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Prevalence of Advanced HIV Disease and Associated Factors among Newly Diagnosed Patients at Public Hospitals in Addis Ababa, Ethiopia, 2023: Multi-Center Retrospective Cross-Sectional Study

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CONTENTS

LIST OF ACRONYMS

AHD: Advanced HIV Disease

AIDS: Acquired Immunodeficiency Syndrome

CD4: Cluster of Differentiation 4

CI: Confidence Interval

HBV: Hepatitis B Virus

HCV: Hepatitis C Virus

HIV: Human Immunodeficiency Virus

LP: Late presentation

MDR: Multidrug Resistant

OIs: Opportunistic Infections

OR: Odds Ratio

PML: Progressive multifocal leukoencephalopathy

SNNPR: Southern Nations and Nationalities Peoples' Region

SSA: Sub-Saharan Africa.

St.: Saint

TB: Tuberculosis

USAID: United States Aid for International Development

WHO: World Health Organization

ABSTRACT

Background: Many patients having HIV present to the health care system with advanced HIV disease. Patients with advanced HIV disease have CD4 cell count of less than 200cells/mm3 or WHO stage III or IV clinical events. The primary culprits responsible for severe morbidity and mortality are tuberculosis, severe bacterial infections and cryptococcal meningitis.

Objective: The aim of this study was to investigate the prevalence and factors associated with advanced HIV disease among newly diagnosed patients at Public Hospitals in Addis Ababa, Ethiopia, 2023.

Methodology: A retrospective multi-centered facility based cross-sectional study was conducted among newly diagnosed HIV patients whose age was ≥ 15 years over a period of one year (October 2023- January 2024). The prevalence of advanced HIV disease was estimated with advanced HIV disease defined as WHO clinical stage 3, stage 4 or CD4 count less than 200 cells/μ. The baseline characteristic of the study participants was compared with and without advanced HIV disease. Pretested and structured questionnaires were adopted. The completed data was collected via web link after being prepared by kobo toolbox, coded, manually checked, and exported to SPSS version 26 for analysis. Descriptive statistics, chi square test, nonparametric tests and multi variable logistic regression were used for data analysis.

Result: Among the 400 patients, 262(65.5%) had advanced HIV disease at presentation. Patients with low BMI had 3.2 times higher odds of having advanced HIV disease in contrast to other patients with normal or higher BMI (AOR 3.2, 95% CI 1.14-8.9, *P* =0.03). Patients having bedridden functional status had 10.6 times higher odds of advanced HIV disease as compared to other groups of patients (AOR 10.6, 95% CI 1.24-91, *P* =0.03). HIV testing reason due to symptoms of opportunistic infections had 44.6 times higher odds of advanced HIV disease as compared to those who had other HIV testing reasons (AOR 44.6, 95% CI 22.8-87.2, *P* <0.001).

Conclusion: The study showed that advanced HIV disease was very high among newly diagnosed HIV patients emphasizing timely intervention to reduce the increased morbidity and mortality associated with advanced HIV disease.

Key words: Advanced HIV disease, Prevalence, Associated factors, CD4 count

1. INTRODUCTION

1.1. Background

In 2021, an estimated 38.4 million people globally were living with HIV. Of these, 1.5 million were newly infected. Nearly half (49%) of new infections occurred in women and girls. Deaths from HIV/AIDS-related illnesses have significantly declined, with 650,000 deaths in 2021 compared to 2 million in 2004 and 1.4 million in 2010. The greatest proportions of individuals affected by HIV primarily reside within nations of low and middle income economy. Low- and middle-income countries have the highest burden of HIV. In 2021, over half (53%) of all diagnosed HIV cases (20.6 million people) were in Eastern and Southern Africa, while 13% (5 million people) were in Western and Central Africa.. In addition, 6 million individuals (15%) were detected in Asia and the Pacific, whereas 2.3 million (5% of cases) were found within Western and Central Europe and North America. According to UNAIDS, 85% of HIV patients knew their status, 75% were accessing ART and 68% were virally suppressed worldwide [1].

Advanced HIV disease (AHD) is defined by a CD4 cell count of less than 200cells/mm3 or by WHO clinical stage III or IV events in adults and adolescents according to WHO criteria. Children under the age of five are all classified as having advanced HIV disease due to their increased risk of disease progression and mortality. Despite no longer being a requirement to initiate treatment, CD4 cell count test is an indispensable tool for identifying individuals with AHD. [2]

Individuals diagnosed with AHD have an increased risk of mortality even following initiation of Antiretroviral Therapy whose risk increase with a drop in CD4 cell count. The primary culprits responsible for severe morbidity and mortality are tuberculosis, severe bacterial infections and cryptococcal meningitis.[3]

Significant strides have been made in the recognition of persons afflicted with HIV and initiating ART so far. 21.7 million out of the projected global population of 36.9 million individuals with HIV are currently on treatment. The number of AIDS related fatalities in 2017 reached an all-time low in the 21st century and the incidence of HIV infections were exceedingly low. But, the above heartening statistical figures obscure the entire narrative.

The 21.7 million persons who commence ART encompasses those who are lost to follow up and redundantly tallied when they re-enter the care. [4]

In spite of concerted endeavors to enhance HIV testing and treatment accessibility, a significant proportion of individuals afflicted with HIV in Sub-Saharan Africa including Ethiopia manifest advanced disease at presentation.[5][6]

Studies done so far indicated that individuals who commence ART at higher CD4 cell counts can have a life expectancy that is nearly equivalent to that of the general population and have substantially low risk of transmitting HIV to others. However, a CD4 count of less than 200 cells/μL is a powerful predictor of severe morbidity like tuberculosis, severe bacterial infections and cryptococcal meningitis and mortality [7][8][9].

1.2. Statement of the problem

In spite of substantial advancements in both HIV prevention and treatment within Ethiopia, advanced HIV disease remains a significant public health concern that has a notable impact on the morbidity, mortality, and healthcare expenditures of both the individuals and countries [10].

Advanced HIV disease is used to describe a CD4 count that is less than 200 cells/mm3, or the presence of a clinical stage 3 or 4 disease at the time of diagnosis, which signifies a severely compromised immune system. Studies have shown that a significant proportion of individuals newly diagnosed with HIV in Ethiopia present with advanced HIV disease at the time of diagnosis.

Advanced HIV disease carries substantial ramifications for both the afflicted individual and the healthcare system. Persons suffering from advanced HIV are at risk of contracting opportunistic infections and ailments resulting in increased morbidity, mortality, and healthcare expenditures. The healthcare system is saddled with the heavy expenses associated with managing advanced HIV affliction, which can be alleviated through timely identification and treatment of the viral infection.

The total population in Ethiopia according to world population prospect estimate in 2018 was 109,224,414. About 666,882 people had HIV as per 2020 SPECTRUM Estimate and HIV national prevalence was 0.88%.

Almost one third of patient presents to health care with AHD and the number is higher in low and middle income countries including Ethiopia despite current recommendation of early initiation of ART upon diagnosis.

A study conducted in the rural SNNP region, Ethiopia showed that 60% of newly diagnosed HIV patients present to the health care system with AHD. Majority of the patients were males and had advanced clinical and immunological diseases. [6]

Knowing the magnitude and associated factors of advanced HIV in newly diagnosed patients is of utmost importance for formulating and executing effective approaches to enhance early recognition and therapy of HIV. A multitude of studies have revealed diverse determinants associated with progressive HIV disease including older age, male sex, lack of formal education, history of tuberculosis, and late presentation to health care services. These determinants imply that socio-economic, cultural, and healthcare system-associated factors influence the punctual detection and management of HIV.[11]

In the end, it is imperative to prioritize measures aiming at decreasing incidence of AHD in newly diagnosed patients. This is a pressing issue that warrants a comprehensive and multi-sectoral approach including individual, socio-economic, cultural, and health system-related factors that contribute to late-stage HIV diagnoses. Among the effective strategies to be considered include community-based testing and counseling, accessibility to HIV testing and treatment services, and targeted interventions aimed at high-risk populations. [7][12]

1.3. Significance of the study

Currently, significant numbers of patients are seen attending the health care system with new diagnosis of AHD in Addis Ababa, Ethiopia.

