COLLEGE OF HEALTH SCIENCE
SCHOOL OF PUBLIC HEALTH

PREVALENCE OF OPPORTUNISTIC INFECTIONS AND ASSOCIATED FACTORS AMONG HIV-INFECTED ADULTS ON ANTIRETROVIRAL THERAPY IN WOLDIA COMPREHENSIVE SPECIALIZED HOSPITAL, NORTH WOLLO, ETHIOPIA, 2023

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WOLDIA UNIVERSITY

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A RESEARCH PROPOSAL SUBMITTED TO WOLDIA UNIVERSITY DEPARTMENT OF PUBLIC HEALTH IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF PUBLIC HEALTH.

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APPROVAL SHEET

The undersigned examining committee certifies that the proposal presented by Birhan Asefie entitled: Prevalence of opportunistic infections and associated factors among HIV-infected adults on antiretroviral therapy in Woldia comprehensive specialized hospital, north Wollo, Ethiopia, 2023**.** Submitted to Woldia University, College of Health Sciences, School of Public Health in partial fulfillment of the requirements for a master's degree in Public Health compiles with the regulation of the University and meets the accepted standards concerning originality and quality.

Place of submission: School of public health, College of Health Sciences, Woldia University.

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Acronyms and abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ART	Anti-Retroviral Therapy
CDC	Centers for Disease Control
CD4	Cluster of differentiation 4
CRFs	Circulating Recombinant Forms
DACA	Drug Administration and Control Authority
FDA	Food and Drug Administration
HAPCO	HIV/AIDS Prevention and Control Office
HIV	Human Immunodeficiency Virus
NNRT	Nucleoside Traverse transcriptase Inhibitors
MTCT	Mother-to-Child Transmission
MOH	Ministry of Health
OI	Opportunistic Infection
PCP	Pneumocystis Carini Pneumonia
PLWHA	People Living With HIV and AIDS
SPSS	Statistical Package for Social Sciences
STI	Sexually Transmitted Infection
UNAIDS	United Nations Program on HIV and AIDS
USAID	United States Agency for International Development
WHO	World Health Organization

Abstract

Introduction – Opportunistic infections are infections occurring due to bacteria, fungi, viruses, or parasites that normally do not cause a disease, but become pathogenic when the body's defense system is impaired. Opportunistic infections associated with HIV infections are lower the quality of life of HIV infected persons, speed up the rate of progression to AIDS, reduce patients' response to treatment and are usually associated with high medical care costs and the leading cause of morbidity and mortality among HIV/AIDS patients. However, studies regarding the magnitude of opportunistic infections in HIV-infected adults on ART are very limited.

Objective - To assess the prevalence of opportunistic infections and its associated factors among HIV- infected adults on anti-retroviral therapy attending Woldia comprehensive specialized hospital.

Methods - Institution based cross sectional study was conducted among 405 HIV-infected adults from January 16, 2023 to February 16, 2023. A structured pre-tested interviewer administered questionnaire was used to collect data. The study participants were selected by the systematic sampling technique. All variables with p-value of ≤ 0.25 in binary logistic regression were taken into multivariable model. Crude and adjusted odds ratios with their 95% confidence intervals were calculated and variables having p value ≤ 0.05 in the multivariate analysis were taken as significant predictors.

Results: A total of 405 HIV-infected adults on antiretroviral therapy participated in this study with a response rate of 100%. The overall prevalence of opportunistic infections among HIV/AIDS patients on ART was 42.2% (95% CI; 37.4 - 47.2). The highest rates of OIs observed were tuberculosis (TB) (27.5%), followed by herpes zoster (25.2%), chronic diarrhea 15.2% and oral and/or esophageal thrush 14.04%. Age between 30-39 (AOR=3.46; 95% CI=1.78, 6.73), 40-49 years (AOR= 2.47; 95% CI, 1.21, 5.04), >= 50 years (3.09; 95% CI, 1.19, 8.03), being on WHO clinical stage III (AOR= 4.63; 95% CI, 2.67, 8.04), Stage IV (AOR=6.63; 95% CI=3.29, 13.35), having CD4 count <= 200 cells/mm3 (AOR=1.91; 95%CI = 1.15, 3.18), chat chewers (AOR= 1.72;95% CI= 1.07, 2.76) and being ambulatory (AOR= 2.18;95%CI; 1.02, 4.63) were predictors of opportunistic infections.

Conclusion: In this study, a high rate of OIs was observed compared with previous studies. Age of respondents, chat chewing, WHO clinical stage III and IV, CD4 count less than or equal to 200 cells/mm3 and being ambulatory were found to be predictors of OIs. More attention should be given to those who have low CD4 count and advanced WHO clinical staging.

Key words: Opportunistic infection, HIV infected patients, ART, Woldia comprehensive specialized hospital

1. Introduction

1.1 Background

Human immunodeficiency virus (HIV), the causal agent for Acquired I Immunodeficiency Syndrome (AIDS) is the world's greatest severe public health and development contest (1). As per global joint estimate of World Health Organization and United Nation Program on HIV/AIDS 2019, since the beginning of the epidemic, 76 million people have been infected with the HIV virus and about 33 million people have died of HIV/AIDS, 38 million of people are living with HIV/AIDS; 1.7 million people newly infected with HIV and 690,000 peoples were died with HIV related diseases (1). There were an estimated 20.6 million people living with HIV in this region, nearly 55% of the global total. This region also contributes 45% of new HIV infection and AIDS related Mortality, with an estimate of 670,000 and 310,000 respectively, to the worldwide burden (2).According to the 2016 Ethiopia Demographic and Health Survey, the national HIV prevalence among adult population aged 15-49 years was 0.9% (3).The prevalence among women was 1.2% and among men 0.6%, with more women in urban areas having the highest risk of infection (4).

Human immunodeficiency virus (HIV) is an infection that attacks the body's immune system, specifically the white blood cells called CD4 cells. HIV destroys these CD4 cells, weakening a person's immunity against opportunistic infections, such as tuberculosis and fungal infections, severe bacterial infections and some cancers. Human Immunodeficiency Virus (HIV) pandemic is among the greatest health crises ever faced by humanity (1, 5)

Opportunistic infections (OIs) are infections that are more frequent or more severe in people with weakened immune systems than in people with healthy immune systems because of immune suppression in HIV infected, and they are the major clinical manifestation of HIV patients (6).The most common opportunistic diseases in HIV patients are Candida esophagi is, Pneumocystis carinii pneumonia (PCP), disseminated Mycobacterium avian complex (MAC)

infection, cytomegalovirus (CMV), Cryptococcus, Kaposi sarcoma, herpes zoster, and tuberculosis (7). Opportunistic infections (OI) are a significant cause of morbidity and mortality in patients with HIV/AIDS. When these infections occur in HIV/ AIDS patients in the form of relapse or re-infection, they are said to be a reoccurrence of the OI (8).

Opportunistic infections are caused by bacteria, viruses, fungi, or protozoa and these take advantage of an opportunity not normally available, such as a host with a weakened immune system, an altered micro biota (such as a disrupted gut flora), or breached integumentary barriers. Many of these pathogens do not cause disease in a healthy host that has a normal immune system as earlier on stated, however, a compromised immune system, a penetrating injury, or a lack of competition from normal commensals presents an opportunity for the pathogen to infect (6, 9).

For many years before the development of effective antiretroviral therapy (ART), these infections inflicted significant morbidity and mortality on patients living with AIDS. Prevention of opportunistic infections (OI) in patients with HIV has since significantly reduced morbidity and mortality in these patients. HIV-related infections and malignancies escalate in frequency and severity as the absolute CD4 T cell count falls toward 200 cells/μl and below (8).The risk for the development 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. And majority of these OI are associated with an increased hazard of death in HIV patients (10).

1.2 Statement of Problem

Worldwide, one in three people seek health care for HIV/AIDS-related opportunistic infections. Opportunistic infections (OIs) are the most significant complication of human immunodeficiency virus (HIV) infection (5). Opportunistic infections (OIs) associated with HIV remain the single main cause of ill-health and death among HIV/AIDS patients in resource poor settings (6). Although there is no adequate information on the reoccurrence rate of OIs in Africa, there were 310,000 OI-related deaths among AIDS patients in the eastern and southern Africa region (11).

Opportunistic infections are a leading cause of poor quality of life, hospitalization, and poor adherence among HIV infected adults in Ethiopia. Besides, OIs remains a major cause of morbidity and mortality among this vulnerable population, which contributes to 74.1% of HIV-

related deaths. OI lower the quality of life of HIV infected persons, speed up the rate of progression to fully blown AIDS, reduces patients' response to antiretroviral treatment especially when HIV-positive patients are co-infected with tuberculosis, increases stigma and limits one's ability to work and are usually associated with high medical care costs (6).

In low- and middle-income countries (LMICs), the global rollout of ART has led to >15 million patients on ART, and a decline in HIV-related deaths by 40% since 2004. However, OIs remain the major driver of HIV-associated morbidity and mortality, accounting for the substantially higher mortality observed in low and middle income countries (12).

HIV infection and OIs have bi-directional relationships (13). Having HIV weakens the immune system and causes the risk of developing opportunistic infections (14). On the other hand, OIs can affect the natural history of HIV/AIDS infection by causing reversibly boosting viral load that speed up HIV progression and increases its transmission (7). HIV weaken immune system and causes the risk of developing opportunistic infections that could accelerate HIV progression and transmission (10).

