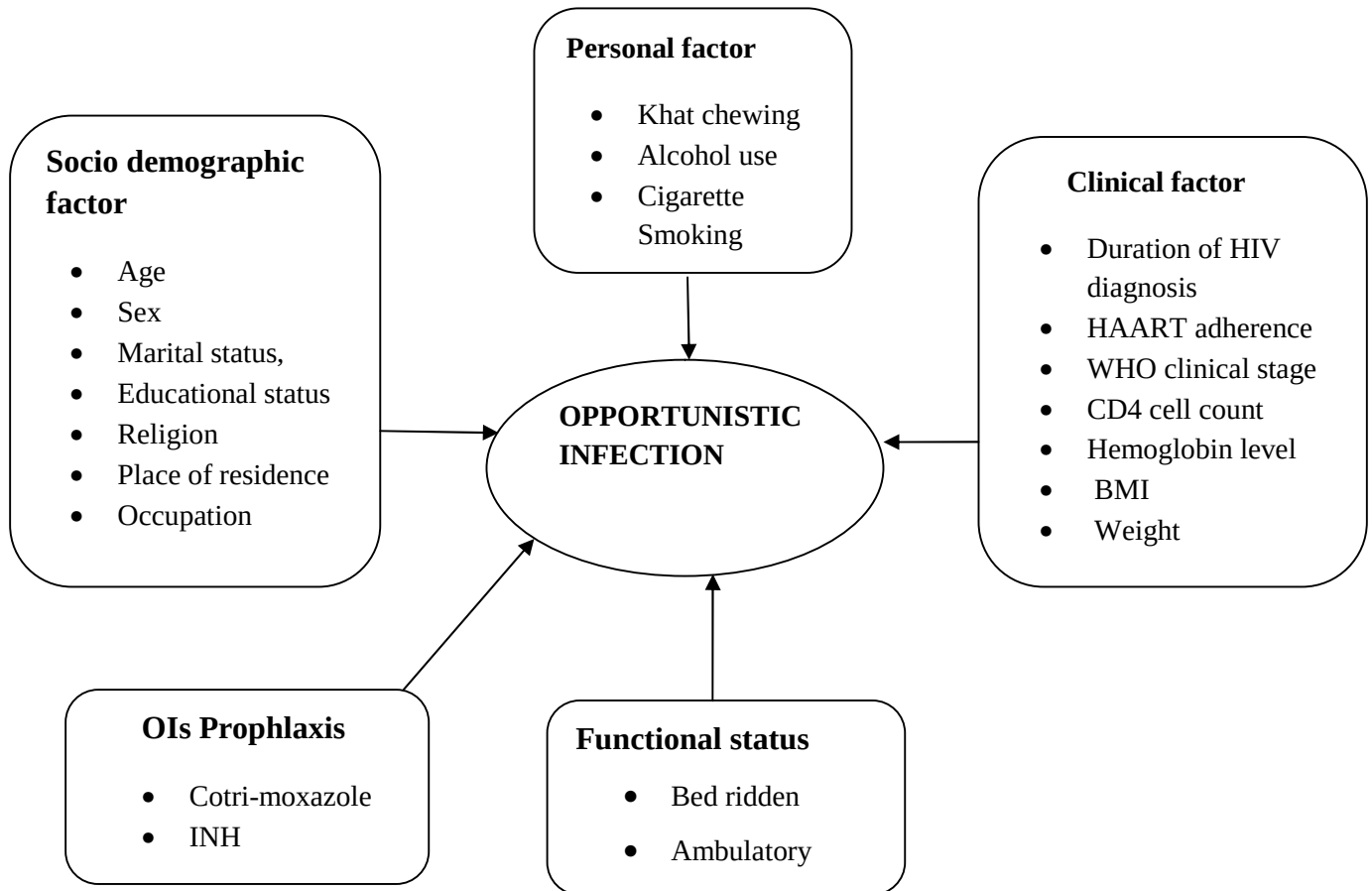


Figure 1 :conceptual frame work developed by principal investigator after literature review(6, 8, 31).

2.6. Justification of the Study

Globally, the number of PLWHA has been increasing over time. OIs have been recognized as common complications of HIV infection and a major cause of hospitalization and death among HIV patients on ART. OIs accounts for more than 90% of HIV/AIDS death and its prevalence varies from country to country. To date, no study was carried on prevalence and associated factor of OIs among HIV positive patients on the new WHO ART initiation protocol in Gedeo zone. So, this study will assess the prevalence and associated factors of opportunistic infections among adult HIV patients on the new antiretroviral treatment protocol in Gedeo Zone All ART offering Health Institutions which can be used as a baseline data for further investigation.

CHAPTER 3: OBJECTIVES OF THE STUDY

3.1. General objective

- ❖ To assess the prevalence of opportunistic infections and associated factors among adult HIV positive patients on the new antiretroviral treatment protocol at health institutions offering ART in Gedeo Zone, Southern, Ethiopia 2018.

3.2 .Specific objectives

- ❖ To assess the prevalence of opportunistic infections among adult HIV patients on the new antiretroviral treatment protocol at health institutions offering ART in Gedeo Zone, Southern, Ethiopia 2018.
- ❖ To identify factors associated with OIs among adult HIV positive patients on the new antiretroviral treatment protocol at health institutions offering ART in Gedeo Zone, Southern, Ethiopia 2018.

CHAPTER 4: METHODS AND MATERIALS

4.1 Study area and period

Data were collected from Gedeo zone of the Southern Nations Nationalities and Peoples Regional States in Ethiopia from April to June, 2018 G.C. Gedeo Zone, which is located at 360kms south from Addis Ababa and 90 km from Hawassa, was established in 1912 E.C. The Zone is bounded by Sidama zone in the east & the rest 3 sides by Oromia region. The total population of the Zone is 1,139,429. The health coverage of Gedeo zone is 83%. Gedeo zone has 38 health institutions. ART program was first launched in Gedeo zone in March 26, 2006. The program was started in Dilla University Referral Hospital, which is the government referral hospital in the zone and currently there are six health centers that are providing ART service. From this Haroresa Health center is located in the Dilla town. The rest health centers i.e. Yirgacheffe, Wonago, Bule, Gedeb and Chelelekitu are located away from Dilla town.

4.2 Study Design

Institutional based retrospective study design was used to collect the quantitative data from adult HIV positive patients (>18 years) on HIV care and ART follow-up at health institutions offering ART in Gedeo Zone.

4.3 Source Population

- ❖ All adult HIV Positive patients on Anti-retroviral therapy who visited health institutions offering ART in Gedeo Zone.

