INCIDENCE RATE OF TUBERCULOSIS AND PREDICTORS OF UNFAVORABLE TREATMENT OUTCOMES AMONG ADOLESCENTS AND YOUNG ADULTS INITIATING ANTIRETROVIRAL THERAPY IN DAR ES SALAAM, 2020 - 2023: A RETROSPECTIVE COHORT STUDY

Mariam Mbwana, BSc. Medical Laboratory Sciences (Bsc. MLS)

MSc Epidemiology and Laboratory Management Dissertation

Muhimbili University of Health and Allied Sciences

October, 2024

Muhimbili university of health and allied Sciences
School of public health and social sciences
Department of epidemiology and biostatistics

INCIDENCE RATE OF TUBERCULOSIS AND PREDICTORS OF UNFAVORABLE TREATMENT OUTCOMES AMONG ADOLESCENTS AND YOUNG ADULTS INITIATING ANTIRETROVIRAL THERAPY IN DAR ES SALAAM, 2020-2023: A RETROSPECTIVE COHORT STUDY

By

Mariam Mbwana

A Dissertation Submitted in Partial Fulfilment of the Requirements for the Degree of Master of Science in Epidemiology and Laboratory Management of Muhimbili University of Health and Allied Sciences

October, 2024

CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance of dissertation entitled Incidence Rate of Tuberculosis and Predictors of Unfavorable Treatment Outcomes among Adolescents and Young Adults Initiating Antiretroviral Therapy in Dar es Salaam From 2020-2023: A Retrospective Cohort Study, in partial fulfilment of the requirements for the degree of Master of Science in Epidemiology and Laboratory Management of Muhimbili University of Health and Allied Sciences.

_____
Dr. Frank Msafiri
(Supervisor)

Date: _____

_____
Dr. Salim Masoud
(Co-Supervisor)

Date: _____

_____
Nelson Edwin Malugu
(Co-Supervisor)

Date: _____

DECLARATION AND COPYRIGHT

I, **Mariam Mbwana** declare that this dissertation is my original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

Signature: …….. Date…….....….....

This dissertation is a copyright material protected under the Berne Convention, the Copyright Act 1999 and other international and national enactments, in that behalf, on intellectual property. It may not be reproduced by any means, in full or in part, except for short extracts in fair dealing, for research or private study, critical scholarly review or discourse with an acknowledgement, without the written permission of the Directorate of Postgraduate Studies, on behalf of both the author and the Muhimbili University of Health and Allied Sciences

ACKNOWLEDGMENT

I would like to express my gratitude to The Management and Development for Health (MDH) for their support and data provision for my dissertation. In light of this, I would like to express my deep appreciations to Dr. Frank Msafiri, and Dr. Salim Masoud, Nelson Edwin Malugu, my supervisors for their assistance and insightful advice during the design, analysis, and writing of my dissertation. I also like to thank the Ministry of Health (MoH) for supporting my studies including the dissertation. Thank you to the Tanzania Field Epidemiology and Laboratory Training Program (TFELTP) for supporting me during my study period. I would especially want to thank Mr. Shabani K. Motto, who sponsored my studies. Finally, but no less, I want to express my gratitude to all of my Muhimbili University of Health and Allied Sciences (MUHAS) for the time we spent and shared learning experiences during the preparation of this dissertation.

DEDICATION

I dedicate this work to my entire family; my beloved Mother, Tausi Ramadhani for her prayers and words of support that pushed me forward in this endeavor. My lovely husband, Shabani K. Motto for his patience, efforts, continuous love, and encouragement. My Sons, Irfaan and Irfad for their supplications and patients when I was away from home. My Siblings, Maulid, Ruqaiyah and Mwanaisha for their prayers, and encouragement.

TABLE OF CONTENTS

ACKNOWLEDGMENT iii
DEDICATION 4
TABLE OF CONTENTS 5
LIST OF TABLES 7
LIST OF FIGURES 8
ABBREVIATIONS 9
ABSTRACT 11
CHAPTER ONE 13
1. INTRODUCTION 13
1.1. Background 13
1.2. Problem statement 14
1.3. Conceptual framework 15
1.4. Rationale 16
1.5. Research questions 17
1.6. Objectives 17
1.6.1. Broad objective 17
1.6.2. Specific objectives 17
CHAPTER TWO 18
2. LITERATURE REVIEW 18
2.1 Overview of TB-HIV Co-infection 18
2.2 Prevalence of TB in Adolescents and Young Adults living with HIV 19
2.3 Incidence of TB among Adolescents and Young Adults (AYA) Living With HIV 19
2.4 TB Treatment Outcomes among HIV Infected AYA 20
2.5 Unfavorable TB treatment outcome among HIV infected AYA 20
2.6 Predictors for unfavorable TB treatment outcomes in HIV-infected AYA 21
2.6.1 Age 21
2.6.2 Sex 22
2.6.3 Residence 22
2.6.4 WHO clinical stage 23
2.6.5 ART adherence 23

2.6.6 CD4 Cell count 24
2.6.7 Type of TB 24
CHAPTER THREE 25
3 METHODOLOGY 25
3.1 Study design and duration 25
3.2 Study area 25
3.3 Study population 25
3.4 Data inclusion and exclusion 25
3.4.1 Inclusion criteria 25
3.4.2 Exclusion criteria 26
3.5 Sampling method 26
3.6 Power of the study 27
Assumptions of power of the study: 27
3.7 Data abstraction procedure and Dataset description 28
3.8 Data analysis 28
3.9 Ethical considerations 29
CHAPETR FOUR 30
4 RESULTS 30
4.1 Descriptive results 30
4.2 Prevalence of TB among HIV infected AYA 31
4.2.1 Prevalence of TB among HIV infected AYA age group 32
4.3 The incidence of TB among HIV infected AY on anti TB 33
4.4 Treatment outcome of TB among HIV infected AYA 35
4.5. Predictors of poor TB treatment outcome among HIV infected AYA 36
CHAPTER FIVE 38
5 DISCUSSION 38
5.1 Study limitation 40
6. CONCLUSION 41
7. RECOMMENDATION 41
REFERENCES 42
APPENDICES 49
Appendix II: Approval letter 51
Appendix III: Data abstraction tool 53

LIST OF TABLES

Table 1. Sociodemographic and clinical characteristics of HIV infected AYA 31
Table 2: Incidence of TB in HIV infected AYA..... 34
Table 3: Treatment outcome among HIV infected AYA.....35
Table 4: Predictors for poor TB treatment outcome among HIV- infected AYA 36

LIST OF FIGURES

Figure 1: Factors associated with poor TB treatment outcomes. 16
Figure 2: Flow chart showing enrolment of study subjects 30
Figure 3: TB prevalence in HIV infected AYA by age group 32
Figure 4: TB prevalence in HIV infected AYA by sex 33

ABBREVIATIONS

AYA	Adolescents and Young Adults
AIDS	Immuno-Deficiency Syndrome
ART	Anti-Retroviral Therapy
ARTI	Annual risk of tuberculosis infection
CD4	Clusters of differentiation 4
CTC	Care and Treatment Centre
HIV	Human Immunodeficiency Virus
LTFU	Lost to Follow Up
MOH	Ministry of Health
MDRTB	Multidrug-resistant tuberculosis
NTLP	National Tuberculosis and Leprosy Program
PTB	Pulmonary tuberculosis
TB	Tuberculosis
TPT	TB Preventive Treatment
WHO	World Health Organization

DEFINITIONS OF TERMS

The definitions in this study are adopted from the World Health Organization

TERM	DEFINITION
An Adolescent	Is any person aged between 10 and 19 years.
Young Adult	Is any person aged between 20 and 24 years.
Adolescent and Young Adult	Is any person between the ages of 10–24 years.
Poor Treatment Outcome	Refers to treatment failure, loss to follow-up/defaulting, and death
Successful Treatment Outcome	Refers to cured tuberculosis infection.
Tuberculosis Treatment Failure	Is a patient whose sputum smear microscopy or culture is positive after five months of anti-tuberculosis treatment.
Death	Refers to a patient with tuberculosis who dies for any reason during treatment.
Lost to Follow-Up	Is a patient with tuberculosis whose treatment is interrupted for two consecutive months or more.
Incidence	Refers to new cases of tuberculosis that were diagnosed between 1st January 2020 to 31st December 2023.

ABSTRACT

Background: Adolescents and young adults (AYA) with HIV infection in sub-Saharan Africa are at high risk of dying from tuberculosis (TB) due to extreme poverty, violence and stigma, and defaulting TB treatment. Despite these risks, estimates of poor TB treatment outcomes among this population are limited in Tanzania as majority of the TB reports divide the population in two group adults (over 15 years old) and children (ages 0-14) ignoring 15-24 years as a distinct group. This study aimed to evaluate the incidence of TB and predictors for poor TB treatment outcomes among 10-24 years old adolescents and young adults (AYA) starting antiretroviral therapy (ART) in Dar es Salaam.

Study objective: To determine the incidence rate of TB and predictors for poor TB treatment outcomes among AYA living with HIV in Dar es Salaam.

Method: A retrospective cohort study, conducted in Dar es Salaam using data collected from Care and Treatment Centre (CTC) 2 database between January 2020 to December 2023. Patients with HIV aged 10 to 24 years who were on ART between January 2020 and December 2023 were included. The incidence of TB was calculated by dividing newly diagnosed cases by person-years of follow-up. TB prevalence was calculated by the number of HIV-infected AYA tested positive for TB over the total number of HIV-infected AYA during the study period. A multivariable Cox proportional hazards regression model was used to identify risk factors for poor TB treatment outcomes.

Result: Among 19,021 HIV-infected AYA, 34 (0.2%) had TB, with a high prevalence in the 20-24 year age group (67.6%). The TB incidence rate was 8.6 per 1000 person year (95% CI; 5.2-14.1/cases per 1000 person year at risk), with the highest rates observed in males 20.5 per 1000 person year (95% CI; 9.2-45.7/1000 person years at risk), young adults 9.1per 1000 person year (95% CI; 5.1-16.1/1000 person years at risk), and WHO clinical stage 4 had 46.3 per 1000 person year (95% CI; 14.9-143.6/1000 person years at risk). The outcome of death was high 11/31 (35.5%). We did not identify significant predictors for poor treatment outcomes in this study.