Late diagnosis of HIV and advanced HIV disease have poor outcomes, such as increased risk of morbidity and mortality. By identifying the factors that contribute to the emergence of advanced HIV disease, targeted interventions can be developed to enhance early HIV diagnosis and linkage to care, leading to better health outcomes for individuals having HIV disease.

Early detection and timely management of HIV infection proves to be a more economically efficient approach as compared to late identification and treatment. Knowledge regarding the determinants leading to late diagnosis and AHD can facilitate the development

of interventions that are not only cost-effective but also substantially alleviate the burden of HIV.

The outcomes of the present study possess the potential to enlighten the development of policies and programs that can enhance the early detection of HIV positive patients and early linkage to care.

Policymakers, healthcare providers, and HIV program managers can utilize these findings to create interventions and tactics tailored to the specific needs of the population, thereby decreasing the prevalence of advanced HIV disease.

Currently, the local prevalence of AHD is not known as there is a scarcity of data regarding the current magnitude of advanced HIV disease at presentation in Ethiopia as well as its temporal trends. There is no much data pertaining to the magnitude and associated factors of advanced HIV disease among newly diagnosed HIV-positive individuals in our set up. This study strives to bridge this gap and provide valuable insights to facilitate further investigations in this area.

Hence, conducting this study will provide a hint as to how to design WHO and national package of implementation strategies to ensure that HIV positive individuals have early diagnosis, early linkage to health care system and initiation of ART, have nearly normal life expectancy and become actively engaged in the productive workforce.

2. Literature Review

2.1. Introduction

HIV/AIDS, a prevalent global pandemic, has afflicted a large number of individuals around the world. Despite considerable progress in HIV treatment and prevention, a significant proportion of newly diagnosed patients experience advanced HIV disease at presentation to the health care system resulting in unfavorable outcomes and increased mortality rates [13].

Global Prevalence and Associated Factors of Advanced HIV Disease

Studies conducted globally have documented a substantial percentage of individuals newly diagnosed with HIV who exhibit advanced stages of the disease at presentation.

In a study conducted in China, 40.1% of newly diagnosed HIV-positive patients had advanced HIV disease [9]. Metanalysis and systematic review conducted in the same country showed that the pooled prevalence of late presentation in Chinese HIV positive population was 43.2%. Age greater than 50, being married and heterosexual contacts were ascribed as a risk factor for late presentation [14]. Another serial cross-section study in China from 2008 to 2020 depicted 55.1% of LP and 28.7% of AHD among 30,251 patients. Married patients, age older than 35 years and heterosexual relationship were found to be the predictors of LP or AHD [8].

The COHERE and EuroSIDA cohorts in Europe showed that out of 18,967 individuals, 48.4% of the patients were late presenters. Late presentation was documented from 36.9% in Estonia and Ukraine to 64.2% in Poland. The prevalence of late presentation was substantially high with the highest estimated number of AHD and excess AIDS-events were reported in Eastern Europe [9]. Retrospective study conducted in India involving 474 patients demonstrated that 75.1% were Late presenters of which 83.99% had AHD. The median CD4 count in the late presenting patients was 134 cells/µl. Age greater than 51 years and living in the rural areas were independently associated with AHD [15].

Between 2004 and 2018, a multicenter cohort study conducted in Spain found that 44.6% of 14,876 individuals diagnosed with HIV were late presenters. Older age, injection drug use and heterosexual intercourse and low educational status were the determinants for LP [16]. A national observational cohort in the Netherlands from 1996-2014 confirmed 53% patients presented with late stage HIV infection and 35% had advanced

disease out of 20 965 patients. Risk factors identified to be correlated with AHD or LP were heterosexual males, injection drug use, age greater than 50 years, country of origin like South East Asia, Sub-Saharan Africa, Caribbean and Latin America. There was no significant association between AHD with socioeconomic status or level of urbanization [17].

Patients with AHD have increased risk of morbidity and mortality. The REALITY randomized trial conducted in Zimbabwe, Uganda, Malawi and Kenya reveals opportunistic infections, notably tuberculosis and cryptococcal meningitis, as still being the major cause of mortality. Furthermore, severe bacterial infections were found to be highly prevalent and had a significant impact on survival. The study also highlights that nearly a third of deaths were consistent with immune reconstitution inflammatory syndrome [18].

The risk of LP and AHD was high according to the Italian MASTER Cohort which had enrolled newly diagnosed HIV positive patients from 1985 to 2013. Among 19,391 patients, 54 % were late presenters and 37.6 % had advanced HIV disease. Male gender, heterosexual relationship, older age and migration were positively correlated with late presentation [19].

Prevalence and Associated Factors of Advanced HIV Disease in Africa

The prevalence of HIV/AIDS in Africa poses a substantial challenge to public health as this region accounts for the majority of the global HIV burden. Although there have been notable advancements in HIV testing and therapy, a significant number of recently diagnosed patients still have advanced stages of the disease which is associated with poor outcomes and increased risk of mortality.

Secondary analysis from three population-based cross-sectional surveys including in Kenya, South Africa and Malawi showed 1 in 10 patients had AHD with 40% of them were not aware of their sero-status. Men had higher proportion of AHD as compared to women [20]. A cluster-randomized HIV-prevention trial conducted in Botswana has shown an overall prevalence of AHD to be 17.2% at the time of presentation. In this study, men were found to have CD4 count less than 200 and increasing age was significantly associated with AHD [11]. Another retrospective cohort study from rural Rwanda involving 957 patient found out that 11% of the patients had AHD at presentation. Patients with AHD were more likely to have low BMI, older and from rural areas. These patients were at exceedingly high rate of mortality and treatment failure at 12 months [21].

A cross-sectional study in Senegal involving 198 individuals found that 71% of patients had AHD at presentation. The median CD4 count was 185. The strongest risk factors of AHD were lack of awareness and age greater than 35 years [5]. Retrospective cohort analysis of 14 487 eligible patients conducted in Nigeria to study trends and determinants of late presentation and AHD, 85.6% of patients were found to be late presenters and 63% of the patients had AHD. Predictors of AHD were found to be male gender, older age, HBV co-infection and unemployment [19].

A study carried out in South Africa to investigate the prevalence and predictors of late presentation among 8138 newly diagnosed HIV patients, 79% of the patients were late presenters, 19% of the patients had WHO stage I, II or CD4 counts between 351-500 and 33% of the patients had AHD. Being males, non-pregnant women, age >30 years and patients seeking in towns were more likely to present late and have AHD [7]. A retrospective cohort study in Tanzania from 2013-2017 involving 2624 patients indicated 50% of them had AHD with 7.8% having TB-coinfection. 58.3% of patients with AHD were female and 80.7% of them were from urban areas [22].

An investigation of 694,138 ART records of adult patients from 10 countries was conducted to determine the prevalence of advanced disease at ART initiation between 2004 to 2015. The results revealed that eight countries had reduction in the prevalence of advanced disease. In Mozambique, Namibia, and Haiti, the prevalence of advanced disease at ART initiation decreased from 73% to 37%, 80% to 41% and 75% to 34% respectively during the period of 2004-2014, 2004-2012, and 2004-2015. Moreover, the remaining seven countries with available data from 2004 to 2011 showed a significant decrease in the prevalence of advanced disease, namely, Nigeria, Swaziland, Uganda, Vietnam and Zimbabwe [23].

From 2005 to 2016 Nationwide laboratory cohort in South Africa, there was a decline in the proportion of patients who entered care with a CD4 count of less than 200 cells/µL, from 46.6% to 32.9%. Between 2012 and 2016, the prevalence of individuals with advanced HIV disease remained relatively stable, fluctuating between 34.8% and 32.9%. However, the proportion of patients with very advanced HIV disease, defined by a CD4 count below 100 cells/µL, declined from 27.7% in 2005 to 18.1% in 2011. Since then, it has remained unchanged at 16.8% in 2016. Notably, men were nearly twice as likely as their female counterparts to initiate care at advanced stages of HIV disease [24].

Late presentation of HIV positive patients remains to be a challenge in Southern Africa according to a study published from population-based nationally representative surveys of Malawi, Zambia and Zimbabwe. Among 1804 adults surveyed, 49% of them were late presenters defined by CD4 count < 350. Male sex and older age were independently associated with late presentation [25].