4.4 Study Population

- ❖ All adult HIV positive individuals who had started antiretroviral therapy from November 2016 to November 2017 and fulfill inclusion criteria.

4.5 Inclusion and Exclusion Criteria

4.5.1. Inclusion Criteria

All adult HIV positive patients who are 18 years old and above who had started ART from November 2016 to November 2017.

4.5.2 Exclusion Criteria

- Clinical records that did not have complete information relevant for the study.
- Transfer out.
- Lost to follow -up.
- Drop out were excluded.

4.7. Sample Size Determination

- Sample size was determined using single population proportion formula.

$$n = \frac{(Z_{\alpha/2})^2 \times P(1-p)}{d^2}$$

$$n = \frac{1.96^2(0.453)(1-0.453)}{0.05^2}$$

$$n = \frac{3.8416 \times 0.453 \times 0.547}{0.0025} n = 381$$

- Since the total population is less than 10,000, correction formula is used as follows:

$$n = \frac{n_0}{1 + \frac{n_0}{N}}$$
$$n = \frac{381}{1 + \frac{381}{666}}$$
$$n = 242$$

Then, considering 10% for patient incomplete data:

$$n = 242 \times 10\% + 242$$

$$n = 266$$

- ❖ **n** = Sample size required for the study
- ❖ **Z $\alpha/2$** = 1.96, standardized normal distribution curve value for the 95% confidence interval
- ❖ **p** = 0.453 from previous study(5).
- ❖ **d** = 0.05 degree of margin of error
- ❖ **N** = Total population for the study

4.8. Sampling Procedure

Simple random sampling technique was used. First the total sample size is allocated to each health institutions by proportion to the number of adult HIV positive patient on ART. Finally, from each institution, study subjects were selected by simple random sampling method.

Proportional allocation, $n_j = \frac{n \times N_j}{N}$

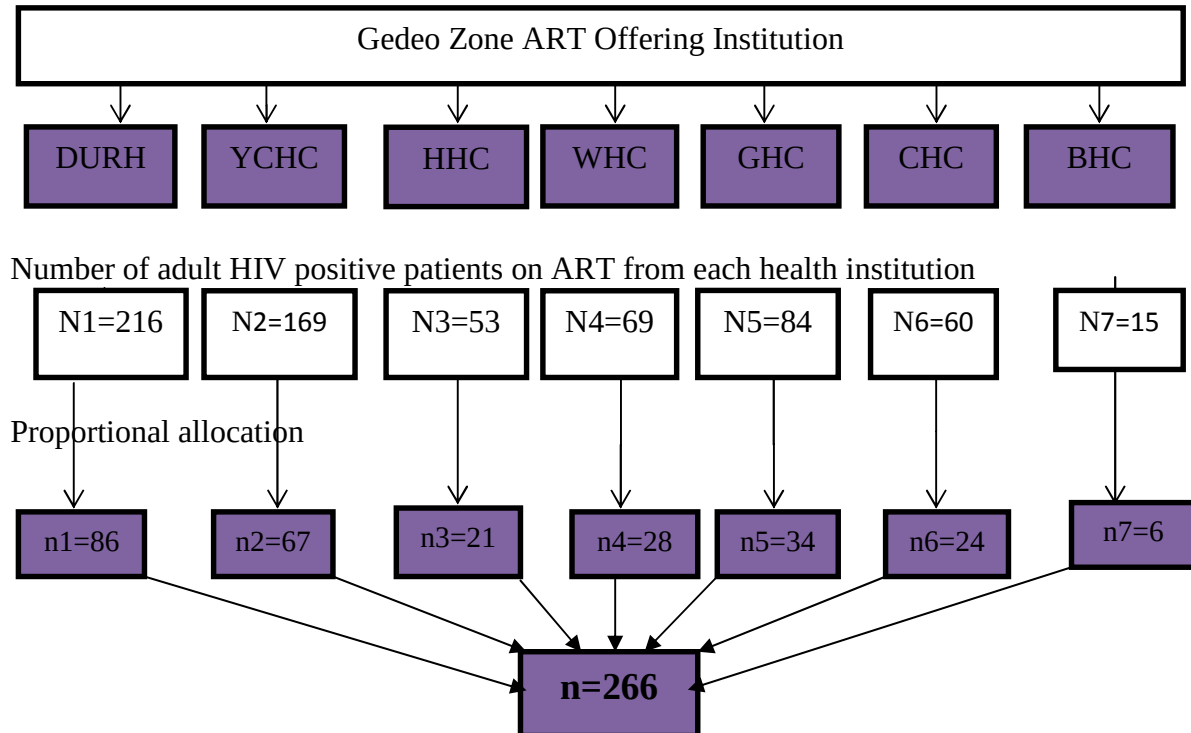
Where: n_j is the sample size of the j th institution

N_j is population size of the j th institution

$n = n_1 + n_2 + n_3 + n_4 \dots$ is the total sample size (**266**)

$N = N_1 + N_2 + N_3 + N_4 \dots$ is total population size (**666**)

K value = $666/266 = 2.504 \approx$ every 2 or 3 card was taken.



Total sample size

Figure2: Sampling procedure used for on assessment of prevalence of opportunistic infections (OIs) and associated factors among adult HIV positive patients on the new antiretroviral treatment protocol at Health Institutions offering ART in Gedeo Zone, Southern, Ethiopia 2018.

4.9. Study Variables

4.9.1 Dependent Variable

- Opportunistic infections among adult HIV positive patients on ART

4.9.2 Independent Variables

- Socio demographic data
 - ✓ Age
 - ✓ sex
 - ✓ Religion
 - ✓ Marital Status
 - ✓ Educational Level
- Clinical factors
 - ✓ Duration of HIV diagnosis
 - ✓ CD4 cell count
 - ✓ Clinical WHO stage of HIV/AIDS
 - ✓ HAART adherence
 - ✓ Hemoglobin level
 - ✓ BMI
- Personal factors
 - ✓ Khat chewing
 - ✓ Alcohol usage
 - ✓ Cigarette smoking
- Functional Status
- OIs prophylaxis
 - ✓ Cotri-moxazole
 - ✓ INH

4.10. Operational Definition

Opportunistic infections-is the occurrence of at least one concomitant infections after ART initiation due to immune suppression by HIV virus.

