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Magnitude of Opportunistic Infections and Associated Factors in Hiv Infected Adults on Art Among Patients Who Visited Tibebe Ghion Specialized Hospital and Felegehiwot Comprehensive Specialized Hospital From September 12,2019 To September 10,2021 Bahir Dar Ethiopia, 2022

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BAHIR DAR UNIVERSITY

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MAGNITUDE OF OPPORTUNISTIC INFECTIONS AND ASSOCIATED FACTORS IN HIV INFECTED ADULTS ON ART AMONG PATIENTS WHO VISITED TIBEBE GHION SPECIALIZED HOSPITAL AND FELEGEHIWOT COMPREHENSIVE SPECIALIZED HOSPITAL FROM SEPTEMBER 12,2019 TO SEPTEMBER 10,2021 BAHIR DAR ETHIOPIA, 2022

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Declaration

I, the under signed, declared that this is my original work, has never been presented in this or any other University, and that all the resources and materials used for the research, have been fully acknowledged.

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Abstract

Background: Opportunistic infections are diseases that cause infections in individuals whose immune systems are compromised. Morbidity and mortality in HIV disease are due to immunosuppression leading to life-threatening opportunistic infections during the natural course of the disease. Human immune virus (HIV/ADIS), with which 36.7 million people were living and 2.1 million infected at the end of 2016, has been a major health problem throughout the world. The commonly reported opportunistic diseases in sub-Saharan Africa among HIV patients are Candidiasis, Pneumocystis carinii pneumonia, disseminated Mycobacterium avium complex infection, Cryptococcus, Kaposi sarcoma, herpes zoster, and tuberculosis

Methods: Institution based cross-sectional study design was applied based on patient record cards. The sample size was 384 and samples were taken by using simple random sampling method. Data were collected by a pre-tested checklist from the medical records of patients with 100% response rat. Data were entered and analyzed for descriptive and logistic regression models by SPSS version 26.0 statistical software. The result declared as statistically significant at $p < 0.05$.

Result: The overall Magnitude of opportunistic infections was 51.3%[95% CI: 46.4-56.5]. The major identified opportunistic infections were recurrent bacterial pneumonia 79 (20.6%), tuberculosis (pulmonary &/or EPTB) 59 (15.4%), candidiasis (Oral & esophageal) 56(14.6%) herpes zoster 38 (9.9%), and Chronic diarrhea 33 (8.6%).

On multivariate analysis, age group of 30-39 [AOR=2.70, 95% CI: 1.09, 6.67] and Being in baseline WHO stage of II, III or IV had 8.2 times **[**AOR=8.20, 95% CI: 3.63, 18.51**]**, 29.19 times [AOR=29.19, 95% CI: 12.40, 68.71] and 22.95 times **[**AOR= 22.95, 95% CI: 5.32, 99.01**]** increased risk of developing OI respectively.

Conclusion: In this study, the overall Magnitude of OIs is high (51.3%) when compared with other studies. This suggests that OIs remain a challenge in RVI patients in Ethiopia despite taking ART. Health officials and clinicians need to give attention to the strengthening of the provision of ART with prophylaxis on early WHO stage. Community awareness creation about the virus should also be facilitated.

Keywords: HIV; Opportunistic Infections; Antiretroviral Therapy

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Lists of Acronyms and Abbreviations

ART Anti Retroviral therapy

BMI body mass index

CDC Center for Disease Control

CKD chronic kidney disease

DM diabetes mellitus

EPTB extra pulmonary tuberculosis

FHCSH Felegehiwot Comprehensive Specialized Hospital

Hgb Hemoglobin

HIV human immunodeficiency virus

KS Kaposi sarcoma

MAC Mycobacterium avium complex infection

OI opportunistic infection

PCP Pneumocystis carinii pneumonia

PI principal investigator

PTB pulmonary tuberculosis

TGSH Tibebe Ghion Specialized Hospital

WHO world health organization

1. INTRODUCTION

1.1. Background of the Study

Opportunistic infections are diseases that cause infections in individuals whose immune systems are compromised[1, 2]**.**Morbidity and mortality in HIV is due to immunosuppression leading to life-threatening opportunistic infections during the natural course of the disease. 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[2, 3]**.**

HIV infection and OIs have bi-directional relationship [4-8]. Having HIV weakens the immune system and causes the risk of developing opportunistic infections. 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 [9-11]. Until effective antiretroviral therapy (ART) was developed, patients generally survived only 1 to 2 years after the initial manifestation of AIDS[9]. The advent of antiretroviral therapy (ART) reduces viral replication, increases the number of CD4 lymphocytes and improves their function, re-establishing the defenses of the host and improving chances of survival [2, 3, 12]. However, it is reported by different studies that there is still high prevalence of opportunistic infections among the HIV-infected patients receiving ART and those in the follow-up. Although, the incidence of opportunistic infections has decreased after the discovery of antiretroviral drugs, they remain an important problem in patients who are unaware of their HIV serologic status, in those not receiving ART, and even in those who are receiving ART due to poor adherence, failure and cross resistance[2, 4-8, 13, 14].

Starting in the late 1980s, the use of chemoprophylaxis, immunization, and better strategies for managing OIs improved quality of life and lengthened survival of persons with HIV. Early antiretroviral drugs and treatment strategies added further benefit. However, the introduction of highly effective combination ART in the mid-1990s has had the most profound influence on reducing OI-related morbidity and mortality in persons with HIV. Despite the availability of multiple safe, effective, and simple ART regimens, and a corresponding steady decline in the incidence of OIs, the Centers for Disease Control and Prevention (CDC) estimates that more than

40% of Americans with HIV are not effectively virally suppressed. As a result, OIs continue to cause preventable morbidity and mortality in the United States[9].