Conclusion: We observed a low prevalence of TB, low incidence of TB, and the most affected age group was 20-24 years in terms of burden, incidence and mortality. To achieve the goal of reducing poor treatment outcomes, it is recommended to sustain the existing

strategies such as the TPT provision and ART adherence, to improve early TB case detection, to strengthen follow-up of 20-24 years after initiation of treatment, further investigation is needed using a large National dataset to get a more comprehensive findings

CHAPTER ONE

1. INTRODUCTION

1.1. Background

In 2021, it was estimated that 10.6 million individuals globally have suffered from tuberculosis (TB). Between 2020 and 2021, there was a 3.6% rise in the number of new cases (incidents) of tuberculosis per 100,000 persons (1). An estimated 1.8 million adolescents (10–19 years old) and young adults (20–24 years old) contract TB annually, accounting for roughly 18% of all TB cases worldwide (2). There were 1.60 million TB cases among adolescents and young adults (AYA) in 2017, based on information from the World Health Organization (WHO). Furthermore, 90,000 deaths from TB occurred in young adults (20-24 years), higher than in young adolescents (10 -14 years) with 11,000 and in older adolescents aged (15-19 years) with 60,000 deaths from TB (3).

HIV and TB are related to public health issues. HIV reduces immunity, which increases the risk of contracting TB and having it recur or reactivate (4). For people who are HIV positive TB is the primary cause of mortality (5). Furthermore, among patients living with HIV (PLHIV), especially AYA, one of the main causes of illness and death is TB (6). AYA are susceptible to TB illness, infection, and unfavorable treatment outcome. Because AYA develop the disease and contribute to its transmission, they provide unique challenges for case detection and treatment (7). During AYA, high TB transmission causes a fast increase in TB incidence.

Additionally, AYAs comprise a half of new HIV infections globally, meaning they are at a high risk of infection (8). In 2019, two out of every seven new cases of HIV infection were brought on by AYA (9). AYA is 1.2 billion, of which 10 million estimated to be HIV positive. Findings revealed that, in Sub-Saharan Africa (SSA) more teenage girls and young females acquired HIV globally than males (10,11). TB development is more likely to occur in AYAs who are HIV positive, leading to unfavorable treatment outcome. Moreover, it advised that TB/HIV patients get antiretroviral treatment (ART) earlier, however it raises the possibility of immune reconstitution inflammatory syndrome (IRIS) for those with subclinical TB within 3 months. Before starting anti-TB treatment, patients on ART were divided into those who started ART 90 days or less, more than 90 days, within 14 days, after 14 days, or did not have ART.

Studies have shown that factors of being older adolescents have a 75% higher risk of loss to follow-up (LFTU) than younger adolescents (11). Those with pulmonary TB had 92% times higher risk of LFTU, treatment failure, and death than those with extra pulmonary TB (12). Having HIV co-infection was 413% times higher risk of LFTU, treatment failure, and death, compared to those without HIV co-infection (13). Moreover, lack of a contact person (a person who takes care of the patient had 37% higher risk of treatment failure, death and LFTU, than those with a contact person (14). Being a males are 152% more likely to experience treatment failures, LFTU, and deaths than females (15). Factor of smear-positive were 88.2% higher risk of LFTU compared to smear negative results (16).

Tanzania reported 22,000 TB patients who were HIV-negative and 16,000 TB patients who were HIV-positive in 2018 (17). The Only 85% of HIV/TB treatments are successful, with 15% having unfavorable results (18). Despite of HIV-infected AYA often overlooked in TB prevention and care strategies. Most of the literature in Tanzania divides the population into children and adults (19,20) ignoring AYA with distinct social, developmental, and biological characteristics that need for specialized methods of case detection for case detection, care, and prevention (21). This study determine the burden of TB and predictors of poor treatment outcomes among AYA living with HIV. The purpose of this study was to improve TB treatment outcomes, reduce transmission of TB, and avoid drug resistance.

1.2. Problem statement

Death from TB among HIV-infected individuals increased to 11% from all deaths in 2017 (22). Likewise in 2019, TB HIV infected people was about 3.4 million, however real TB burden among HIV-positive AYA is uncertain, which reveals that the AYA population is a neglected group (23,24). AYAs face age-related challenges in accessing issues of healthcare services, especially in TB-endemic places without concentrating on adolescent health services. Despite WHO and other organizations emphasizing the need for healthcare services to address the specific needs of AYAs with HIV infection. Still HIV HIV-infected AYAs are at risk for TB infection, illness, and unfavorable outcomes in TB treatment since this age group faces social, developmental, and physiological characteristics that require dedicated approaches to increase attention in case identification, treatment, and prevention within the worldwide End TB Strategy.

In Tanzania, more initiatives aimed at reducing the TB burden in two age groups as children and/or adults living with HIV, while the AYAs group was disregarded in prevention and care policies. The specific needs of HIV-infected AYAs must be considered and addressed to improve outcomes in the AYA group.

There is little information on the TB burden and predictors of poor TB treatment outcomes among HIV-infected AYA in Tanzania. This study assessed the burden of TB and predictors of death, LTFU, and treatment failure among HIV-infected AYA in Dar es Salaam, aimed to improve treatment outcomes, reduce TB transmission, and avoid drug resistance.

1.3. Conceptual framework

Young adults had a 57% times higher risk of LTFU compared to young adolescents (25). Previously reported males had two times higher risk of LTFU than females (26). Additionally, compared to patients who received Antiretroviral Therapy (ART) more than 8 weeks after their TB diagnosis, those who had never been on ART but received it less than that period had a 59% decreased chance of dying. The WHO clinical stage had a 118% increased risk of death in every increase of the WHO stage (27).TB HIV coinfection patients was 350% times higher risk of adverse treatment outcomes compared to non-HIV TB patients (28).

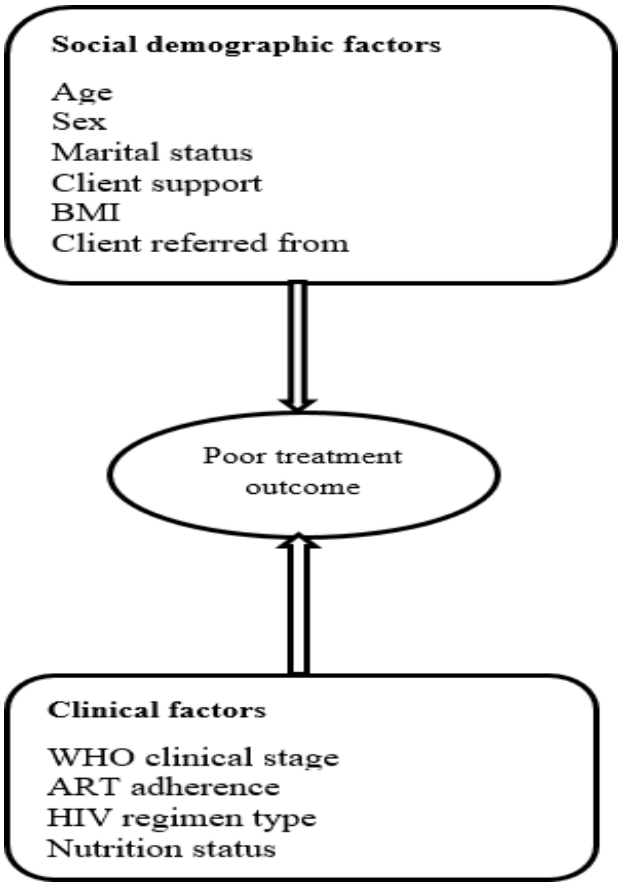


Figure 1: Factors associated with poor TB treatment outcome among AYA living with HIV.

1.4. Rationale

HIV infected AYA faced challenges of stigma, economic and education factors in TB treatment and cause poor treatment outcome, however many studies and other organization in Tanzania focusing in children and adults ignoring AYA age group. The findings will be used to improve treatment outcome for TB and prevent further TB transmission among HIV infected AYA. Moreover, the finding will help Ministry of Health (MoH) through National Tuberculosis and Leprosy Program (NTLP) to advise, evaluate the policies and strategies to age specific friendly services for AYA. Additionally, NTLP they may benefit from the findings by using it to improve the epidemiological data by age disaggregation of TB data. Further, it will help the health care provider to take into account and tend to AYAs' particular demands in their health facilities.

1.5. Research questions

What is the incidence of TB and predictors of unfavorable treatment outcomes among newly diagnosed AYA (10-24 years) initiating ART in Dar es Salaam, 2020-2023?

1.6. Objectives

1.6.1. Broad objective

To assess the incidence of TB and predictors of poor TB treatment outcomes among AYA (10-24 years) initiating ART in Dar es Salaam.

1.6.2. Specific objectives

a. To determine the prevalence of TB among HIV-infected AYA after initiation of antiretroviral therapy
b. To determine the incidence of TB among HIV-infected AYA after initiation of antiretroviral therapy.
c. To determine treatment outcomes among HIV-infected AYA on anti-TB treatment.
d. To determine the predictors for poor TB treatment outcome among HIV-infected AYA on anti-TB treatment.

CHAPTER TWO

2. LITERATURE REVIEW

2.1 Overview of TB-HIV Co-infection

TB is among opportunistic infection (OI) which are infections that affect persons with weakened immunity more frequently or more severely than they affect those with healthy immune systems. HIV impairs the immune system, exposing HIV-positive individuals at higher risk for TB. The combination of HIV and TB infection known as HIV/TB coinfection. Compared to people without HIV, persons with HIV are more likely to get TB illness from an untreated latent TB infection (29). HIV and TB have well-documented epidemiological and biological interactions that affect the prevalence, course, and outcomes of both illnesses. The global increase of TB cases is mostly due to the HIV epidemic, and the largest risk factor for acquiring TB is HIV infection (30). Globally, patients living with HIV (PLHIV) are eighteen times more likely to get active TB compared to individuals without HIV. Similarly, the approximate number of TB cases were 10 million, 8.2% of the population had HIV in 2019 (31).

WHO reported, SSA has the highest rate of HIV and TB co-infection in the globally, where the co-infection continues to have severe effects on the human population. The burden of co-infection differs significantly between Regions and Nations. In Ghana showed the increase in prevalence of TB HIV, a research conducted in Accra in 2020 found a prevalence of TB/HIV of 22.9%. Furthermore, demographic research from the Volta area revealed that TB/HIV prevalence reached 19.1% in 2019 after 18.2% in 2017 (32). The frequency of TB-HIV co-infection is quite high in South Africa (23%), which maintaining two separate and frequently overlapping TB and HIV treatment programs it identified as an inefficient use of resources, hence policymakers advocated for the unification of TB and HIV treatments (33).

Tanzania is a country with a high TB burden as well as a high TB/HIV burden 31% (48,000) of the 154,000 newly reported cases of TB in Tanzania in 2017 were also HIV positive, according to estimates from WHO (2018). According to Mollel et al. (2019), incidence of TB was 2.08 for every 1,000 person-years, and recognized as the main cause of death for those living with HIV, making it crucial to closely monitor its prevalence in this population (34).