Some patients do not have a sustained response to antiretroviral agents for multiple reasons including poor adherence, drug toxicities, drug interactions, or initial acquisition of a drug resistant strain of HIV-1. Therefore OIs continue to cause substantial morbidity and mortality in patients with HIV-1 infection despite use of ART (15). HIV causes progressive depletion of the CD4 T cells, which leads to life-threatening OIs or malignancies during the natural course of the disease. More than 90% of OIs are responsible for the development of AIDS morbidities and mortalities (16, 17).

Majority of opportunistic infections are associated with an increased hazard of death in HIV patients. Patients experiencing morbidity from opportunistic diseases may have interruptions in antiretroviral therapy causing more rapid progression of HIV disease. In addition studies found that opportunistic infections cause an up regulation in HIV replication and higher viral loads. Severely immune-compromised HIV patients may develop a variety of opportunistic infections that have a significant impact on their well-being, quality of life, health care costs, and their survival. It affects different body parts such as mainly the nervous, gastrointestinal, respiratory systems, and the skin (18).

Despite the fact that different studies have been conducted on the prevalence of individual OIs among HIV-infected adult patients on ART in Ethiopia, information about the magnitude and associated factors of OIs is limited in Woldia. Therefore, this study tried to assess the prevalence of OIs and identify associated factors in patients taking ART drugs in Woldia referral hospital, North Wollo, Ethiopia 2023.

1.3 Significance of the study

After HIV Infection and the development of AIDS various kinds of OIs develop in the patients that differ from country to country. The research will be used to establish the existence of opportunistic infections among patients attending ART at Woldia referral hospital and how these infections affect the health status of these individuals. In addition, the research will also contribute to the efforts being made by the country as a whole to reduce on the cases of morbidity and mortality rates in HIV patients due to opportunistic infections.

Furthermore, the information obtained from this study will also be used to provide sensitization on how the way of life of these individuals predisposes them to various opportunistic infections and so help them adopt behaviors that can help them reduce the risks of acquiring these infections as well as create self-awareness among these individuals regarding the risks and complications associated with the different OIs and finally to help stake holders plan effective intervention formulate policies and developmental programs to help address the problems identified.

This study will be to provide information on the magnitude and associated factors of the most frequent OIs observed in the ART clinics for health workers, mangers and responsible bodies. Recommendations for prevention, control and effective treatment for the OIs will be presented to the concerned bodies. This study will be used as source of reference for the future researchers.

2. Literature review

2.1 Magnitude of opportunistic infection

Worldwide, one in three people seek health care for HIV/AIDS-related opportunistic infections (OIs)(5). The rate of reoccurrence of OIs is increasing. For instance, in 2017 there were 160,684 recurrent tuberculosis (TB) cases, which represented an increase from the previous year, 2016, when there were around 150,000 (19). Although there is no adequate information on the reoccurrence rate of OIs in Africa, there were 310,000 OI-related deaths among AIDS patients in the eastern and southern Africa region (11).

A study that was done to screen for the presence of opportunistic infections in a tertiary hospital in India using both clinical, laboratory and radiological method was done in 80 patients (20). In this study 68.25% of the patients had evidence of OIs. Pulmonary tuberculosis (31%) and chronic diarrhea (12.5%) was the most common observed opportunistic infections. Candida infections (7%), recurrent herpes zoster (3.5%), Cryptococcus meningitis (2.5%), PCP (1.5%), CNS toxoplasmosis (1.25%) were the other observed infections(20, 21).

Among different types of OIs, pulmonary tuberculosis (TB) is the major reoccurring OI. TB reactivation in HIV-uninfected individuals is less than 10%, but the rate of reoccurrence is greater than 10% per year in HIV-positive individuals. Recurrent TB among HIV/AIDS patients is a major challenge for TB control programs, as it is associated with drug resistance and low cure rates(22).

A survey conducted to determine the prevalence of OIs from patients attending 5 major hospitals in one of the states of Nigeria (Kebbi state) found that out of 1950 patients attending the hospitals 606 (31%), were HIV seropositive and 374(61%) were infected with one or more of the following infections; these were; STD/Gonorrhea (22%) ascariasis (15%), Giardiasis (13%), Trichomoniasis (10%), candidacies (8.6%), tuberculosis (TB) (6.7%)(23). The study concluded that these findings in the state were in line with reports from other areas especially Sub-Saharan Africa and concluded that the state government should enforce control strategies against the spread of HIV/AIDS, enhance improved hygiene/environmental sanitation to reduce the level of

OI parasitic disease transmission, and enforce mass health education against HIV/AIDS as well as OIs (7, 23).

In the Ethiopian context a one year prospective study of consecutive patients admitted to the medical wards of Tikur Anbessa teaching hospital had shown the morbidity and mortality patterns of patients with HIV/AIDS with the following findings (20, 24). Oro-pharyngeal candidacies 136 (57.4%), tuberculosis 131 (55%), CNS mass Lesions 74 (31.2.%), sepsis 56 (24.9 %), herpes zoster 40 (16.9%), PCP 34 (14.3%), bacterial pneumonia 22(9.3%), Cryptococci meningitis 14(5.9%) and others 82 (34.6%). The authors concluded that OIS were the major causes of morbidity and mortality among HIV patients and many of the common OIS were both preventable and treatable (25).

Cross-sectional study was conducted in Arba Minch Town, Southern Ethiopia, 119 HIV/AIDS patients (26.4%) were diagnosed with reoccurrence of OIs. Pulmonary tuberculosis was the major reoccurring OI(22). A hospital-based retrospective study was conducted in eastern Ethiopia; the overall of 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 candidacies (9.5%)(16).

A retrospective observational cohort study is conducted on HIV/AIDS patients who started ART clinic in St. Paul's Hospital Millennium Medical College from September 2014 to August 2015, From the total patients 264 (83.8%) developed Opportunistic infections. TB of all forms was 137 (43.49%), 111(35.2%) have oral candidacies, 60(19%) have herpes zoster had the highest prevalence. CD4 count had an independent association with the distribution of the different forms of the opportunistic infections(25).

A comparative cross-sectional study was conducted among adult patients infected with HIV and who were on Pre-ART or On-ART and followed up from 2012 to 2016 in Zewditu Memorial Hospital, Addis Ababa, the overall prevalence of opportunistic infections was found to be 33.6% (95% CI; 28.9–38.5). The prevalence of opportunistic infections among the Pre-ART group (38%) was higher than On-ART group (29.2%) (P-value = 0.04). Pulmonary tuberculosis was the most common opportunistic infection observed in both Pre-ART and On-ART groups(26).

A facility-based cross-sectional study was conducted, Leku, Bona and Yirgalem Hospitals in Sidama Zone, Southern Ethiopia, 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% (27).

Cross sectional study was conducted in Gondar town shows that the overall prevalence of OIs was (19.7%). Tuberculosis (9.72%) followed by oral candidacies (5%) and diarrhea (3.3%) were the most frequently observed OIs (28).

Studies from Tercha Hospital Dawro zone, indicates that the overall all prevalence of opportunistic infection was (88.4%) developed OIs. Pulmonary tuberculosis, (18%), severe community acquired pneumonia (16.3%) and oral candidacies (15.6%) were the most common opportunistic infections (29).

A health facility based single centered cohort study Mekelle, the incidence of OIs after HAART was 7.5 cases/100person years. Tuberculosis, oral candidacies, pneumonia and toxoplasmosis were the leading OIs after HAART (30).

2.2Associated factors for opportunistic infections among HIV infected adult patients on ART

2.2.1 WHO staging and CD4 count

In India the prevalence of opportunistic infection was 50.63% with a significant positive association with WHO clinical staging and CD4 count as associated risk factors (31). In Addis Ababa, among the patients with OIs, patients with stage III and II were with higher percentage 25.34% and 12.44%, respectively. Patients with baseline, WHO stage III and stage IV1.698 times odds of having OIs with a statistical significance (P= 0.016), were statistical significance with occurrence of OIs. Patients with poor ARV adherence 4.04 times (P=0.004) were more likely to acquire OIs as compared to patients with good ARV adherence. Moreover, patients with the following variables had increased likelihood of OIs: hypertension (AOR: 5.457; P=0.010), and Hemoglobin level, < 10g/dL (COR: 13.442;P= 0.014)and patients under first-line ART regimen, 77.5% (32).

The risk for the development 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. Antiretroviral therapy (ART) increases the length and quality of life and productivity of patients by improving survival, and decreases the incidence of OIs in HIV-infected people through reduction of the viral load and increasing the level of CD4 cells.4 The widespread use of ART has had the most profound influence on reducing OI-related mortality in HIV-infected persons in those countries in which these therapies are accessible and affordable (33).

According to the Arba Minch Towns, Ethiopia, age, rural residence, chronic disease, baseline anti-retroviral therapy (ART) adherence, current hemoglobin level, and current cell differentiation-4 (CD4) count were factors significantly associated with reoccurrence(22). A hospital-based retrospective study was conducted in eastern Ethiopia shows that Baseline CD4 cell count,200 cells/mm3(adjusted odds ratio [AOR] =1.645, 95% CI =2.187, 3.983), baseline World Health Organization (WHO) clinical stage III clinical stage III (AOR =2.801, 95% CI =1.958, 7.165) and IV(AOR =3.856; 95% CI =2.691, 10.390) , and not using prophylaxis (AOR =1.912, 95% CI =1.444, 3.824) were found to have strong association with acquisition of OIs (16).

Study in St. Paul's Hospital Millennium Medical College, Ethiopia, from September 2014 to August 2015; conducted on HIV/AIDS patients who started ART clinic CD4 count had an independent association with the distribution of the different forms of the opportunistic infections. The Odds of having the severe forms of the opportunistic infections was 6.162 times higher in the patients who had CD4 count less than 200 (25).