Durable viral suppression eliminates most but not all OIs. Tuberculosis, pneumococcal disease, and dermatomal zoster are examples of infectious diseases that occur at higher incidence in persons with HIV regardless of CD4 count. When certain OIs occur, most notably tuberculosis and syphilis, they can increase plasma viral load, which both accelerates HIV progression and increases the risk of HIV transmission. Thus, clinicians continue to need to be knowledgeable about the prevention and management of HIV related OIs[9].

1.2. Statement of the Problem

Human immune virus (HIV/ADIS), with which 36.7 million people were living and 2.1 million infected at the end of 2016, has been a major health problem throughout the world[15]. From the total people currently living with HIV worldwide, 52% reside in sub-Saharan Africa (SSA)[16].

The commonly reported opportunistic diseases in sub-Saharan Africa among HIV patients are Candidiasis, Pneumocystis carinii pneumonia (PCP), disseminated Mycobacterium avium complex (MAC) infection, Cryptococcus, Kaposi sarcoma, herpes zoster, and tuberculosis[17, 18].

Ethiopia is a country with a large percentage of HIV infected population with a total of 737,186 population living with HIV where the occurrence of opportunistic infection is considered as minor infections until they present with life-threatening complications[10].

Most of the states in Ethiopia have an HIV prevalence of 1% and more. For example, Gambella, Addis Ababa, Dire Dawa, and Harari have an HIV prevalence of 4.8%, 3.4%, 2.5%, 2.4%, respectively[11]**.**

Even though nationally representative and comprehensive data regarding the magnitude of opportunistic infections lack in Ethiopia, some regional studies have shown the prevalence ranging from 19.7% to 48%.14,16. The prevalence of OIs among HIV patients on ART is still high namely; oral candidiasis 11.8%, followed by chronic diarrhea, 9.9% and tuberculosis 9.7% at Debre Markos referral hospital in Ethiopian[7]

1.3. Significance of the Study

In developing countries including Ethiopia, the occurrence and determinant factors of opportunistic infections on ART receiving patients are not well studied and OIs remain the main causes of morbidity, mortality, and deterioration of clinical conditions.

In the previous studies, the effect of other co morbidities especially DM, CKD and chronic steroid use was not assessed. This study includes the possible impact of such co morbidities.

This study was designed to see the determinants of opportunistic infections in the study area and to minimize potential challenges. Health planners, researchers as well as clinicians can also get important insights from this work. The finding of this research can also be used as baseline data for other researchers interested in the area

1.5 Hypothesis

The factors such as demographic characteristics, baseline clinical condition of the patient and possible risk factors for opportunistic infection has no association with Magnitude of opportunistic infections in RVI patients who are on ART.

2. Literature review

Magnitude of opportunistic infections

In a report which included 126 different studies done in 38 countries in sub-Saharan Africa, Asia, and Latin America, During the first year of ART, the risk of all OIs declined to <2%,except for unspecified tuberculosis (4.2%), PTB (3.5%), herpes zoster (2.3%), and oral candidacies (2.3%), which remained the most common OI. In Meta regression analysis of those studies, it is found that the greatest effect of ART was seen during the first year of treatment, and ranged from a 57%–91% reduction. There were few studies providing information on risk after the first year of ART except for unspecified tuberculosis and PTB. The magnitude of effect of ART during the first year was greatest for oral candidacies , cerebral toxoplasmosis, and PCP [19].

A study done in china reviewed total of 954 cases of HIV infection, and found that bacterial pneumonia (25.8%) was the most common OIs, followed by Candida infection (18.3%), *Pneumocystis jiroveci* pneumonia (11.9%), tuberculosis (11.5%), infectious diarrhoea (9.3%), Cryptococcus infection (7.3%), *cytomegalovirus* infection (4.9%), toxoplasmosis (4.6%), hepatitis C (4.0%), nontuberculous mycobacteria desease (2.2%) and *Penicillium marneffei* infection(0.3%)[20].

A study which was done in Nigeria, Out of 339 patients, 76 had diagnosed OIs giving an overall prevalence of 22.4%. There were a total of 96 opportunistic infections diagnosed in the 76 patients. 55 (16.2%) patients had single OI, 20 (5.9%) had dual OIs while 1 (0.3%) had triple OIs. The most frequent conditions were candidiasis, 29 (8.6%); TB, 26 (7.7%); dermatitis 19 (5.6%); chronic diarrhea, 5 (1.5%); and sepsis 5 (1.5%). Bacterial pneumonia was diagnosed in 3 (0.9%) patients, cryptococcal meningitis, herpes zoster, genital herpes, and genital warts were each diagnosed in 2 (0.6%) patients while only 1 (0.3%) patient had Kaposi's sarcoma. In relative terms, candidiasis, TB and dermatitis, constituted 38.2%, 34.2%, and 25% of the OIs respectively[12].

A retrospective descriptive and analytical study carried out in 12 accredited HIV treatment centers in Cameroon, involving a total of 1,617 HIV-infected patients sampled, 419 (25.9%) had at least one OI[21].

In a retrospective study done in Dawro Zone hospital: Out of 744 individuals, 658 (88.4%) developed OIs, of which 232 (35.2%), 157 (23.9%), 146 (22.2%), and 123 (18.7%) developed 2, 3, ≥ 4, and 1 OI respectively. The spectrum of OIs was ranging from the common oral candidiasis to the life threatening CNS toxoplasmosis and the fungal cryptococcal meningitis. Pulmonary tuberculosis, 118 (18%) was the most common OI. Next to TB, Severe community acquired pneumonia (SCAP) 107 (16.3%) and oral candidacies 103 (15.6%) were the most common OIs in this study. Only 5 and 2 individuals were affected by Toxoplasmosis and KS respectively[22]

In a Comparative Cross Sectional Study done in Addis Ababa, The overall prevalence of opportunistic infections was found to be 33.6% and the prevalence of OIs among HIV patients on ART was 29.2%.Pulmonary tuberculosis was the most common opportunistic infection[23].