2.2 Prevalence of TB in Adolescents and Young Adults living with HIV

There are many people in this age group worldwide nearly 2 billion people, or 90% of those in the 15–24 age range, reside in low-income nations, which frequently have the highest rates of TB (35). A study in South Africa showed, TB/HIV co-infection in young adults (33.1%) had the highest prevalence, following that, older adolescents (12.9%) and younger adolescents (18.5%) (36). In Gaborone, the percentage of TB registrations with unreported HIV status is 1.8% among adults, 4.8% among 20–24-year-olds, and 9.2% among those aged 10–19 (37). In study conducted in rural areas of India revealed that prevalence of TB infection was 16.7% in adolescents (38). In Tanzania, the Prevalence of TB was 19% of 12 and 16 years old in Mwanza (39). To the best of knowledge there is a little available information on the prevalence of TB in HIV infected AYA in Tanzania.

2.3 Incidence of TB among Adolescents and Young Adults (AYA) Living With HIV

In 2012 an estimated 1.78 million AYA became infected with TB every year, making up around 18% of the annual worldwide TB incidence. The largest number of TB cases were in the WHO African region. Among AYA, with 534,000 cases in the same year (40). According to the report of the CDC in Ghana, it is estimated that in 2020 the incidence of TB in HIV-infected individual was 143 for every 100,000 people (41). Moreover, in 2013, worldwide TB incidence has decreased by 2% and a 4% African decline. However, reported 10 million newly identified cases of TB in 2017, with 87% occurring in 30 African nations and Tanzania is one of the nation having a high TB burden. Currently, SSA the incidence rate of TB in individuals living with HIV continues to be highly variable, both within individual countries (such as Tanzania, Uganda, South Africa, and Ethiopia) and across the continent (42). However, this finding regardless of AYA's HIV status, these results apply to all ages. In SSA the incidence rate of HIV-positive children and adolescents once treatment began was lower 5.4 per 100 person-years, than prior to the initiation of combination antiretroviral treatment was 10.5 per 100 individual years (42)

Additionally, Tanzania is a country with a high TB burden as well as a high TB/HIV burden. Based on the research that was done, by Majigo et al showed general population, overall incidence rate of TB among individuals who tested positive for HIV was high in persons not using ART (43)

2.4 TB Treatment Outcomes among HIV Infected AYA

A study done in India revealed that co-infected individuals who were not receiving antiretroviral therapy (ART) had a considerably lower treatment success rate (54%) than those who were (80%); also, the non-ART group had greater risks of mortality and default (44). On top of that, a study reveals that the success rate of treatment for TB/HIV co-infection was 58.0% and the rates of treatment failure were 0.5% treatment failure, 24.2% LTFU, and 4.5% death. Although a majority of deaths, 80% happened two months after anti-TB treatment was started (45). Additionally, TB HIV co infected individuals have a 5.6% treatment failure rate. For individuals with co-infections of HIV and TB, the treatment success rate was 86.4% (46). Moreover, a study done in rural Kenya revealed that individuals with co-infections of HIV and TB had poor treatment results for TB of 80% complete treatment, 12% death, and 4.2% LTFU than those with HIV-negative patients of 86% complete treatment, 5.6% death, and 4.4 LTFU, however these findings not detailed AYA age group (47). In Tanzania, only 85% of HIV/TB patients in Tanzania receive successful treatment, and the remaining 15% have unsatisfactory treatment (48). Furthermore, NTLP noticed in 2020, the total success rate of treatment for both new and relapsed TB patients was 96%. and the remaining 4% was unsuccessful treatment with 0.08% non-completing patients, 3.3% died while receiving the treatment, and 0.92% were lost to follow-up in all age group TB patients (49). Nevertheless, the HIV-infected AYA age group has not been taken into consideration in these findings.

2.5 Unfavorable TB treatment outcome among HIV infected AYA

HIV TB co-infection prevalent were 56% of patients who were unsuccessful in treatment outcome of death, lost to follow up and treatment failure. This shown that individuals with HIV positive have a significantly higher risk of being unsuccessful treatment for TB than patients with HIV negative status (50). In addition, loss to follow-up, death and treatment failure in TB treatment was 72% higher in those with HIV and TB coinfection than in those without (51).

Another study revealed HIV TB co-infected patients were 76% times more risk of death compared to those with HIV negative (52). Additional findings from Tanzania by Njiro BJ et al. 2024 showed that patients with TB-HIV co-infection accounted for 62% extra odds of

unfavorable treatment outcomes compared to their HIV-negative, however, this study done for recurrent TB in the age group of children and adults (20). Another study carried out in Mumbai, India, poor outcome were seven individuals (64%) where by four patients (36.5%) died, one patient died 16 days after treatment started, whereas three of these individuals who passed away never got TB or antiretroviral therapy. These may be due to HIV co-infection increases the probability of death in MDR- TB patients. Similarly, Co-infected people may experience severe Immune Reconstitution Inflammatory Syndrome (IRIS) after starting antiretroviral therapy (ART), which has been linked to death (36).

A study done in Mumbai showed that 64% had poor treatment outcomes with three (27%) treatments failed with the reason of illness severity also drug resistance, notably to fluoroquinolones, also linked to poorer treatment results (38). Western Cape Province, individuals with HIV co-infection aged 15–19 and 20–24 years had a high risk of treatment failure of 0.3%. This reported as due to disengagement from treatment could make it more likely that others will contract TB (53).

In a study conducted in 2020 revealed, that loss to follow-up was more frequent among those 10 to 18 years old than those under five (23). In another study revealed that, when treatment began, older adolescents and young adults were 70% higher of loss to follow up in care than younger adolescents (54). Adolescents lack the ability to manage their own finances, solve problems, and make long-term plans. Other causes include factors like home instability and poverty. Adolescents with HIV co-infection face additional difficulties in sticking to complicated ongoing treatment plans, adverse medication reactions, and the stigma associated with co-infection with both HIV and TB, all of which might negatively affect their coping strategies and result in unsatisfactory treatment outcomes.

2.6 Predictors for unfavorable TB treatment outcomes in HIV-infected AYA

2.6.1 Age

There was a larger risk of a LTFU in the participant groups that were young adults age of 15-18 years of LTFU in the study conducted in Netherlands (55). Another study revealed the highest LTFU as a poor treatment outcome rates in South Africa were 15% and 16% for TB/HIV co-infected 15–19 and 20–24 year olds, respectively (56). Moreover, another study

in Cape Town, South Africa, a place with high rates of TB and HIV, discovered that adolescents with drug-susceptible TB had a higher death risk (57).

In this factor, different age groups are faced with various challenges, such as developmental factors, socioeconomic factors, and psychological issues that might cause poor treatment outcomes of either death or Lost to follow up. However, no assessment of age in relation to unfavorable TB treatment outcomes in HIV-infected AYA in Tanzania.

2.6.2 Sex

Different studies showed that, sex associated with poor treatment outcome such as being a male young adults had a higher mortality risk than female young adults (57). In a study conducted in Cape Town, South Africa, a region with a high prevalence of TB and HIV, it was discovered that among adolescents with drug-susceptible TB aged 15 to 19 years, female adolescents had a mortality risk that was more than twice as high as that of male adolescents. A study in Nigeria done by Chukwuma B. et al. revealed, males had higher levels of treatment failure, loss to follow up and death than females, although female had higher treatment success rates (92.4%) than their male counterparts (71.8%) (58). Several research have supported this pattern of lower success rates among men, However, the age of poor treatment outcomes in HIV-infected AYA was not categorized in this study.

Biological variations between sexes can also have a role, for example female, may have various adverse effects from ART, which might impact their adherence and overall health outcomes.

Nevertheless, sex in relation to predictors of unfavorable TB treatment outcome in HIV infected AYA in Tanzania not evaluated.

2.6.3 Residence

The distance, transportation, cost, availability, and acceptance of TB services are just a few of the obstacles that AYA residing in rural locations may encounter while trying to access healthcare. AYAs who reside in metropolitan areas may experience more difficulties finishing therapy due to factors like prejudice, stigma, mobility, or loss of follow-up (59).Living in rural areas has a 174% higher risk of treatment failure, death, and LFTU compared to urban dwellers (60). TB notification, case detection, treatment start, treatment adherence, and treatment outcomes among AYA living in rural or urban regions vary

depending on where you live.

Individuals living in remote area frequently encounter obstacles such as restricted access to healthcare facilities, transportation concerns, and a lack of healthcare resources. These restrictions can result in a greater incidence of LTFU and death. While those residing in urban often have stronger healthcare facilities, factors like stigma, congested clinics, and socioeconomic inequality can all contribute to LTFU and mortality.

Hence, this study also aimed at establishing the association between residence and predictors of unfavorable TB treatment outcome in HIV infected AYA in Tanzania

2.6.4 WHO clinical stage

There was an increased in three times more risk of a poor result from TB therapy in individuals with initial WHO stage III, nevertheless individuals in WHO stage IV were six times more likely of increased risk of unsatisfactory treatment outcome compared to those WHO stage II patients (61) . In addition, patients who are in WHO stage IV have three times higher odds of having a poor treatment outcome than patients who are not in WHO stage IV (62).

Advanced stage of HIV is frequently accompanied by visible symptoms, which can enhance stigma and discrimination. This social pressure could discourage AYA from completing their therapy and follow-up visits and death may occur.

Findings observed in other studies are contradicting, therefore this study predicts WHO clinical stage in relation to unfavorable TB treatment outcome in HIV infected AYA in Tanzania

2.6.5 ART adherence

According to the study revealed that, poor ART adherence to treatment for TB is associated with LTFU as a poor treatment outcome (63). Furthermore, another study done in Malaysia it is encouraged to enhance adherence counseling so that the causes can be found and dealt with. This is crucial since poor treatment compliance and frequent treatment pauses can result in the emergence of resistant TB, treatment failure, relapse, prolonged infections, and even death (64). However, the study population was not categorized in Adolescents and Young Adults with HIV infection.

2.6.6 CD4 Cell count

Numerous studies revealed that the strongest clinical factor of death in TB/HIV co-infected patients is a low CD4 T-lymphocyte count. A study done in Uganda by Lumu I, et al. 2023 revealed a CD4 count of less than 200 cells/mL had 81% higher risk of mortality among HIV-positive individuals compared with a CD4 count of greater than 200 cells/ mL (65). Furthermore, Patients who had a CD4 count of less than 200 cells/mL were 289% increased risk of mortality compared to those who had a CD4 count of more than 200 cells/mL (66).