Adherence: Adherence to medication defined as the act of conforming to the recommendations made by the provider with respect to timing, dosage, and frequency of medication taking. And assessed by using both tablet counting and self-reporting methods, is defined as poor, fair and good, poor if adherence is <85 %(>6 dose of 30 doses or >9 dose of 60 dose is missed). Fair, if adherence is between 85 % and 95 % (3-5 doses of 30 doses or 3-9 dose of 60 doses is missed). and good if adherence is >95% (<2 doses of 30 doses or <3 dose of 60 dose is missed)(40).

Functional status: Is an individual's ability to perform normal daily activities required to meet basic needs, fulfill usual roles and maintain health and well-being. Functional status is classified in to the following categories:

Working- Able to perform usual work in or out of the house, harvest, go to school.

Ambulatory-Able to walk to or at treatment unit and walks at home unaided.

Bedridden-Most of time in bed at home(40).

Personal factor: are factors related to an individual habit like alcohol, khat and smoking that cannot be measured in amount but can be assessed HIV positive patient to be answered as Yes or No according to HIV care refill form (40).

Body Mass Index: A measurement used to assess nutritional status and measured as weight divided by height square. For adult, if not malnourished (BMI>18.5), if moderate malnutrition (BMI 16-18.5), if severe malnutrition (BMI<16)(40).

WHO Clinical Staging: is a way to categorize HIV disease severity based on new or recurrent clinical events. There are 4 WHO clinical stages which range from mild symptoms (WHO clinical stage 1) to severe symptoms (WHO clinical stage 4)(37).

4.11. Data Collection technique and instrument

Data collection format or checklist were prepared to extract the necessary data for the study based on the patient registration form for HIV care and ART clinic intake of the FMOH are adapted from previous studies and patient monitoring guidelines for HIV care and ART(30, 31, 37).A structured log book were prepared for each health center and hospital then the necessary data for the study were taken and registered on it. The structured log book was pretested in one health institution which is not part of the study hospitals. Fourteen BSc Nurses who are working in the ART clinics were recruited for data collection and for supervision respectively. Seven Bsc nurses who have experience in data collection and seven Bsc nurses who have experience of supervision in data collection were recruited. The data collectors and the supervisor were trained before actual data collection on sampling methods, ethical issues and on the use of the log book for one day.

4.12. Data Quality Control

The checklist was pre-tested on 5% of the sample size at Kebado health center to modify the checklist two weeks before the actual data collection period. The data collectors were trained before actual data collection and the principal investigator was supervising the data collector closely. During data collection, both principal investigator and data collectors were check the data for its completeness and missing information at each point. After data collection each check list was also checked during entry into the computer before analysis.

4.13. Data Analysis

After the collection of data, the checklist was checked for completeness and consistency. Then, the data template format was prepared, coded and entered in to Epi Data version 4.2. Then data was exported to SPSS version 23 for analysis. Descriptive analysis was employed to describe the percentages and distributions of the respondents for socio-demographic characteristics. Bivariate and multivariate analysis was used for association of independent variable with dependent variable. Crude and adjusted odds ratios with the corresponding 95% confidence intervals were computed. P-value <0.05 was considered statistically significant in this study. Then, the results were presented in the form of tables and charts.

4.14. Ethical consideration

This study was carried out after getting ethical clearance and formal letter of co-operation were obtained from Addis Ababa University, College of Health Sciences, School of Allied Health Sciences, Department of Nursing and Midwifery to conduct the study. Following the approval official letter of co-operation were write to Gedeo zone health bureau and Dilla university referral hospital from Department of Nursing and Midwifery of AAU. Permission were then obtained from Gedeo zone health bureau and hospitals ethical intuitional review board /IRB/. The purpose of the study was then explained to each ART clinic's head and all research ethical issues to keep the privacy, confidentiality, beneficence and justice to make the study under the legal framework of the institutional board review was strictly adhered. All the necessary precautions were taken to keep all documents in a safe and secure place. Names and other identification of the study subjects were omitted during data collection.

4.15. Dissemination of results

The result of this study will be disseminated to Addis Ababa University collage of Health sciences, School of Nursing and Midwifery, Addis Ababa. In addition, copies of the result will be given to Gedeo zone health bureau, Woreda health bureaus of study area and Dilla university Referral Hospital to utilize the information for further development of strategic and educational plan to prevent opportunistic infections. Finally, the manuscript will be submitting to scientific journals for possible publication.

CHAPTER 5: RESULT

5.1. Socio-Demographic Characteristics

This study assessed the prevalence and associated factors for OIs. A total of 266 HIV/AIDS patients who were in ART from November 2016 to November 2017 were participated in the study. Out of 266 reviewed cards, 160(60.2%) were males. The mean age of individuals on the reviewed cards was 37.10 year with $SD \pm 11.882$. Majority 104(39.1%) of individuals on the reviewed cards were age between 30-39 and regarding to religion 132(49.6%) were orthodox Christian. All socio-demographic characteristics are presented in the table below (table 1).

Table 1: Socio-demographic characteristics and Functional status of adult HIV positive patients taking Anti-Retroviral Therapy at health institutions offering in ART Gedeo Zone, Southern Ethiopia; 2018 (n=266).

Variables		Frequency(n)	Percentage (%)
Age	18-29	70	26
	30-39	104	39.1
	40-49	48	18.0
	≥50	44	16.5
Sex	Male	160	60.2
	Female	106	39.8
Marital status	Single	25	9.4
	Married	184	69.2
	Divorced	36	13.5
	Widowed	19	7.1
	Separated	2	0.8
Religion	Orthodox	132	49.6
	Muslim	55	20.7
	Protestant	77	28.9
	Catholic	2	0.8
Occupation	Gov't Employee	36	13.5
	Private Employee	12	4.5
	Daily Laborer	38	14.3
	House Wife	55	20.7
	Merchant	73	27.4
	Factory worker	5	1.9
	Farmer	30	11.3
	Others	17	6.4
Educational status	No education	77	28.9
	Primary	100	37.6
	Secondary	58	21.8
	Tertiary	31	11.7
Place of residence	Urban	167	62.8
	Rural	99	37.2

5.2 Clinical Characteristics and functional status of study participant

Many study participants 148 (55.6%) were at baseline WHO clinical stage I/II. Regarding to baseline CD4 cell count, the majority of the participants 82(30.8%) were CD4 count <200 cells/mm³ and concerning functional status, most 150 (56.4%) of patients were working personnel and many participants 169(63.5%) were patients had good adherence. In addition, 179(67.3%) of participants had >10 mg/dl hemoglobin level and 159(59.8%) weighed <60 kg, respectively. All clinical characteristics and functional status are presented in the table below (Table 2).