In a cross sectional study done on total of four hundred patients in southern zone of Tigray and parts of Amhara, 195 had diagnosed OIs, with an overall prevalence of 48.75% .There were a total of 221 OIs diagnosed in the 195 patients. About 41.5%, 13.75% of the study participants had single and multiple OIs, respectively. The most frequent OIs were oral candidacies and ulcers mouth, genital (11%) followed by herpes zoster 10.8% and tuberculosis at 9.5%[24].

A study done at Selected Public Hospitals in Sidama National Regional State showed that, The overall magnitude of opportunistic infections was 39.6%, and the Major identified opportunistic infections were oral candidiasis 96 (23.2%), recurrent bacterial pneumonia 89 (21.5%), herpes zoster 26 (6.3%), pulmonary tuberculosis 25 (6.0%), extrapulmonary TB 24 (5.8%), and Crypto coca meningitis 9 (2.2%)[25]

Risk factors for opportunistic infections

There was heterogeneity between the incidence of OIs across studies and regions, and the most important sources of heterogeneity were baseline CD4 count for cryptococcal meningitis (I2 = 56.4% for CD4 counts 200–499 cells/μL) and oral candidiasis (I2 = 54.9% for unspecified CD4 count), but no factor was identified that predominately explained the source of this heterogeneity. The use of CTX prophylaxis did not explain the heterogeneity in incidence of PCP or toxoplasmosis, where estimates of I2 were high for all categories of CTX exposure [19].

The socio-demographic variables that had significant positive association with the presence of OIs on univariate analysis included the following: age ≤ 40 years, household income ₦ 20,000 , and having >2 people per room . Although the risk of having OIs was higher in individuals with lower socio-economic status, the deference did not attain statistical significance. The risk of OIs did not significantly diff er according to gender, place of residence or marital status.

Occurrence of OIs had a significant positive association with duration of HIV diagnosis <3 years duration of HAART <36 months, and HAART non-adherence. The following baseline parameters were positively associated with increased risk of OIs: WHO clinical stage 3, CD4 cell count < 200 cells/µl, and hemoglobin <10 g/ dl . In addition, the risk of OIs was significantly higher in participants with the following current parameters: CD4 cell count <200 cells/µl , and hemoglobin <10 g/dl. The risk of OIs was higher in patients with BMI <25 kg/m2 but the deference was not statistically significant. There was no significant relationship between OIs and cotrimoxazole prophylaxis, diabetes, hypertension, alcohol consumption or smoking[12].

According to the study in Cameroon, There was a significant relationship between the male gender and the onset of OI. Age ≥ 50 years was associated with the occurrence of OI. and CD4 count of <200/mm3 was also associated with the risk of developing an OI[21].

According to the study done in Dawro Zone hospital , WHO stage , CD4 level, ART adherence and hemoglobin level showed significant association with OIs. PLHIV who are on WHO stage II–IV were 3 times more likely to develop OI than those who are on stage I. Poor adherence became a predictor for developing OI in which the odds of developing OI among those individuals who have poor ART adherence was three times higher than those who have good adherence [22].

Based on the findings of the study done Selected Public Hospitals in Sidama, The highest number of OIs and had statistically significant association on bivariable analysis were among older aged 35 or above years were 78 (50.6%), which followed by 66 (38.6%) were grouped b/n 25–34 years. Also, the highest magnitude of OIs among no formal education 15 (60.0%), attending elementary school 48 (47.1%), and 46 (48.9%) the study respondents who did not disclosed their HIV status to their family and relatives were exposed to OIs with P-value <0.05. In the multivariate analysis age of respondents, household monthly income, initial CD4 count,

education, had no extra medicine additional to ART (prophylaxis), taking ART medicines properly, and Khat chewing remained as the determinant of opportunistic infections. This study result shows that advancing in the age had about 3.5 times more exposed to develop OIs, as compared with younger age. No formal education had, more exposed to OIs as to their counterparts. Initial CD4 count less than 200 cells/mm3, the study participants who interrupt ART medicines and Khat chewing were more exposed to OIs when compared to their counterparts[25]

In the study done in Southern Tigray and parts of Amhara, the prevalence of OIs among males (54.0%) and females (56.4%) was comparable. The highest prevalence of OIs was found in those individuals divorced (79.3%), the age group of 18-29 and 30-39 years old (56.8%) (57.3%) respectively. more or less similar, with secondary school educational level (57.4%), rural dwellers (57.7%) and with body weight >60kg (59.0%). However, the prevalence of OIs was not statistically different among the above variables (P.0.05). In bivariate analysis, study participants in marital status, divorced were more likely to develop OIs than single and married, those secondary school, college and above were less likely to develop OIs. Concerning WHO clinical stages III and IV were more likely to develop OIs compared to those participants at WHO clinical stages I. Those participants with CD4 cell count of <200 cells/mm3 were more likely to develop OIs than their counterparts with higher CD4 cell count. Participants who were 50 and above years old age were more likely to develop OIs compared to patients 18-29 years old. In addition, participants who were >60kg weight were less likely develop OIs compared to their counterparts who were <60kg WHO clinical stage was significantly associated with the presence of OIs. The odds of college and above educational level were less likely to develop OIs compared to illiterate. The odds of having OIs in WHO clinical stage I were less likely to have OIs compared to WHO clinical stage III and V [24]

In the study done in Debre Berhan Referral Hospital, Drinking alcohol, BMI <18.5, previous history of opportunistic infections were independent predictors of opportunistic infections in people living with HIV/AIDS on HAART[26].