Prevalence and Associated factors of Advanced HIV Disease in Ethiopia

Despite national and WHO guidelines highlighting rapid ART initiation, substantial number of patients manifest advanced disease.

There was a study conducted in the rural SNNP region of Ethiopia involving 1799 adults newly diagnosed HIV patients in 32 district hospitals and health center. Advanced HIV disease was present in 66% of males and 56% of females attending the health care system with overall prevalence of AHD being 60%. This study showed that males had lower CD4 count, lower BMI and poor health status. Moreover, they had chronic diarrhea, fevers, cough, pain, fatigue and weight loss [6]. CD4 T lymphocyte count <200 cells /μl and advanced WHO HIV clinical stages were powerful indicators of OIs and increased mortality [26]. In 2019, an unmatched case-control study was carried out in public health facilities in West Arsi Zone. The study aimed to explore predictors of late presentation among patients with HIV. The sample size included 500 individuals (167 cases and 333 controls). Several risk factors were identified including residing in rural areas, fear of losing job security and chronic medical conditions. Interestingly, being single emerged as the sole protective factor associated with late presentation for HIV/AIDS care [27].

A cross-sectional study was carried out to determine the magnitude and associated factors of delayed initiation of ART among individuals infected with HIV at the ART Clinic of Nekemte Referral Hospital in Western Ethiopia. This study took place from January 1, 2016 to December 31, 2019 and involved a total of 417 patients. The average age of the participants was 33.49 (with a standard deviation of ±9.81) years. Approximately one-third (34%) of the individuals had delayed initiation of ART, which was started 7 days after a confirmed diagnosis of HIV. Several factors were found to be significantly associated with this delay. These factors included having a normal nutritional status (BMI=18.5–24.9), CD4 count ≥351 cells/mm3, co-infection with TB, using traditional treatment methods and not being aware of any other ART users [28].

A systematic review was conducted with the aim of determining the prevalence of HIV and the underlying risk factors, identifying areas of high transmission, determining the key populations at risk, evaluating the accessibility and utilization of services, and addressing the obstacles in the prevention and control of the HIV epidemic in Addis Ababa. It is evident that the prevalence of HIV remains stable, yet it varies across different areas and socio-demographic groups. The most prevalent areas in Addis Ababa are those where establishments such as bars, grocery stores, guest houses, hotels, brothels, massage parlors, khat houses, shisha lounges, nightclubs and tourist settings are concentrated. The primary population at risk is female sex workers. There is a mixing of high-risk populations, such as female sex workers with the general population. Various behavioral, biological, and socioeconomic risk factors contribute to the spread of the HIV epidemic and corresponding measures, encompassing behavioral, biomedical, and structural interventions, have been identified to address the issue in the presence of challenges and gaps [29].

A systematic review and meta-analysis was done to determine the prevalence of late presentation of HIV positive patients and its predictors in Ethiopia in 2019. 8 studies with 7, 568 patients were included for analysis. The pooled prevalence of LP was 52.89%. Regular alcohol use, fear of social stigma, chronic illness, and the presence of symptoms at the time of HIV diagnosis were ascribed for late presentation [10].

Conceptual framework

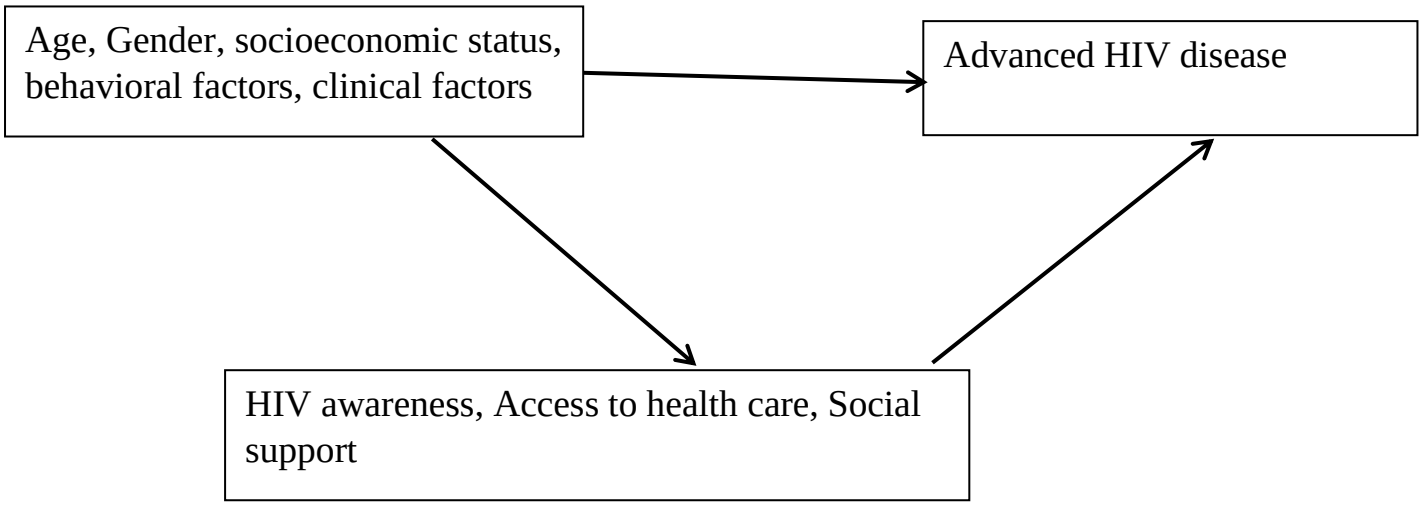

Fig 1: Conceptual framework on determinants of advanced HIV disease among newly diagnosed HIV patients presenting to Public Hospitals, Addis Ababa, Ethiopia, 2023 [16][15][8][12][30].

3. OBJECTIVES

3.1. General Objective

To assess the prevalence of advanced HIV disease and associated factors among newly diagnosed patients at Public Hospitals, Addis Ababa, Ethiopia, 2023.

3.2 . Specific Objectives

1. To assess the prevalence of advanced HIV disease among newly diagnosed patients in Public Hospitals from October 2022 to October 2023.
2. To identify associated factors of advanced HIV disease among newly diagnosed HIV patients.

4. METHODS

4.1. Study Area

The study was conducted at Tikur Anbessa Specialized Hospital, Yekatit 12 Hospital Medical College, St. Peter Specialized Hospital and Zewuditu Memorial Hospital, Addis Ababa, Ethiopia from October 2023 – February 2024.

Tikur Anbessa Specialized Hospital is the largest referral and teaching hospital in Addis Ababa and Ethiopia. It is found in Lideta sub city. It was established in 1972 as the only site for training in the country.

Yekatit 12 Hospital Medical College is one of the teaching and referral hospital found in Arada Sub-city, Addis Ababa, Ethiopia. It was formerly called Bethsaid Hospital. It was renamed to Yekatit 12 hospital in the commemoration of the massacre and imprisonment of Ethiopians by the occupation of Italian forces on February 19, 1937.

St. Peter Specialized Hospital is the other referral hospital found in Gulele Sub-city, Addis Ababa, Ethiopia. It was founded by the Ethiopian Catholic Church in 1960 and has been providing clinical services to the population of Addis Ababa and its surroundings over six decades.

Zewuditu Memorial hospital is one of the oldest and largest public hospitals found Kirkos sub-city, Addis Ababa and serves as a major healthcare facility. The hospital is named after Empress Zewuditu, who ruled Ethiopia from 1916 to 1930. It was established in 1922 as a maternity clinic and has since expanded to provide a wide range of medical services.

4.2. Study Design

A Multi-Centered Facility based retrospective cross-sectional design was employed to conduct the study. The public hospitals were picked up by lottery methods.

Non-probability total enumerative sampling method was utilized where every newly diagnosed HIV patient meeting the inclusion criteria was selected from each hospital until the required sample size was obtained.

4.3. Source Population

All HIV positive patients who have follow up at the public hospitals in Addis Ababa, Ethiopia.

4.4. Study Population

Adult patients with newly diagnosed HIV infection from October 2022 – October 2023 at the study hospitals were the study population.

