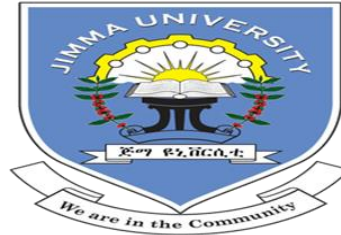


JIMMA UNIVERSITY
INSTITUTE OF HEALTH SCIENCE DEPARTMENT OF EPIDEMIOLOGY



DETERMINANTS OF UNSUCCESSFUL TB TREATMENT OUTCOME AMONG TB PATIENTS ON DOTS: A CASE CONTROL STUDY IN JIMMA TOWN HEALTH FACILITIES, SOUTH WEST ETHIOPIA, 2022GC

BY
DEREJE TEKA BEYENE

A RESEARCH THESIS SUBMIT TO JIMMA UNIVERSITY INSTITUTE OF HEALTH SCIENCE DEPARTMENT OF EPIDEMIOLOGY; IN PARTIAL FULFILLMENT FOR THE REQUIREMENT OF MASTERS IN PUBLIC HEALTH (GMPH)

DETERMINANTS OF UNSUCCESSFUL TB TREATMENT OUTCOME AMONG TB PATIENTS ON DOTS: A CASE CONTROL STUDY IN JIMMA TOWN HEALTH FACILITIES, SOUTH WEST ETHIOPIA 2020GC

BY

DEREJE TEKA BEYENE

ADVISORS

1. DR. SAHILU ASSEGID
2. MR. MAMO NIGATU

Jimma University
January, 2022

ABSTRACT

Background: Failure to treatment completion or cure was believed to be the main determinants for difficulties in controlling a disease. Identification of the determinants was therefore crucial for the improvement of future control and prevention strategies. Thus, this study assessed determinants for unsuccessful TB treatment outcome among patients on DOTS in Jimma town, south west Ethiopia.

Methods: Unmatched case control study was conducted from April 1 to June 1 2021. 118 cases and 472 controls were required for this study. Cases were TB cases with unsuccessful treatment course whereas controls were those of successful treatment. After obtained Ethical clearance and Letter of permission data collection was done from 10 health facilities by allocating cases and controls proportionally for each facility and randomly from each facility. Data Quality control was done by checking completeness and consistence of collected data at field. Analysis was done using backward method and Binary logistic regression model were used for AOR at 95% CI.

Result: After controlling for possible confounders, the independent variables that associated with unsuccessful treatment outcome were age > 34.7 years p-value 0.0015 (AOR 1.9(95% CI 1.14-3.2), lack of contact person p-value 0.000 AOR 27(95% CI 15.8-46.3), HIV positive P-value 0.000 AOR 7.3(95% CI 3.7-14.2)) and malnourished p value 0.006 (AOR 4.5(95% CI 1.5-12.9). On the other hand, the factors significantly and negatively associated with unsuccessful treatment were Unknown nutritional status with p-value 0.001 AOR .188(95% CI 0.07-0.5).

Conclusion and recommendations: factors for unsuccessful treatment outcome were advanced age those who haven't contact person, HIV positive and malnourished. Therefore, targeted measures should be considered to reduce the poor TB treatment outcome among the high-risk. Furthermore, careful monitoring, screening and management of risk factors are highly recommended.

Key words:

Unsuccessful treatment outcome, TB, south west Ethiopia

ACKNOWLEDGMENT

First and foremost my heartily felt thanks go to the Almighty God. I would also like to acknowledge Department of Epidemiology for the chance it delivered me in doing this thesis. My earnest gratitude goes to my advisors Dr. Sahilu Assegid and Mrs. Mamo Nigatu for their unreserved assistance, timely comments and relevant guidance throughout developing the full Thesis. I would like also to thank Jimma town health office and health facilities for their cooperation and assistance by giving me relevant information.

CONTENTS

Topic	Page No.
ACKNOWLEDGMENT	iii
LIST OF TABLES.....	vii
LIST OF FIGURES.....	viii
ABBREVIATION/ ACRONYMS	ix
JHC- Jimma health center	ix
CHAPTER ONE: INTRODUCTION	1
1.1 Back ground information	1
1.2 Statement of the problem	3
CHAPTER TWO: LITERATURE REVIEW	5
2.1 Introduction.....	5
2.2 Factors that contribute for unsuccessful treatment outcome.....	5
2.2.1 Socio demographic factors.....	5
2.2.2 Clinical related factors	6
2.2.3 Health care and system-related factors	10
2.2.4 Treatment related factors	11
2.3 Limitations	11
2.4 Significance of the study.....	12
2.5 Conceptual Framework.....	12
CHAPTER THREE: OBJECTIVES	13
3.1 General Objective:	13
3.1.1 To determine factors for unsuccessful TB treatment outcome among patients on DOTS in Jimma town, south west Ethiopia.	13
3.2 Specific Objectives:	13
CHAPTER FOUR: METHODS AND MATERIALS	14
4.1 Study Area:	14
4.2 Study period:	15
4.5 Study Design:.....	15
4.6 Sample size Determination	15
4.7 Definition of cases and controls.....	16

4.7.1 Definition of cases	16
4.7.2 Definition of controls	16
4.8 Inclusion and Exclusion criteria	16
✓ Inclusion criteria for cases	16
✓ Inclusion criteria for controls	16
✓ Exclusion criteria for controls	17
✓ Exclusion Criteria for case	17
4.9 Sampling technique.....	17
4.9.1 Sampling of cases.....	17
4.9.2 Sampling of controls	17
4.10 Sampling frame	18
4.10.1 Selection of cases	18
4.10.2 Selection of controls.....	19
4.11 Data collection Instrument.....	19
4.12 Data collection Tools.....	19
4.13 Variables of the study	19
4.14 Data collection procedures.....	19
4.15 Data Quality Control.....	20
4.16 Data processing and analysis	20
4.17 Operational definitions.....	20
4.18 Ethical considerations	21
4.19. Dissemination plan.....	21
CHAPTER FIVE: RESULT	22
5.1 General information	22
5.2 Sociodemographic Characteristics related factors	22
5.3 Clinical and investigations related characteristics-including HIV test result:.....	23
5.4. Treatment related factors.....	24
5.5 Health care and system-related factors	25
5.6 Test for significance.....	26
5.7 Predictors for unsuccessful treatment outcomes	30
CHAPTER SEVEN: CONCLUSSION AND RECOMENDATIONS	35
REFERENCES	36