1. Conceptual Framework

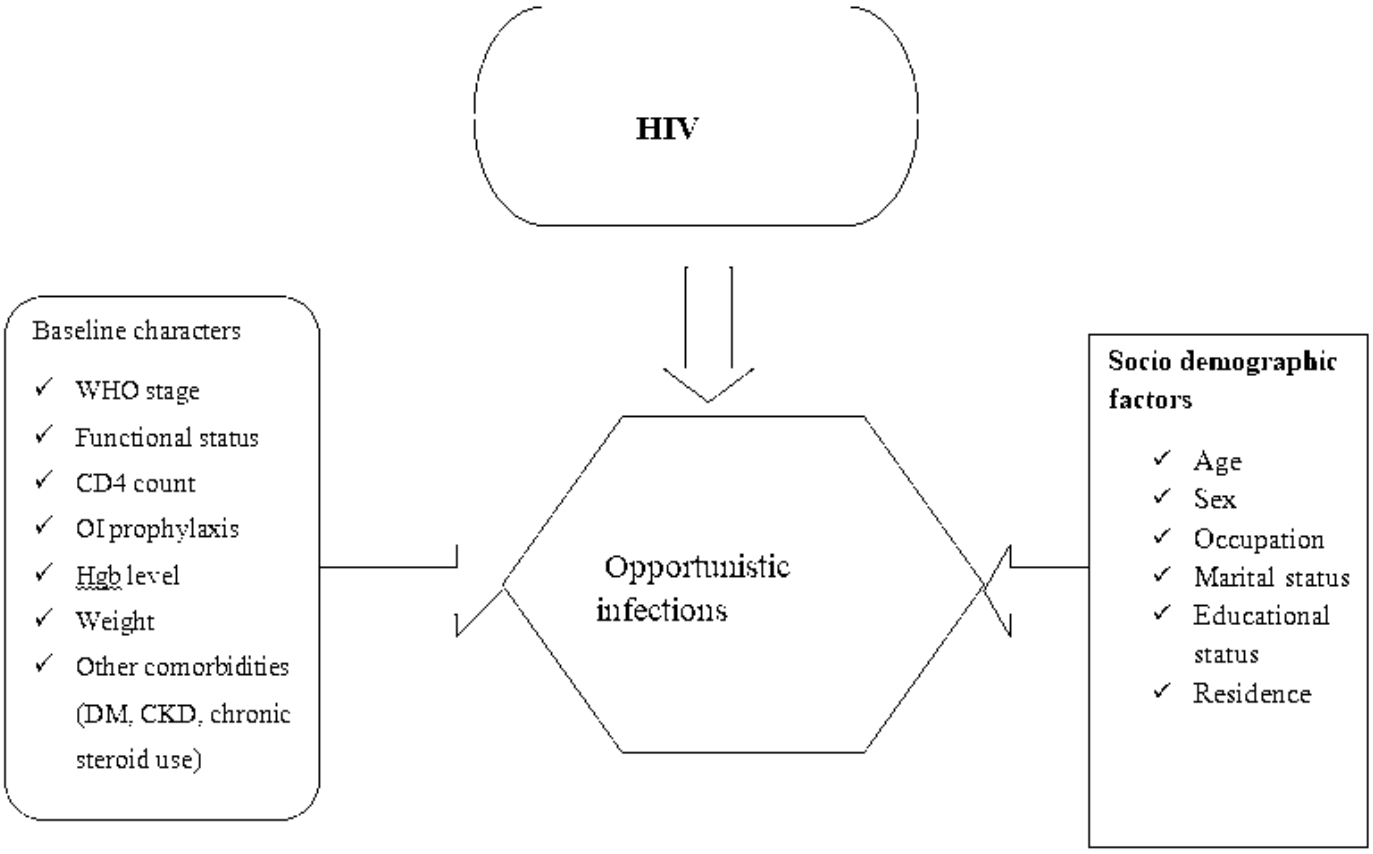

Figure 1 Conceptual frame work of proportion of OI and its associated factors among HIV patients who visited TGSH and FHCSH

4. Objectives of the study

4.1. General Objective

- ✓ To assess the Magnitude and associated factors of OIs in HIV infected adults on ART among patients who visited TGSH and FHRH from September 12,2019 to September 10,2021 Bahir Dar Ethiopia, 2022 G.C

4.2. Specific Objectives

- ✓ To determine the Magnitude of OIs in HIV infected adults on ART
- ✓ To identify associated factors those increase the magnitude of OIs

5. Methods

5.1. Study Design

Institution based cross-sectional study design was applied based on patient record cards from September 12, 2019 to September 10, 2021.

5.2. Study Area and Period

Bahir Dar is situated on the southern shore of Lake Tana, the source of the Blue Nile (locally called Abay). Bahir Dar city (one of the ten most beautiful cities in Africa and one of the twelve UNESCO Learning Cities Awardee of 2015) .The city is located approximately 565 km (360 miles) north-northwest of Addis Ababa, and an elevation of 1,840 meters (6,036 foot) above sea level. Tibebe Ghion specialized hospital is located about 10km south from the city center and about 7 km from the new bus station ('Addisu Meneharia') on the way to Adet District and about 23 km from the Blue Nile Falls (locally called 'Tis Esat' (Smoke of Fire). It is a tertiary university teaching hospital with 450 bed capacity. The hospital receives patients who are referred from across the Amhara region and gives outpatient and inpatient services in all major departments. Felegehiwot comprehensive specialized hospital is located in Bahirdar City.

The study was conducted in Tibebe Ghion Specialized Hospital and Felegehiwot comprehensive specialized hospital starting from August 2022 to October 2022.

5.3. Source Population

All HIV infected adults who visited TGSH and FHCSH from September 12, 2019 to September 10, 2021 were the source population.

5.4. Study population

All adults on ART among HIV infected adult patients who visited TGSH and FHCSH from September 12, 2019 to September 10, 2021 were the study population**.**

5.5. Inclusion Criteria

Patients on ART

Age ≥ 18 years

Those who had history of Admission to medical ward or started follow up at ART clinic or medical referral clinic and continued follow up at these two hospitals.

5.6. Exclusion Criteria

Those patients with incomplete records on their cards and who were lost from follow up were excluded.