4.5. Inclusion and exclusion criteria

4.5.1. Inclusion criteria

1. Newly diagnosed HIV patients between October 2022 - October 2023
2. Adult patients who aged above 15 years

4.5.2. Exclusion criteria

3. Individuals who have already started ART treatment outside the study period.
4. Patients with incomplete records.
5. Patients who lost follow up or transferred to any other areas.

4.6. Sample size determination

Sample size was determined based on the following assumptions; the confidence level to be 95%, margin of error <0.05 to be significant.

$n=\frac{z^2 p(1-p)}{d^2}$ where n= number of sample, **z**= standard score at 95% CI which is 1.96, **d**= margin of error, **P**= the prevalence of advanced HIV disease was **60%** according to a study conducted in the rural SNNP region that was published in 2019 [6].

Hence, n=**369**. Taking 10% non-response rate, the final sample size will be **406.**

4.7. Sampling procedures

The sampling procedure employed non-probability total enumerative sampling method. Therefore, all patients were picked up from ART registry log book who satisfied the inclusion criteria.

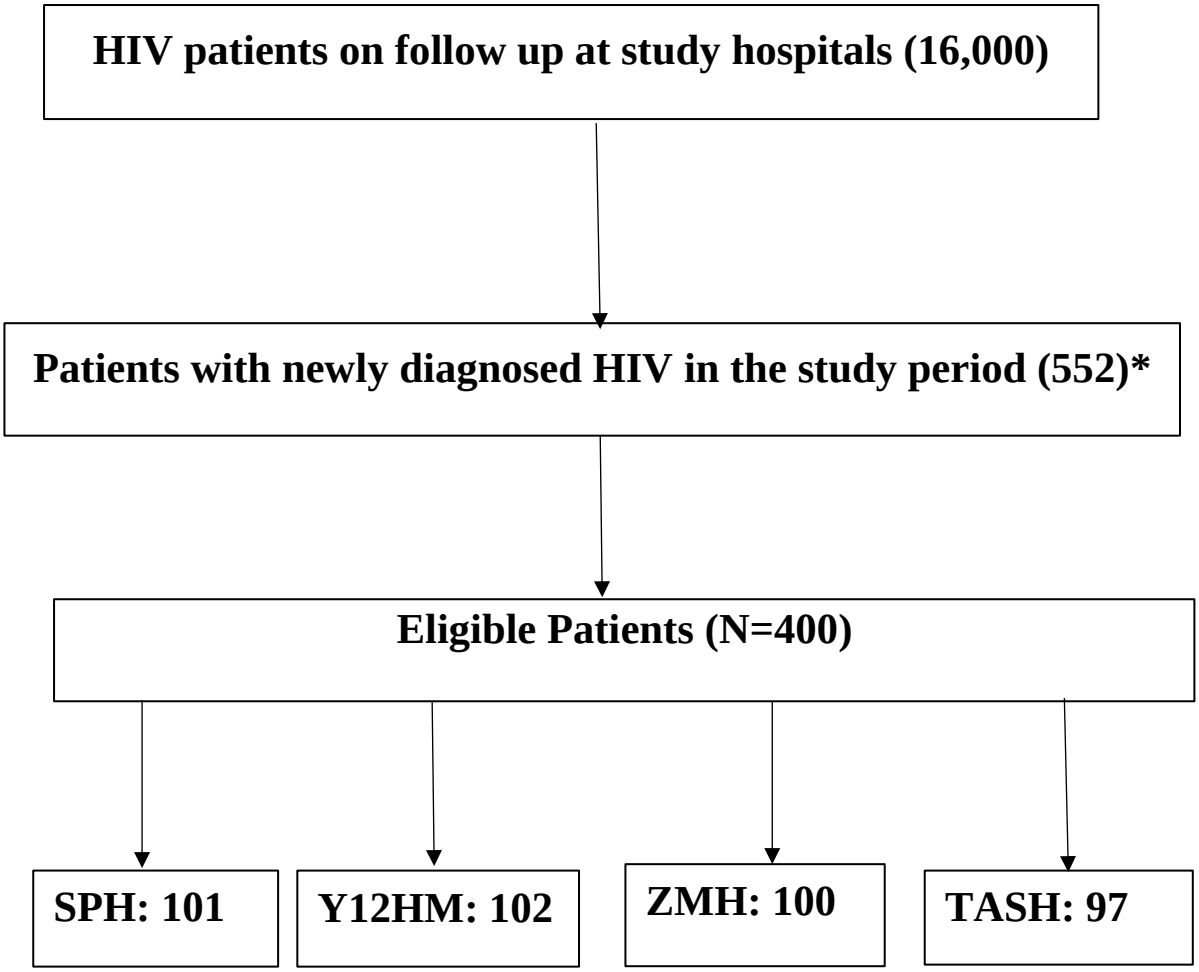

Fig 2: Hospital Allocation of Study Participants.

*: 152 patients were excluded from the study due to incomplete documentation (105), lost to follow up at study hospitals (29) and absence of their charts (18).

4.8. Study variables

4.8.1. Dependent variables

Prevalence of Advanced HIV disease

4.8.2. Independent variables

Demographic factors: Age, gender, educational level, address and occupation

Clinical factors: CD4 count, OIs, comorbidities, constitutional symptoms

Behavioral factors: Drug use, smoking and alcohol consumption

4.9. Operational definitions

Prevalence: refers to the proportion of patients at public hospital, Addis Ababa, Ethiopia, 2023 who have advanced HIV disease at presentation.

HIV: is Human Immunodeficiency Virus that affects human immune system causing to advanced HIV disease and puts patients at greater risk of OIs and malignancies.

Advanced HIV disease: refers to patients with WHO stage 3 or stage 4 defining clinical events or CD4 counts less 200 cells/mm³.

Newly diagnosed HIV Patient: refers to patients who were diagnosed with HIV disease from October 2022 – October 2023 at the study hospitals.

Late presentation: refers to patients who present with CD4 count less than 500 cells/mm³ but greater than 200 cells/mm³ or WHO stage 1 or 2 defining clinical events.

Associated factors: refers to the socio-demographic, clinical and other factors that can be associated with advanced HIV disease among newly diagnosed patients based on multivariable logistic regression analysis.

Data collection and materials

Data was collected from patients' medical chart using pretested and structured questionnaires which were adapted by reviewing various literatures ([31], [21], [6]). The questionnaires were closed ended including socio demographic factor, clinical presentation, certain laboratory values and other factors. It was prepared in English and uploaded onto Kobotool box for ease of data collection. The data collector was the investigator himself with helps stretched from his friends and colleagues.

4.10. Data quality assurance and analysis

The data collected through Kobo Toolbox was processed and exported to SPSS version 26 for analysis. Qualitative nominal variables were represented using absolute counts and relative percentages. For non-normally distributed continuous and ordinal data, the median along with the interquartile range was utilized. Before applying these measures, the normality of the data was assessed using the Shapiro-Wilk test. Independent variables and the primary outcome variable were presented through frequency tables and cross-tabulations, which were subsequently evaluated using the Chi-Square Test. Additionally, the median of continuous data was compared using non-parametric tests such as the Mann Whitney U test. Finally,

a multivariable logistic regression was conducted to explore the association between advanced HIV disease and various independent variables (such as age, gender, CD4 count, clinical factors), while controlling for other relevant factors. The results of the regression analysis were reported as OR with 95% confidence interval. P-value less than 0.05 were considered to be statistically significant.

4.11. ETHICAL CLEARANCE

Ethical clearance was obtained from Department of Internal Medicine, School of Medicine, College of Health Sciences, Addis Ababa University, Ethical Board Review of Addis Ababa Health Bureau and St. Peter Specialized Hospital.

An informed consent was not necessary as the data was obtained from secondary sources. However, privacy and confidentiality of collected information was ensured throughout the process.

4.12. Dissemination of the result

The result of this study will be submitted to Department of Internal Medicine, School of Medicine, College of Health Sciences, Addis Ababa University, Addis Ababa Health Bureau and St. Peter Hospital. Publication in scientific journal and online dissemination will be considered after defense presentation.

5. RESULTS

5.1. Baseline Characteristics of Study Participants

From October 2022 to October 2023, a total of 400 study participants were enrolled in the current study from the four public hospitals in Addis Ababa, Ethiopia.