ANNEXES	39
I. QUESTIONNAIRE	39
Section I socio- demographic information of the patient.....	40
Section II- Clinical characteristics	40
Section III Treatment related factors.....	41

LIST OF TABLES

Content	Page No.
Table 1. Shows allocation of cases and control for each health facility	18
Table 2: Socio-demographic characteristics related factors of study subjects, Jimma town health facilities, south west Ethiopia, 2013 EC	22
Table 3: Clinical and investigations related characteristics-including HIV test result of the study subjects, Jimma town health facilities, south west Ethiopia, 2013 EC	23
Table 4: Treatment related factors of the study subjects, Jimma town health facilities, south west Ethiopia, 2013 EC	25
Table 5: Health care and system-related factors, Jimma town health facilities, south west Ethiopia, 2013 EC	26
Table 6: Association of sociodemographic factors with Unsuccessful outcome of the study subjects, Jimma town health facilities, south west Ethiopia, 2013 EC	27
Table 7: Predictors for unsuccessful treatment outcomes among patients on DOTs, Jimma town health facilities, south west Ethiopia, 2013 EC	31

LIST OF FIGURES

Content	Page No.
Figure 1: Conceptual frame work for determinants of successful TB treatment outcome among TB patients on DOTS (Source: developed by principal investigator based on literature review)	12
Figure 2 Map of Jimma town	14

ABBREVIATION/ ACRONYMS

AFB- Acid fast bacilli

AIDS-Acquired Immune Deficiency Syndrome

ART-Anti Retroviral Therapy

CDC-Center of Disease Control

DOT- Directly observed treatment

EPTB- Extra pulmonary tuberculosis

H2HC Higher two health center

HIV- Human immune virus

JHC- Jimma health center

JU-Jimma University

JUMC-Jimma University medical center

LTFU: - Lost to follow up

MKHC- Mendera kochi health center

MOC Mission of charity

PTB- Pulmonary tuberculosis

SGGH- Shenen Gibe General Hospital

SPSS- Statistical Package for Social Sciences

TB- Tuberculosis

TSR- Treatment success rate

VCT-Voluntary Counseling Technique

WHO - World Health Organization

CHAPTER ONE: INTRODUCTION

1.1 Back ground information

TB is a major public health problem throughout the world. About a third of the world's Population is estimated to be infected with tubercle bacilli and hence at risk of developing active disease(1).

According to the WHO Global TB Report 2015, 9.6 million people are estimated to have fallen ill with TB in 2014 while an estimated 1.5 million people died of TB. In addition, an estimated 3.3% of these new TB cases and 20% of the previously treated cases have believed to harbor MDR-TB whereas, an estimated 190 000 people died of MDR-TB(2).

Ethiopia is among the 30 High TB, HIV and MDR-TB Burden Countries, that accounted for 80% of all estimated TB cases worldwide, with annual estimated TB incidence of 207/100,000 populations and death rate of 33 per 100,000 populations for 2012. Among the notified TB cases in 2014, 1300(1.6%) of new TB cases and 11.8% of previously treated TB cases were estimated to harbor MDR TB(3).

While treatment is integrated into general health services and DOTS geographical coverage is 95%, TB remains a major health problem in Ethiopia. Cure rate of 67% remains well below the 85% rate of WHO recommendation(3).

Upon an individual TB patient completed receiving full course of treatment or reached to the point of evaluation, the TB focal should analyze patient information and assign one final outcome and register on unit TB register as treatment result. There are seven possible outcomes to be assigned and one patient could only have one possible result as follows: cure, complete, Treatment failure, Died, Lost to follow up (LTFU) and Not Evaluated. When we say successful TB treatment outcome includes Cure and treatment complete and Unsuccessful treatment outcomes includes treatment failure, Death and LTFU(4).

A retrospective study from north Ethiopia depicts the treatment success rate of tuberculosis patients was unsatisfactory(5).

An earlier study on the impact of DOTS in the Southern Ethiopia reported one in five TB patients still continued to result with unsuccessful treatment outcome. Defaulted is one of the unsuccessful forms of TB treatment outcome and a serious problem in the TB program of Ethiopia. According to the retrospective study in rural hospital in South Ethiopia defaulted from treatment rate was 11.4%. Another study from Northern part of the Country also revealed among unsuccessful treatment outcome, 18.3% were defaulted followed by death and treatment failure account 10.1% and 0.2% respectively(5)(6).

Also the study found that the treatment outcome of TB patients treated under DOTS program in Benishangul Gumuz Region was low. The treatment success rate of all cases was 60.77%. This finding is higher than the study reported by Shargie et al. in southern Ethiopia that has shown the treatment success rate of all TB cases was 49% and the study reported in ref. that indicated the treatment success rate of all TB cases was 29.5% in Gondar University Teaching Hospital, northwest Ethiopia. However, it is lower than the WHO international target of 87% (updated target 2011–2015). The low treatment success rate observed in this study as compared to WHO's average might be due to high not evaluated rate 775 (21.19%), loss to follow up rate 315 (8.61%) death rate 341 (9.32%), particularly the high loss to follow up rate and death rate deserve special attention(7).

In effort to reach the global target of 85% treatment success, it is compelling to identify, describe, and deal with factors determining poor treatment outcome. Several reasons and risk factors for unsuccessful TB treatment outcomes have been reported from different countries (3)(8).