5.7. Study Variables

5.7.1. Dependent Variables

- Magnitude of opportunistic infections in HIV/AIDS patients on ART at TGSH and FHCSH from September 12, 2019 to September 10, 2021

5.7.2. Independent Variables

- Age
- Sex
- Occupation
- Marital status
- Residence
- Educational status
- WHO stage
- Functional status
- Baseline CD4 count
- OI prophylaxis
- Baseline Hgb level.
- Baseline weight
- Other comorbidities(DM, CKD, chronic steroid use)

5.8. Sampling Size Estimation

The sample size was determined using computer-based Epi info7 software Stat Cal, by using Single population proportion formula used to determine the sample size with a 95% confidence interval within a 5% marginal error (W) and the magnitude from previous studies was 40%.So the sample was 349 and by assuming 10% non-response rate it became 384.

5.9. Sampling Technique

From a total of 6369 patients who visited TGSH and FHCSH from September 12, 2019 to September 10, 2021, 384 samples were taken by using simple random sampling method.

5.10. Data Collection Procedure

A checklist that measures the socio-demographic characteristics of patients, clinical information & type of OIs and risk factors was used to collect the data. As a result, the checklist was prepared based on feasibility to the objective. A pretest was done to see the practicability of the check list contents and parameters. The part that was not practical in the check list was removed.

5.11. Data Quality Assurance

The data was collected by the principal investigator. Data quality was assessed every day after data collection and it checked for completeness

5.12. Data Processing and Analysis

The principal investigator collected the data and incomplete documents were cleaned, checked for quality and Coding of different variables was carried out prior to data entry. Data entry, cleaning, and analysis were done by SPSS version 26.0 statistical software. Descriptive analysis including simple frequency distribution and the percentage was made to describe socio-demographic characteristics, clinical information & risk factors for OI, to determine the type and magnitude of the opportunistic infections. All factors were checked by bivariable logistic regression analysis, the variables with p-value <0.25 are candidates for multivariable logistic models to control confounding effects. The Hosmer-Lemeshow goodness-of-fit statistic was used to assess whether the necessary assumptions for the application of multiple logistic regression are fulfilled. Adjusted odds ratios (AOR) with 95% Confidence Intervals (CI) were calculated. Finally, p-value <0.05 was declared a significant association.

5.13. Operational definition

Other comorbidities: DM, CKD, chronic steroid use

Private business: merchant, farmer

Working: able to perform usual work in or out of the house; harvest, go to school

Ambulatory: able to perform activities for daily living;

Bedridden: not able to perform activities of daily living[27]

6. Results

Socio Demographic Characteristics of Participants

A total of 384 HIV-positive adults who were taking ART were enrolled in the study. Charts of those 384 adults were reviewed (response rate of 100%). More than half of the studied participants 201 (52.3%) were female and 142 (37%) in the age category of 30–39 years old. 199 (51.8%) of them were married and 342(89.1%) were living in Urban area.

Regarding educational status, 124(32.3 %) of them attended secondary school and 80 (20.8%) of them had no formal education

The occupational status of the participants, 159 (41.4%) of them run private business and 59 (15.4%) of them were daily laborer (Table 1).

Table 1: socio demographic characteristics of RVI patients on ART, who visited TGSH and FHCSH from September 12, 2019 to September 10, 2021, Bahirdar Ethiopia, 2022

Variable	Category	Frequency(n=384)	Percent (%)
Sex	Male	183	47.7
	Female	201	52.3
Age	18-29	71	18.5
	30-39	142	37.0
	40-49	114	29.7
	50 & above	57	14.8
Marital status	never married	67	17.4
	Married	199	51.8
	Divorced	84	21.9
	Widowed	34	8.9
Educational Status	no formal education	80	20.8
	primary school	118	30.7
	secondary school	124	32.3
	college/university	62	16.1
Occupational status	no work/house wife	95	24.7
	daily labor	59	15.4
	private business	159	41.4
	government employee	71	18.5
Residence	Urban	342	89.1
	Rural	42	10.9

The Magnitude of Opportunistic Infections

The overall Magnitude of opportunistic infections was 51.3% [95% CI: 46.4-56.5]. Those participants were found to be infected by one or more opportunistic infections. The major identified opportunistic infections were recurrent bacterial pneumonia 79 (20.6%), tuberculosis (pulmonary &/or EPTB) 59 (15.4%), candidiasis (Oral & esophageal) 56(14.6%) herpes zoster 38 (9.9%), and Chronic diarrhea 33 (8.6%) (Table3).

Associated Factors for Opportunistic Infections

The highest number of OIs with statistically significant association on bivariable analysis were among male sex 108(59%), age group of 30-39years 81(57%) & 40-49 years 64(56.14%). There is also the highest proportion of OIs among private business workers 90(56.60%) and daily laborers 33 (55.93%). Among the risk factors, participants with baseline WHO stages [stage IV 47(90.38%), stage III 106 (83.46%), & stage II (47.76%)], functional status [Bedridden 8(88.89%) & Ambulatory 56(88.89%)], CD4 cell count < 200 cells 134(69.79%), No OI prophylaxis 28 (93.33%), Cotrimoxazole only prophylaxis 32(88.89%), low Baseline Hgb level 27 (75%) and the presence of other comorbidities 10(66.67%) are associated with higher magnitude of OIs with P-value <0.25(table 2).

In multivariate analysis, age of respondents and Baseline WHO stage remained as the determinant of opportunistic infections.