2.6.7 Type of TB

A Cameroonian research found, having extra pulmonary were 89% times more risk of mortality than those who had pulmonary TB (67). Additionally, another study showed that children with extra-pulmonary TB infection were a 190% times higher risk of mortality than those with infection of pulmonary TB (68). These might result from the challenge of extra-pulmonary TB diagnosis in our clinical environment with limited resources, which is frequently exacerbated by patients' inability to afford timely, targeted diagnostic testing.

CHAPTER THREE

3 METHODOLOGY

3.1 Study design and duration

This was retrospective cohort study, based on routinely collected data from 92 Care and Treatment Clinics (CTC) out of 249 CTCs in Dar es Salaam. The data included in this study was from January 2020 to April 2024. Enrolment time was from January 2020 to December 2023. Follow up time was from January 2020 to April 2024. The start time was taken from 1 January 2020, or the date of first enrollment at the CTC if enrollment was after 1 January 2020. Patients were followed for the first episode of TB to happen. End time was defined as whichever came first among the following; the date there were last seen at a CTC, the date of death, transferred out, treatment failure or loss to follow up or 31st April 2024.

3.2 Study area

This study was carried out at Dar es Salaam CTCs, supported by the Management and Development for Health (MDH). MDH is a non-governmental organization that works in Tanzania and is supported by the US Centers for Disease Control and Prevention (CDC) under the President's Emergency Plan for AIDS Relief (PEPFAR) to offer HIV management and care as well as access to ART in Tanzania. These clinics receive technical assistance, laboratory services, and infrastructure from MDH. Dar es Salaam is Tanzania's largest city and its main commercial city, with almost 6 million populations.

3.3 Study population

All AYA living with HIV who are attending CTC initiating ART in Dar es Salaam.

3.4 Data inclusion and exclusion

3.4.1 Inclusion criteria

HIV infected patients aged 10-24 years, who were on ART January 2020 and December 2023.

3.4.2 Exclusion criteria

All adolescents and young adults 10-24 years missing Outcome variables of TB results and the final treatment outcome of TB required for analysis

3.5 Sampling method

Purposive sampling methods of CTC selection was used. All AYA meeting the inclusion criteria were enrolled into the study.

3.6 Power of the study

The formula for estimating the power of cohort studies was

$$Power = \Phi\left(\frac{\sqrt{(n_1 * \Delta^2)} - z_{1-\alpha/2}\sqrt{(1+1/\kappa) * p * q}}{\sqrt{(p_1 * q_1) + (p_2 * q_2 / \kappa)}} \right)$$

Where

Δ = difference of risk of disease between exposed group and unexposed group

κ = ratio of sample size: unexposed group / exposed group

p1= risk of disease among the exposed group;

p2= risk of disease among the unexposed group;

p = (p1*n1+p2*n2) / (n1+n2)

q= 1-p

n1= available sample size among the exposed group.

Assumptions of power of the study:

The following assumptions were used in order to calculate the power of the study: The two-sided confidence interval of 95% was used. HIV only cases were considered as a non-exposed group and coinfected TB/HIV cases as an exposed group. The number of coinfected TB/HIV cases were 34 while HIV only cases were 18,987. The ratio of sample size among non-exposed group and exposed group (K) was 0.002. Risk of poor treatment outcome among exposed was 55.9% while risk of poor treatment outcome among non-exposed was 0.1%. Power calculation using OpenEpi software Version 3.01 available at https://www.openepi.com/Menu/OE_Menu.htm yielded a power of 100%.

3.7 Data abstraction procedure and Dataset description

Data was abstracted from CTC2 electronic data systems. The database store demographic and clinical information that is collected from CTC2 card for the HIV infected patients. Primary data generated in the CTC was captured on facility-held information collection tools designated as CTC2 card.

Data were exported from the CTC 2 database systems to Microsoft Excel 2016 and then imported into Stata Version 15.0 for analysis. Before analysis, data were cleaned and checked to ensure that the data lie within the maximum and minimum fixed values and are logical. The outcomes were TB, and TB treatment outcome. Independent variables were socio-demographic and clinical characteristics available in the CTC 2 database. Social demographic factors includes BMI, age, sex, and client referred from. Clinical characteristics included ART adherence, WHO clinical stage, HIV regimen used, nutrition status and duration of HIV treatment.

In the database, these variables were recorded as follows, age as a continuous variable which categorized as (10-14 years, 15-19 years, and 20–24 years), sex (male and female), client referrals from (OPD, , IPD, Community and Laboratory), ART adherence (Yes, No), WHO clinical stage (1^{st}stage, 2^{nd}stage, 3^{rd}stage, 4^{th}stage), HIV regimen used (1^{st}line, 2^{nd}line), BMI (Underweight, Normal, Overweight, Obese) and duration of HIV treatment (<=1year, >1year).The dependent variables was recorded as treatment outcome (cured: A TB patient with confirmed TB at the beginning of treatment who was smear or culture-negative in the last month of treatment, death: refers to a TB patient who dies for any reason during treatment and lost to follow up: is a TB patient whose treatment is interrupted for two consecutive months or more.

3.8 Data analysis

Categorical variables summarized using frequency and proportions, numerical variables was summarized using measures of mean and Standard Deviation (SD).

The time between enrollment in CTC and TB diagnosed was time in months, TB negative were censored. The time in months between TB treatment initiation until cured, loss to follow up, transferred out and death was used. Patients who were cured who had their

treatment classified as success were censored at the outcome date.

The incidence of TB was calculated as the number of HIV-infected AYA newly diagnosed TB started anti TB medications divided by the person-month of follow-up.

The prevalence of TB was calculated as the number of HIV-infected AYA tested positive for TB as the numerator and the total number of HIV-infected AYA tested as the denominator for the entire patient population who are at risk in the of year January 2020-December 2023).
To handle missing data, missing key variables was omitted and large sample size was included in this study, so that may not affect the power of the study.

An extended Cox model (time-dependent Cox proportional model) was used for univariate and multivariate analyses after verification of the proportional-hazard assumption using the Schoenfeld's test. Factors that were statistically significant at a p-value of ≤ 0.2 in the univariate analysis were considered as potential risk factors and included in the multivariable model. We assessed both a main effects multivariable model and a model including significant two-way interaction terms between covariates.

3.9 Ethical considerations

Ethical approval and waiver of informed consent was sought from the Institutional Review Board (IRB) at Muhimbili University of Health and Allied Sciences (MUHAS). Permission to use HIV data was obtained from data manager at The Management and Development for Health (MDH). To ensure data security, the patient unique Identification number was used instead of using patient names. In additional, computer that contain data had password protected and access was only be granted to people who was authorized. (Appendix I and II)

CHAPETR FOUR

4 RESULTS

4.1 Descriptive results

Data were extracted and analyzed from records of 19,039 AYA enrolled in HIV care and treatment services between January 2020 and December 2023. 18 HIV infected AYA were excluded due to missing of outcome variables. 19,021 Participants were enrolled in this study. Participants who had no symptoms of TB were 18,890 and 131 HIV infected AYA they had TB symptoms, 34 were positive TB and 97 were TB negative. Figure 2.

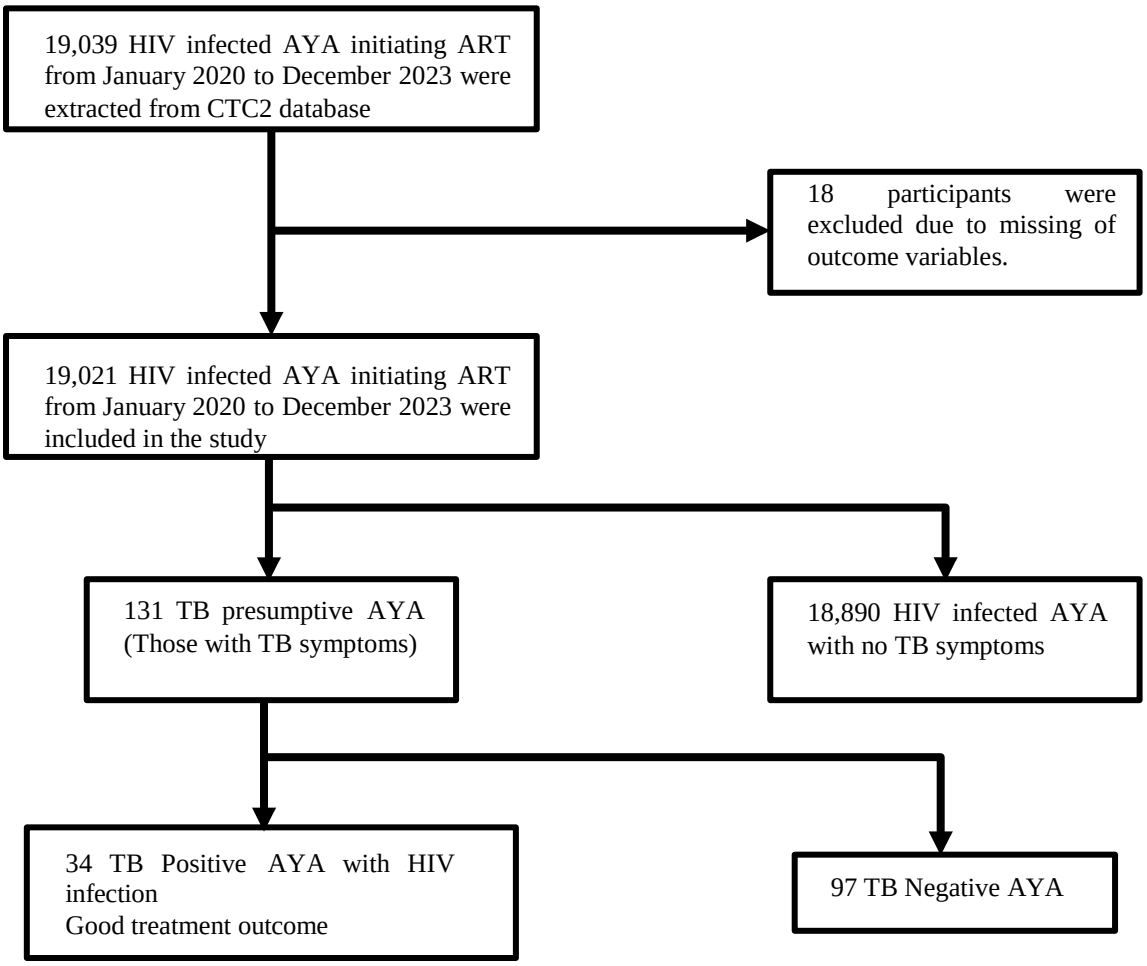


Figure 2: Flow chart showing the procedure used to select subjects

4.2 Prevalence of TB among HIV infected AYA

This study involves 19,021 participants of HIV infected AYA on ART from January 2020 to December 2023. Majority 14,921 (78.4%) of the study cohort were aged between 20-24 years and the mean (SD) age was 20 ± 3.6 years. Female sex were accounted for 15,429 (81.1%) among the study population. Those who were referred from the community had 10,081 (54.9%). Among all participants, those with no TB symptoms were 18,890 (99.3%). The overall prevalence of TB in HIV infected AYA is 0.2. Among those who were TB presumptive majority 92 (0.4%) were cured. Table 1.