The Federal Ministry of Health of Ethiopia (FMOH) has been implementing a number of strategies specific to TB, TB/HIV, and MDR-TB. Direct Observed Treatment Short-course (DOTS) was recommended by WHO since the mid-1990s. DOTS have been started in Ethiopia in 1992 as a pilot and since then Ethiopia has been implementing DOTS. So far, TB treatment outcomes in Ethiopia were evaluated in a limited number of easily accessible health facilities. However, treatment outcomes are dependent on adherence to the treatment protocol which is also dependent on the knowledge and commitment of patients and health professionals. This implies that patients who live in less accessible and geographically distant places could have low level of knowledge that may contribute to the reduced adherence to treatment. Studies indicated that

treatment success rate (TSR) in Ethiopia varies from 26% to 94.4% depending on different factors(9). Therefore, evaluating the treatment outcomes of specific localities such as that of the Jimma town could play an important role in addressing the TB control problems of the town.

1.2 Statement of the problem

Failure to treatment completion or cure is believed to be the main reason for difficulties in controlling a disease that is far from new.

While treatment is integrated into general health services and DOTS geographical coverage is 95%, TB remains a major health problem in Ethiopia. Cure rate of 67% remains well below the 85% rate of WHO recommendation(3).

Upon an individual TB patient completed receiving full course of treatment or reached to the point of evaluation, the TB focal should analyze patient information and assign one final outcome and register on unit TB register as treatment result(4).

In effort to reach the global target of 85% treatment success, it is compelling to identify, describe, and deal with factors determining poor treatment outcome. Several reasons and risk factors for unsuccessful TB treatment outcomes have been reported from different countries (3)(8).

An earlier study on the impact of DOTS in the Southern Ethiopia reported one in five TB patients still continued to result with unsuccessful treatment outcome. Defaulted is one of the unsuccessful forms of TB treatment outcome and a serious problem in the TB program of Ethiopia. According to the retrospective study in rural hospital in South Ethiopia defaulted from treatment rate was 11.4%. Another study from Northern part of the Country also revealed among unsuccessful treatment outcome, 18.3% were defaulted followed by death and treatment failure account 10.1% and 0.2% respectively(5)(6).

For these reasons, determination of the pattern of unsuccessful treatment outcome and factors that predicts the unsuccessful treatment outcomes helps to design the possible future of TB treatment and control in the community. Therefore, this study was aimed to describe pattern of unsuccessful TB treatment outcome and associated factors among health institutions providing

DOTS in Jimma town, south west Ethiopia Thus, Monitoring the treatment outcome and understanding of reasons for unsuccessful treatment outcome are also essential in order to improve treatment outcome.

In our country trend of TB case is similar to global cases it is important to avert the problem of Unsuccessful TB treatment outcome and crucial to conduct retrospective case control study in health facilities found under Jimma town health office and providing the results and forward the possible recommendation to persons it may concern.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

The implementation and expansion of DOTS strategy have been substantially improved the success rate of TB treatment outcomes. However, the strategy is being challenged by poor treatment outcomes especially in low and middle-income countries. Therefore, routine monitoring of TB treatment performances and analysis of determinants responsible for poor treatment outcomes are vital to prevent further adverse outcomes. This study describes the characteristics of patients with TB and their Treatment outcome over a past 5-years period in health institutions that provide DOTS in Jimma town, south west Ethiopia.

2.2 Factors that contribute for unsuccessful treatment outcome

Several reasons and risk factors for poor TB treatment outcome have been reported by previous studies in other settings. Male sex, lack of education, old age, multidrug resistance, HIV co-infection, accessibility of health facilities, low socio-economic status, low awareness to the disease and its treatment, Absence of contact(1)(2)(10).

2.2.1 Socio demographic factors

The study done in Southern Ethiopia shows the chance of developing poor treatment outcome was higher among subjects older than 35 years of age (AOR=2.4; 95% CI: 1.6-3.4) . A significant association between poor outcome and older age may be partly explained by the reason that older individuals often have concomitant diseases, general physiological deterioration with age, are less able to reach health facilities. The study in Debretabor shows that the burden of TB was higher among the age groups of 15–24 and 25–34 years. This is in line with many similar studies that confirm as TB mainly affects sexually active and reproductive age groups. This might also be due to high HIV prevalence in these age groups. Also males were 1.6 times more likely to develop poor treatment outcome (AOR=1.6; 95% CI: 1.1-2.3) when compared to females This could be attributed to the fact that men are the bread winners in the most family, who are highly exposed to cigarette smoking, alcohol consumption and thus find it difficult to comply with daily clinic attendance. Study shows that subjects from rural area were 1.5 times more likely to develop poor outcome than urban dwellers (AOR=1.5; 95%CI: 1.0-2.2) The lower

treatment success rate in rural patients is probably due to lower awareness of TB treatment and the long distance between their homes and the treatment centers. This study also shows male patients were more likely to have poor treatment outcome when compared to females (AOR: 1.81; 95% CI: 1.06–3.10; $P = 0.031$) the reason may being highly exposed to cigarette smoking, alcohol consumption and HIV prevalence and travelling a long distance for economic reasons might contribute to poor treatment success rate in men. Related to residence the study shows Patients from rural areas were more likely to have poor treatment outcome than urban dwellers (AOR = 1.173; 95% CI: 1.02–2.91; $P = 0.041$) because of lower awareness and information about TB, HIV and their treatments, long distance between their homes and treatment centers, fear of stigma and discrimination, and poor socio-economic status might contribute to lower treatment success rate in rural patients.

2.2.2 Clinical related factors

Regarding the type of TB, subjects who had smear negative PTB (PTB-) and EPTB were respectively 2.4 and 2.5 times more likely to develop poor outcome referred to smear positive PTB. This is probably due to low rate of identification of illness and delay to start treatment, long treatment duration, the case that monitoring of treatment outcome of PTB- and EPTB is only based on clinical condition and their diagnosis is difficult often resulting in treatment delay. The study done in Easter Ethiopia shows out of the total reviewed patients' record more proportion of patient with unsuccessful treatment outcome were pulmonary negative compared to those successfully completed the treatment (47.3% of cases and 32% of controls, $P < 0.001$). HIV positive (AOR=2.4; 95% CI: 1.6 3.5) and unknown HIV status (AOR=2.5; 95%CI: 1.3-5.1) were associated with more than two-fold increase in odds for poor treatment outcome. Among the total of patient with unsuccessful treatment outcome ($n=330$) 64.2% were because of death, Contrary similar study conducted in North Ethiopia showed defaulter was more cause of unsuccessful treatment outcome than death (11). A study from Taipei, Taiwan among adult also showed death was the main cause of unsuccessful treatment outcome of Tuberculosis patients(12). Contrary similar study conducted in North Ethiopia showed defaulter was more cause of unsuccessful treatment outcome than death(11). The difference might be related with starting of using strategies such as health extension workers to increase public awareness on the importance of effective completion of TB

treatment; use of phone of contact person to ascertain reason for lost follow up are being undertaken so that might contribute to the decreasing of defaulter from TB treatment.