According to the study in Zewditu Memorial Hospital, Ethiopia, adults on Pre-ART or On-ART and followed up from 2012 to 2016 shows that Being in the WHO clinical Stage III (AOR = 2.1; 95% CI 1.1–3.9)or Stage IV(AOR = 3.6; 95% CI 1.7–7.7) were independent predictors for the development of opportunistic infections (26).

A facility-based cross-sectional study was conducted, Southern Ethiopia, the magnitude of opportunistic associated with; 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/mm3 [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 when compared to their counterparts[AOR=5.52, 95% CI: 2.42-12.56] (27).

Research conducted in Gondar town, Ethiopia, shows CD4 count less than 200/mm3(AOR = 4.933, P < 0.001), World Health Organization (WHO) clinical stage III (AOR = 9.418, P < 0.001)and IV(AOR = 22.665, P < 0.001) were found to have strong association with acquisition of OIs (28).

A retrospective conducted at Tercha Hospital Dawro zone, Ethiopia, Disease stage[AOR=3.22:95% CI 1.76–5.66], CD4 level[AOR=2.53:95% CI 1.19–5.37], drug adherence [AOR=3.02:95% CI 1.57–5.77] and hemoglobin[AOR=2.49:95% CI 1.34–4.62] showed significant association with OIs (29).A health facility based single centered cohort study Mekelle A bed ridden functional status at initiation of HAART, presence of OIs before HAART, non-adherence and low hemoglobin level were predictors for the occurrence of OIs after HAART (30).

2.2.2 Age

Research conducted in south India, shows majority of the HIV positive patients with opportunistic infections were in the age group of 30-39 years. So it was observed that the frequency of opportunistic infections was highest in the sexually active age group of the society (33).A facility-based cross-sectional study was conducted, Southern Ethiopia with opportunistic infections were; older age [AOR=2.61, 95% CI: 1.30-5.23], compared to younger age (27).

2.3 High risk behaviors for opportunistic infections among patients with HIV.

2.3.1 Alcohol consumption

The prevalence of alcohol use disorders (AUDs) appears to be high among people living with HIV (PLHIV) compared to the general population. AUDs are associated with premature mortality in PLHIV, thought to occur due to alcohol enhancing the toxicity of antiretroviral treatment (ART), increasing liver damage from concurrent infection with hepatitis C virus, and increasing the risk of opportunistic infection due to decreased effectiveness of ART and exacerbation of immune suppression (34, 35).

2.3.2 Tobacco smoking

As mortality due to AIDS-related causes has decreased with the use of antiretroviral therapy, there has been a rise in deaths related to non–AIDS-defining illnesses. Given the exceedingly high prevalence of cigarette smoking among individuals living with HIV infection, tobacco has been implicated as a major contributor to this paradigm shift. Evidence suggests that smoking-related illnesses, such as cardiovascular disease, respiratory illnesses, and certain malignancies, contribute substantially to morbidity and mortality among HIV-infected persons (36).

Evidence demonstrates that cigarette smoking adversely affects the immunologic response to ART. In a longitudinal study of a large HIV-infected cohort, Feldman and coworkers found that, compared with nonsmokers, smokers receiving ART had poorer viral responses, poorer immunologic response, greater risk of virology rebound (AOR, 1.39; 95% CI, 1.06–1.69) and more frequent immunologic failure(AOR, 1.52; 95% CI, 1.18–1.96) (37).

2.4. Conceptual framework

The conceptual framework of this study is based on literature findings that showed factors which have been cited as reasons for opportunistic infections which includes socio-demographic and economic variables and individual factors (Figure1). Other consistent factors for opportunistic infections include behavioral and intervening factors (38).

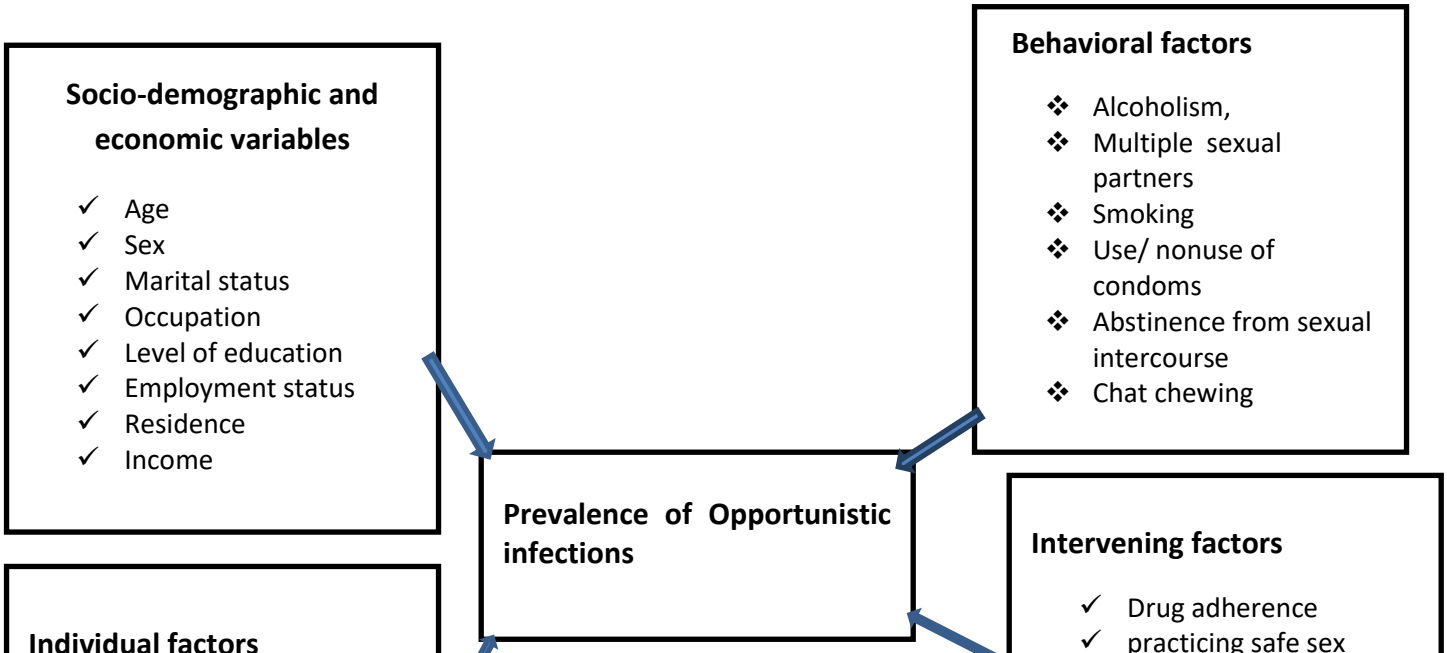

Figure 1:- The conceptual framework to identify factors associated with the occurrence of opportunistic infection among adult HIV-patients at Woldia comprehensive specialized hospital (By reviewing different literatures)

2.5. Research questions

The research aims at answering the following questions;

1. What is the prevalence of opportunistic infections among patients attending ART at Woldia comprehensive specialized hospital?

2. What are the associated factors for development of opportunistic infections among HIV patients attending ART at Woldia comprehensive specialized hospital?

3. Objective

3.1 General objective

- To assess the prevalence of opportunistic infections and associated factors among HIV-infected adults on antiretroviral therapy in Woldia comprehensive specialized hospital, North Wollo zone, Ethiopia, 2023.

3.2 Specific objectives

- To assess prevalence of opportunistic infections among HIV-infected adults on antiretroviral therapy in Woldia comprehensive specialized hospital, North Wollo zone, Ethiopia.
- To identify associated factors for opportunistic infections among HIV-infected adults on antiretroviral therapy in Woldia comprehensive specialized hospital, North Wollo zone, Ethiopia.

4. Methods

4.1 Study setting

This study was conducted at Woldia town which is located in the Amhara region, 521 km from Addis Ababa. It sits at a latitude and longitude of 11˚46050'N 39˚3600'E, with an elevation 2, 112 meters above sea level. Based on the 2014 national population projection conducted by the Central Statistical Agency of Ethiopia, Woldia Town has a total population of 180,000, of whom 81,750 are men and 98,250 women(39). The town administration contains ten kebeles (the smallest administration unit in Ethiopia). The health services include one public hospital, two public health centers, and more than 10 private clinics(40).

Woldia comprehensive specialized hospitals one of government hospitals found in the north Wollo zone and has ART service delivering facility. Woldia comprehensive specialized hospital has a total of 358health professionals. The Woldia comprehensive specialized hospital currently delivers comprehensive HIV/AIDS services in the following areas; HIV counseling and testing, provision of ART, provision of co-trimoxazole and isoniazid prophylaxis, palliative care, TB/HIV treatment, sexually transmitted infections diagnosis and treatment and post-exposure prophylaxis for HIV. Woldia comprehensive specialized hospital has a total of 3859 on adult clients ART.

4.2 Study design and period

Facility based cross-sectional study was conducted among adult HIV clients to assess the prevalence of OIs and associated factors at Woldia comprehensive specialized hospital from January 16, 2023 to February 16, 2023.

4.3 Population

4.3.1 Source population

The source populations were all HIV/AIDS patients who are on ART follow up and who visited the ART clinic at Woldia comprehensive specialized hospital.

4.3.2 Study population

All the adult clients enrolled in the Woldia comprehensive specialized hospital for chronic HIV/AIDS care and ART follow up were the study population. Only those who attended the hospital during the study period should be considered as study population.