This study result shows that being in the age group of 30-39 had about 2.7 times risk of developing OIs [AOR=2.70, 95% CI: 1.09, 6.67] , as compared with the other age groups. Being in baseline WHO stage of II, III and IV had 8.2 times **[**AOR=8.20, 95% CI: 3.63, 18.51**]**, 29.19 times [AOR=29.19, 95% CI: 12.40, 68.71] and 22.95 times **[**AOR= 22.95, 95% CI: 5.32, 99.01**]** more risk of developing OI/OIs respectively. (Table 4 and table 5 :)

Table 2: clinical information & proportion of Associated Factors for Opportunistic Infections of RVI patients on ART, who visited TGSH and FHCSH from September 12, 2019 to September 10, 2021, Bahirdar Ethiopia, 2022, (n=384)

Variable	Category	Frequency	Percent (%)
Baseline WHO Stage	I	138	35.9
	II	67	17.4
	III	127	33.1
	IV	52	13.5
functional status	Working	312	81.3
	Ambulatory	63	16.4
	Bedridden	9	2.3
Baseline CD4 cell count	< 200	192	50.0
	200 & above	192	50.0
Prophylaxis for OI	both cotrimoxazole & INH	224	58.3
	INH	94	24.5
	Cotrimoxazole	36	9.4
	No prophylaxis	30	7.8
Baseline Hgb	<10	36	9.4
	10 & above	348	90.6
Baseline Weight	<60 kg	267	69.5
	60kg & above	117	30.5
Other comorbidities	Yes	15	3.9
	No	369	96.1

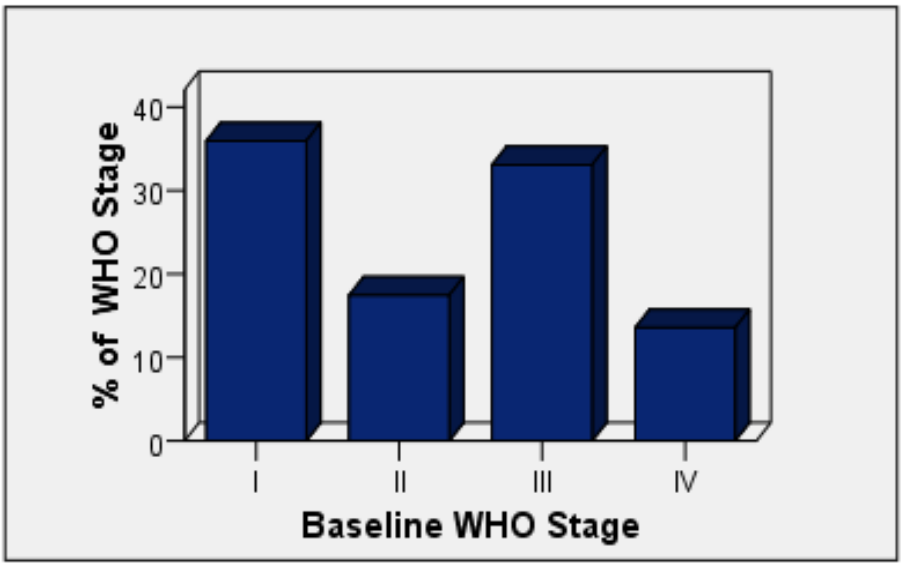

Figure 2: percentage of each WHO stage in the study.

Table 3: Magnitude of Opportunistic infections in RVI patients on ART, who visited TGSH and FHCSH from September 12, 2019 to September 10, 2021, Bahirdar Ethiopia, 2022

	Frequency(n=384)	Percent (%)
Total OIs	197	51.3
Bacterial pneumonia	79	20.6
TB (Pul &/or EPTB)	59	15.4
Candidiasis	56	14.6
Herpes Zoster	38	9.9
Chronic diarrhea	33	8.6
CNS Toxoplasmosis	14	3.7
Cryptococcal meningitis	6	1.6
PCP	4	1
Kaposi sarcoma	1	0.3

Table 4: Bivariable Logistic Regression Analysis for OIs Among RVI patients on ART, who visited TGSH and FHCSH from September 12, 2019 to September 10, 2021, Bahirdar Ethiopia, 2022

Variables		Opportunistic infections		COR(95% CI)	p-value
		Yes (n=197, 51.3%), %	No(n=187),%		
Sex	Female	89(44.28)	112(55.72)	1	
	Male	108(59.01)	75(40.98)	1.812 (1.208-2.718)	0 .004*
Age in years	18-29	23(32.39)	48(67.60)	1	
	30-39	81(57.04)	61(42.95)	2.771 (1.524,5.039)	0.001*
	40-49	64(56.14)	50(43.86)	2.671(1.438,4.964)	0.002*
	50 &above	29(50.88)	28(49.12)	2.161(1.053,4.435)	0.036*
Marital status	never married	38(57.72)	29(43.28)	1	
	Married	89(44.72)	110(55.28)	0.617(0.353,1.079)	0.091
	Divorced	50(59.52)	34(40.48)	1.122 (0.585,2.151)	0.728
	Widowed	20(58.82)	14(41.18)	1.090 (0.472, 2.517)	0.840
Educational status	no formal education	38(47.5)	42(52.5)	1	
	primary school	55(46.61)	63(53.39)	0.965 (0.546, 1.704)	0.902
	secondary school	73(58.87)	51(41.13)	1.582(0.898,2.787)	0.112
	college/university	31(50)	31(50)	1.105 (0.569 2.146)	0.768
Occupation	no work/housewife	35(36.84)	60(63.16)	1	
	daily labor	33(55.93)	26(44.07)	2.176 (1.123,4.217)	0.021*
	private business	90(56.60)	69(43.40)	2.236 (1.327,3.767)	0.002*
	governmental employee	39(54.93)	32(45.07)	2.089(1.117,3.909)	0.021*
Residence	Rural	19(45.24)	23(54.76)	1	
	Urban	178(52.05)	164(47.95)	0.761(0.400,1.449)	0.406
Baseline WHO Stage	I	12(8.69)	126(91.30)	1	
	II	32(47.76)	35(52.24)	9.600 (4.481,20.565)	0.000*
	III	106(83.46)	21(16.53)	53.000 (24.915,112.745)	0.000*
	IV	47(90.38)	5(9.62)	98.700 (32.995,295.249)	0.000*
functional status	Working	133(42.63)	179(57.37)	1	
	Ambulatory	56(88.89)	7(11.11)	10.767(4.756,24.377)	0.000*
	Bedridden	8(88.89)	1(11.11)	10.767(1.330,87.131)	0.026*
Baseline CD4	200 & above	63(32.82)	129(67.18)	1	
	< 200	134(69.79)	58(30.21)	4.731(3.075,7.279)	0.000*
Prophylaxis for OIs	Both cotrimoxazole & INH	124(55.36)	100(44.64)	1	
	INH	13(13.83)	81(86.17)	0.129(0.068,0.246)	0.000*
	Cotrimoxazole	32(88.89)	4(11.11)	6.452 (2.208,18.852)	0.001*
	No prophylaxis	28(93.33)	2(6.67)	11.290(2.626,48.544)	0.001*
Baseline Hgb	10 & above	170(48.85)	178(51.15)	1	
	<10 mg/dl	27(75.00)	9(25.00)	3.141(1.435,6.874)	0.004*
Baseline wt in Kg	60 & above	52(44.44)	65(55.56)	1	
	<60	145(54.31)	122(45.69)	1.486(0.960,2.300)	0.076*
Other comorbidities	No	187	182	1	
	Yes	10(66.67)	5(33.33)	1.947(0.653 ,5.805)	0.232*