Table 1. Social and clinical characteristics of HIV infected AYA initiated ART from January 2020 to December 2023 in Dar es Salaam (N= 19,021)

Variable	Frequency	Percentage
Age		
10 - 14	145	0.8
15 - 19	3,955	20.8
20 - 24	14,921	78.4
Mean 20±3.6SD		
Sex		
Male	3,592	18.9
Female	15,429	81.1
Client referred from		
OPD	8,808	46.3
IPD	120	0.6
CTC	32	0.2
Community	10,061	52.9
TB presumptive		
Yes	131	0.7
No	18,890	99.3
TB results		
Positive	34	0.2
Negative	18,987	99.8

4.2.1 Prevalence of TB among HIV infected AYA age group

In the present study we observed the overall prevalence was 0.2 with high prevalence of TB in young adults' age group of 20-24 years compared to other age groups of adolescents as shown in figure 3. TB prevalence in this study found to be high in female compared to male shown in figure 4 below

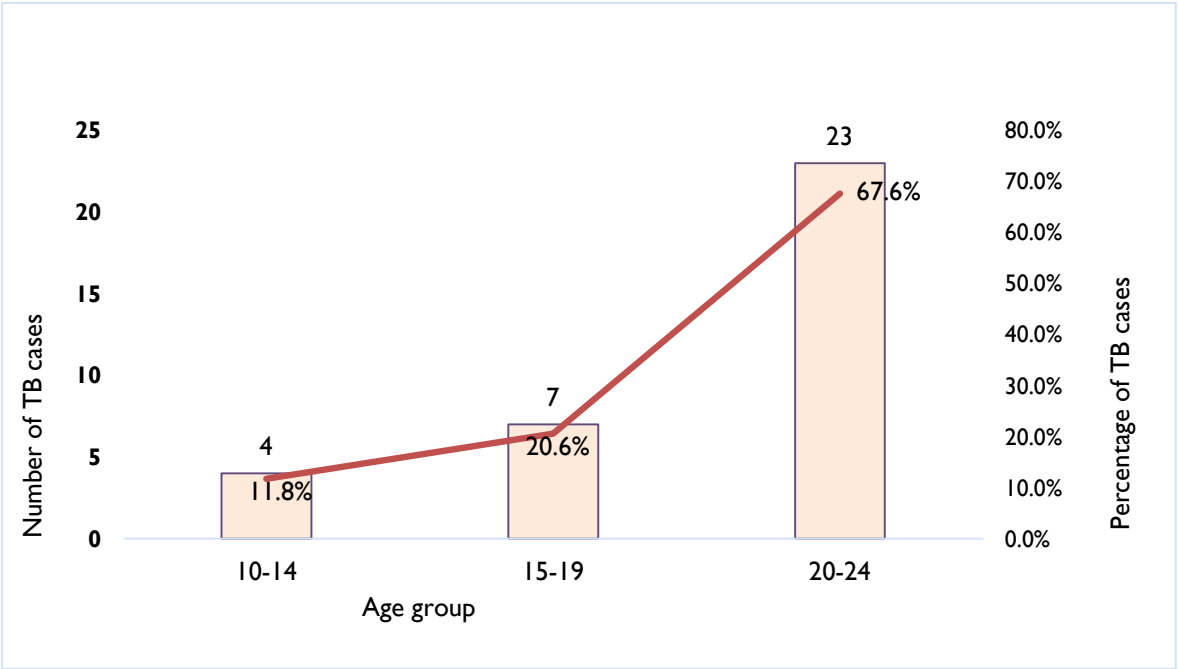


Figure 3: TB prevalence in HIV infected AYA by age group

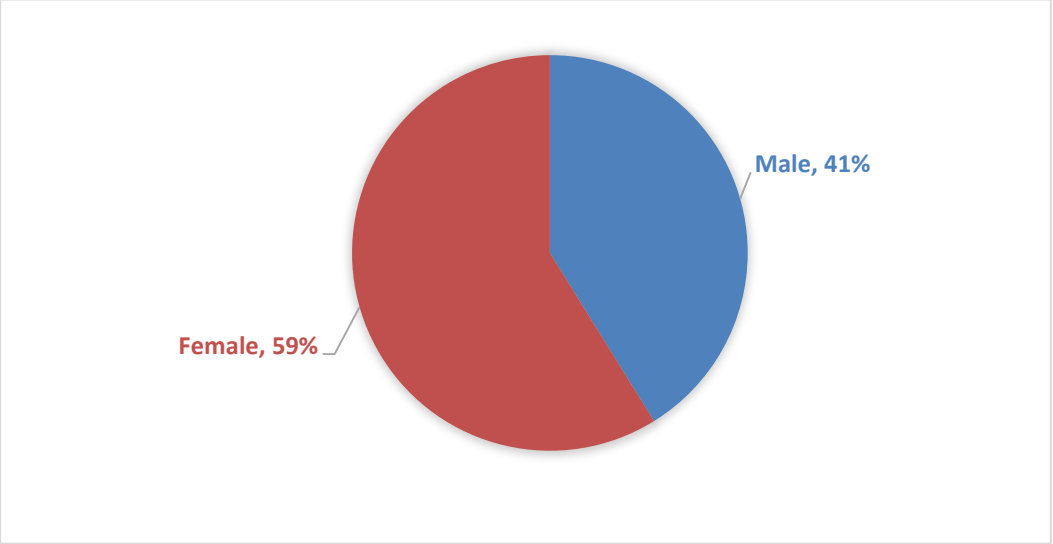


Figure 3: TB prevalence in HIV infected AYA by sex

4.3 The incidence of TB among HIV infected AY on anti TB

We found, the total follow up time of 1,853.3 person year in 19,021 HIV infected AYA and 16 (0.1%) TB cases was obtained. The overall incidence rate of TB in HIV infected AYA 8.6 per 1000 person years at risk (95% CI; 5.2-14.1/1000 person year at risk).

Male had high TB incident rate than female 20.5 per 1000 person years at risk (95% CI; 9.2- 45.7/1000 person year at risk). The age group of young adults (20-24 years) had high incident rate of 9.1 per 1000 person years at risk (95% CI 5.1-16.1/1000 person year at risk) than other age group. WHO clinical stage 4 had high TB incident rate of 46.3 per 1000 person years at risk (95% CI; 14.9-143.6/1000 person year at risk) compared to other stages, however WHO clinical stage 2 than stage 1 had low TB incident rate of 3.4 per 1000 person years at risk (95% CI 0.85-13.6/1000 person year at risk) due to few number of TB cases. Table 2.

Table 2: Incidence of TB in HIV infected AYA initiated ART from January 2020 to December 2023 in Dar es Salaam

Characteristics	**Number of TB cases**	**1000 Person year**	**TB incident rate/1000 person-years (95%CI)**
Overall	**16**	**1,853.3**	**8.6 (5.2-14.1)**
Sex			
Male	6	292.2	20.5 (9.2 – 45.7)
Female	10	1561.1	6.4 (3.4 – 11.9)
Age group			
10-19	4	534.2	7.5 (2.8 – 19.9)
20-24	12	1561.1	6.4 (3.4 -11.9)
WHO clinical stage			
1	5	806.7	6.2 (2.9 - 65.0)
2	2	585.9	3.4(0.85-13.6)
3	6	395.9	15.1(6.8 – 33.7)
4	3	64.7	46.3(14.9-143.6)

4.4 Treatment outcome of TB among HIV infected AYA

In our study we found that, poor treatment outcome of death proportion was 11/31 (35.5%) during the TB treatment compared to other poor treatment outcome of Loss to follow up. Table 3.

	Treatment outcome		
Variables	**Cured n (%)**	**Dead n (%)**	**LTF n (%)**
Total	**15 (48.4)**	**11 (35.5)**	**5(16.1)**
Sex			
Male	5(33.3)	5(45.5)	2(40.0)
Female	10(66.7)	6(54.5)	3(60.0)
Age group			
10-14	2(13.3)	2(18.2)	0(0)
15-19	4(26.7)	2(18.2)	1(20.0)
20-24	9(60.0)	7(63.6)	4(80.0)

Table 3: Treatment outcomes among HIV infected AYA

4.5. Predictors of poor TB treatment outcome among HIV infected AYA

In bivariate analyses, five predictors of Client referred from, ART adherence, WHO clinical stage, HIV regimen used and Duration of HIV treatment had P value of <0.2 as shown in table 4. Accordingly, these variables were subjected to multivariate Cox regression analysis and found no factors with significance associated with the poor TB treatment outcome.

Table 4: Bivariate analysis of predictors for poor TB treatment outcome among HIV- infected AYA on anti-TB treatment, January 2020 to December 2023, Dar es Salaam

Variables	**Treatment outcome of TB**		**P Value**
	Favorable (%)	**Unfavorable (%)**	
Age			0.397
10-19	6(54.5)	5(45.5)	
20-24	9(39.1)	14(60.9)	
Total	15(44.1)	19(55.9)	
Sex			0.409
Male	5(35.7)	9(64.3)	
Female	10(50.0)	10(50.0)	
Total	15(44.1)	19(55.9)	
Marital status (n=30)			0.411
Single	7(46.7)	8(53.3)	
Married/ Cohabiting	6(54.6)	6(45.4)	
Widow	0(0)	1(100)	
Divorced	0(0)	2(100)	
Total	13(44.8)	17(55.2)	
BMI			0.841
Underweight	13(44.8)	16(55.2)	
Normal	2(40.0)	3(60.0)	
Overweight	0(0)	0(0)	
Obese	0(0)	0(0)	
Total	15(44.1)	19(55.9)	
Client referred from			0.129
OPD	3(25.0)	9(75.0)	
IPD	2(66.7)	1(33.3)	
Community	10(52.6)	9(47.4)	
Total	15(44.1)	19(55.9)	

Variables	Treatment outcome of TB		P Value
	Favorable (%)	Unfavorable (%)	
ART adherence			0.253
Yes	14(42.4)	19(57.6)	
No	1(100)	0(0)	
Total	15(44.1)	19(55.9)	
WHO clinical stage			0.06
1st stage	2(20.0)	8(80.0)	
2nd stage	6(85.7)	1(14.3)	
3rd stage	6(40.0)	9(60.0)	
4th stage	1(50.0)	1(50.0)	
Total	15(44.1)	19(55.9)	
HIV regimen used			0.253
1st line	14(42.4)	19(57.6)	
2nd line	1(100)	0(0)	
Total	15(44.1)	19(55.9)	

CHAPTER FIVE

5 DISCUSSION

The purpose of this study was determine the prevalence of TB, incidents of TB, treatment outcomes, and predictors of poor treatment outcomes of HIV-infected AYA in Dar es Salaam from January 2020 to December 2023. The overall TB prevalence of AYA with HIV infection was low 0.172 (172 cases/1000 population). The overall incidence rate of TB in HIV-infected AYA was low 8.6 (95% CI 5.2-14.1) cases per 1000 person-year. The study found a high proportion of poor treatment outcome of death (35.5%). The most affected age group was the age of 20-24years. This study did not determine predictors of poor treatment outcomes of TB in HIV-infected AYA.