4.4 Inclusion and Exclusion Criteria

4.4.1 Inclusion Criteria

All HIV positive adults aged 18 years and above were included in the study.

4.4.2 Exclusion Criteria

All HIV-infected patients admitted to the intensive care unit those who cannot able to speak, those who have mental illness and seriously ill patients during the study period were excluded from the study.

4.5. Study variables

4.5.1. Dependent variable:

- Opportunistic infections

4.5.2. Independent variables

- **Demographic and socioeconomic variables:-** Age, sex, marital status, occupation, level of education, employment status, residence, ethnicity, religion, income,
- **Behavioral factors :-** Alcoholism, multiple sexual partners, smoking, use/ nonuse of condoms, abstinence from sexual intercourse, chat chewing
- **Individual factor /client related factors**: WHO clinical staging, baseline CD4 count, BMI, viral load,
- **Intervening factors:** Status of immune system, drug adherence, practicing safe sex, OI treatment availability, availability and uptake of condoms, ART adherence counseling, OI diagnosis and treatment.

4.6. Operational definitions

Opportunistic Infections: If the HIV-infected adults on antiretroviral therapy are diagnosed with at least one or more opportunistic infections; any infections of bacteria, viruses, fungi, Parasitic or protozoa or multiple infections reported on their medical record. HIV-infected adults on antiretroviral therapy who developed opportunistic infections any time after the start of the treatment and diagnosed having OIs (41).

ART adherence:

Good adherence: Good adherence: If PLHIV are adherent >95% (i.e. the percentage of missed doses is < 2 (tabs) doses of 30 doses or < 3(tabs) doses of 60 doses), as documented by ART health personnel (42).

Fair adherence: If PLHIV are adherent 85–94% (i.e., the percentage of missed doses is 3–5 doses of 30 doses or 3–9 doses of 60 doses), as documented by ART health personnel (42).

Poor adherence: If PLHIV are adherent <85% (i.e. the percentage of missed dose is > 6 doses of 30 doses or >9 doses of 60 doses), as documented by ART health personnel (42).

Functional Status:

Working: Able to perform usual work in or out of the house.

Ambulatory: Able to perform activities of daily living.

Bedridden: Not able to perform activities of daily living (43).

4.7. Sample Size Determination

4.8.1 Sample size calculation to estimate the prevalence of opportunistic infections

Sample size was determined by single population proportion formula, that is

$$n = za/_2{}^2 * \frac{p(1-p)}{d^2}$$

where; n=minimum sample size, Z is the level of significance corresponding to 95% confidence interval (1.96), p = anticipated value (Prevalence of opportunistic infection (39.6%)from studies

conducted in Sidama (44) and d= desired absolute precision which was taken as 5%. Then sample size was calculated as 368 with design effect and none response rate of 10%.

$$n = (1.96)^2 * \frac{0.396(1 - 0.396)}{(0.05)^2}$$

n= 368 by adding 10% of non-respondent rate of 37 which is equal to 405. The computed sample size was 368 and by taking 10% non-response rate, the total sample size computed is 405.

3.8.2 Sample size calculation to assess the associated factors

Using Epi-info version-7.2.5 and using different factors such functional status, severe anemia, WHO clinical staging and utilization of prophylaxis are used to determine the sample size. And non-response rate of 10% is made the total sample size in the (table 1) below.

Table 1. Sample size calculation for the second objective from prior related studies for some related factors associated with opportunistic infection occurrence among adult HIV/AIDS patients on ART in Woldia comprehensive specialized hospital, 2023

S. No	Factors	Confidence level	Power	Exposed–to-non exposed ratio	Prevalence of occurrence of Opportunistic infection Among non-exposed	Odds ratio	Non response rate	Calculated sample size
1	Functional status	95% (1.96)	80%	1:1	39.6*	3.9	10%	92
2	WHO clinical staging	95% (1.96)	80%	1:1	42.8**	4.7	10%	77
3	Prophylaxis	95% (1.96)	80 %	1:1	48***	1.9	10%	372

***Sidama ** Debre-Markos *** Eastern Ethiopia**

Finally, from the calculated sample size for the two objectives (prevalence and the factors) the largest sample size is 405, therefore for this study the final sample size required was 405.

4.8. Sampling procedures

From the total 3859 HIV/AIDS patients who were on ART chronic care, in order to select 405 participants, according to the hospital report, on average 28-35 on ART clients were visiting the Woldia comprehensive specialized hospital daily. The study participants were selected by the systematic sampling technique making a continuous list of subjects from the first to last day of data collection. The first subject was selected from first day registration of patient one to two by using the lottery method and then taking every 2^{nd} individual from the list of clients using sampling fraction formula K=N/n, where k= sampling fraction, N = total expected monthly clients attending the Woldia comprehensive specialized hospital ART clinic during the study period and n= the sample size (sampling fraction is k= N/n = 900/405 =2) and going on serially until the total number was found. Using the office hours and taking the first client as case one, every second of the daily attended clients during the data collection period were included and interviewed until the required sample were obtained.

Each patient was studied only once, on his/ her first visit during the study period, if selected. Repeat visits were excluded by recording registration numbers of each client at the time of interview and checking thereafter for avoidance of possible repetition.

4.9. Data Collection Tool and Procedures

The data were collected by face to face interviews by using semi structured interviewer administered questionnaire using a pre-tested questionnaire; a pre-tested checklist done to collect information regarding OIs from patient's interview and medical records of the patients were reviewed. Data were collected by three clinical nurses and supervised by one public health professionals. A pre-tested structured questionnaire was utilized to collect: Socio-demographic characteristics (age, sex, marital status, and Residence, ethnicity, religion, and employment & Educational status), Clinical information's (CD4 level, WHO stage, Adherence, weight, co-morbidities) and other risk factors. Three data collectors and one supervisor were recruited and two days training were given. Training and practical demonstrations on interview techniques and document extraction procedures based on the checklist were given to data collectors and supervisors for two consecutive days assessed for competency. The data collection process was followed daily by the supervisor and principal investigators.

4.10. Data Quality Management

The questionnaire was adapted and modified in to our context from previous literatures. It was prepared first in English and then translated into the local language Amharic, and then retranslated back to English by an expert who is fluent in both languages to maintain its consistency. Training was given for data collectors and the supervisor. The questionnaires were pretested and validated before two weeks in the study time in Woldia health center on 5% of HIV positive adult patients who attend ART clinic which is outside of the study area and necessary modifications were done based on the findings. Data collection process was strictly followed day to day by the supervisor and principal investigators. After the data collection process, the data were checked for completeness and any incomplete or misfiled questionnaires filed again. To ensure the quality of data, the questionnaires and medical record were evaluated for completeness and all the needed information were checked. To avoid bias, Patient clinical records with redundant, incomplete or missing information was omitted.

4.11. Data Processing and Analysis

Questionnaires were checked for completeness, coded, and entered into SPSS version 25 statistical package. Data cleaning and assumption checking was performed prior to proceeding to analysis. Frequencies, cross tabulation and percentages, were calculated for all the categorical variables. To claim statistically significant effect, crude and adjusted odds ratio with 95% confidence interval (CI) were employed. The finding from all analysis were summarized and presented by graphs, tables and other summery measures. Binary logistic regression analyses were computed to assess the association of the various factors against the level of opportunistic infection. Variables with a p-value of less than 0.25 in the bi-variable analysis was entered into the final multiple logistic regression model. The Hosmer -Lemeshow goodness-of-fit statistic was used to assess whether the necessary assumptions for the application of multiple logistic regression are fulfilled. At 95% confidence interval, explanatory variables with P-value ≤ 0.05 in multiple logistic regression analysis were considered as significantly associated.

5. Ethical Considerations

Ethical clearance was obtained from Institutional Review Board of Woldia University; official letters were submitted to the North Wollo Zonal health department. The zonal health department ethical review board approved and gives us a formal letter to Woldia comprehensive specialized hospital. Supervisors and data collectors were trained on confidentiality. The purpose and importance of the study was explained to the study participants and written informed consent was obtained from all participants before starting the interviews. They were also informed about the possibility to refuse participation at any time of data collection. Confidentiality of the data were assured and kept anonymously; code number was assigned to the study participants without mentioning the name, the information that will be collected by the study were kept in a file and locked with key. By participating in this study and answering our questions, you will not receive any direct benefit. You in this study will not involve any risks. If a question makes you feel uncomfortable, you may choose not to answer.

6. Results

Socio-demographic characteristics of study participants

A total of 405 HIV-infected adults on antiretroviral therapy on ART were interviewed in the current study with response rate of 100%. The mean age of study HIV-infected adults on antiretroviral therapy was 36 (SD ±8.974) years and ranging from 18–78 years. Most of HIV-infected adults on antiretroviral therapy were in the age group of 30–39 years (42.2%), were female (62.7%), rural (55.3%), and Unable to read and write (44.0%) (Table 2).