Sputum test positive for AFB result at 2nd month after initiation of treatment was significantly high among unsuccessful treatment outcome compared to those successful treatment outcome (OR= 14.23(5.52-36.46). study showed sputum smear negative pulmonary TB at the beginning of treatment is a factor that predict unsuccessful TB treatment outcome (OR 1.83, 95% CI 1.3-5.51) This might because of probability of miss diagnosis of the patients which resulted with poor treatment response. . The main concern about TB/HIV co-infection is that , different study result from different part of the world showed the TB treatment outcome probability are significantly different between HIV+ and HIV negative TB patients. The prevalence of HIV co-infection was 35.9% among patients with unsuccessful treatment outcome which is 24.2% among successfully complete treatment. This showed the risk of unsuccessful TB treatment outcome is significantly high among patients with HIV positive compared to HIV negative sero status (OR= 2.33(1.34-5.73, P<0.01). It is comparable with many studies that have found that HIV co-infections are associated with poorer outcomes compared to HIV-negative patients(6). One can understand that HIV is continued to be double challenge both increasing the risk of developing and poor outcome to treatment of TB. Sputum test positive for AFB result at 2nd month after initiation of treatment was significantly high among unsuccessful treatment outcome compared to those successful treatment outcome (OR= 14.23(5.52-36.46). This result is in line with a study from Yunnan, China which showed positive 2-month smear test result is one of the risk factors for unsuccessful treatment outcome(13). Study in Eastern Ethiopia showed sputum smear negative pulmonary TB at the beginning of treatment is a factor that predict unsuccessful TB treatment outcome (OR 1.83, 95% CI 1.3-5.51). The finding is in line with previous studies from Ethiopia and other countries(14). This might because of probability of miss diagnosis of the patients which resulted with poor treatment response. The proportion of PTB+, PTB-, and EPTB cases were 24.5%, 38.7%, and 36.9%, respectively. The proportion of PTB+ cases was relatively lower when compared to the national average reported by the WHO between 2011 and 2015, of 32.4%. Moreover, bacteriologically confirmed TB is also much lower than the national average of 54%. However, there are similar reports showing lower notification rates of PTB+ cases and high numbers of EPTB cases in the northern part Ethiopia. The causes for this are not yet identified and some reports suggest that it might have something to do with the host genomic base, but this

needs further investigation. On top of this, due to limited resources, most of the health facilities in Ethiopia have been using AFB microscopy, which has low sensitivity (40–45%) and might contribute to lower notification rates of PTB+ (observation). The results of this study could be used to support the country's strategy to use rapid, sensitive, and specific point-of-care diagnostic technologies such as GeneXpert among vulnerable groups (children, HIV positive people, etc.). The proportion of TB/HIV co-infection cases was 24.2%, which is much higher than the national prevalence of 8%. This could partly be explained by the fact that the subjects in the present study were individuals with active TB, who might have underlying immunological defect like HIV. On top of this, the national TB/ HIV co-infection estimate was based on the community based survey. At the same time, our findings are from one site, while the national data is countrywide and thus disparity is likely. However, similar findings to the present study have also been reported by other studies conducted in Ethiopia.

This study in JUMC found that TB diagnosed patients with unknown HIV test result were almost eight times more likely to have an unsuccessful treatment outcome than HIV-positive TB patients. These findings are in line with other studies done elsewhere. Reasons for unsuccessful treatment outcomes probably associated with any presence of comorbidities (diabetes mellitus and other chronic disorders) that impair cell-mediated immunity, not only targeting the CD4 T lymphocytes as in the case with HIV infection but also by interfering with the function and activation of other immune cells. The unsuccessful treatment outcome was significantly higher among smear-negative PTB patients and two times more likely than smear-positive PTB patients with the incidence of default (8.8%) was significantly higher compared with other study (0.8%) in other parts of Ethiopia, and in Pakistan, which was (2.6%). Therefore, specific measures are needed to improve compliance among TB patients in the study area, focusing on addressing the challenges in defaulters and promoting adherence. In this study, there were lower TSR for TB cases in comparison with the End TB Strategy targeted by the WHO until 2025. On the other hand, high TSR was observed in this study than those of the findings from Gambella hospital (63.4%) and Gondar town (70.5%), both studies were reported from Ethiopia. This difference may be due to the fact that MRC in this setting has a greater involvement in accordance with functionality to provide training and access. There were low transferred out proportions in this study. This

finding was low in comparison with other findings, 17.12% and 13.8% in studies conducted in Gambella and Gondar University hospitals, respectively. This is probably due to the expansion of DOTS facilities in the region have contributed to this low number of transferred out cases in this study. TB infection control has been a growing concern among health-care workers in developed countries, but it is a neglected problem among individuals working in health facilities in southwest part of Ethiopia. This study revealed that in each of the 5 years, between 3.7% and 12.5% of TB patients registered for DOTS at JUMC were working in any health facilities. The primary reason for this occupational TB infection may be due to low awareness and poor commitment to follow the effective implementation of infection control practices in their workplace setting(15). In study conducted in North Ethiopia, HIV status had no significant association with TB treatment failure. A study in Thailand and Addis Ababa showed also that HIV status was not significantly associated with TB treatment failure. A study in Ukraine showed that HIV positive individuals had a 50% higher risk of developing TB treatment failure at their first TB infection. This is because being HIV positive is one risk factor for drug susceptible TB, which is related to immune system suppression. Being HIV positive might carry the same risk of infection with MDR-TB but may not contribute to the change of a drug-susceptible strain of TB to MDRTB.