Table 2: Clinical characteristics and Functional status of adult HIV positive patients taking Anti-Retroviral Therapy at Health Institutions offering ART in Gedeo Zone, Southern, Ethiopia 2018.(n=266).

Variables		Frequency(n)	Percentage (%)
Baseline WHO clinical stage	Stage I/II	148	55.6
	Stage III/IV	118	44.4
Baseline CD4 cell count	<200	82	30.8
	200-350	62	23.3
	350-500	58	21.8
	≥500	64	24.1
HAART Adherence	Good	169	63.5
	Fair	38	14.3
	Poor	59	22.2
Duration of HIV diagnosis	<1 year	152	57.1
	>1year	114	42.9
Baseline Hgb	<10g/dl	87	32.7
	>10g/dl	179	67.3
Baseline BMI	>18.5kg/m2	167	62.8
	16-18.5kg/m2	83	31.2
	<16kg/m2	16	6.0
Current BMI	>18.5kg/m2	204	76.7
	16-18.5kg/m2	56	21.1
	<16kg/m2	6	2.3
Baseline Weight	<60kg	159	59.8
	>60kg	107	40.2
Current Weight	<60kg	143	46.2
	>60kg	123	53.2
Functional status at the beginning of ART	Working	150	56.4
	Ambulatory	53	19.9
	Bedridden	63	23.7

Abbreviations: ART, antiretroviral therapy; BMI, body mass index; Hgb, hemoglobin; HAART, highly active anti-retroviral therapy; WHO, world health organization, n, number of patients.

5. 3. Personal habit and usage of OIs prophylaxis

The majority 172 (64.7%) were receiving IsoNicotinyHydrazine (INH) prophylaxis, while 94(35.3%) of the participants were not receiving. Concerning personal habit majority 250(94.0%) of participants were not used alcohol while 16(6.0%) were used alcohol. All personal habit and usage of OIs prophylaxis are presented in the table below (Table3).

Table 3: Personal habit and usage of OIs prophylaxis of adult HIV positive patients taking Anti-Retroviral Therapy at Health Institutions offering ART in Gedeo Zone, Southern, Ethiopia 2018.(n=266).

Variables		Frequency(n)	Percentage (%)
Cotri-moxazole	Yes	114	42.9
	No	152	57.1
INH	Yes	172	64.7
	No	94	35.3
Alcohol usage at the beginning of ART	Yes	16	6.0
	No	250	94.0
Chat chewing at the beginning of ART	Yes	60	22.6
	No	206	77.4
Cigarette smoking at the beginning of ART	Yes	13	4.9%
	No	253	95.1%

Abbreviations: INH, IsoNicotinyHydrazine; ART, antiretroviral therapy; n, number of patients.

5.4. Prevalence of opportunistic infections

Out of 266 patients a total of 119 OIs were observed from the study participants during the study period. The overall prevalence of OIs among the study participants were 38.7 % (103/266). From these; 87(84.4%) of patients had only one opportunistic infection during study period, while 16(15.6%) of patients had double OIs per one patient during the study period respectively. The most frequent OIs among HIV patients on ART in the current study area were oral candidiasis 28(10.5%), followed by tuberculosis 26(9.8%) and Herpes zoster 15 (5.6%). The overall prevalence of OIs is presented in the figure below and prevalence of each OIs are presented table below (Figure3&table 4).

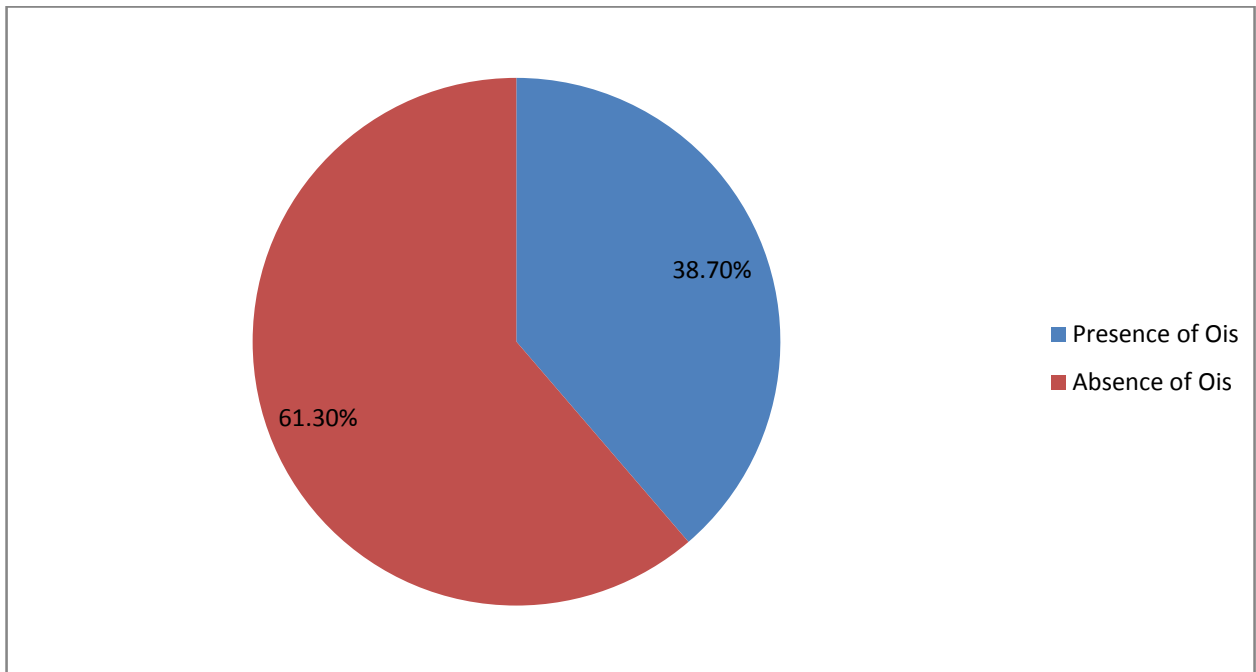


Figure 3: Pie chart showed that the overall prevalence of opportunistic infections among adult HIV/AIDS patients on ART at Health Institutions offering ART in Gedeo Zone, Southern, Ethiopia 2018.

Table 4: Prevalence of each opportunistic infections among adult HIV positive patients taking Anti-Retroviral Therapy at Health Institutions offering ART in Gedeo Zone, Southern, Ethiopia 2018 (n=266).