The findings from this study found the prevalence of TB in HIV-infected AYA is low. This might be due to several reasons, the improvement in treatment and care of HIV simply because ART in HIV patients it prevents the inactive form of TB from developing to active form of TB disease. Another factor could be due to the implementation of collaborative TB and HIV activities in Tanzania. Similar findings observed in a study done in Tanzania between 2011 to 2014 revealed the prevalence of TB decreased in PLHIV on ART than those who are not on ART (43). Contrary with the study done in DRC, Mukuku et al reported 20.95% prevalence of TB in HIV infected children (69). The difference might be due to differences in HIV burden, access to health services, and quality of the health services.

According to this study, young adults were more affected than adolescents. This finding may be explained by the possibility of different social and behavioral patterns, such as increased mobility or substance use, which may be related to higher rates of TB transmission. Moreover, may encounter challenges while seeking to get access to healthcare, including testing and treatment for HIV and TB, which can cause a delay in TB diagnosis and treatment. Our findings supported by a study done on AYA in South Africa by Mulongeni P et al result showed the young adults had high prevalence of TB/HIV co- infection than adolescents (11). Moreover, similar findings were reported in a study done among AYA in Botswana by Enane et al 2020 (37).

In the present study, we found the overall TB incidence was a low among HIV-infected AYA. Similar findings were observed in the study done by Said K et al. 2017 in Tanzania with the overall TB incidence among HIV-infected adults was low (0.8 per 100 PY), this could be due to the effectiveness of health interventions in TB management and also improvement in national interventions such as the uptake of ART, provision of IPT (70).

In this study we observed male gender had a higher incidence of TB than females, these findings might be due these findings might be due to less health seeking behavior of men, causing men to be more likely to get TB due to undiagnosed and untreated HIV co-infection. The similar findings observed in the studies done by Mollel et al in the Tanzania (34).

Compared to other age groups, our study found that young adults had a greater incidence of TB. This may be because of the stigma facing this age group, quality of counseling provoded, and challenges in adherence to TPT and ART due to movement of young adults such that, attending school or in economic activities. Similarly findings in the studies done in Botswana and South Africa (11,37).

In our findings, WHO clinical stage 4 showed high TB incidence among HIV-infected AYA compared to other stages, this corresponds to advanced HIV disease with severe immunosuppression. At this point, patients are particularly susceptible to opportunistic infections like TB. These findings were supported by the study that revealed advanced WHO stages 3 & 4 had high TB incidence in HIV-infected patients (71). Another study showed a similar finding that WHO stage 3 & 4 was significantly associated with TB incidence (72). However this study showed WHO clinical stage 2 had low TB incidence rate than stage 1, it could be due to low number of new TB cases in stage 2.

In our study, we observed out of the total reviewed AYA records high proportion of patients had unsuccessful treatment outcomes. Most of the AYA with poor treatment outcomes, more than half had outcome of death than LTF. Comparable results were observed in a study done by Amante et al. that, a high proportion of poor treatment outcomes, and among the participants with unsuccessful treatment outcomes majority were because of death (14). A study in Ethiopia, done by Katana et al. 2022 in Kenya

revealed high Mortality of 7.3% (51). The reasons could be due to depression of the patients, lack of social support, early presentation to CTC for management and treatment.

In this study we found death was high in the age group of 20-24years. Similar findings observed in the study by to Osman et al. 2021 conducted in South Africa, showed the age of 20-24 years had high death proportion than other age group (57). Contrast findings observed in study done in Tanzania by E M Bukundi at al. 2021, revealed mortality rate was high in advanced aged might be due to disrupted immunity and age- related co-morbidities that contributed to an increased risk of TB mortality among this age group (73)

In the present study we found out five predictors of poor treatment outcome of TB; Client referred from, ART adherence, WHO clinical stage, HIV regimen used and Duration of HIV treatment had P value of <0.2 in bivariate analysis. Those predictors were failed to run in a mathematical model due to few observations of outcome variable. However different studies observed there are predictors for poor TB treatment outcome.

5.1 Study limitation

The study had limitation of few variables of interest limited the statistical power to identify independent risk factors. Likewise some variables were missing in the data set such as CD4, client information support and type of TB**.** Missing variables were not included in the analysis.

6. CONCLUSION

Our study showed an improvement in TB HIV integration services. This study found the overall prevalence of TB in HIV-infected AYA was low. Also we observed the overall Incidence rate of TB in HIV-infected AYA was low. Moreover, the prevalence of TB, the incidence of TB and Mortality of TB in HIV infected AYA the most affected age group was 20-24 years.

7. RECOMMENDATION

In order to achieve and maintain the WHO end-of-TB milestones, which involve a 95% reduction in poor treatment outcomes, we recommend to sustain the existing strategies such as the TPT provision to PLHIV and ART adherence. Additionally, to improve early TB case detection, especially in the population of 20-24 years who were HIV infected. Moreover, to strengthen follow-up of 20-24 years after initiation of treatment to reduce mortality in this group. Lastly, further investigation is needed using a large National dataset to get a more comprehensive picture

REFERENCES

1. World Health Organization (WHO). Evidence and research gaps identified during development of policy guidelines for tuberculosis. 2021. 1–36 p. Available from: https://www.who.int/publications/i/item/9789240040472
2. Snow KJ, Sismanidis C, Denholm J, Sawyer SM, Graham SM. The incidence of tuberculosis among adolescents and young adults : a global estimate. Eur Respir J. 2018;(1702352). Available from: http://dx.doi.org/10.1183/13993003.02352-2017
3. World Health Organization (WHO). World Health Organization. Maternal, newborn, child and adolescent health and ageing. WHO. 2023. Available from: https://platform.who.int/data/maternal-newborn-child-adolescent-ageing/%0Aadolescent-data/adolescent---mortality-causes-of-death
4. World Health Organization. HIV and Tuberculosis. 2021. Available from: https://cdn.who.int/media/images/default-source/health-topics/hiv/210311_who_tbday_infographic.14.jpg?sfvrsn=bb221ae5_7
5. World Health Organization (WHO). Global tuberculosis report 2015. Geneva 27, Switzerland; 2015. Available from: www.who.int/about/licensing/copyright_form/en/index.html
6. World Health Organization (WHO). Global health estimates: Leading causes of death. WHO. 2023; Available from: https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death
7. Unaids. AIDS epidemic update. Aids. 2000;37(6):1287–96. Available from: http://whqlibdoc.who.int/unaids/2007/9789291736218_eng.pdf
8. Wilson CM, Wright PF, Safrit JT, Rudy B. Epidemiology of HIV Infection and Risk in Adolescents and Youth. NIH Public Access. 2011;54(Suppl 1):1–5.
9. Joint United Nations Programme on HIV/AIDS (UNAIDS). Young people and HIV. 2021.
10. United Nations Programme on HIV/AIDS (UNAIDS). The path that ends AIDS: UNAIDS Global AIDS Update 2023. Geneva; 2023. Available from: http://www.wipo.int/amc/en/mediation/rules
11. Mulongeni P, Hermans S, Caldwell J, Bekker L, Wood R, Kaplan R. HIV prevalence and determinants of loss-to- follow-up in adolescents and young adults with tuberculosis in Cape Town. PLoS One. 2019;1–16.
12. Mohammed T, Daniel K, Helamo D, Leta T. Treatment outcomes of tuberculosis patients in

nigist Eleni Mohammed general hospital , hosanna , southern nations , nationalities and peoples region , Ethiopia:a five year (June 2009 to August 2014)retrospective study.Arch Public Heal. 2017;1–10.

13. Zeramariam Z, Id A, Kibreab F, Kibrom AA, Mebrahtu H, Girmatsion MG, et al. Determinants of unsuccessful tuberculosis treatment outcome in Northern Red Sea. PLoS Med. 2022;1–13. Available from: http://dx.doi.org/10.1371/journal.pone.0273069
14. Tariku Dingeta Amante et al. Risk factors for unsuccessful tuberculosis treatment outcome (failure, default and death) in public health institutions, Eastern Ethiopia. Pan African Med Journa. 2015;8688:1–8.
15. Melese A, Zeleke B. Factors associated with poor treatment outcome of tuberculosis in Debre Tabor , northwest Ethiopia. BMC Res Notes. 2018;1–6. Available from: https://doi.org/10.1186/s13104-018-3129-8
16. Enane LA, Lowenthal ED, Arscott-mills T, Eby J, Caiphus C, Kgwaadira B, et al. Investigating Outcomes of Adolescents and Young Adults (Ages 10–24) Lost to Follow-Up From Tuberculosis Treatment in Gaborone, Botswana. Pediatr Infect Dis J. 2020;38(10):1–8.
17. WHO. Global tubercolosis report 2018. Vol. 63, World Health Organization. 2018. Available from: https://apps.who.int/iris/handle/10665/274453
18. De Oliveira MCB, Sant'Anna CC, Luiz RR, Kritski AL. Unfavorable outcomes in tuberculosis: Multidimensional factors among adolescents in Rio de Janeiro, Brazil. Am J Trop Med Hyg. 2020;103(6):2492–500.
19. Sabasaba A, Mwambi H, Somi G, Ramadhani A, Mahande MJ. Effect of isoniazid preventive therapy on tuberculosis incidence and associated risk factors among HIV infected adults in Tanzania : a retrospective cohort study. 2019;1–8.
20. Id BJN, Kisonga R, Joachim C, Sililo GA, Nkiligi E, Ibisomi L, et al. PLOS NEGLECTED TROPICAL DISEASES Epidemiology and treatment outcomes of recurrent tuberculosis in Tanzania from 2018 to 2021 using the National TB dataset. 2024;49:1–19. Available from: http://dx.doi.org/10.1371/journal.pntd.0011968
21. UNFPA. Young people and HIV and AIDS: Taking action to realize the 90-90-90 targets. UN. 2018;25(2):200–11.
22. Chan CK, Wong KH, Lee MP, Chan KCW, Leung CC, Leung ECC, et al. Risk factors associated with 1-year mortality among patients with HIV-associated tuberculosis in areas with intermediate tuberculosis burden and low HIV prevalence. Hong Kong Med J.