Study in Addis Ababa shows that the proportion of persons with a successful treatment outcome was lower among underweight patients compared with normal or overweight patients (85.3% versus 93.4%). The odds of successful treatment outcomes were 2.15 times higher in normal or overweight TB patients versus those that were underweight at baseline(19). Study conducted in Ethiopia university hospital showed that unsuccessful treatment outcomes of were significantly higher in weight category 30–39.9 than weight categories ≥ 55 kg with p-value .000 and AOR 1.508 (1.102–2.065)(19). One study in Addis Ababa revealed that body weight at initiation of anti-TB treatment (<35 kg) was a significant risk factor of death during anti tuberculosis treatment period (12). In contrast study done in in South Africa shows that wt. with unsuccessful treatment outcome has not significantly associated with unsuccessful treatment outcome (13). The unsuccessful treatment outcome in TB with malnutrition could be related to malabsorption of key anti TB drugs, late diagnosis and treatment, malnutrition which implies that their immunity was subsidized and causes difficulty for them to battle the side effects of the drug and

the comorbidities, in addition early TB diagnosis and treatment may decrease the mortality rate.(33).

2.2.3 Health care and system-related factors

In this study, subjects started their anti-TB medication before the year 2011 were more likely to have poor treatment outcome (AOR=2.1; 95% CI=1.3-3.4) when compared to subjects started their medication after 2011. This difference might be due to improvements in DOTS performance in the subsequent years, TB treatment regime changed from EH to RH based treatment in the continuation phase, improvement in patient awareness about TB transmission and treatment because of health education and promotion, and health extension workers involvement in the community(10). study also depicts lack of registered contact person was also the risk factor associated with unsuccessful treatment outcome (OR=1.37(1.14-2.91, $p<0.024$)(16). Study in Eastern Ethiopia depicts lack of registered contact person was also the risk factor associated with unsuccessful treatment outcome (OR=1.37(1.14-2.91, $p<0.024$)(14). The difference might be related with starting of using strategies such as health extension workers to increase public awareness on the importance of effective completion of TB treatment; use of phone of contact person to ascertain reason for lost follow up are being undertaken so that might contribute to the decreasing of defaulter from TB treatment. This study also depicts lack of registered contact person was also the risk factor associated with unsuccessful treatment outcome (OR=1.37(1.14-2.91, $p<0.024$).

Study in west wolega showed that treatment success rate was significantly varied across treatment centers. Unfavorable treatment outcome was observed in Anger Gute health center than others (AOR: 2.27; 95% CI: 1.18–4.38; $P = 0.015$), the possible reasons might be differences in human resources and their productivity, workload and heterogeneity of service provision. Study conducted in East Ethiopia [(14)] and study done in Somalia, Mogadishu(17) Shows that person who do not have contact person have higher risk of unsuccessful treatment outcome, The difference might be related with starting of using strategies such as health extension workers to increase public awareness on the importance of effective completion of TB treatment; use of phone of contact person to ascertain reason for lost follow up are being undertaken so that might contribute to the decreasing of defaulter from TB treatment.

2.2.4 Treatment related factors

Study done in Tigray the bivariate analysis also showed that individuals who missed to take one or more first-line anti-TB drugs whether forgot or intentionally missed had increased risk for development of TB treatment failure(11). It is also similarly with study conducted in Addis Ababa showed that individuals who did not take first-line anti-TB drugs regularly had increased risk for development of MDR-TB(4).

Related to treatment history previously treated patients were more likely to have poor treatment outcome than newly treated ones (AOR = 1.72; 95% CI: 1.16–6.39; P = 0.022) this due to Prior suboptimal therapy, poor compliance and high prevalence of multidrug resistant TB might contribute the observed variation(16). In the study, the proportion of patients with successful treatment outcomes (cured and completed) was found to be 90.9%, which is higher than the WHO target set for the Millennium Development Goal (MDG) of 85% and comparable to that of the milestone target set globally for 2025 of > 90%.

Findings were reported by study done in Tigray shows the use of HAART during treatment for tuberculosis significantly protected against mortality when compared with HIV infected patients who did not receive antiretroviral medications or who received regimens other than HAART. Similar study stated that HIV infections without the use of ART were a factor that reduced the probability of cure(18). But a study done in southern region shows initiation of CPT (AOR=0.931; p=0.917) and HAART (AOR=2.781; p=0.056) for HIV+ had shown no significant association with unsuccessful TB treatment outcome(10).

2.3 Limitations

There are some limitations to this study. First, the retrospective nature of the study is a methodological limitation. Second, they used only routine program data; so that the Ethiopian health institution TB log book might be no enough check lists to identify full history of TB patients' characteristics, thus it is possible that there might be other associated factors left to examine. The analysis can only provide evidence of statistical association between those items and unsuccessful treatment outcome and cannot show cause-effect relationships. Despite these limitations, the study findings are useful to inform policy and programmers that aim to improve management of TB patients in Ethiopia and other comparable settings.

2.4 Significance of the study

Unsuccessful TB treatment outcome was the main challenge for global and National TB control program. Since, there is limited study about determinants of unsuccessful outcome among TB patient in the country and study area, this study is aimed to identify the determinants factors of unsuccessful treatment outcome among TB patients on DOTs in health facilities found in Jimma town, South west Ethiopia using case control study.