Table 5: Multivariable Logistic Regression Analysis for OIs among RVI patients on ART, who visited TGSH and FHCSH from September 12, 2019 to September 10, 2021, Bahirdar Ethiopia, 2022

Variables		Opportunistic infections		COR(95% CI)	AOR(95%)	P-value
		Yes (n=197, 51.3%), %	No(n=187)%			
Sex	Female	89(44.28)	112(55.72)	1	1	
	Male	108(59.01)	75(40.98)	1.81 (1.21-2.72)	0.99(0.50,1.99)	0.983
Age in years	18-29	23(32.39)	48(67.60)	1	1	
	30-39	81(57.04)	61(42.95)	2.77 (1.52,5.04)	2.70(1.09,6.67)	0.031*
	40-49	64(56.14)	50(43.86)	2.67(1.44,4.96)	2.01 (0.79,5.11)	0.144
	50 &above	29(50.88)	28(49.12)	2.16(1.05,4.44)	1.24(0.41,3.77)	0.700
Occupation	no work/housewife	35(36.84)	60(63.16)	1	1	
	daily labor	33(55.93)	26(44.07)	2.18 (1.12,4.22)	1.68 (0.60,4.70)	0.325
	private business	90(56.60)	69(43.40)	2.24 (1.33,3.77)	1.10(0.46,2.62)	0.823
	government employee	39(54.93)	32(45.07)	2.09(1.12,3.91)	0.93(0.35,2.46)	0.883
Baseline WHO Stage	I	12(8.69)	126(91.30)	1	1	
	II	32(47.76)	35(52.24)	9.60 (4.48,20.57)	8.20(3.63,18.51)	0.000*
	III	106(83.46)	21(16.53)	53.00(24.92,112.75)	29.19(12.40,68.71)	0.000*
	IV	47(90.38)	5(9.62)	98.70(32.99,295.25)	22.95(5.32,99.01)	0.000*
functional status	Working	133(42.63)	179(57.37)	1	1	
	Ambulatory	56(88.89)	7(11.11)	10.77(4.76,24.34)	2.67 (0.87,8.24)	0.087
	Bedridden	8(88.89)	1(11.11)	10.77(1.33,87.13)	1.69 (0.15,18.75)	0.671
Baseline CD4	200 & above	63(32.82)	129(67.18)	1	1	
	< 200	134(69.79)	58(30.21)	4.73(3.08,7.29)	1.33 (0.67,2.63)	0.413
Prophylaxis for OIs	Both cotri.& INH	124(55.36)	100(44.64)	1	1	
	INH	13(13.83)	81(86.17)	0.13(0.07,0.26)	0.41(0.16,1.01)	0.051
	Cotrimoxazole	32(88.89)	4(11.11)	6.45(2.21,18.85)	3.31(0.91,12.05)	0.069
	No prophylaxis	28(93.33)	2(6.67)	11.29(2.63,48.54)	3.04(0.56,16.65)	0.200

Baseline Hgb	10 & above <10 mg/dl	170(48.85) 27(75.00)	178(51.15) 9(25.00)	1 3.141(1.435,6.874)	1 1.29(0.42,3.93)	0.667
Baseline wt in Kg	60 & above <60	52(44.44) 145(54.31)	65(55.56) 122(45.69)	1 1.49(0.96,2.30)	1 1.38(0.70,2.74)	0.355
Other comorbidities	No Yes	187 10(66.67)	182 5(33.33)	1 1.95(0.65,5.81)	1 0.56(0.14,2.26)	0.418

Note: NB: * in the Bivariable analysis, statistically significant p-value (<0.25) and in the multivariable analysis. Statistically significant p-value (<0.05)

Abbreviations: COR, crude odds ratio; AOR, adjusted odds ratio; CI, confidence interval; 1, reference.

7. Discussions

This Institution based cross-sectional study revealed that 51.3%[95% CI: 46.4-56.5] of RVI patients on ART had one or more opportunistic infections. The major identified opportunistic infections in this study were recurrent bacterial pneumonia 20.6%, tuberculosis (pulmonary &/or EPTB) 15.4%, candidiasis (Oral & esophageal) 14.6% herpes zoster 9.9%, Chronic diarrhea 8.6%,CNS Toxoplasmosis 3.7%, Cryptococcal meningitis 1.6% and PCP 1%. Only 1 patient was diagnosed to have Kaposi sarcoma (0.3%)

This result is higher when compared to 22.4% in Nigeria with the most frequent conditions were candidiasis, (8.6%); TB (7.7%); dermatitis (5.6%); chronic diarrhea, (1.5%); and sepsis (1.5%). Bacterial pneumonia was diagnosed in 3 (0.9%) patients, cryptococcal meningitis, herpes zoster, genital herpes, and genital warts were each diagnosed in 2 (0.6%) patients while only 1 (0.3%) patient had Kaposi's sarcoma[12].

It's also higher than that of 25.9% in Cameroon, 33.6% in Addis Ababa and 39.6% in Selected Public Hospitals in Sidama National Regional State[21, 23, 25].