2018;24(5):473–83.

23. de Oliveira MCB, Sant'Anna CC, Raggio RL, Kritski AL. Tuberculosis among children and adolescents in Rio de Janeiro, Brazil – Focus on extrapulmonary disease. Int J Infect Dis. 2021;105:105–12.
24. Sonko I, Chung MH, Hou WH, Chen WT, Chang PC. Predictors of HIV testing among youth aged 15–24 years in The Gambia. PLoS One. 2022;17(2 February):1–17. Available from: http://dx.doi.org/10.1371/journal.pone.0263720
25. Berry KM, Rodriguez CA, Berhanu RH, Ismail N, Mvusi L, Long L, et al. Treatment outcomes among children, adolescents, and adults on treatment for tuberculosis in two metropolitan municipalities in Gauteng Province, South Africa. BMC Public Health. 2019;19(1):1–17.
26. Vision W. Technical Guideline for Tuberculosis (TB) and TBHIV Program Implementation. Vol. 13, Technical Guideline for Tuberculosis (TB) and TB-HIV Program Implementation. 2017.
27. Mandalakas AM, Kay AW, Bacha JM, Devezin T, Golin R, Simon KR, et al. Tuberculosis among children and adolescents at HIV treatment centers in Sub-Saharan Africa. Emerg Infect Dis. 2020;26(12):2933–43.
28. Hayibor KM, Bandoh DA, Asante-poku A, Kenu E. Predictors of Adverse TB Treatment Outcome among TB / HIV Patients Compared with Non-HIV Patients in the Greater Accra Regional Hospital from 2008 to 2016. Tuberc Res Treat. 2020;2020(1097581):8.
29. NIH. HIV and Tuberculosis (TB) | NIH. Nih. 2021. Available from: https://hivinfo.nih.gov/understanding-hiv/fact-sheets/hiv-and-tuberculosis-tb
30. Kruk A, Bannister W, Podlekareva DN, Chentsova NP, Rakhmanova AG, Horban A, et al. Tuberculosis among HIV-positive patients across Europe: Changes over time and risk factors. BMC Infect Dis. 2014;25(12):1505–13.
31. World Health Organization 2020. Global HIV Programme. World Health Organization. 2020. Available from: https://www.who.int/data/gho/data/themes/hiv-aids/data-on-the-size-of-the-hiv-aids-epidemic%0Ahttps://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/hiv/strategic-information/hiv-data-and-statistics
32. Osei E, Der J, Owusu R, Kofie P, Axame WK. The burden of HIV on Tuberculosis patients in the Volta region of Ghana from 2012 to 2015: Implication for Tuberculosis control. BMC Infect Dis. 2017;17(1):1–9.

33. L Page-Shipp, Lima YV De, Clouse K, Vos J de, Evarts L, Bassett J, et al. TB/HIV integration at primary care level: A quantitative assessment at 3 clinics in Johannesburg, South Africa. South Afr J HIV Med. 2012;3(1):1–17.
34. Mollel EW, Maokola W, Todd J, Msuya SE. Incidence Rates for Tuberculosis Among HIV Infected Patients in. Front Public Heal. 2019;7(October):1–9.
35. García-basteiro AL, Schaaf HS, Diel R, Migliori GB. Adolescents and young adults : a neglected population group for tuberculosis surveillance. Eur Respir J. 2018;1–4. Available from: http://dx.doi.org/10.1183/13993003.00176-2018
36. Moscibrodzki P, Enane LA, Hoddinott G, Brooks MB, Byron V, Furin J, et al. The Impact of Tuberculosis on the Well-Being of Adolescents and Young Adults. Pathogens. 2021;1–17. Available from: https://doi.org/10.3390/ pathogens10121591
37. Enane LA, Eby J, Argabright S, Caiphus C, Kgwaadira B, Steenhoff AP, et al. TB and TB-HIV care for adolescents and young adults. Int J Tuberc Lung Dis. 2020;24(2):240–9.
38. Isaakidis P, Paryani R, Khan S, Mansoor H, Manglani M. Poor Outcomes in a Cohort of HIV-Infected Adolescents Undergoing Treatment for Multidrug-Resistant Tuberculosis in Mumbai , India. PLoS One. 2013;8(7).
39. Jeremiah K, Lyimo E, Ritz C, PrayGod G, Rutkowski KT, Korsholm KS, et al. Prevalence of Mycobacterium tuberculosis infection as measured by the QuantiFERONTB Gold assay and ESAT-6 free IGRA among adolescents in Mwanza, Tanzania. PLoS One. 2021;16(6 June):1–12. Available from: http://dx.doi.org/10.1371/journal.pone.0252808
40. Global T, Secretariat F, Council Y, Fund G, Council TY, Africa S, et al. Youth Council Terms of Reference. 2020;(January):1–5.
41. Palmer VE. Ghana: Strategic Focus. CDC Div Glob HIV TB Ctry profile. 2022;(September):2022. Available from: https://www.cdc.gov/globalhivtb/where-we-work/Ghana.pdf
42. Wondmeneh TG, Mekonnen AT. The incidence rate of tuberculosis and its associated factors among HIV-positive persons in Sub-Saharan Africa: a systematic review and meta-analysis. BMC Infect Dis. 2023;23(1):1–24.
43. Majigo M, Somi G, Joachim A, Manyahi J, Nondi J, Sambu V, et al. Prevalence and incidence rate of tuberculosis among HIV-infected patients enrolled in HIV care , treatment , and support program in mainland Tanzania. Trop Med Health. 2020;1:1–8.
44. Shastri S, Naik B, Shet A, Rewari B, De Costa A. TB treatment outcomes among TB-HIV co-

infections in Karnataka, India: How do these compare with non-HIV tuberculosis outcomes in the province? BMC Public Health. 2013;13(1):5–10.

45. Lakoh S, Jiba DF, Adekanmbi O, Poveda E, Sahr F, Deen GF, et al. Diagnosis and treatment outcomes of adult tuberculosis in an urban setting with high HIV prevalence in Sierra Leone: A retrospective study. Int J Infect Dis. 2020;96:112–8. Available from: https://doi.org/10.1016/j.ijid.2020.04.038
46. Alayu Alemu M, Yesuf A, Girma F, Adugna F, Melak K, Biru M, et al. Impact of HIV-AIDS on tuberculosis treatment outcome in Southern Ethiopia – A retrospective cohort study. J Clin Tuberc Other Mycobact Dis. 2021;25:100279.
47. Ngari MM, Rashid MA, Sanga D, Mathenge H, Agoro O, Mberia JK, et al. Burden of HIV and treatment outcomes among TB patients in rural Kenya : a 9 - year longitudinal study. BMC Infect Dis. 2023;1–11.
48. Mollel EW, Todd J, Mahande MJ, Msuya SE. Effect of tuberculosis infection on mortality of HIV-infected patients in Northern Tanzania. 2020;
49. NTLP Annual Report 2020. Ministry of health, community development, gender, elderly and children (mohcdgec) 2020. Accessed 10th March 2023.
50. Tweya H, Feldacker C, Phiri S, Ben-Smith A, Fenner L, Jahn A, et al. Comparison of treatment outcomes of new smear-positive pulmonary tuberculosis patients by HIV and antiretroviral status in a TB/HIV clinic, Malawi. PLoS One. 2013;8(2).
51. Katana GG, Ngari M, Maina T, Sanga D, Abdullahi OA. Tuberculosis poor treatment outcomes and its determinants in Kilifi County , Kenya : a retrospective cohort study from 2012 to 2019. Arch Public Heal. 2022;1–13.
52. Ingrid V. Bassett, MD, MPH, Senica Chetty, MSc, Bingxia Wang, PhD, Matilda Mazibuko, Janet Giddy, MBChB, MFamMe, Zhigang Lu, MD, Rochelle P. Walensky, MD, MPH Kenneth A. Freedberg, MD, MSc and Elena Losina P. Loss to follow-up and mortality among HIV-infected people co- infected with TB at ART initiation in Durban, South Africa. NIH Public Access. 2012;23(1):1–7.
53. Snow K, Hesseling AC, Naidoo P, Graham SM, Denholm J, Preez K. Tuberculosis in adolescents and young adults : epidemiology and treatment outcomes in the Western Cape. INT J TUBERC LUNG DIS. 2017;21(February):651–7.
54. Reif LK, Rivera V, Bertrand R, Rouzier V, Kutscher E, Walsh K, et al. Outcomes across the tuberculosis care continuum among adolescents in Haiti. Public Heal Action. 2018;I(3):103–9.

55. Gafar F, Boveneind-vrubleuskaya N Van. Nationwide analysis of treatment outcomes in children and adolescents routinely treated for tuberculosis in the. Eur Respir J. 2019;54(July).
56. Laycock KM, Enane LA. Tuberculosis in Adolescents and Young Adults : Emerging Data on TB Transmission and Prevention among Vulnerable Young People. Trop Med Infect Dis. 2021;6(6030148):17.
57. Osman M, du Preez K, Seddon JA, Claassens MM, Dunbar R, Dlamini SS, et al. Mortality in South African children and adolescents routinely treated for tuberculosis. Pediatrics. 2021;147(4):1–22.
58. Duru CB, Uwakwe KA, Nnebue CC, Diwe KC, Merenu IA, Emerole CO, et al. Tuberculosis Treatment Outcomes and Determinants among Patients Treated in Hospitals in Imo State , Nigeria. Open Access Libr J. 2016;3:1–17.
59. Lee JY, Kwon N, Goo G, Cho S. Inadequate housing and pulmonary tuberculosis : a systematic review. BMC Public Health . 2022;1–12.
60. Adamu AL, Aliyu MH, Galadanci NA, Musa BM, Lawan UM, Bashir U, et al. The impact of rural residence and HIV infection on poor tuberculosis treatment outcomes in a large urban hospital : a retrospective cohort analysis. Int J Equity Health. 2018;1–11.
61. Gezae KE, Abebe HT, Gebretsadik LG, Gebremeskel AK. Predictors of Time to Death among TB/HIV Co-Infected Adults on ART at Two Governmental Hospitals in Mekelle, Ethiopia, 2009-2016: A Retrospective Cohort Study OPEN ACCESS. Ann Infect Dis Epidemiol. 2020;5(1):7.
62. Belayneh M, Giday K, Lemma H. Treatment outcome of human immunodeficiency virus and tuberculosis co-infected patients in public hospitals of eastern and southern zone of Tigray region, Ethiopia. Brazilian J Infect Dis. 2015;19(1):47–51.
63. Leddy AM, Jaganath D, Triasih R, Wobudeya E, Oliveira MCB De, Sheremeta Y, et al. Social Determinants of Adherence to Treatment for Tuberculosis Infection and Disease Among Children , Adolescents , and Young Adults : A Narrative Review. J Pediatric Infect Dis Soc. 2022;11(Suppl 3):79–84.
64. Selimin DS, Ismail A, Ahmad N, Ismail R, Farhana N, Azman M, et al. Tuberculosis Treatment Outcome in Patients with TB-HIV Coinfection in Kuala Lumpur , Malaysia. J Trop Med. 2021;2021:10.
65. Lumu I, Musaazi J, Semeere A, Handel I, Castelnuovo B. Survival and predictors of mortality after completion of TB treatment among people living with HIV: a 5-year analytical cohort.