2.5 Conceptual Framework

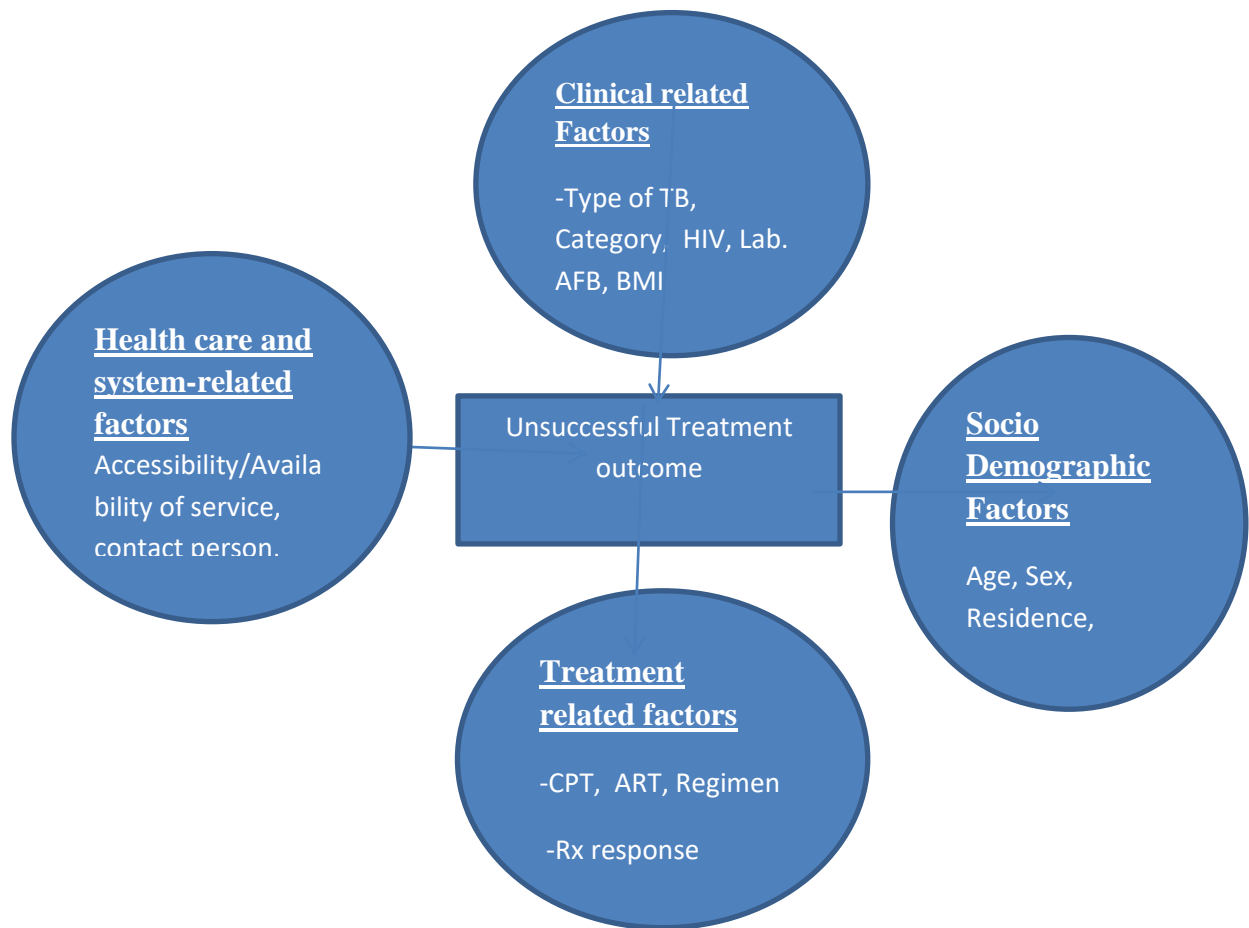


Figure 1: Conceptual frame work for determinants of successful TB treatment outcome among TB patients on DOTs (Source: developed by principal investigator based on literature review)

CHAPTER THREE: OBJECTIVES

3.1 General Objective:

3.1.1 To determine factors for unsuccessful TB treatment outcome among patients on DOTS in Jimma town, south west Ethiopia.

3.2 Specific Objectives:

3.2.1 To determine socio- demographic factors associated with unsuccessful treatment between cases and controls

3.2.2 To determine clinical factors associated with unsuccessful treatment between cases and controls

3.2.3 To determine Treatment related factors associated with unsuccessful treatment between cases and controls

3.2.4 To determine Health care and system-related factors associated with unsuccessful treatment between cases and controls

CHAPTER FOUR: METHODS AND MATERIALS

4.1 Study Area:

Jimma town is located 357 Kms South West of Addis Ababa and has total area of 4,623 hectares. It is bounded by Kersa Woreda in East, Manna Woreda in West, Manna and Kersa Woreda in North and Seka Woreda in South. The town is divided in to 3 Woreda or Higher and 13 Kebeles .The total projected population of the town is 130,254 (CSA 2007). The town has a temperature that ranges from 20-30 °C, an average annual rainfall of 800-2500mm³ and an altitude of 1750-2000m above sea level. The town has 5 hospitals (2 governmental and 3 private), 4 governmental Health centers and 16 Private clinics among those 6 governmental health facilities and 4 private facilities provides DOTS for TB treatment.