Hundred two (25.5%) of the study participants were from Yekatit 12 Hospital Medical College, 101(25.3%) from St. Peter Specialized Hospital, 100(25%) from Zewuditu Memorial Hospital and 97(24.3%) were from Tikur Anbessa Specialized Hospital.

Out of the total study participants, 205 (51.3**%**) were female and 195 (48.8**%**) male and the median age was 38 years (IQR 30-48). One hundred seventy-three of the study participants (43.3%) were married, 100 (25%) were divorced, 98 (24.5%) were single and 29 (7.3%) were widowed. Most of the study participants (51.1%) were employees; 31.1% were unemployed, 5.5% were students, 3.3% were merchants, 2.5% were farmer and 6.5% had other jobs.

Majority of the study participants were Orthodox Christian (78.8%), 13.3% were Protestant, 7.5% were Muslims and 2 of them were other religion followers. When it comes to education, 157 of the study participants (39.3%) had tertiary level of education, 114 (28.5%) had attended secondary high school, 88 (22%) went to primary school and 41(10.3%) had no formal education.

The largest number of the study participants 347(86.8%) were from Addis Ababa followed by 39(9.8%) from Oromia region, 6(1.5%) from Amhara region, 5(1.3%) from Tigray region, 2(0.5%) from SNNRP and 1(0.3%) from Dire Dawa.

Seventy-nine (81.4%) of the study participants from Tikur Anbessa Specialized Hospital had advanced HIV disease at presentation followed by those from St. Peter Specialized Hospital by 67.3%, Yekatit 12 hospital medical college by 66.7% and Zewuditu Memorial Hospital by 47%.

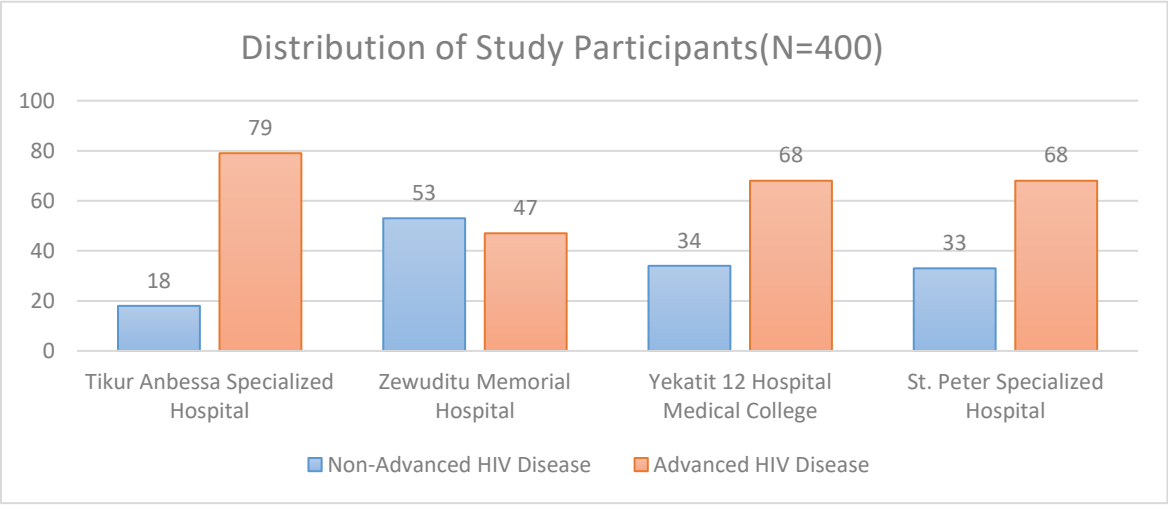

Table 1*: Baseline Characteristics of Study Participants (*N *= 400)*

Characteristics	*Frequency*	*Percent*
Hospital		
Tikur Anbessa Specialized Hospital	97	24.3%
Zewuditu Memorial Hospital	100	25%
Yekatit 12 Hospital Medical College	102	25.5%
St. Peter Specialized Hospital	101	25.3%
Gender		
Male	195	48.8%
Female	205	51.3%
Age		
< 25	50	12.5%
24-44	211	52.8%
>45	139	34.8%
Marital Status		
Single	98	24.5%
Married	173	43.3%
Divorced	100	25%
Windowed	29	7.3%
Education		
No formal Education	41	10.3%
Primary School(grade 1-8)	88	22%
Secondary School(grade 9-12)	114	28.5%
Tertiary education	157	39.3%
Occupation		
Student	22	5.5%
Unemployed	124	31.1%
Farmer	10	2.5%
Merchants	13	3.3%
Employed	204	51.1%
Others	26	6.5%
Religion		
Orthodox Christian	315	78.8%
Muslim	30	7.5%
Protestant	53	13.3%
Catholic	1	0.3%
Other religions	1	0.3%
Address		
Addis Ababa	347	86.8%
Amhara	6	1.5%
Dire Dawa	1	0.3%
Oromia	39	9.8%
SNNPR	2	0.5%
Tigray	5	1.3%

5.2. Clinical Profiles of the Study Participants

With regards to gender distribution of advanced HIV disease, more than two-thirds (70.3%) of male had advanced disease at presentation where as 61% of female presented with advanced HIV disease. Seventy-five percent of divorced study participants had advanced HIV disease at presentation. The cumulative proportion of advanced HIV disease among new presenters is 65.5%.

Two hundred fifty-four of the participants (63.5%) were diagnosed with HIV because of signs and symptoms consistent with opportunistic infections. Fourteen percent were diagnosed with HIV by means of patients' request and VCT. Reason for testing with HIV was not known in 64 (16%) of the study participants. Eleven percent of the study groups were diagnosed with HIV during ANC follow up. Eleven percent of the participants received HIV diagnosis concomitant with STI diagnosis. Sixty-two of the study participants (15.5%) had other comorbidities; 16(4%) of them were smokers and 41(10.3%) were alcoholics. One study participant was IV drug user.

Two hundred eleven of the study participants (72.8%) had CD4 count below 200 cells/µL. The median CD4 count was 138.5 (IQR 58.75 – 214.5). Seventeen percent of the study participants had BMI lower than 18.5 kg/m2. The median BMI was 20.1(IQR 19.2 - 22). One hundred sixty-six of the study participants (41.5%) were able to work; 179(44.8%) were ambulatory and 55(13.8%) were bedridden.

When it comes to clinical manifestations, the study participants had pulmonary tuberculosis 125(31.3%), extra pulmonary tuberculosis 82(20.5%), cerebral toxoplasmosis 50(12.5%), severe bacterial infections 38(9.5%), oral candidiasis 37(9.3%), Pneumocystis carinii pneumonia 32(8%), unintentional weight loss > 10% 32(8%), unintentional weight < 10% 31(7.8%), cryptococcal meningitis 15(3.8%), lymphoma 16(4.1%), recurrent upper respiratory tract infections 16(4%) and asymptomatic HIV infection 123(30.8%) respectively.

One hundred thirty-four (33.5%) of the study participants had WHO stage 1 HIV disease, WHO Stage 2 HIV disease 20 (5%), WHO Stage 3 HIV disease 109 (27.3%) and WHO Stage 4 HIV disease 137(34.3%).