Types of opportunistic infections	Frequency(n)	Percentage (%)
Oral candidacies	28	10.5
Pulmonary TB	26	9.8
Herpes zoster	15	5.6
Chronic diarrhea	12	4.6
Esophageal candidacies	9	3.4
PCP	8	3.0
Recurrent bacterial pneumonia	7	2.6
Kaposi's sarcoma	4	1.5
Extra pulmonary TB	3	1.1
Cryptococcal meningitis	3	1.1
Toxoplasmosis of the CNS	2	0.8
Cervical cancer	2	0.8

Abbreviations: ART, antiretroviral therapy; CNS, central nervous system; PCP, pneumocystis carnie pneumonia; TB, tuberculosis; n, number of patients.

5.5: Risk factors of opportunistic infections

Bivariate and multivariate analysis was conducted to identify the associated factors for occurrence of OIs among HIV positive patients taking ART. The highest prevalence of OIs was found in those individuals with primary school educational level (37.6%), urban dwellers (62.8%), with baseline body weight <60 kg (59.8%) and current body weight<60kg (53.8%). However, the prevalence of OIs was not statistically different among the above variables ($P>0.05$). The independent variables were found to have association with occurrence of OIs in bivariate analysis were, study participants in WHO clinical stages III and IV were more likely develop OIs compared to those participants at WHO clinical stages I and II (COR = 4.391;95% CI =2.594, 7.433). Those participants with CD4 cell counts of <200 cells/mm³ were at high risk to OIs development than their counterparts with higher CD4 cell counts (COR =1.878; 95% CI =2.070, 3.298).

Participants who were bedridden (COR=15.078; 95%CI=5.482,41.470) and ambulatory (COR =2.826; 95% CI =1.542,5.181) were more likely to develop OIs compared to patients at work during initiation of ART, individuals who used chat chewing had risk for OIs occurrence (COR=5.012;95%CI= 2.696,9.318). Poor HAART adherence was found to be a higher risk for OI occurrences(COR=10.793;95%CI=5.254,22.170) compared to good HAART adherence and those who had baseline BMI<16kg/m² was found to be a risk to develop OIs(COR=1.451;95%CI=0.494,4.262). In order to determine the independent predictors of OIs, sex, age, WHO clinical stages, CD4 cell count, functional status of patients at the beginning of ART, baseline BMI, HAART Adherence, using alcohol, chat chewing, baseline hemoglobin levels, and current body weight were included in multivariate analysis, as they all had P=<0.25 on univariate analysis.

Those participants in WHO clinical stage III/IV were about 2.717 times (AOR =2.717; 95% CI =14.20, 5.198) more likely develop OIs compared to those in WHO clinical stage I/II. Participants with CD4 cell counts of <200 cells/mm³ were about 9.136 times (AOR = 9.136; 95% CI=2.747, 30.386) and 200-350cells/mm³ were about 9.449 times (AOR=9.449; 95%CI=2.701,33.057) more likely develop OIs compared to those with CD4 cell counts ≥500 cells/mm³. Those bedridden HIV/AIDS patients were 3.266 times (AOR=3.266; 95% CI=1.637,6.518) and were ambulatory 2.397 times (AOR =2.397; 95% CI =1.142, 5.031) more likely develop OIs when compared with patients at work, those who used to chew khat was at risk of developing OI 2.839 times(AOR=2.839;95%CI=1.211,6.652) more likely than those who did not chew, patients with poor HAART adherence were almost 10.052 times at risk of OI(AOR=10.052;95%CI=4.3062,3.464). In addition, patients with <16 baseline BMI had 1.804 times OIs with (AOR=1.804;95%CI=0.526,6.192) than participants with>18.5 while 16-18.5 baseline BMI had 0.802 times OIs with (AOR=0.802;95%CI=0.245,2.624) than participants with >18.5 baseline BMI to develop OIs.

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Table 5: Results of bivariate and multivariate analysis of factors s associated with opportunistic infections among adult HIV positive patients taking Anti-Retroviral Therapy at Health Institutions offering ART in Gedeo Zone,Southern,Ethiopia 2018(n=266).P<0.05*, P<0.01, P<0.001*****

Variables		OIs		COR(95%CI)	AOR(95%CI)
		Yes n(%)	No n(%)		
Sex	Male	71(44.3)	89(55.7)	1.845(1.098,3.100)	1.300(.592, 2.854)
	Female	32(30.1)	74(69.9)	1	
Age	18-29	27(38.5)	43(61.5)	1	
	30-39	33(31.8)	71(68.2)	1.214(.552, 2.668)	1.899(.595,6.065)
	40-49	28(58.3)	20(41.7)	.899(.425, 1.898)	.937(.323,2.723)
	≥50	15(34.0)	29(66.0)	2.707(1.160,6.315)	1.780(.534,5.935)
Functional status	Working	104(69.3)	46(30.6)	1	
	Ambulatory	31(58.5)	22(41.5)	1.604(.840,3.065)	2.397(1.142,5.031) *
	Bedridden	28(44.4)	35(55.6)	2.826(1.542,5,181)	3.266(1.637,6.518)***
Baseline CD4 count	<200	46(56.0)	36(44.0)	15.078(5.482,41.470)	9.136(2.747,30.386) ***
	200-350	32(51.6)	30(48.4)	12.587(4,449,35.609)	9.449(2.701,33.057) ***
	350-500	20(34.4)	38(65.6)	6.211(2.149,17.951)	5.758(1.710,19.387)**
	≥500	5(7.9)	59(92.1)	1	
HAART adherence	Good	45(26.7)	124(73.3)	1	
	Fair	11(29.0)	27(71.0)	1.123(.515, 2.448)	.850(.340, 2.128)
	Poor	47(79.7)	12(20.3)	10.793(5.252,22.170)	10.052(4.306,23.464)***
WHO clinical stage	I/II	35(23.7)	113(76.3)	1	
	III/IV	68(57.7)	50(42.3)	4.391(2.594,7.433)	2.717(1.420, 5.198)**
Baseline Hgb	<10g/dl	48(55.1)	39(44.9)	2.775(1.636, 4.707)	1.502(.671, 3.364)
	>10g/dl	55(30.7)	124(69.3)	1	
Baseline BMI	>18.5	52(44.4)	115(55.6)	1	
	16-18.5	44(53)	39(47)	0.581(0.205,1.646)	0.802(0.245,2.624) *
	<16	7(43.8)	9(56.2)	1.451(0.494,4.262)	1.804(0.526,6.192)*
Current weight	<60kg	69(48.2)	74(51.8)	2.441(1.460, 4.079)	1.553(.689, 3.498)
	>60kg	34(25.6)	89(67.4)	1	
Khat chewing	Yes	41(49.9)	62(60.1)	5.012(2.696,9.348)	2.839(1.211, 6.652)*
	No	19(11.7)	144(88.3)	1	
Alcohol drinking	Yes	11(10.7)	92(89.3)	3.778(1.273, 11.214)	2.351(.519, 10.646)
	No	5(6.0)	158(94.0)	1	

CHAPTER 6: DISCUSSION

The broad purpose of this study was to better understand the prevalence and associated factors of OIs among adult HIV-positive patients taking ART and this study gives important findings as well as possible improvement measures that could be implemented in an effort to reduce the occurrence of opportunistic infections. Review of available literature reveals a wide variation in the prevalence of opportunistic infections within different geographical regions and also within the same country(41).