➤ MAP

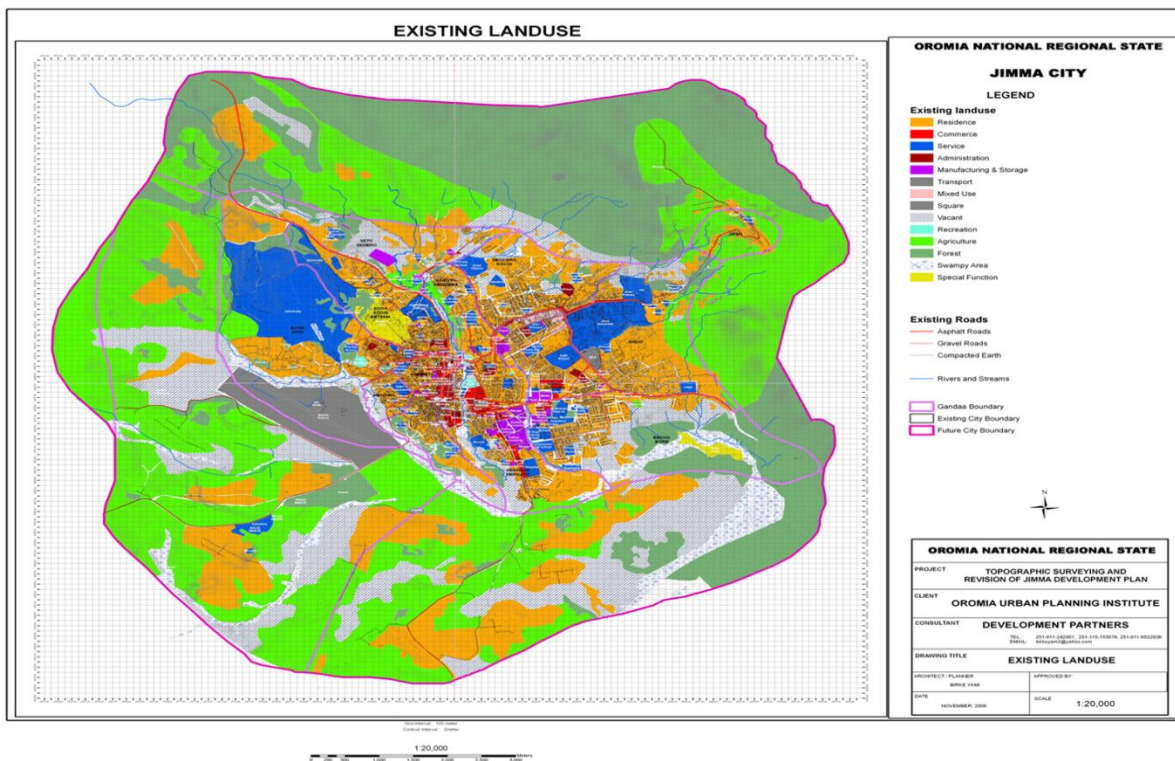


Figure 2 Map of Jimma town

4.2 Study period:

Study was conducted from April 1 to Jun 1/2021

4.3. Source population:

The documents of all TB patients who registered in TB unit register from July 1, 2015, to Jun 30, 2020, were source population.

4.4 Study population

The documents of randomly selected TB patients who registered in the TB treatment providing facilities from July 1, 2015, to Jun 30, 2020, were study population.

4.5 Study Design:

Unmatched Case control study to evaluate determinants of unsuccessful TB treatment outcome among TB patients was conducted from April 1 to Jun 1/2021GC in Jimma town health facilities.

4.6 Sample size Determination

To estimate précis proportion of unsuccessful TB treatment outcome; unsuccessful treatment outcome determinant factors; and the mean deference of two groups (control and cases) unsuccessful treatment outcome were used. To determine the required sample size two population proportion estimation formulas were used.

$$P = \frac{P_1 + rP_2}{1+r}$$

$$n_1 = \left[\frac{\left[Z_{\alpha/2} \sqrt{\left(1 + \frac{1}{r}\right) P(1-P)} + Z_{\beta} \sqrt{P_1(1-P_1) \frac{P_2(1-P_2)}{r}} \right]^2}{(P_1 - P_2)^2} \right]$$

Where;

P_1 = proportion cases who PTB negative = .0.529 (14)

P_2 = proportion controls who PTB negative =0.38(14)

$Z_{\alpha/2}$ = 1.96

Z_{β} =0.84

n_1 = No. of cases required

n_2 = No. of controls required

$r = n_2/n_1 = 4$

AOR (Odds ratio) = 1.83

Accordingly the number of cases and controls will be 117 and 468 respectively.

Adding 10% for non-response, the final number of cases and controls were 129 and 516 respectively

4.7 Definition of cases and controls

4.7.1 Definition of cases

Cases: was any person aged >15 years of age on DOTS between July 1, 2015, to Jun 30, 2020 subsequently classified as unsuccessful treatment (Treatment failure, LTFU or death) according to the national guideline

4.7.2 Definition of controls

Controls: was any person aged >15 years of age on DOTS from July 1, 2015, to Jun 30, 2020 subsequently classified as successful treatment (Cure or Treatment complete) according to the national guideline

4.8 Inclusion and Exclusion criteria

✓ Inclusion criteria for cases

The cases were patients with TB treatment failures (smear-positives after 5 months of treatment), default (interrupted treatment for two consecutive months or more after registration), or death (died from any cause during the course of treatment) with the resolution of symptoms according to WHO criteria on treatment outcomes adopted by FMOH between 1st July, 2015 and 30th June 2020(20).

Age >15 years

✓ Inclusion criteria for controls

patients who were declared cured (negative smear microscopy at the end of treatment and on at least one previous follow-up test) or completed treatment according to WHO criteria on treatment outcomes adopted by FMOH between 1st July, 2015 and 30th June 2020(20).

Age > 15 years

✓ **Exclusion criteria for controls**

Registries in which treatment outcomes were missing and patients were transferred to other districts, retreatments, MDR treatment and age < 15 will exclude from the study

✓ **Exclusion Criteria for case**

Registries in which treatment outcomes were missing and patients were transferred to other districts, retreatments, MDR treatment and age < 15 will exclude from the study.

4.9 Sampling technique

4.9.1 Sampling of cases

To allocate Unsuccessful (cases) to each facility under study were calculated as:-

Number of cases (Treatment failure, LTFU and death) divided by Total number of unsuccessful in all health facilities (=149) multiplied by Total Unsuccessful (cases) required.

4.9.2 Sampling of controls

To improve the comparison of cases and controls for one case (Unsuccessful treatment outcome) to four controls (successful treatment outcome) that started the treatment in the same week in the same institution was included. If more than four controls start with in same week with cases the nearest to the case was selected for control.

4.10 Sampling frame

Table 1. Shows allocation of cases and control for each health facility

Success	Health Facility Name										
	Jim ma HC	JMC	SGG H	MK HC	Hig her 2 HC	Bach o bore HC	Awet u hospi tal	MO C	Ethio Africa	Unive rsal Clinic	Total
Total Unsuccessful during July 1, 2015, to Jun 30, 2020	18	10	5	4	13	2	8	86	2	2	149
Total Successful July 1, 2015, to Jun 30, 2020	389	622	237	122	232	78	104	511	83	43	2421
Sample selected among unsuccessful (Cases)	16	9	4	3	11	2	7	73	2	2	129
Sample selected among successful	64	36	16	12	44	8	28	292	8	8	516

4.10.1 Selection of cases

Selection from the list of cases (Unsuccessful treatment outcome) by simple random sampling, that the allocated cases were drawn from each facility.