Table 2:- Socio-demographic characteristics of HIV-infected adults on antiretroviral therapy in Woldia comprehensive specialized hospital, 2023(n=405)

Variable (n= 405)		Frequency	Percentage
Age	18-29	91	22.5
	30-39	171	42.2
	40-49	106	26.2
	>=50	37	9.1
Residence	Rural	224	55.3
	Urban	181	44.7
Religion	Muslim	215	53.1

	Orthodox	176	43.5
	Protestant	14	3.5
Educational status	Unable to read and write	178	44.0
	Able to read and write	66	16.3
	Primary school	65	16.0
	Secondary school	83	20.5
	College/University	13	3.2
Marital status	Single	100	24.7
	Married	229	56.5
	Divorced	50	12.3
	Windowed	15	3.7
	Separated	11	2.7
Sex	Male	151	37.3
	Female	254	62.7
Ethnicity	Amhara	375	92.6
	Afar	16	4.0
	Tigrie	10	2.5
	Oromo	4	1.0
Occupational status	House wife	104	25.7
	Merchant	57	14.1
	Daily laborer	34	8.4
	Government employee	41	10.1
	Private employee	52	12.8
	Farmer	107	26.4
	Student	10	2.5
Income	<= 1000	318	78.5
	1001-1999	42	10.4
	>=2000	45	11.1
Family size	1-2	121	29.9
	3-4	166	41.0
	5 and above	118	29.1

Behavioral and Environmental related characteristics of study participants

Two hundred sixty five (65.4%) HIV-infected adults on antiretroviral therapy were living in the mud floor house and four hundred three (99.5%) HIV-infected adults on antiretroviral therapy had a latrine. The main source of drinking water was 372 (91.9%) pipe water. Regarding behavioral related factors, 182 (44.9%), were chat chewers and 128 (6.9%) were cigarette smokers. Regarding alcohol consumption, 322 (79.5 %) had ever drunk alcohol, 83 (20.5%) were current alcohol drinkers (Table 3).

Table 3:- Behavioral and Environment related characteristics of HIV-infected adults on antiretroviral therapy in Woldia comprehensive specialized hospital, 2023(n=405)

Variable		Frequency	Percentage
Drinking alcohol	Yes	83	20.5
	No	322	79.5
Chewing chat	Yes	182	44.9
	No	223	55.1
Smoking	Yes	28	6.9
	No	377	93.1
Condom use	Yes	85	21.0
	No	320	79.0
Floor of Living house	Mud	265	65.4
	Cement	140	34.6
Availability of latrine	Yes	403	99.5
	No	2	.5
Source of water	Pipe	372	91.9
	river/spring	33	8.1
Living with domestic animals and pets	Yes	34	8.4
	No	371	91.6

Clinical condition of the study participants

In this study 45.7% of HIV-infected adult on antiretroviral therapy were at WHO clinical stage I and 29.1% were at clinical stage III. Concerning duration of ART, 44.0% of HIV-infected adults on antiretroviral therapy were taking more than five years of duration. Three hundred sixty eight (90.9%) of the HIV-infected adults on antiretroviral therapy had good adherence to ART, 24.9% of the HIV-infected adults on antiretroviral therapy were currently receiving cotrimoxazole during the study period, while 15.3% were receiving isoniazid (INH) prophylaxis. About 30.1 % of HIV-infected adults on antiretroviral therapy had a CD4 count less than or equal to 200 cells/mm3. In addition, about 17.3% and 35.6% of HIV-infected adults on antiretroviral therapy had 12 mg/dL hemoglobin level and less than or equal to 18.49 BMI, respectively (Table 4).

Table 4:- Clinical condition of HIV-infected adults on antiretroviral therapy in Woldia comprehensive specialized hospital, 2023(n=405)

Variable		Frequency	Percentage
Duration of ART taking (in month)	<=36	143	35.3
	37-59	84	20.7
	>=60	178	44.0
Functional status of HIV-infected adults on ART	Working	333	82.2
	Ambulatory	45	11.1
	Bed ridden	27	6.7
WHO clinical staging	stage I	185	45.7
	Stage II	41	10.1
	stage III	118	29.1
	Stage IV	61	15.1
Adherence to ART	Good adherence	368	90.9
	Fair adherence	29	7.2
	Poor adherence	8	2.0
Taking cotrimoxazole	Yes	101	24.9
	No	304	75.1
taking isoniazid	Yes	62	15.3
	No	343	84.7
BMI	<=18.49	144	35.6
	18.5-24.99	250	61.7
	>=25	11	2.7
CD4 count	<=200	122	30.1
	>200	283	69.9
Hemoglobin level	<12	70	17.3
	>=12	335	82.7

Prevalence and types of Opportunistic infections

Out of 405 patients, 171 were diagnosed having OIs, yielding an overall prevalence of 42.2 % (95% CI; 37.4 - 47.2) (Figure 2). The most frequent OIs were Tuberculosis (both pulmonary and extra-pulmonary) 47(27.5%), Herpes zoster at 43 (25.1%), chronic diarrhea 26 (15.2%) and oral and/or esophageal thrush at 24 (14%) (Figure 3).

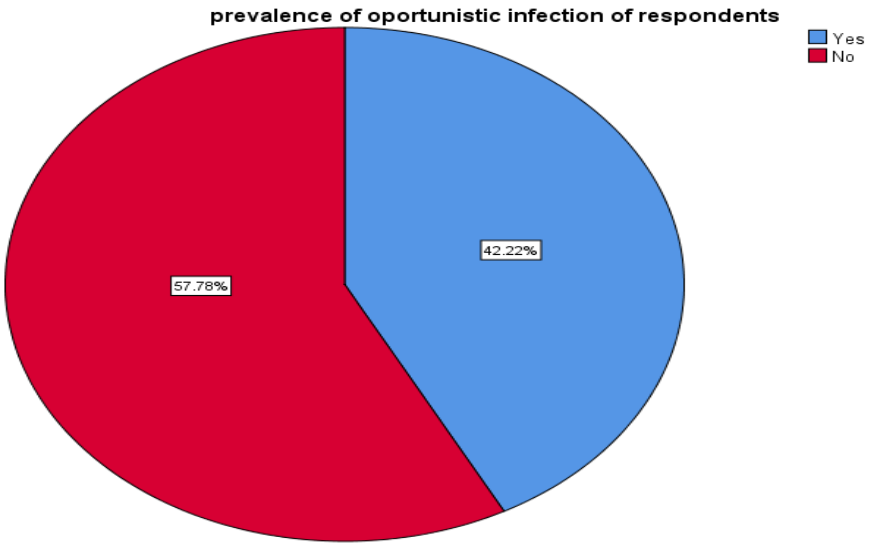

Figure 2:- Prevalence of opportunistic infections among HIV-infected adults on antiretroviral therapy in Woldia comprehensive specialized hospital, 2023

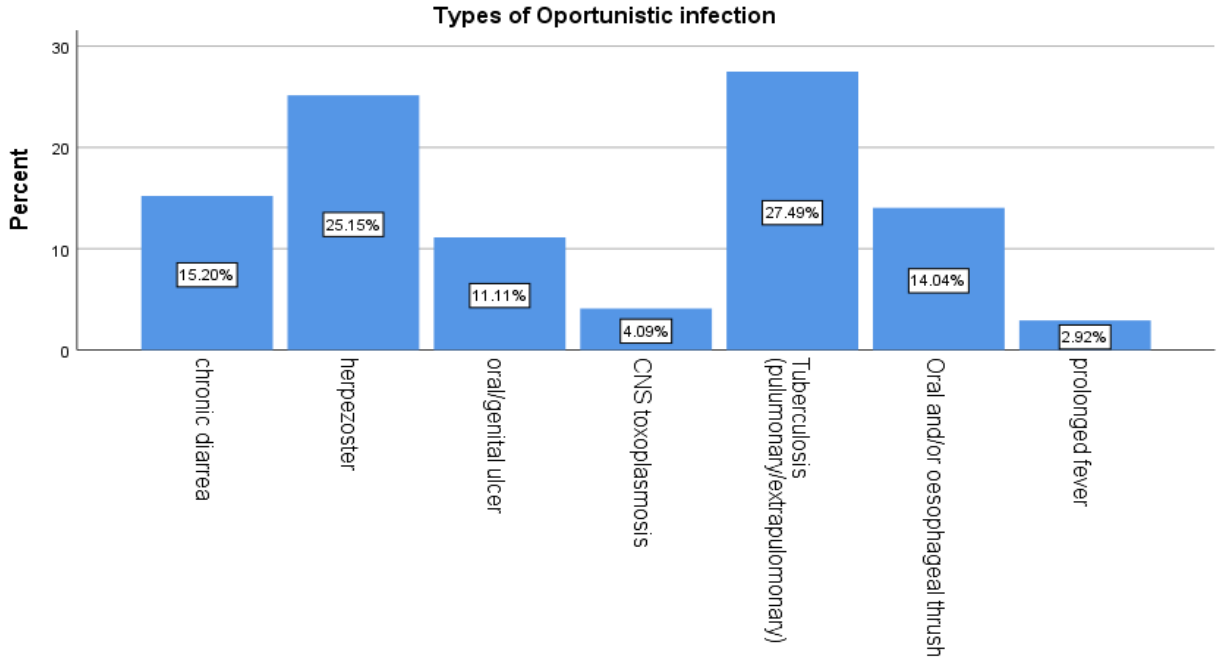

Figure 3:- Common opportunistic infections among HIV-infected adults on antiretroviral therapy in Woldia comprehensive specialized hospital, 2023