The current study found that overall prevalence of opportunistic infections to be 38.7%. This finding was comparable to the 33.3% reported in a study conducted in Debre Markos(31). This finding is higher than similar studies carried out in Ethiopia in Gondor and Nigeria, which documented 19.7%,22.4% respectively(6, 33).This difference might be due to variation of the degree of host immunity and methodological difference in selecting study subjects. These studies were conducted among HIV patients taking ART fromNovember2016 to November 2017. The risk of developing an OIs for a person receiving ART is highest during the initial month of therapy(8).A study conducted in Eastern Ethiopia showed that the prevalence of OIs to be 48%, and Wolaita Sodo 45.3% which is greater than the current study. The discrepancy might be due to the result of deference in study design, host immunity and sample size. I.e this study involves patients taking ARTfromNovember2016 to November 2017 cross-sectional data while the study conducted in Wolaita Sodo were a five-year retrospective data and the sample size of this study were266 while Wolaita Sodo 377 and Eastern Ethiopia were 358.

Majority of the current study participants 87(84.4%) had one opportunistic infection while only 16(15.6%) had a co-infection. The most common predominant OIs were Oral candidiasis, pulmonary tuberculosis and Herpes zoster. This is the same with a study-conducted in Wolaita Zone, Southern Ethiopia, Debre Markos, Eastern Ethiopia and Gonder. However, the current study also revealed that the most prevalent OI was oral candidiasis 10.5 % (28/266). The prevalence rate of oral candidiasis was in agreement with finding reported from Nigeria 8.6%, Debre Markos, Ethiopia 11.8%, and Hiwot Fana Specialized University Hospital, Eastern Ethiopia (9.5%).However; it was fewer rates than compared to Wolaita Zone (17.7%) and India (21.3%)(5, 6, 8, 31).

Following oral candidiasis, TB and Herpes zoster were the second and the third most prevalent OIs in the present study, at 9.8% (26/266) and 5.6% (15/266), respectively. Next to oral candidiasis pulmonary tuberculosis is the second most common OIs in this study (9.8%). However, it was comparable prevalence reported from two areas in Ethiopia (9.7%) and two areas in Africa, Nigeria(7.7%) and Uganda(11%)which also revealed TB as a major OI(6, 31, 42). The rate was also lower compared to a TB prevalence of 8% in India and Hiwot Fana Specialized University Hospital(21.23%)(8, 43).The present study also revealed that Herpes zoster is the predominant OI identified(5.6%).However this finding is comparable with India(4.2%)(43). This rate was higher than the study conducted in Nigeria 0.6%(6). However, higher prevalence of Herpes zoster were reported in wolaita Zone(15.5%)(5).The chronic diarrhea,12(4.6%); and Esophageal candidiasis9(3.4%).PCP was diagnosed in 8(3.0%), Recurrent bacterial pneumonia was diagnosed in 7 (2.6%) and Kaposi's sarcoma was diagnosed in 4(1.5%) patients, cryptococcal meningitis, Extra pulmonary TB, were each diagnosed in 3 (1.1%) patients while only 2 (0.8%) patient had Toxoplasmosis of the CNS and Cervical cancer. In relative terms, Oral candidiasis, TB and Herpes zoster, constituted 10.5%, 9.8%, and 5.6% of the OIs respectively.

However, the study further shows that the burden of OIs was still considerable in spite of availability of HAART. This is probably because these OIs are endemic in the country and will always manifest at the slightest opportunity or they could still occur because of associated with the ART regimen currently in use, poor immunological status at HAART initiation, poor adherence to HAART, and other factors that me comprise the effectiveness of HAART.

Factors associated with occurrence of OIs among adult HIV patients taking ART were also assessed. Accordingly, advanced baseline WHO stage, baseline CD4 cell count, HAART adherence, chat use, functional status, and baseline BMI were found to be associated factor for OIs occurrence. In this study around 64 participants had ≥ 500 cells/mm³ baseline CD4 cell count during ART initiation time and this is a new WHO recommendation for ART initiation. So, regarding baseline CD4 cell count, among the total 64 participants who had ≥ 500 baseline CD4 cell count only 2(1.9%)had OIs in this study. This shows that ≥ 500 cells/mm³ baseline CD4 cell count is protective than those with < 500 cells/mm³ baseline CD4

cell count for development of OIs. Previous studies show that timely access to HAART ($CD4count \geq 500 \text{ cells/mm}^3$) is highly protective against OIs and associated death(42).

However, also in this study HIV-infected patient with $CD4$ counts of $<200 \text{ cells/mm}^3$ had 9.136 times higher OI occurrence ($AOR = 9.136$; $95\% \text{ CI} = 2.747, 30.386$) compared to those with $CD4$ counts of $200-350 \text{ cells/mm}^3$, $350-500 \text{ cells/mm}^3$ and $\geq 500 \text{ cells/mm}^3$, while $CD4$ counts of $200-350 \text{ cells/mm}^3$ had 9.449 times had risk to develop OIs ($AOR = 9.449$; $95\% \text{ CI} = 2.701, 33.057$) compared to $CD4$ cell count $350-500 \text{ cells/mm}^3$ and $\geq 500 \text{ cells/mm}^3$ and $CD4$ cell count $350-500 \text{ cells/mm}^3$ had 5.758 times ($AOR = 5.758$; $95\% \text{ CI} = 1.710, 19.387$) to develop OIs. This finding is concordant with other studies from Gondar, Ethiopia which reported that HIV-infected patients with $CD4$ counts of $<200 \text{ cells/mm}^3$ were more likely to develop OIs compared to the reference group of patients with $CD4$ counts $>350 \text{ cells/mm}^3$ (33). Other studies from India also reported high risk of developing OIs such as TB, *Pneumocystis carinii* pneumonia, and Cryptococcal meningitis occurs among patients with $CD4$ counts $<200 \text{ cells/mm}^3$. This finding appears accurate, since $CD4$ cells play a central role in the activation of both humoral and cellular immune response to fight against infection. Hence, low $CD4$ count increases susceptibility to OIs (8, 33).