BMC Infect Dis. 2023;23(1):1–10.

66. Ismail I, Bulgiba A. Predictors of Death during Tuberculosis Treatment in TB/HIV Co-Infected Patients in Malaysia. PLoS One. 2013;8(8):1–7.
67. Bigna JJR, Noubiap JJN, Agbor AA, Plottel CS, Billong SC, Ayong APR, et al. Early mortality during initial treatment of tuberculosis in patients co-infected with HIV at the Yaoundé Central Hospital, Cameroon:An 8-year retrospective cohort study (2006-2013). PLoS One. 2015;10(7):1–13.
68. Nigussie J. "Predictors of Mortality Among Children Co-Infected with Tuberculosis and Human Immunodeficiency Virus in Region, North Ethiopia, Retrospective Follow- Up Study." Biomed J Sci Tech Res. 2021;39(1):1–10.
69. Olivier Mukuku, Augustin Mulangu Mutombo, Christian Ngama Kakisingi, Jacques Mbaz Musung, Stanislas Okitotsho Wembonyama ONL. Tuberculosis and HIV co-infection in Congolese children: risk factors of death. Pan African Med Journal. 2018;8688:1–9.
70. Said K, Verver S, Kalingonji A, Lwilla F, Mkopi A, Charalambous S, et al. Tuberculosis among HIV-infected population : incidence and risk factors in rural Tanzania. African Heal Sci Vol. Vol 17(Issue 1):208–15.
71. Tesfaye B, Alebel A, Gebrie A, Zegeye A, Tesema C, Kassie B. The twin epidemics: Prevalence of TB/HIV coinfection and its associated factors in Ethiopia; A systematic review and meta-analysis. PLoS One. 2018;13(10):1–18.
72. Ahmed A, Mekonnen D, Shiferaw AM, Belayneh F, Yenit MK. Incidence and determinants of tuberculosis infection among adult patients with HIV attending HIV care in north-east Ethiopia: A retrospective cohort study. BMJ Open. 2018;8(2):1–14.
73. Bukundi EM, Mhimbira F, Kishimba R, Kondo Z, Moshiro C. Journal of Clinical Tuberculosis and Other Mycobacterial Diseases Mortality and associated factors among adult patients on tuberculosis treatment in Tanzania : A retrospective cohort study. J Clin Tuberc Other Mycobact Dis. 2021;24:100263.

APPENDICES

Appendix I: Ethical clearance

UNITED REPUBLIC OF TANZANIA
MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY
MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES
OFFICE OF THE DIRECTOR – RESEARCH, PUBLICATIONS AND INNOVATIONS

Ref. No.DA.282/298/01.C/ Date: 19/12/2023

MUHAS-REC-12-2023-2002
Mariam Mbwana
Shool of Public Health and Social Sciences
MUHAS

RE: APPROVAL FOR ETHICAL CLEARANCE FOR A STUDY TITLED: Burden of Tuberculosis and Predictors of Unfavorable Treatment Outcomes among Adolescents and Young Adults Initiating Antiretroviral Therapy in Dar es Salaam: A Retrospective Cohort Study

Reference is made to the above heading.

I am pleased to inform you that the Chairman has on behalf of the University Senate, approved ethical clearance of the above-mentioned study, on recommendations of the Senate Research and Publications Committee meeting accordance with MUHAS research policy and Tanzania regulations governing human and animal subjects research.

APPROVAL DATE: 19/12/2023
EXPIRATION DATE OF APPROVAL: 19/12/2024

STUDY DESCRIPTION:
Purpose:
The purpose of this retrospective observational cohort study is to determine the burden of TB and predictors of unfavorable TB treatment outcomes among 15-24-year-old adolescents and young adults (AYA) starting antiretroviral therapy (ART) in Dar es Salaam.

The approved protocol and procedures for this study is attached and stamped with this letter, and can be found in the link provided:
https://irb.muhas.ac.tz/storage/Certificates/Certificate%20-%2015178.pdf and in the MUHAS archives.

The PI is required to:

1. Submit bi-annual progress reports and final report upon completion of the study.
2. Report to the IRB any unanticipated problem involving risks to subjects or others including adverse events where applicable.
3. Apply for renewal of approval of ethical clearance one (1) month prior its expiration if the study is not completed at the end of this ethical approval. You may not continue with any research activity beyond the expiration date without the approval of the IRB. Failure to receive approval for continuation before the expiration date will result in automatic termination of the approval for this study on the expiration date.
4. Obtain IRB amendment (s) approval for any changes to any aspect of this study before they can be implemented.
5. Data security is ultimately the responsibility of the investigator.
6. Apply for and obtain Data Transfer Agreement (DTA) from NIMR if data will be transferred to a foreign country.
7. Apply for and obtain Material Transfer Agreement (MTA) from NIMR, if research materials (samples) will be shipped to a foreign country.
8. Apply for and obtain permission to publish the results from National Institute for Medical Research. The application should be before submitting to a publisher and not concurrently through the email publications@nimr.or.tz.
9. Any researcher, who contravenes or fail to comply with these conditions, shall be guilty of an offence and shall be liable on conviction to a fine as per NIMR Act No. 23 of 1979, PART III section 10 (2)
10. The PI is required to ensure that the findings of the study are disseminated to relevant stake holders.
11. PI is required to be versed with necessary laws and regulatory policies that govern research in Tanzania. Some guidance is available on our website https://drp.muhas.ac.tz/.

Dr. Nahya Salim Masoud,
Chairperson, MUHAS Research and Ethics Committee

Appendix II: Approval letter

Data request form

Name of Requester: Mariam Mbwana

Date of Request: 23/02/2024

Organization: Muhimbili University of Health and Allied Sciences (MUHAS)

MDH Contact Person: Mr. Fikiri Chisonjela and/ Ms. Angelica Rugarabamu

Please describe how the data will be used: Data will be used for academic purpose

Please describe / list the variables needed:

Dependent variables are:

1. Burden of Tuberculosis among AYA initiating ART
2. Treatment outcomes
    - Unfavorable treatment outcome (Lost to follow up, Death, Treatment failure)
    - Favorable treatment outcome (Treatment completion and Cured)

Independent Variables:

Social demographic information

- Age
- Sex
- Area of Residence
- Marital status
- Client supporter
- BMI
- Client referred from

Clinical information

- ART adherence
- CD4 COUNT
- WHO clinical stage
- Duration on HIV treatment
- HIV regimen used
- Nutrition status

Please list names of individual staff with access to data and security procedures:
Mariam Mbwana, Dr. Frank Msafiri, Dr. Salim Masoud, and Nelson Edwin Malugu.
Do you plan to publish data or submit in a report? **YES**, this study will be submitted in a report and also published

If **YES**, please describe and indicate all authors including MDH authors:
Mariam Mbwana, Dr Salim Masoud, Nelson E. Malugu, Prof Michael J. Mahande, Rugarabamu, Fikiri Chisonjela, Dr, Lameck Machumi Dr Frank Msafiri, Dr David Sando

Approvals:

I recommend/ ~~not recommend~~ the proposed request: ___  _____

Signature –**DSI**

I approve/ disapprove the proposed request:

_____

Signature- **CEO** or COO

Appendix III: Data abstraction tool

HIV/TB CO-INFECTION ABSTRACTION FORM		
Section A. Demographic information		
Facility name: Patient ID Code:		
Sex	Male	Female
Age		
Resident	Region	District
Marital status	Single	Married
	Widow	
Client referred from	OPD	CTC
	Other:	
Client support	Yes	No
BMI		
Section B: Clinical **information**		
WHO clinical stage	1st stage	2nd stage
	3rd stage	4th stage
Duration on TPT	4month	6month
Duration on HIV treatment	<1 year	>1year
ART adherence	Yes	No
CD4 count	<200	>200
Outcome for current TB case	Cured	Death
	Transferred out	lost to follow up
Nutrition status	Good	Moderate
	Severe	Obese

turnitin

Digital Receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is displayed below.

Submission author:	Mariam Ramadhan
Assignment title:	Dissertation Reports
Submission title:	Burden of Tuberculosis and Predictors of Unfavorable Treat...
File name:	Mariam_Mbwana_Dissetertion_Report_v28062024.docx
File size:	1.1M
Page count:	56
Word count:	11,384
Character count:	61,411
Submission date:	28-Jun-2024 03:33PM (UTC+0300)
Submission ID:	2409828394



Burden of Tuberculosis and Predictors of Unfavorable Treatment Outcomes among Adolescents and Young Adults Initiating Antiretroviral Therapy in Dar es Salaam From 2020 - 2023: A Retrospective Cohort Study

Mariam Mbwana (BSc. Medical Laboratory Sciences)

MSc Epidemiology and Laboratory Management Dissertation
Muhimbili University of Health and Allied Sciences

June 2024

Copyright 2024 Turnitin. All rights reserved.

Burden of Tuberculosis and Predictors of Unfavorable Treatment Outcomes among Adolescents and Young Adults Initiating Antiretroviral Therapy in Dar es Salaam From 2020 - 2023: A Retrospective Cohort S

ORIGINALITY REPORT

28%	24%	19%	9%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Submitted to Muhimbili University of Health and Allied Sciences Student Paper	5%
2	dspace.muhas.ac.tz:8080 Internet Source	2%
3	researchonline.lshtm.ac.uk Internet Source	1%
4	irb.muhas.ac.tz Internet Source	1%
5	journals.plos.org Internet Source	1%
6	bmcinfectdis.biomedcentral.com Internet Source	1%
7	www.ncbi.nlm.nih.gov Internet Source	1%
8	www.frontiersin.org Internet Source	1%