Associated Factors for Opportunistic Infections

In the multi-variable analysis age, chat chewers, initial CD4 count less than or equal to 200 cells/mm3, advancing WHO clinical stage III, stage IV and being ambulatory were found to be factors associated with occurrence of opportunistic infections. This study result shows that the odds of the occurrence of opportunistic infections among HIV-infected adults on antiretroviral therapy who were within the age group 30-39 years were 3.46 times more likely to develop OIs [AOR = 3.46; 95% CI: 1.78–6.73], 40-49 years were 2.47 time more likely to develop OIs [AOR = 2.47; 95% CI: 1.21 –5.04], and age greater or equal to 50 years were 3.09 time more likely to exposed to OIs [AOR = 3.09; 95% CI: 1.19–8.03] compared with younger age. The odds of the occurrence of opportunistic infections among HIV-infected adults on antiretroviral therapy who were chat chewers were 1.72 times more likely to develop OIs than compared to their counterparts [AOR = 1.71, 95% CI: 1.07– 2.76]. Similarly the odds of the occurrence of opportunistic infections among HIV-infected adults on antiretroviral therapy who were in the WHO clinical Stage III were 4.63 times more likely to exposed to OI higher as compared to those who were in the WHO clinical Stage I[AOR = 4.63, 95% CI: 2.67–8.04]. In addition, the odds of the occurrence of opportunistic infections among HIV-infected adults on antiretroviral therapy who were in the WHO clinical Stage IV were 6.63 times more likely to be exposed to OIs as compared to those who were in the WHO clinical Stage I[AOR= 6.63; 95% CI, 3.29-13.35]. Furthermore, HIV-infected adults on antiretroviral therapy with initial CD4 count less than or equal to 200 cells/mm3 were 1.91 times more likely to develop OIs as compared to those with CD4 cell counts > 200 cells/mm3 [AOR = 1.91, 95% CI: 1.15–3.18] and being ambulatory functional status of HIV-infected adults on antiretroviral therapy were 2.18 times more likely to develop OIs as compared to working [AOR= 2.18; 95% CI, 1.02-4.63] (Table 6).

Table 5:- Multi-variable logistic regression analysis of prevalence of OI and associated factors among HIV-infected adults on antiretroviral therapy in Woldia comprehensive specialized hospital, 2023(n=405)

Variable		Opportunistic infection		COR 95% CI	AOR 95% CI
		Yes	No		
Age	18-29	24(26.4%)	67(73.6%)	1	1
	30-39	81(47.4%)	90(52.6%)	**2.512(1.44, 4.37)***	**3.46(1.78, 6.73)****
	40-49	46(43.4%)	60(56.6%)	**2.140(1.170, 3.916)***	**2.47(1.21, 5.04)****
	>=50	20(54.1%)	17(45.9%)	**3.284(1.480, 7.289)***	**3.09(1.19, 8.03)****
Educational	Unable to read and write	75(42.1%)	103(57.9%)	.850(.274, 2.631)	1.142(.279, 4.676)

status	Able to read and write	21(31.8%)	45(68.2%)	.544(.163, 1.821)	.807(.185, 3.513)
	Primary school	37(56.9%)	28(43.1%)	1.542(.466, 5.097)	2.277(.517, 10.034)
	Secondary school	32(38.6%)	51(61.4%)	.732(.226, 2.374)	1.215(.281, 5.263)
	College/university	6(46.2%)	7(53.8%)	1	1
Sex	Male	65(43.0%)	86(57.0%)	1	1
	Female	106(41.7%)	148(58.3%)	.948(.631, 1.424)	.995(.591, 1.675)
Income	<=1000	131(41.2%)	187(58.8%)	.613(.328, 1.147)	.604(.277, 1.318)
	1001-1999	16(38.1%)	26(61.9%)	.538(.229, 1.266)	.512(.179, 1.464)
	>= 2000	24(53.3%)	21(46.7%)	1	1
Chewing chat	Yes	88(48.4%)	94(51.6%)	**1.579(1.061, 2.351)***	**1.72(1.07, 2.76)****
	No	83(37.2%)	140(62.8%)	1	1
WHO Clinical staging	Stage I	45(24.3%)	140(75.7%)	1	1
	Stage II	15(36.6%)	26(63.4%)	1.795(.875, 3.683)	1.618(.726, 3.606)
	Stage III	71(60.2%)	47(39.8%)	**4.7(2.854, 7.738)***	**4.63(2.67, 8.04)****
	Stage IV	40(65.6%)	21(34.4%)	**5.93(3.169, 11.081)***	**6.63(3.29, 13.35)****
BMI	<= 18.49	75(52.1%)	69(47.9%)	1.304(.381, 4.467)	1.153(.257, 5.18)
	18.5- 24.99	91(36.4%)	159(63.6%)	.687(.204, 2.313)	.642(.147, 2.81)
	>=25	5(45.5%)	6(54.5%)	1	1
CD4 count	<=200	74(60.7%)	48(39.3%)	**2.956(1.907, 4.583)***	**1.91(1.15, 3.18)****
	>200	97(34.3%)	186(65.7%)	1	1
Functional status of HIV-infected adults on ART	Working	132(39.6%)	201(60.4%)	1	1
	Ambulatory	26(57.8%)	19(42.2%)	**2.084(1.109, 3.916)***	**2.18(1.02, 4.63)****
	Bedridden	13(48.1%)	14(51.9%)	1.414(.644, 3.104)	1.414(.590, 3.390)

****statistically significant**

7. Discussion

This facility-based cross-sectional study revealed the prevalence of opportunistic infections and associated factors among HIV-positive patients taking ART at Woldia comprehensive specialized hospital. The current study found that the prevalence of opportunistic infections was 42.2% (95% CI; 37.4 - 47.2). This study result is consistent with the study findings in Wolaita Zone, Southern Ethiopia 43.3% (45), Debre-Markos 42.8% (46) and Uganda 43% (47). The similarity may be due to the same information access to opportunistic infection and access to health care (29). However this finding was lower than studies in Taiwan 47.6% (48) and in eastern Ethiopia 48% (49), and in Nigeria 61.7% (50). This different result among different studies could be explained by the discrepancy in health care awareness of the population and variation in the degree of host immunity and may be due to methodological difference in selecting participants or due to sample size variation (51). However, it is higher than when compared to, similar studies carried out in Ethiopia in Gondar, which reported 19.7% (28), 22.4% Nigeria (50). The discrepancy might be due to high exposure to infectious agents, the accessibility of higher health facilities, social-economic status, drug resistance, immunity and nutrition, may affect the magnitude of OIs (27).

Major identified opportunistic infections were tuberculosis (both pulmonary and extra-pulmonary) 27.5%, Herpes zoster 25.2%, chronic diarrhea 15.2% and oral and/or esophageal thrush 14.04%. In line with this a study in Gondar (28) showed that TB as the commonest OI followed by oral candidiasis and diarrhea were the major OIs encountered by HIV-infected patients. A study conducted in Debre-Markos (46) in their study found that oral candidiasis, chronic diarrhea, and TB as common types of OI. Another study in Dawro zone showed that the common co-infections/OIs were TB followed by oral candidiasis (29), while study conducted in Addis Ababa showed that the most common OIs were oro-pharyngeal candidiasis followed by TB (32). This might be because of their diagnosis is relatively easy to identify from patients than other OIs and also could be due to difference in laboratory detection, CD4 level, and patient drug adherence (29, 46).

A number of factors have been associated with the occurrence of OIs. One of the factors associated with occurrence was the patient's age. These study results revealed that advancing in

ages were exposes HIV positive people to OIs as compared with younger age. Being age 30-39 years, 40-49 years and > =50 years were associated with OI occurrence. This finding is in line with several previous studies (52, 53). Although scientific evidence suggests that several physiological and biochemical protective factors deteriorate with increasing age, further research needs to be conducted to determine the exact effect of age on the development of OIs. 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 (27, 29). However, in contrast to this finding, a study in Tanzania found that as the age of the patient increases, the risk of acquiring an OI will decrease (17).

Those patients with initial CD4 count less than or equal to 200 cells/mm3 were more likely to developed OIs as compared with higher CD4 count. This study finding agrees with the studies conducted in eastern Ethiopia (16), and the Amhara region, Ethiopia (54). This might be due to the low body defense mechanism which favors the OIs. This finding sounds true since CD4 cells play a central role in the activation of both hormonal and cellular immune response to fight against infection. Hence, low CD4 count increases susceptibility to OIs (16). This implies that HIV-positive adults need more attention on counseling for early initiation of ART and took their ART drugs as prescribed reduce exposure to the OI s (27, 29).

This study result showed that chat chewing was more likely to expose to OIs. Similarly studies done in Northwest Ethiopia (46), and eastern Ethiopia (16) showed that chat chewing was more likely to expose to OIs . The possible reasons may be, chewing Chat causes malnutrition due to poor appetite and it affects health-seeking behavior by temporary relief. This may be due to unclean and raw harvested chat which grows on unclean environment which was not free from open defecation and can lead to more exposure to the OIs. Another possible reason may be people who chew chat spent more money and time which may lead to economic problems to afford well-nourished foods and affects health-seeking behavior by temporary relief. This suggest why health officials and health-care providers should act by using different strategies to occurrence of the reduce the infection and consequences of the OIs among HIV-positive adults (27, 46).

In addition, functional status of patients was strongly associated with increased morbidity with opportunistic disease. This study revealed that clients with ambulatory were more likely to

develop OIs as compared to working functional status. Similar study conducted at Hiwot Fana Hospital, Eastern part of Ethiopia (16), and national level cross sectional study in Ethiopia (55). These study reports opportunistic diseases are significantly associated with PLHIV being bed ridden or ambulatory. This could be explained by lack or limited mobility of patients who may begin to lose interest in eating because they are not getting enough stimulation on a regular basis and unable to care for themselves, which can further result in compromised immunity their by putting them at risk of developing OIs. (55).