Participants with advanced WHO stages III and IV had 2.717 times OIs with ($AOR = 2.717$; $95\% \text{ CI} = 1.420, 5.198$) than those with WHO stage of I and stage II respectively. This finding is in agreement with two studies from Gondar and Debre Markos, Ethiopia (31, 33). The study conducted in Gondor reported that WHO clinical stages III and IV HIV-infected patients were 9.4 ($p < 0.001$) and 22.6 ($p < 0.001$) times more likely to develop OIs compared to those in clinical stage I, respectively. The study conducted in Debre Markos reported that patients with advanced WHO stages III and IV were 4.76 times more likely to develop OIs with ($AOR = 4.76$, $95\% \text{ CI} = 2.16, 10.47$) than those with a WHO stage I and stage II. Similar finding were also observed in studies conducted in India, and Nigeria with ($AOR = 9.49$; $95\% \text{ CI} = 4.20, 21.42$), which reported that advanced clinical stage of the disease were significantly associated with development of OIs among patients on ART (6, 43).

Peoples who use khat along with ART medications had 2.839 times OIs with ($AOR = 2.839$; $95\% \text{ CI} = 1.211, 6.652$) than those who don't use Khat. Similar studies conducted in Debre Markos reveals that 4.73 times had OIs with ($AOR = 4.73$, $95\% \text{ CI} = 1.19, 18.92$) than those who

don't use khat. Alcohol use and cigarette smoking were not found to be association for occurrence of OIs. Similar study conducted in Nigeria and Debre Markos also found alcohol consumption and smoking to have no association to develop OIs(6, 31).

In the current study, peoples with poor HAART adherence also had 10.052 times occurrence of OIs with (AOR=10.052; 95%CI=4.3062, 3.464) compared to peoples with good adherence. Similar studies conducted in Nigeria with (AOR=5.28; 95%CI=2.52, 11.08) and Debre Markos with (AOR=0.16, 95%CI=0.05, 0.52) support this result. This might be because of good adherence for HAART will suppress viral replication and would increase CD4 cells that intern decrease risk of new opportunistic infection.(6, 31).Additionally, current study revealed that those HIV/AIDS patient who were bedridden had 3.266 times with (AOR=3.266; 95% CI=1.637, 6.518) and were ambulatory 2.397 times with (AOR =2.397; 95% CI =1.142, 5.031) increased risk for occurrence of OIs compared with patients at work. Similar study conducted in Eastern Ethiopia also showed that patients who were bedridden had 7.812times OIs with(AOR=7.812;95%CI=4.676, 9.421) while patients who were ambulatory had 4.464 time OIs with (AOR=4.464;95%CI=3.647, 6.845) than patients at work(8). And also in this study participants with <16 baseline BMI had 1.804 times OIs with (AOR=1.804; 95%CI=0.526, 6.192) than participants with>18.5 while 16-18.5 baseline BMI had 0.802 times OIs with (AOR=0.802;95%CI=0.245,2.624) than participants with >18.5 baseline BMI.

CHAPTER 7: STRENGTH AND LIMITATIONS OF THE STUDY

7.1. Strength

- This study is the first study that included individual who had baseline CD4 cell count ≥ 500 cells/mm³ based on new WHO ART initiation recommendation in assessing prevalence of OIs in Ethiopia.
- Data quality control was maintained thoroughly by giving intensive training.
- The study included all ART offering health institution in Gedeo zone to make study representative.

7.2. Limitations

- The health institutions where this study was conducted did not perform cultures for the diagnosis of OIs. Hence, the majority of the OIs were diagnosed clinically, which may have affected the diagnostic accuracy.
- Data Collection technique and instrument was a secondary data. Therefore, some data were missing.
- The study included only individuals who have one year of follow-up.

CHAPTER 8: CONCLUSIONS AND RECOMMENDATIONS

8.1. Conclusions

According to this finding, the prevalence of OI among HIV positive patients receiving ART was still high. This shows nearly four in ten HIV positive patients develops OIs. CD4 cell count, advanced WHO stage, adherence, functional status, baseline BMI and khat chewing are predominantly mentioned factors associated with occurrence of OIs among HIV positive patients. Therefore, this indicate that these factors may need great attention to alleviate them.

8.2. Recommendations

Based on the result of the study, the following recommendation was provided

- ❖ To GedeoZone Health bureau
 - Should provide interventions designed to promote early HIV testing and early enrollment of HIV-infected individuals into ART services.
 - Should create awareness on the advantage of having balanced diet.
- ❖ To Gedeo Zone Hospitals and health centers health professionals who are assigned to ART clinics.
 - Should give necessary education on adherence of medications for PLWHA who are on HAART.
 - Individuals who continue to have low CD4 cell counts while on ART should be aggressively evaluated for OIs, and practical efforts to optimize their immunological recovery should be made.
- ❖ To Stakeholders and other researchers
 - Should conduct longitudinal studies in order to identify risk factors for respective opportunistic infections.
 - The future research need to focus on the factors that have direct and indirect association with the prevalence of OI and that are not included in this study.

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CHAPTER 10: ANNEXES

Annex I: Information Sheet

Title of the research project: prevalence of opportunistic infections and associated factors among adult HIV-positive patients on the new antiretroviral treatment protocol at Health Institutions offering ART in Gedeo Zone, Southern, Ethiopia 2018.

Name of Investigator: Genet G/Michael (BSc.)

Name of the Organization: Addis Ababa University, College of Health sciences, school of nursing and midwifery.

Name of the Sponsor: Addis Ababa University

Introduction: This information sheet is prepared for Dilla university referral hospital, Haroresa, Yirgacheffe, Wonago, Bule, Gedeb, Chelelekitu health center Gedeo zone, Ethiopia. The aim of the form is to make the above concerned office clear about the purpose of research, data collection procedures and get permission to conduct the research.

Purpose of the Research Project: To assess the prevalence and associated factors of opportunistic infections among adult HIV positive patient on ART at health institutions offering ART in Gedeo zone.

Procedure: In order to achieve the above objective, information which is necessary for the study will be taken from HIV care refill form and ART follow-up record forms. In order to come up with the above mentioned findings, total document of program clients enrolled during November 2016 to November 2017 will be selected and a reviewed of the required information from the records will be made by using checklist.

Risk and /or Discomfort: Since the study will be conducted by taking appropriate information from medical chart, it will not inflict any harm on the patients. The name or any other identifying information will not be recorded on the checklist and all information taken from the chart will be kept strictly confidential and in a safe place. The information retrieved will only be used for the study purpose.