Table 2: ***Clinical Profiles***

Characteristics	(N = 400/%)	Non-Advanced HIV	Advanced HIV
Clinical Manifestations			
Asymptomatic	123 (30.8)	114 (92.7)	9 (7.3)
Persistent generalized lymphadenopathy	3 (0.8)	2 (66.7)	1 (33.3)
Acute retroviral syndrome	6 (1.5)	2 (33.3)	4 (66.7)
Unintentional weight < 10%	31 (7.8)	6 (19.4)	25 (80.6)
Mucocutaneous manifestations	13 (3.3)	8 (61.5)	5 (38.5)
Herpes zoster within previous 5 years	5 (1.3)	2 (40)	3 (60)
Recurrent upper respiratory tract infections	16 (4)	8 (50)	8 (50)
Unintentional weight loss > 10%	32 (8)	2 (6.3)	30 (93.8)
Chronic diarrhea > 1 month	18 (4.5)	3 (16.7)	15 (83.3)
Oral candidiasis	37 (9.3)	2 (5.4)	35 (94.6)
Pulmonary tuberculosis	125 (31.3)	3 (2.4)	122 (97.6)
Severe bacterial infections	38 (9.5)	1 (2.6)	37 (97.4)
Unexplained cytopenias	9 (2.3)	0 (0)	9 (100)
HIV wasting syndrome	3 (0.8)	0 (0)	3 (100)
Pneumocystis carinii pneumonia	32 (8)	0 (0)	32 (100)
Toxoplasmosis of the brain	50 (12.5)	0 (0)	50 (100)
Cryptococcal Meningitis	15 (3.8)	0 (0)	15 (100)
Cytomegalovirus disease	1 (0.3)	0 (0)	1 (100)
Mucocutaneous herpetic infection	1 (0.3)	0 (0)	1 (100)
Progressive multifocal leukoencephalopathy	2 (0.5)	0 (0)	2 (100)
Esophageal Candidiasis	12 (3)	0 (0)	12 (100)
Extra pulmonary tuberculosis	82 (20.5)	0 (0)	82 (100)
Lymphoma	16(4.1)	0 (0)	16(100)

Table 3: ***Clinical Profiles***	***Frequency/percent***
WHO Staging	
Stage 1	134 (33.5)
Stage 2	20 (5.)
Stage 3	109 (27.3)
Stage 4	137 (34.3)
BMI, Median (IQR)	20.1 (19.2 – 22.0)
CD4 Count, M (IQR)	139 (59 – 214)
≤ 200	211 (72.8)
201 – 350	42 (14.5)
351 – 500	21 (7.2)
>501	16 (5.5)
Functional Status	
Bedridden	55 (13.8)
Ambulatory but not working	179 (44.8)
Working	166 (41.5)
Reason for HIV Testing	
HIV related symptoms	254 (63.5)
HIV contact history	1 (0.3)
ANC follow up	11 (2.8)
Patient request (VCT)	56 (14)
Diagnosis of STI	11 (2.8)
Unknown	64 (16)
Others	3 (0.8)
Others	
IV drug use	1 (0.3)
Comorbidities	62 (15.5)
Alcohol	41 (10.3)
Smoking	16 (4)

5.3. Factors associated with advanced HIV disease

Chi-square test for independent variables and Mann-Whitney test for BMI and CD4 count were carried out to look for association with outcome variable, ‘’advanced HIV disease’’. Binary and multivariate logistic regressions were performed after chi-square and nonparametric tests for which p- value in the bivariate analysis based on Wald test from the logistic regression less than 0.2 was taken to examine the effect of hospitals, gender, marital status, BMI, functional status and reason for HIV testing on advanced HIV disease. The Hosmer-Lemeshow test was employed to evaluate the goodness of fit for the model. The data includes crude odds ratios (COR) and adjusted odds ratios (AOR) with 95% confidence intervals.

Among the variables that were examined, having follow up at Tikur Anbessa Specialized Hospital ($\chi 2$ of 26.3 with P <0.001). being male ($\chi 2$ of 3.8 with P=0.05), divorced marital status ($\chi 2$ of 8.0 with P=0.02), low BMI (P <0.001), bedridden functional status ($\chi 2$ of 139.3 with P <0.001) and HIV testing reason due to symptoms of opportunistic infections ($\chi 2$ of 227 with P<0.001) had statistically significant association with advanced HIV disease.

On multivariate logistic regression, patients with low BMI had 3.2 times higher odds of having advanced HIV disease in contrast to other patients with normal or higher BMI (AOR 3.2, 95% CI 1.14 -8.9, P =0.03). Patients having bedridden functional status had 10.6 times higher odds of advanced HIV disease as compared to other groups of patients (AOR 10.6, 95% CI 1.24-91, P =0.03). HIV testing reason due to symptoms of opportunistic infections had 44.6 times higher odds of advanced HIV disease as compared to those who had HIV testing reasons (AOR 44.6, 95% CI 22.8-87.2, P <0.001).

No significant difference was obtained when comparison was made among patients having follow up at Tikur Anbessa Specialized Hospital and other hospitals, between male and female and marital status.

Table 4: Factors associated with advanced HIV disease

Characteristics	(N = 400/%)	Non-Advanced HIV	Advanced HIV	χ^2-test	p-value
Hospital					
TASH	97 (24.3)	18 (18.6)	79 (81.4)	26.3	.000
ZMH	100 (25.0)	53 (53)	47 (47)		
Y12HMC	102 (25.5)	34 (33.3)	68 (66.7)		
SPSH	101 (25.3)	33 (32.7)	68 (67.3)		
Gender					
Male	195 (48.8)	58 (29.7)	137 (70.3)	3.8	.05
Female	205 (51.3)	80 (39)	125 (61)		
Marital Status					
Single	98 (24.5)	43 (43.9)	55 (56.1)	8.0	
Married	173 (43.3)	61 (35.3)	112 (64.7)		
Divorced	100 (25.0)	25 (25)	75 (75)		.02
Widowed	29 (7.3)	9 (31)	20 (69)		
BMI, Median (IQR)	20.1 (19.2 – 22.0)	20.5 (20 – 23)	20.0 (18.9 – 21.8)		.000*
CD4 Count, Median (IQR)	139 (59 – 214)	404 (285 – 505)	103 (50 – 165)		.000*
Functional Status					
Bedridden	55 (13.8)	1 (1.8)	54 (98.2)	139.2	.000
Ambulatory but not working	179 (44.8)	25 (14)	154 (86)		
Working	166 (41.5)	112 (67.5)	54 (32.5)		
Reason for HIV Testing					
HIV related symptoms	254 (63.5)	19 (7.5)	235 (92.5)	227	.000
HIV contact history	1 (0.3)	1 (100)	0 (0)		
ANC follow up	11 (2.8)	10 (90.9)	1 (9.1)		
Patient request (VCT)	56 (14.0)	48 (85.7)	8 (14.3)		
Diagnosis of STI	11 (2.8)	8 (72.7)	3 (27.3)		
Unknown	64 (16.0)	50 (78.1)	14 (21.9)		
Others	3 (0.8)	2 (66.7)	1 (33.3)		

*: Refers to p-value obtained by Mann-Whitney U test

TASH: Tikur Anbessa Specialized Hospital, Y12HMC: Yekatit 12 Hospital Medical College, ZMH: Zewuditu Memorial Hospital, SPSH: St. Peter Specialized Hospital.

Table 5: ***multivariate binary logistic regression***

Independent Variables	p-value	95% CI			p-value	95%CI		
		COR	Lower	Upper		AOR	Lower	Upper
BMI	**0.000**	3.6	1.80	7.4	**0.03**	3.2	1.14	8.9
Functional Status	**0.000**	35.6	4.9	260.1	**0.03**	10.6	1.24	91
Reason for HIV Testing	**0.000**	56.6	30.1	106.4	**0.000**	44.6	22.8	87.2
Hospital	**0.000**	2.9	1.6	5.1	**0.3**	1.5	0.7	1.6
Gender	**0.05**	1.5	1.0	2.3	**0.3**	0.7	0.4	1.4
Marital Status	**0.02**	1.8	1.1	3.02	**0.3**	1.4	0.7	3.2

6. DISCUSSION

HIV disease is a global problem that has affected large proportion of individuals around the world. In spite of significant progress in the treatment and prevention of HIV disease, large number of newly diagnosed patients have advanced HIV disease at presentation resulting in increased morbidity and mortality rates [13].

Although more than half of both male and female patients had advanced HIV disease at presentation in many studies, males were more prone to manifesting with stage III or IV HIV disease or having CD4 counts below 200 cells per cubic millimeter according to WHO reports despite less gender disparity in this study [6].

In this study conducted at four public hospitals in Addis Ababa, 400 HIV-positive patients who were diagnosed newly from October 2022 to October 2023 were included. The prevalence of advanced HIV was 65.5% among newly diagnosed HIV positive patients based on WHO staging system of advanced HIV disease as clinical stage 3, stage 4 or CD4 count < 200 cells/µL. One hundred thirty-seven (70.3%) of male study participants had advanced HIV disease and 125(61%) of female study participant had advanced HIV disease at presentation. The prevalence was higher than studies conducted in rural parts of SNNPR where the prevalence of advanced HIV disease upon entering into care was 60%([6]). It was lower than Senegal (71%), higher than South Africa (22%-26%) and Botswana (24.7%) [21].