WHO clinical staging is also the significant predictor of opportunistic infections according to the finding of the present study. HIV-infected patients in stage III and stage IV were more likely to develop opportunistic infections than those who were in WHO Stage I. This finding of the study is consistent with other studies conducted in other parts of Ethiopia, namely; Bahir Dar (56), Eastern Ethiopia (16), Arbaminch (57), Gondar (28) and Debre-Markos (46). Similar finding were also observed in a study conducted in Nigeria showing that advanced WHO clinical stage at baseline to be an independent clinical risk factors for the occurrence of OIs (50). This could be because of lower immunity as WHO clinical staging is higher those further predispose for different types of OIs. Majority of HIV-infected adults on antiretroviral therapy also start treatment at their advanced stage of AIDS that will be difficult to reverse the stage easily with treatment. In addition, severity of HIV progression (WHO HIV clinical stage III and IV) makes an increasing susceptibility of infection and depends on patients' degree of immunosuppression (16, 50).

Limitations of the Study

The hospital 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. Viral load test for HIV-infected adults on antiretroviral therapy is incomplete and not done regularly. So, the immunological conditions of the HIV-infected adults on antiretroviral therapy were not assessed. Documentation and determination of the viral load had important factor for knowing further distribution of OIs. A prospective study was not done because prospective studies take very long time, costly and need more resources.

8. Conclusion and Recommendation

8.1 Conclusions

In this study, a high rate of OIs was observed compared with previous studies. This suggests that OIs remain a challenge in patients receiving ART in Ethiopia. The most common opportunistic infections were of tuberculosis (pulmonary and extra-pulmonary), herpes zoster, chronic diarrhea and oral and/or esophageal thrush. Advancing age, chat chewing, initial CD4 count, advancing WHO clinical stage III, stage IV and being ambulatory were found to be factors associated with the occurrence of opportunistic infections among people living with HIV.

8.2. Recommendations

Interventions need to be designed to promote early HIV testing and early enrollment of HIV-infected individuals into ART services. The ART clinic health professionals need to have given attention to older age , WHO clinical stage III and IV, being ambulatory HIV-infected adults on antiretroviral therapy and initial CD4 count less than or equal to 200 cells/mm^3 for proper diagnosis and management of the prevalent OIs. TB of all forms has high contribution to the disease burden and it is the leading OI presenting in 27.5% of the HIV-infected adults on antiretroviral therapy. Therefore, strengthening of the implementation of the TB/HIV collaboration activity is of vital importance.

To:- North Wollo Health Department

Need to look and have a policy or guideline to tackle morbidity and mortality due HIV-related to opportunistic infections. Because of opportunistic infection problems are very common among HIV/AIDS adults on ART attention needs to be given to opportunistic infection treatment facilities.

To :- Woldia Comprehensive Specialized Hospital

Close monitoring and evaluation of health workers as well social workers about how to give opportunistic infection counseling for people living with HIV. Update health professional's skill of HIV treatment protocol in relation to opportunistic infection.

To:- Health workers managing people living with HIV/AIDS

Consistent and proper diagnosis and treatment of OI should be a vital part of HIV management and a prerequisite to the planning of general care and support for people living with HIV. Early initiation of HAART and early treatment of opportunistic infection and HIV related infections are very important for the reduction of morbidity and mortality in people living with HIV.

To:- Study subjects

They have to take medical care as soon possible when they get sick, close follow up regularly when they have low CD4 count, WHO clinical stage III and IV, having aging, avoiding chat chewing and follow the health professional advice.

To:- Researchers

Further study is recommended to conduct comparative study and clinical study that could discover more risk factors for opportunistic infection.

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10. Appendices

10.1. Appendix 1. Participants informed consent form (English version)

Introduction

My name is ----------. I am a student at Woldia University, who is doing a research for the partial fulfillment of master's degree in public health at Woldia University. This questionnaire is intended to assess the magnitude of opportunistic infection and associated factors in HIV-infected adults on antiretroviral therapy at Woldia referral hospital, North, Wollo, Ethiopia.

Research title: Prevalence of opportunistic infections and associated factors among HIV-infected adults on antiretroviral therapy in Woldia referral hospital, North Wollo, Ethiopia, 2023

Purpose: purpose of the project is to identify the prevalence and associated factors affecting the occurrence of opportunistic infection in HIV infected adults on ART. The other purpose is for the fulfillment of my master degree in public health. The information you provide here will be very helpful to the investigator of this study to write a research paper for the requirement in completion of master's program. The finding of this project could help in designing priority intervention strategies for better management of opportunistic infection that enables to meet much more planned management and prevention of opportunistic infection.

Duration of the study period: From January 16, 2023 to February 16, 2023 G.C

Benefit and Risks: By participating in this study and answering our questions, you will not receive any direct benefit. However, the information will help the researcher to understand factors influencing the occurrence of opportunistic infection in order to appropriately identify future interventions related to problem to be found. You in this study will not involve any risks. If a question makes you feel uncomfortable, you may choose not to answer.

Confidentiality: you will not be asked your name on to be written the survey questions. All the information you give to us will be kept private. Whatever information you provide will be kept strictly confidential. The information you give will be kept in a locked file cabinet. Only the researcher will have access to see the answers you give. No information identifying you will ever be released to anyone outside of this data collection activity.

Participation: participation in the survey is completely voluntary. If you are not comfortable in answering any question(s), you can leave it blank. You can stop filling out the questionnaire at any time without giving a reason and your relationship with the community or any other body will not be affected in any way.

Address of principal investigator

Name: BirhanAsefe phone no: 0930980948 E-mail: ----------

Address of advisor

Name: AYELIGN MENGESHA phone no_____ e.mail_____

I thank you in advance for taking your time to answer questions. Would you be willing to participate in the study?

If yes, I am inn advance to ask you.

If no, please stop here.

Consent to the participants

I the undersigned have been informed that the purpose of this research project. Based on the above information I agree to participate in the research voluntarily.

_____ _____

Signature of participant date

10.2. Appendix II: questionnaire English

Questionnaire English version

Health facility---------- interviewer no----------interviewee no----------

Date of interview----------

Part I socio demographic conditions

Code	Questions	Possible responses	Skip to question
101	Age	--------	
102	Residence	1. Rural 2. Urban	
103	What is your ethnicity?	1. Amhara 2. Tigrie 3. Oromo 4. Afar 5. Others(specify)----------	
104	Occupation	1. House wife 2. Merchant 3. Daily laborer 4. Government employee 5. Private employee 6. Student 99. Others (specify)----------	
105	Religion	1. Muslim 2. Orthodox	

		3. Protestant 4. Catholic 99. Others (specify)----------	
106	Educational status	1. Illiterate 2. Able to read and write 3. Primary school 4. Secondary school 5. Grade 12 complete 6. College and above	
107	Sex	1. Male 2. Female	
108	Family size	---------	
109	Income	----------birr/monthly	
110	Marital status	1. Single 2. Married 3. Widowed 4. Divorced 5. Separated 99.Others(specify)_____	

Part II: Behavioral and environmental factors

Code	Questions	Possible response	Skip to question
201	Do you drinking alcohol?	1. Yes	

		2. No	
202	Chewing chat	1. yes 2. no	
303	Smoking	1. yes 2. no	
204	Condom use	1. Yes 2. No	
205	Floor of living house	1. Mud 2. Cement 3. Wood 99. Other(specify)----------	
206	Latrine available	1. Yes 2. no	
205	Source of water for drink	1. Pipe 99. others(specify)-------	
208	Living with domestic animals and pets	1. Yes 2. No	

Part III. Medical condition of the participants

Code	Questions	Possible response	Skip to
301	Are you starting ART?	1.Yes 2.No	If no go to 303
302	If yes for Q 301 what is the duration of starting ART	_____month	

	treatment (in month)		
303	Functional status	1. Working 2. Ambulatory 3. Bedridden	
304	CD4 count (data collector will fill this)	----------cells/mm3	
305	WHO Clinical staging (data collector will fill this)	1. Stage I 2. Stage II 3. Stage III 4. Stage IV	
306	Adherence to ART(data collector will fill this)	1. Good 2. Fair 3. Poor	
307	Base line hemoglobin gm/dl(data collector will fill this)	--------	
308	Taking cotrimoxazole prophylaxis	1. Yes 2. No	
309	Taking ionized prophylaxis	1. Yes 2. No	
310	Weight (data collector will fill this)	----------kg	
311	Height (data collector will fill this)	----------meter	
312	Opportunistic infection now or before?	1. yes 2. no	If no go to question no 413

313	If yes for question no 411 which type of opportunistic infection does the client have? (Data collector will look at the card and do physical examination to fill and more than one answer possible)	1.Chronic diarrhoea > 1month 2.Herpezoster 3. Oral/Genital ulcer 4.CNS toxoplasmosis 5.Tuberculosis 6.Oral candidiasis and/or oesophageal thrush 7.Prolonged fever >1month 99.Other (specify).....	

Thank you!!!