This higher Magnitude of OIs when compared to the previous studies is due to the fact that majority of RVI patients Visit higher Hospitals after they developed serious opportunistic infections. In addition, there is no habit of early/timely visit to health institution when the patients feel ill.

The result of this study is lower when compared to 88.4% in Dawro Zone hospital where prevalence of Pulmonary tuberculosis, (18%) was the most common OI, followed by Severe community acquired pneumonia (16.3%) & oral candidacies (15.6%). And Only 5 and 2 individuals were affected by Toxoplasmosis and KS respectively [22].

The study is nearly comparable to 48.75% in Southern zone of Tigray and parts of North Wollo Amhara where the most frequent OIs were oral candidacies and ulcers mouth, genital (11%) followed by herpes zoster 10.8% and tuberculosis at 9.5% [24]

In this study the magnitude of Cryptococcal meningitis 6 (1.6%),PCP 4 (1%), and Kaposi sarcoma 1(0.3%) is relatively low when compared to magnitude of opportunistic diseases reported in sub-Saharan Africa and in china [17, 18,20].

This is likely due to missing the diagnosis of those OIs as a result of limited investigation modalities

The highest number of OIs with statistically significant association on bivariable analysis was among male sex (59%), age group of 30-39years (57%) & 40-49 years (56.14%). There is also the highest magnitude of OIs among private business workers (56.60%) and daily laborers (55.93%).

Among the risk factors, participants with baseline WHO stages [stage IV (90.38%), stage III (83.46%), & stage II (47.76%)], functional status [Bedridden & Ambulatory (88.89% each)], CD4 cell count < 200 cells (69.79%), No OI prophylaxis (93.33%), low Baseline Hgb level (75%).This is similar to the study done in Dawro Zone hospital, Nigeria and Cameroon [12, 21, 22].

The presence of other comorbidities (66.67%) had higher magnitude of OIs. This is because comorbidities mainly DM and CKD can further suppress the immunity of RVI patients and make double trouble for them. In this study chronic steroid use was included as comorbidity but no patient had history of chronic steroid use among the samples.

In multivariate analysis, age of respondents and Baseline WHO stage remained as the determinant of opportunistic infections.

This finding is consistent with the findings of the study done in Selected Public Hospitals in Sidama, Dawro Zone hospital, and in the study done in Southern Tigray and parts NorthnWollo Amhara [22, 24, 25].

The risk of OIs did not significantly diff er according to place of residence, marital status or educational status.

Limitations

This study has potential limitations as the study is cross-sectional in design. In addition to this, the odds ratios of the cross-sectional study did not show the strength of an association.

Furthermore, my study was based on patient's information on their medical documentations. Some of their charts lack clear and proper documentation of their clinical information.

8. Conclusion and Recommendation

In this study, the overall Magnitude of OIs is high (51.3%) when compared with other studies. This suggests that OIs remain a challenge in RVI patients in Ethiopia despite taking ART.

The major identified opportunistic infections were recurrent bacterial pneumonia, tuberculosis (pulmonary &/or EPTB), candidiasis (Oral & esophageal), herpes zoster and Chronic diarrhea.

Baseline WHO stages III & IV, initial CD4 count <200, and not getting OI prophylaxis were found to be strongly associated with the high proportion of opportunistic infections. So that, interventions need to be designed to promote early HIV testing and early enrollment of HIV infected individuals into ART services.

Individuals who presented with advanced WHO clinical stage, and low CD4 cell count should be followed closely and OI prophylaxis should be given early if the patient fulfills the criteria. Health officials and clinicians need to give attention to the strengthening of the provision if ART with OI prophylaxis on early WHO stage and Community awareness creation about the virus should also be facilitated.

For better conclusive information, Future research should be done including patients in health facilities of rural areas.

Ethical approval and consent

Ethical clearance was obtained from Bahir Dar University College of Medicine and Health Sciences Ethical Committee. A support letter was sent to Tibebe Ghion Specialized Hospital and Felegehiwot comprehensive specialized hospital. Names were not used in collecting the data from the medical files. Confidentiality was maintained by keeping the data collection forms locked in a secure cabinet and the electronic data file was kept securely in a password protected computer. Data obtained in the course of study was handled by the researcher only.

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APPENDIX

Check list to assess the socio demographic characteristics of patients, and magnitude, & associated factors of OIs in HIV patients who visited TGSH and FHCSH from September 12, 2019 to September 10, 2021.

Part I

Check list for identification, socio-demographic and clinical characteristics of the study participants from September 12, 2019 to September 10, 2021.

	Card number	
No-	**Variables**	**Category**
1	Sex	Male
		Female
2	Age group, years	18–29
		30–39
		40–49
		≥50
3	Marital status	Single
		Married
		Divorced
		Widowed
4	Educational status	Illiterate
		Primary school (1st–8th grade)
		Secondary school (9th–12th grade)
		College/University
5	Occupation	No work
		Daily labor

		Private business
		Government employee
6	Residence	Urban
		Rural
7	WHO stage	I
		II
		III
		IV
8	Functional status	Working
		Ambulatory
		Bedridden
9	OI prophylaxis	Cotrimoxazole
		INH
10	Baseline CD4 cell count, cells/mm3	<200
		≥200
11	Baseline hemoglobin level, g/dL	<10
		≥10
12	Baseline weight, kg	<60
		≥ 60
13	Other co morbidities	DM, CKD, chronic steroid use

Part II.

Check list for prevalence of opportunistic infections among HIV/AIDS patients on ART Who visited TGSH and FHCSH from September 12, 2019 to September 10, 2021.

Opportunistic infections	yes	No
Herpes zoster	yes	No

Tuberculosis	yes	No
Bacterial pneumonia	yes	No
Oral candidacies	yes	No
Chronic diarrhea	yes	No
Pneumocystis carini pneumonia	yes	No
CNS toxoplasmosis	yes	No
Cryptococcal meningitis	yes	No
Kaposi sarcoma	yes	No