The true prevalence of advanced HIV disease in the study hospitals might be higher than the reported prevalence because patients with advanced HIV disease have exceedingly high risk of death even before linkage to HIV care (reference).

Eighty-one percent of patients who were seen at Tikur Anbessa Specialized Hospital had advanced HIV disease as compared to other patients seen in the other hospitals. This might be due to many of the patients having complicated and advanced disease have been referred for specialists' evaluation at tertiary care. St. Peter Specialized Hospital and Yekatit 12 Hospital Medical College were also a high burden sites of advanced HIV disease having a prevalence rate of 67.3% and 66.7% respectively. Zewuditu Memorial Hospital had relatively lower prevalence of advanced HIV disease at presentation (47%) in contrast to other hospitals.

The commonest opportunistic infections diagnosed in patients who had advanced HIV disease at presentation to health cares were pulmonary tuberculosis (31.3%), extra pulmonary tuberculosis (20.5%), cerebral toxoplasmosis (12.5%), severe bacterial infection (9.5%), oral and esophageal candidiasis (9.6%), PCP (8%), lymphoma 16(4.1%), cryptococcal meningitis (3.8%) and two patients (0.5%) had PML. One hundred twenty-three (30.8%) of the study participants were asymptomatic upon linkage into the HIV care. More than seventy percent of the study participants (72.5%) had CD4 counts at diagnosis. Of these, 72.8% of them had CD4 counts less 200cells/μL. The median CD4 count was 139 with inter quartile range of 59-214.

Consistent with the previous studies, men were more likely to have various WHO clinical stage 3 and 4 defining illnesses, lower CD4 count and lower BMI upon presentation to hospitals. Bedridden patients and those who were diagnosed with HIV due to symptoms of OIs had advanced HIV disease while entering into care.

There was a significant association between lower BMI and advanced HIV disease (AOR 3.2, 95% CI 1.14-8.9, P=0.03), bedridden functional status and advanced HIV disease (AOR 10.6, 95% CI 1.24-91, P=0.03) and HIV diagnosis due to symptoms of OIs and advanced HIV disease (AOR 44.6, 95% CI 22.8-87.2, $P < 0.001$) after adjusting for other independent variables like age, education, gender, marital status, occupation and hospitals. There was no association between older age and male gender with advanced HIV disease although it was reported in other studies [21].

The current finding shows that many patients from Addis Ababa have advanced HIV disease at presentation to health care which is consistent with many studies from SSA (6). There may

be various reason for advanced HIV disease at presentation (6). These factors include lack of awareness to HIV status, absence of universal HIV screening and impact of COVID global pandemic. A prospective study is needed to evaluate the factors contributing to late presentation and the development of advanced HIV disease.

The study's strength is its inclusion of all individuals who were diagnosed with HIV at the study hospitals within the study period. Nevertheless, the result needs to be interpreted in the context of specific limitations. The hospitals incorporated in this study are presumably not indicative of all healthcare facilities that provide HIV care and treatment in Addis Ababa.

6.1. Strength of the study

The study has relatively larger sample by including all patients at the study sites. Important information including date of diagnosis and clinical profiles were documented.

6.2. Limitation of the study

One limitation is that it is a retrospective study limited to Public Hospitals in Addis Ababa. The other limitation of the study is it only involved specialized hospital and it wouldn't reflect the true picture of advanced HIV disease in Addis Ababa. Some important information like CD4 count, reason for testing, sociodemographic characteristics in certain patients and BMI have not been determined. For instance,110(28.2%) patients had no CD4 count highlighting the importance of complete patient evaluation and documentation of clinical and laboratory data. There is some incongruity between WHO clinical staging of patients and their actual diagnoses documented on their charts.

6.3. Conclusion and Recommendation

This study provides a snapshot of the current situation regarding advanced HIV disease among newly diagnosed HIV patients in Addis Ababa. The prevalence of advanced HIV disease stands at 65.5%, reflecting a recent steady increase. Urgent and effective interventions are necessary for raising awareness and scaling up HIV testing rates to address this critical public health issue. The high incidence of advanced HIV disease poses challenges for prevention and control efforts. Therefore, targeted programs focused on early detection, public awareness, and universal testing access are crucial to alleviate the burden while patients enter into care.

7. REFERENCES

[1] UNAIDS, "Global HIV Statistics," *Fact Sheet 2021*, no. June, pp. 1–3, 2021.

[2] A. T. Boyd *et al.*, "Addressing advanced HIV disease and mortality in global HIV programming," *AIDS Res. Ther.*, vol. 17, no. 1, pp. 1–7, 2020, doi: 10.1186/s12981-020-00296-x.

[3] P. Brief, "Providing care to people with advanced hiv disease who are seriously ill".

[4] G. A. Update, "Ending AIDS," 2017.

[5] N. A. Benzekri *et al.*, "Prevalence, predictors, and management of advanced HIV disease among individuals initiating ART in Senegal, West Africa," *BMC Infect. Dis.*, vol. 19, no. 1, pp. 1–8, 2019, doi: 10.1186/s12879-019-3826-5.

[6] A. R. Lifson *et al.*, "Advanced HIV Disease among Males and Females Initiating HIV Care in Rural Ethiopia," *J. Int. Assoc. Provid. AIDS Care*, vol. 18, pp. 1–7, 2019, doi: 10.1177/2325958219847199.

[7] H. N. Fomundam *et al.*, "Prevalence and predictors of late presentation for HIV care in South Africa," *South African Med. J.*, vol. 107, no. 12, pp. 1058–1064, 2017, doi: 10.7196/SAMJ.2017.v107i12.12358.

[8] L. Shi *et al.*, "Trends of late HIV presentation and advance HIV disease among newly diagnosed HIV cases in Jiangsu, China: A serial cross-sectional study from 2008 to 2020," *Front. Public Heal.*, vol. 10, 2022, doi: 10.3389/fpubh.2022.1054765.

[9] H. Jiang *et al.*, "Prevalence of and factors associated with advanced HIV disease among newly diagnosed people living with HIV in Guangdong Province, China," *J. Int. AIDS Soc.*, vol. 23, no. 11, pp. 1–11, 2020, doi: 10.1002/jia2.25642.

[10] G. M. Belay, A. Endalamaw, and A. D. Ayele, "Late presentation of HIV positive adults and its predictors to HIV/AIDS care in Ethiopia: A systematic review and meta-analysis," *BMC Infect. Dis.*, vol. 19, no. 1, pp. 1–8, 2019, doi: 10.1186/s12879-019-4156-3.

[11] R. Lebelonyane *et al.*, "Advanced HIV disease in the Botswana combination prevention project: Prevalence, risk factors, and outcomes," *Aids*, vol. 34, no. 15, pp. 2223–2230, 2020, doi: 10.1097/QAD.0000000000002627.

[12] M. Lahuerta *et al.*, "Advanced HIV disease at entry into HIV Care and Initiation of Antiretroviral Therapy during 2006-2011: Findings from four sub-saharan African countries," *Clin. Infect. Dis.*, vol. 58, no. 3, pp. 432–441, 2014, doi: 10.1093/cid/cit724.

[13] N. Ford and V. Hepatitis, "Advanced HIV Disease Update from WHO Slow decline in AIDS-related deaths," 2022.

[14] C. Sun *et al.*, "HIV/AIDS late presentation and its associated factors in China from 2010 to 2020: a systematic review and meta-analysis," *AIDS Res. Ther.*, vol. 18, no. 1, pp. 1–14, 2021, doi: 10.1186/s12981-021-00415-2.

[15] S. Rao, S. Av, B. Unnikrishnan, D. Madi, and A. K. Shetty, "Correlates of Late Presentation to HIV care in a South Indian Cohort," vol. 99, no. 5, pp. 1331–1335, 2018, doi: 10.4269/ajtmh.18-0386.

[16] O. Bisbal *et al.*, "Late presentation for HIV remains a major health issue in Spain : Results from a multicenter cohort study , 2004 – 2018," pp. 2004–2018, 2021, doi: 10.1371/journal.pone.0249864.

[17] E. L. M. Op De Coul *et al.*, "Factors associated with presenting late or with advanced HIV disease in the Netherlands, 1996 2014: Results from a national observational cohort," *BMJ Open*, vol. 6, no. 1, 2016, doi: 10.1136/bmjopen-2015-009688.