Benefits: The research have no direct benefit for one whose document/ record is included in this research. But the indirect benefit of the research for the participant and other clients in the program is clear. This is because if program planners are preparing predicted plan there is

a benefit for clients in the program of getting appropriate care and treatment services. Of all, the research work has a paramount direct benefit for health care planners and managers, especially for those on HIV prevention, treatment and support program planning and management.

Confidentiality: To reassure confidentiality the data on the chart were collected by those individuals who are working on the HIV care clinic in the facility and information will be collected without the name of the clients. The information collected from this research project will be kept confidential and will be stored in a file. In addition, it will not be revealed to anyone except the principal investigator and it will be kept in key and locked system with computer pass ward.

Person to contact: This research project will be reviewed and approved by the institutional review board of College of Medicine and Health Science, AAU. If you want to know more information, you can contact the committee through the address below. If you have any question you can contact any of the following individuals (Investigator and Advisors) and you may ask at any time you want.

1. Genet G/Michael, AAU University, College of Medicine and Health Science, Department of Adult Nursing: principal investigator.

Cell phone: +251-909495581 E-mail: genetgmichael@yahoo. com

2. Daniel Mengistu (RN,Bsc, Msc,Asst.Prof), AAU University, College of Medicine and Health Science, School of Nursing and midwifery: Main-Advisor.

Cell phone: +251-911119597 E-mail: mengistudaniel@yahoo.com

3. Niguse Tadele(BSc, MSc) AAU University, College of Medicine and Health Sciences School of Nursing and midwifery: Co- Advisor.

Cell phone: +251-9 13163130 E-mail: niguse.tadele@aau.edu.et

Annex II: - Consent Form For Hospitals and Health Center

I have read all the process and the objective of the study. I'm willing to provide you all necessary document for your study entitled "prevalence of opportunistic infections and associated factors among adult HIV positive patients on the new antiretroviral treatment protocol in Gedeo zone all ART offering health institutions, southern, Ethiopia 2018". I have informed the purpose and procedure of the study. I have also informed the benefit of the study that the research has no direct benefit for one whose document/ record is included in this research but it helps program planners to develop strategies that improve care of PLWHA on ART. I have understood that information provided will be kept confidential and providing documents will have no effect on me and patients. I know whom to contact if have any question or if I want any clarification.

So, are you willing to provide me the necessary documents?

_____ Yes, I can provide you.

_____ No, I don't want provide you (Thank you very much!).

Witness: Signature_____ Date _____

Data collector

Name_____Signature_____Date____/____/____

Checked by Supervisor:

Name_____Signature_____Date____/____/____

Annex III: Checklist

Table 6: Checklist used for assessment of prevalence of opportunistic infection and associated factor among adult HIV positive patient on new antiretroviral treatment protocol at health institutions offering ART in Gedeo Zone,southern,Ethiopia,2018.

General information

For each question, make a circle around a Number that corresponds to answer; fill the blank answer.

Unique ART number_____

Unique patient ID number_____

Part 1: Socio-demographic characteristic

No	Variable	Descriptive Categories
1.1.	Age	_____
1.2.	Sex	1. Male 2. Female
1.3.	Marital Status	1. Single 2. Married 3. Divorced 4. Widowed 5. Separated
1.4.	Religion	1. Orthodox 2. Muslim 3. Protestant 4. Catholic 5 Other_____

1.5.	Occupation	1. Government employee 2. Private employee 3. Daily laborer 4. House wife 5. Merchant 6. Factory worker 7. Other _____
1.6.	Residence	1. Urban 2. Rural
2.1.	Part II: Functional status	1.working 2.Ambulatory 3.Bedridden

Part III: Clinical characteristic

No.	Variables	Descriptive categories
3.1.	Duration of HIV diagnosis	_____
3.2.	Baseline WHO Clinical Stage	_____
3.3.	Baseline CD4 Cell count	_____
3.4.	Baseline Hemoglobin level	_____
3.5.	HAART Adherence	1. Good 2. Poor 3. Fair
3.6.	Weight	Baseline _____ Current _____
3.7.	BMI(Body Mass Index)	Baseline _____ Current _____
Part IV: OIs Prophylaxis		
4.1.	Co-trimoxazole	1. Yes 2. No
4.2	INH	1. Yes 2. No

Part v: Personal habits or Factors

No.	Variables	Descriptive categories
5.1	Khat chewing at the beginning of ART	1.Yes 2.No
5.2	Alcohol drinking at the beginning of ART	1.Yes 2.No
5.3	Cigarette smoking at the beginning of ART	1.Yes 2.No

Part VI: Diagnosed opportunistic infections

Taken from HIV care or ART follow- up form.

No	Types of opportunistic infection	
6.1.	Oral candidacies	1. Yes 2.No
6.2.	Pulmonary TB	1. Yes 2.No
6.3.	Esophageal candidacies	1. Yes 2.No
6.4.	Herpes zoster	1. Yes 2.No
6.5.	Pneumocystis carnie pneumonia (PCP)	1. Yes 2.No
6.6.	Recurrent bacterial pneumonia	1. Yes 2.No
6.7.	Extra pulmonary TB	1. Yes 2.No
6.8.	Kaposi's sarcoma	1. Yes 2. No
6.9.	Toxoplasmosis of the CNS	1. Yes 2.No
6.10.	Cryptococcal meningitis	1. Yes 2. No

6.11.	Chronic diarrhea	1. Yes 2. No
6.12.	Lymphoma	1. Yes 2. No
6.13.	Cervical cancer	1. Yes 2. No
6.14.	Others(specify)	

APPROVAL SHEET
ADDIS ABABA UNIVERSITY
COLLEGE HEALTH SCIENCES
SCHOOL OF NURSING AND MIDWIFERY

I, the undersigned MSc Nurse Student, declare that I have submitted my original work on a title for the Prevalence of opportunistic infections and associated factors among adult HIV positive patients on the new antiretroviral treatment protocol at Health Institutions offering ART in Gedeo Zone, Southern, Ethiopia 2018.

Submitted by:

Genet G/Michael (Bsc)

Name of student

Signature

Date

This research thesis work has been submitted for examination with my approval as an advisor.

Approved by:

1. Daniel Menigstu(RN, Bsc, Msc, Ast.Prof)

Name of Major Advisor

Signature

Date

2. Nigusse Tadele (Bsc,Msc,Ast.Prof)

Name of Co-Advisor

Signature

Date