10.3. Annex 3. Amharic version questionnaire

አማርኛ መጠይቅ

የመረጃና የስምምነት ውልቅፅ

ሀ. መግቢያ-

ጤናይስጥልን!---------እባላለሁ።ወልድያ ዩኒቨርሲቲ የህብረተሰብ ጤና ተማሪ ስሆን አሁን የሁለተኛ ዲግሪ ማሟያ ጥናታዊ ፅሑፍ/ምርምር/ በማድረግ ላይ እገኛለሁ። ይህ መጠይቅ የተዘጋጀው በወልድያ ሆስፒታልውስጥበመሄድየጸረኤችአይቪኤድስህክምናአገልግሎትተጠቃሚዎችንየተጓዳኝበሽታችግርስርጭት ንማወቅናተያያዥምክንያቶችንለማወቅቃለመጠይቅእያደረግሁኝእገኛለሁ።እርስዎምየጥናቱተሳታፊይሆኑዘ ንድተመርጠዋል።

የምርምሩ/የጥናቱርዕስ፡-

በወልድያሆስፒታልውስጥበመሄድየጸረኤችአይቪኤድስህክምናአገልግሎትተጠቃሚዎችንየተጓዳኝበሽታችግ ርስርጭትንመጠንማወቅናተያያዥምክንያቶችንለመለየት

የጥናቱዓላማ፡-

በወልድያሆስፒታልውስጥበመሄድየጸረኤችአይቪኤድስህክምናአገልግሎትተጠቃሚዎችንየተጓዳኝበሽታችግ ርስርጭትንመጠንማወቅናተያያይዥነትያላቸውነገሮችንመዳሰስሲሆንበሚገኝውምየጥናትውጤትምችግሩ ንለመቅረፍየሚያስችሉትንስልቶችንማመላከትይሆናል

ሌላዉአላማበህብረተሰብጤናየሁለተኛድግሪማሟያፅሑፍለማቅረብሲሆንእርሰዎየሚሰጡንመረጃነዉ።የተ ጓዳኝበሽታችግርዙሪያለሚሰሩአካላት/ሀላፊዎች/ ዕቅድ፤ ዝግጅትና ትግበራ ላይ ማሻሻያ ለማድረግ አስፈላጊነቱ የላቀይ ሆናል።

የጥናቱጊዜ፡-ጥናቱ ከጥር 16/2014 እስከጥ የካቲተ 16 /2015ዓ.ም.ይካሄዳል።

አተገባበር፡-

ከላይየተመለከተዉንጥናትለማካሄድየተለያዩጥያቄዎችይኖሩናል።ጥናቱውጤታማሊሆንየሚችለውዕርስዎ

በሚሰጡትትክክለኛመልስላይበመሆኑጥያቄዎቹንበጥንቃቄእንዲመልሱልንፍቃደኝነትዎንበትህትናእንጠይ
ቃለን።ተጋብዘዋል።በፕሮጀክቱለመሳተፍፈቃደኛከሆኑውሉሊገባዎትናሊፈርሙይገባል።ከዚያምበመረጃሰብ
ሳቢዎችጥቂትደቂቃዎች (ሰላሳ)
ለሚወስዱጥያቄዎችመልስእንዲሰጡበአክብሮትይጠየቃሉ።ለእያንዳንዱጥያቄለሚሰጡትምላሽማንምበማ
ያገኘውመለያቁጥርሚስጥራዊነቱየተጠበቀይሆናል።

የጥናቱጥቅምናጉዳት፡-

እርስዎበዚህጥናትተሳታፊበመሆንዎበቀጥታሊያገኙየሚችሉትነገርላይኖርይችላል።በዚህጥናትበመሳተፍዎ
ምንምዓይነትጉዳትአይደርስብዎትም።በመጠይቁውስጥለመመለስየማይፈጉትጉዳይካለምምላሽእንዲሰጡ
አይገደዱም።

<u>ምስጢራዊነት</u>፡-

እርሰዎየሚሰጡትማንኛዉምዓይነትመረጃምስጢራዊነቱየተጠበቀሲሆንየርስዎምስምበመጠይቁላይእንዲ
ፃፍአይጠየቁም።

ተሳትፎ፡-

በዚህጥናትላይመሳተፍ/አለመሳተፍ/ሙሉበሙሉበርስዎፈቃደኝነትላይየተመሰረተነዉ።ለሚጠየቁትጥያቄ
ዎችሁሉይመልሳሉብዬተስፋአደርጋለሁ።ነገርግንከሚጠየቁትጥያቄዎችለተወሰኑትአሊያለሁሉምመልስያለ
መመለስመብትአለዎት።እንዲሁምያለምንምቅጣትናመብትመጓደልበፈለጉሰአትጥናቱንየማቋረጥሙሉመ
ብትአለዎት።

በጥናቱተሳታፊለመሆንፍቃደኛነዎት?

አዎ---------- አዎከሆነይቀጥሉ

አይደለሁም ---------- አመስግነውወደሚቀጥለውተሳታፊይሂዱ.

የቃለ-ምልልስቁጥር (ኮድ)_____

መረጃውንየሰበሰበውባለሙያስም----------ፊርማ------ ቃለምልልሱየተካሄደበትቀን ____

ክፍልአንድ : ማህበራዊናኢኮኖሚያዊሁኔታመጠይቆች

መለያኮድ	ጥያቄዎች	ለጥያቄውመልስሊሆንየሚችሉአማራጮች	ወደቀጣይእለፍ
101	እድሜ?	------ አመት	
102	መኖሪያ ቦታ	1. ገጠር 2. ከተማ	
103	ስራዎ?	1. የቤትእመቤት 2. ነጋዴ 3. የቀንሰራተኛ 4. የመንግስትተቀጣሪ 5. መንግስታዊያልሆነድርጅት 6. ተማሪ 99. ሌሎች (ይግለጥ)------	
104	ብሄርዎምንድንነው?	1. አማራ 2. አፋር 3. ትግራይ 4. ኦሮሞ 99. ሌላ (ይገለፅ) -----	
105	ሃይማኖትዎምንድንነው ?	1.ሙስሊም 2. ኦርቶዶክሰ 3. ፕሮቴስታንት 99 ሌሎች(ያብራሩ) ------	
106	የትምህርትደረጃዎ?	1. ያልተማረች 2. መፃፍናማንበብየምትችል 3. አንደኛደረጃያጠናቀቀ 4. 2ኛደረጃያጠናቀቀች 5. 12 ኛክፍልያጠናቀቀ 6. ኮሌጅናከዚያበላይ	

107	የጋብቻሁኔታ	1. ያላገባች 2. ያገባች 3. የሞተባት 4. የተፋታች 5. ሌላካለይግለጽ----------	
108	ጸታ	1. ወንድ 2. ሴት	
110	የወርገቢ	----------ብር	

ክፍል 2: ስነ-ባህሪእናአካባቢያዊሁኔታዎች

ኮድ	ጥያቄ	ለጥያቄውመልስሊሆንየሚችሉአማራጮች	ወደቀጣይእለፍ
201	አልኮልይጠጣሉ?	1. አዎ 2. አይ	
202	ጫትይቅማሉ?	1. አዎ 2. አይ	
203	ሲጋራያጨሳሉ?	1. አዎ 2. አይ	
204	ኮንዶምይጥቀማሉ?	1. አዎ 2. አይ	
205	የመኖሪያቤትወለል	1. ጭቃ 2. ሲምንቶ/ 99. ሌላካለይገልጽ	
206	መጸዳጃቤት	1. አለ 2. የለም	
207	የመጠጥዉሀምንጭምንድንነዉ	1.ቧንቧ	

		99. ሌላካለ(ይግልጹ)-------	
208	ከቤትእንሰሳናከቤትእንሰሳጋርመኖር	1.አዎ 2. አይ	

ክፍል 3. ያለፈውናያሁኑየበሽተኛውሁኔታዳሰሳ

ኮድ	ጥያቄ	ለጥያቄውመልስሊሆንየሚችሉአማራጮች	ወደቀጣ ይእለፍ
301	የፀረ-ኤችአይቪመድሃኒትጀምረዋል	1. አዎ 2. አይ	አይከሆነ ወዴ 303 ይለፉ
302	የጸረኤችአይቪህክምናከጀመሩስንትጊዜሆ ነዎት (በወራት)	----------ወራት	
303	የበሽተኛውየመስራትአቅም	1. መስራትየሚችል 2. ተንቀሳቃሽ 3. የአልጋቁራኛ	
304	የ CD4 መጠንስንትነው	----------cells/mm3	
305	በአለምጤናድርጅትየህመምተኞችደረጃ መስፈርትመሰረትበአሁኑጊዜየበሽተኛው ደረጃስንትነው(በመረጃሰብሳቢውየሚሞላ)	1. ደረጃ 1 2. ደረጃ 2 3. ደረጃ 3 4. ደረጃ 4	
306	ጸረ-ኤችአይቪመድሀኒትጀምረውከሆነከመድ ሀኒቱጋርየለዎትቁርኝትምንይመስላል	1. ጥሩቁርኝት (Good adherence) 2. መካከለኛቁርኝት (Fair adherence) 3. ደካማቁርኝት (Poor adherence)	
307	ሄሞግሎቢንgm/dl	--------	
308	ኮትሮሞዛዞልይወስዳሉ	1.አዎ	

		2. አይ	
309	አይሶኒያዝድይዎስዳሉ	1. አዎ 2. አይ	
310	ክብደት	----------ኪግ	
311	ቁመት	----------ሜትር	
312	ተጓዳኝበሽታይዞዎትነበር	1. አዎ 2. አይ	አይከሆነ ወዴ 314 ይለፉ
313	አዎከሆነመልሶየትኛውአይነትተጓዳኝበሽታነበረብዎ (መረጃሰብሳቢውየበሽተኛውንካርድበማትና የአካል ምርመራ በማድረግ ይሞላል)	1. የቆየተቅማጥ> 1 ወር 2. ሄርፐዞስተር 3. የአፍ/የብልትቁስለት 4. የጭንቅላትቶክሶፕላስሞሲስ 5. የሳንባነቀርሳ (ቲቢ) 6. የአፍውስጥወይምየጉሮሮፈንገስ 7. የቆየትኩሳት>1 ወር 99. ሌላካለይገለጽ	

ስለሰጡኝመልስአመሰግናለሁ !!!!