[18] A. Calmy, N. Ford, and G. Meintjes, "The Persistent Challenge of Advanced HIV Disease and AIDS in the Era of Antiretroviral Therapy," vol. 66, no. Suppl 2, pp. 103–105, 2018, doi: 10.1093/cid/cix1138.

[19] P. A. Agaba *et al.*, "Patients who present late to HIV care and associated risk factors in Nigeria," *HIV Med.*, vol. 15, no. 7, pp. 396–405, 2014, doi: 10.1111/hiv.12125.

[20] M. L. Chihana *et al.*, "Distribution of advanced HIV disease from three high HIV prevalence settings in Sub-Saharan Africa: a secondary analysis data from three population-based cross-sectional surveys in Eshowe (South Africa), Ndhiwa (Kenya) and Chiradzulu (Malawi)," *Glob. Health Action*, vol. 12, no. 1, 2019, doi: 10.1080/16549716.2019.1679472.

[21] G. Musengimana *et al.*, "Characteristics and clinical outcomes of patients presenting with advanced HIV disease in the 'treat all' era: a retrospective cohort study from rural

Rwanda," *BMC Infect. Dis.*, vol. 22, no. 1, pp. 1–9, 2022, doi: 10.1186/s12879-022-07692-w.

[22] F. E. Hassan *et al.*, "Implementation of WHO guidelines on management of advanced HIV disease and its impact among TB co-infected patients in Tanzania: a retrospective follow-up study," *BMC Public Health*, vol. 22, no. 1, pp. 1–9, 2022, doi: 10.1186/s12889-022-13498-x.

[23] A. F. Auld, R. W. Shiraishi, I. Oboho, C. Ross, M. Bateganya, and V. Pelletier, "Trends in Prevalence of Advanced HIV Disease at Antiretroviral Therapy," *Morb. Mortal. Wkly. Rep.*, vol. 66, no. 21, pp. 2–7, 2017.

[24] S. Carmona *et al.*, "Persistent High Burden of Advanced HIV Disease among Patients Seeking Care in South Africa's National HIV Program: Data from a Nationwide Laboratory Cohort," *Clin. Infect. Dis.*, vol. 66, no. Suppl 2, pp. S111–S117, 2018, doi: 10.1093/cid/ciy045.

[25] A. D. Haas *et al.*, "Prevalence of and factors associated with late diagnosis of HIV in Malawi, Zambia, and Zimbabwe: Results from population-based nationally representative surveys," *PLOS Glob. Public Heal.*, vol. 2, no. 2, p. e0000080, 2022, doi: 10.1371/journal.pgph.0000080.

[26] B. Z. Woldegeorgis, Z. Zekarias, B. G. Adem, M. S. Obsa, and A. A. Kerbo, "Prevalence and determinants of opportunistic infections among HIV-infected adults receiving antiretroviral therapy in Ethiopia: A systematic review and meta-analysis," *Front. Med.*, vol. 10, no. February, 2023, doi: 10.3389/fmed.2023.1087086.

[27] S. Degno *et al.*, "Predictors of late presentation for hiv/aids in west arsi zone public health institutions, south ethiopia: Unmatched case–control study," *HIV/AIDS - Res. Palliat. Care*, vol. 13, pp. 759–766, 2021, doi: 10.2147/HIV.S313139.

[28] L. Bayisa, A. Tadesse, M. M. Reta, and E. Gebeye, "Prevalence and factors associated with delayed initiation of antiretroviral therapy among people living with hiv in nekemte referral hospital, western ethiopia," *HIV/AIDS - Res. Palliat. Care*, vol. 12, no. September, pp. 457–465, 2020, doi: 10.2147/HIV.S267408.

[29] M. Adal, "Systematic review on HIV situation in Addis Ababa, Ethiopia," *BMC Public Health*, vol. 19, no. 1, pp. 1–12, 2019, doi: 10.1186/s12889-019-7885-8.

[30] X. Hu *et al.*, “HIV late presentation and advanced HIV disease among patients with newly diagnosed HIV/AIDS in Southwestern China: A large-scale cross-sectional study,” *AIDS Res. Ther.*, vol. 16, no. 1, pp. 1–10, 2019, doi: 10.1186/s12981-019-0221-7.

[31] F. Terefe Asfaw *et al.*, “Proprtion of Late Presentation to Hiv/Aids Care in Yekatit 12 Hospital Medical College, Addis Ababa. 2020GC,” *Am. J. Infect. Dis. Microbiol.*, vol. 11, no. 2, pp. 30–39, 2023, doi: 10.12691/ajidm-11-2-2.

7.1. English Version Questionnaire

1. Data collector's name: _____
2. What is the date of data collection?
3. What is the MRN of the patient?
4. What is the site of data collection?
5. TASH B. ZMH C. Y12H D. SPH
6. What is the age of the patients?
7. What is the sex of the patient?
8. 1. Male, 2. Female
9. What is the religion of the patient?
10. 1. Orthodox, 2. Muslim, 3. Protestant, 4. Catholic, 5. other
11. What is the educational status of the patient?
12. No formal education, 2. Grade 1-8, 3. Grade 9-12, 4. Higher education
13. Where is the region of residency of the patient?
14. AA, 2. Afar, 3. Amhara, 4. Benshangul Gumuz, 4. Dire Dawa, 5. Gambela, 6. Harari, 7. Oromia, 8. Sidama, 9. Somali, 10. South west Ethiopia People region, 11. SNNRP, 12. Tigray
15. What is the marital status of the patient?
16. Single, 2. Married, 3. Divorced, 4. Widowed
17. What is the occupation of the patient?
18. Student, 2. Unemployed, 3. Farmer, 4. Merchant, 5, employ, 6. other
19. What is the height of the patient?
20. What is the weight of the patient?
21. What is the BMI of the patient?
22. Does the patient have history of smoking?
23. Yes, 2. No
24. Does the patient have history of alcohol intake?
25. Yes, 2. No
26. Does the patient have history of injection drug use?
27. Yes, 2. No
28. What is the reason for HIV testing?
29. HIV related symptoms, 2. HIV contact History, 3. ANC follow up, 4. Patient request or VCT, 5. Diagnosis of STI, 6. Unknown, 7. Other
30. What is the functional status of the patient?
31. Bedridden, 2. Ambulatory but not working, 3. Working
32. Does the patient have a CD4 count at diagnosis?
33. Yes, 2. No
34. If Yes to Q33, mention the CD4 count
35. What is the WHO stage of the HIV at diagnosis?
36. Stage 1, 2. Stage 2, 3. Stage 3, 4. Stage 4
37. Does the patient have advanced HIV disease?
38. Yes, 0. No
39. Which one of the following diseases does the patient have at diagnosis?
    1. Asymptomatic infection
    2. Persistent generalized lymphadenopathy

3. Acute Retroviral (HIV) Syndrome
4. Unintentional weight loss < 10% body weight
5. Minor mucocutaneous manifestations
6. Herpes zoster within previous 5 years
7. Recurrent upper respiratory tract infections
8. Unintentional weight loss > 10% body weight
9. Chronic diarrhea > 1 month
10. Prolonged fever > 1 month
11. Oral candidiasis
12. Oral hairy leukoplakia
13. Pulmonary tuberculosis
13. Severe bacterial infections
14. Vulvovaginal candidiasis
15. Unexplained anemia, neutropenia or chronic thrombocytopenia
16. HIV wasting syndrome
17. Pneumocystis carinii pneumonia
18. Toxoplasmosis of the brain
19. Cryptosporidiosis with diarrhea > 1 month
20. Isosporiasis with diarrhea > 1 month
21. Cryptococcosis, extrapulmonary
22. Cytomegalovirus disease
23. Herpes simplex virus infection, mucocutaneous
24. Progressive multifocal leukoencephalopathy
25. Any disseminated endemic mycosis
26. Esophageal Candidiasis
27. Atypical disseminated mycobacteriosis
28. Non-typhoid Salmonella septicemia
29. Extra pulmonary tuberculosis
30. Lymphoma
31. Kaposi's sarcoma
32. HIV encephalopathy
33. Visceral Leishmaniasis

40. Does the patient have any comorbidities?
    1. Yes 2. No
41. Mention the comorbidities the patient has.