4.10.2 Selection of controls

Selected from the list of controls, that the allocated control was drawn that started the treatment in the same week in the same institution were included. If more than four controls start with in same week with the cases the nearest to the case were selected for control.

4.11 Data collection Instrument.

Date was collected through observation method (record review). Patient data, including year of treatment, age, sex, residence, TB type, TB, category, Lab investigations including HIV test and AFB, treatment history, Anthropometric measurements and treatment outcomes, were extracted from TB patient medical records using a well-structured checklist.

4.12 Data collection Tools

Data collection tool were structured questioners established after review of relevant literatures that can address particular objectives. Adopted from various similar studies in different parts of the world and modified according to local context.

4.13 Variables of the study

- The dependent variable was treatment outcome (successful/unsuccessful) while the
- independent variables were
 - Socio demographic (Age, sex, residence)
 - Clinical, Laboratory/investigations (Type of TB, Category, HIV, Lab. AFB), BMI, Wt.
 - Treatment/complication/course (ART, Cotrimox., Regimen, Rx response follow-up)
 - Health care and system-related factors (type of Institution which provides DOT, Accessibility, availability, Years of treatment, contact person, Distance from facility)

4.14 Data collection procedures

Date was collected through observation method (record review). Patients data, including year of treatment, age, sex, residence, TB type, TB, category, Lab investigations including HIV test and AFB, treatment history, Anthropometric measurements and treatment outcomes were extracted from TB patient medical records using a well-structured checklist. Data were collect by 10 experienced nursing staffs working in TB treatment unit and. Data collectors were trained for 2 days and collect under the strict supervision by supervisor.

4.15 Data Quality Control.

The raw data were collected by trained nurses and trained supervisor. The completeness and consistence of collected data was checked at field; and missing data and Outliers were checked at office and data entry was done by EPI DATA.

4.16 Data processing and analysis

After checking for completeness and consistency, data was entered into SPSS (IBM 23) for descriptive and inferential analysis. Binary logistic regression was used to determine the dependent variable on the basis of continuous and/or categorical independent variables, and factors with P value ≤ 0.25 in bivariate analysis were candidates for multivariate analysis. In multivariate analysis selection of variables were done by backward Wald and factors with P value ≤ 0.05 in the final model were statistically significant. The degree of association between dependent and independent variables was assessed using AOR at 95% CI.

4.17 Operational definitions

The following term/s used in the study were operationally defined accordingly

- **Cured:** - A pulmonary TB patient with bacteriologically confirmed TB at the beginning of treatment who was smear-ve or culture-negative in the last month of treatment and on at least one previous occasion.
- **Treatment completed:-** A TB patient who completed treatment without evidence of failure but with no record to show that sputum smear or culture results in the last month of treatment and on at least one previous occasion were negative, either because tests were not done or because results are unavailable.
- **Treatment failure:** - A TB patient whose sputum smear or culture is positive at month 5 or later during treatment.
- **Lost to follow up (LTFU)** for TB patient who has discontinued TB treatment for eight or more consecutive week after initiated on Anti-TB treatment
- **Died:** -for TB patient who is reported dead while receiving TB treatment, cause of death may not be related to TB.
- **Treatment success:** - The sum of cured and treatment completed.
- **Treatment un-success:** - The sum of treatment failed, defaulted and died.

- **New TB patients-** have not previously been treated for TB and are now diagnosed and started the current treatment.
- **Transfer in TB patients:** - A patient who has been transferred from another Facility to Continue DOTs treatment.
- **Associated factors:** factors that directly affect success of outcome either negatively or positively

4.18 Ethical considerations

Ethical approval was obtained by ethical approval committee of College of Health Sciences, Jimma University (JU). Letter of permission was written to Jimma town health office and to the respective health facilities to access patients' data. All information collected from TB unit register was kept strictly confidential and names of patients were not included in the data extraction form. All data were fully anonymous before access by the researchers. Confidentiality was keep throughout the study. The collected data was used for the intended purpose only.

4.19. Dissemination plan

Finding of this study will be presented and submitted to Jimma University, Jimma town health office and Health facilities. Effort will also be made to publish in peer reviewed journal and will be presented in different national and international conferences and seminars.

CHAPTER FIVE: RESULT

5.1 General information

During the study period Unit TB register were reviewed. A total of 118 cases and 472 controls were included in the study, therefore analysis were made based on 590 samples. After controlling for possible confounders and checked for collinearity analysis was done.

5.2 Sociodemographic Characteristics related factors

A total of 590 patient records were analyzed and the mean age of the cases was 39.8 years with SD 16.6, and that for the controls was 33.45 years with SD of 14.06. Majority of the cases and controls were males, comprising 75(63.8%) and 287(60.8%) respectively. Majority of cases 64(54.2%) and controls 346(73.3%) were Urban resident.

Table 2: Socio-demographic characteristics related factors of study subjects, Jimma town health facilities, south west Ethiopia, 2013 EC

Variable	Category	Cases No.(%)	Controls No.(%)	Total No.(%)	Control: Case
Sex	Males	75(63.8)	287(60.8)	362(61.3)	3.83
	Females	43(36.2)	185(39.2)	228(38.7)	4.30
	Total	118(100)	472(100)	590(100)	4.00
	Mean age	39.83(SD 16.6)	33.45(SD 14.06)		
Age in Years	≤34.7	53(44.9)	290(61.4)	342(63.1)	5.47
	>34.7	65(55.1)	182(38.6)	247(36.9)	2.8
	Total	118(100)	472(100)	590(100)	4
Residence	Urban	64(54.2)	346(73.3)	410(69.5)	5.41
	Rural	54(45.8)	126(26.7)	180(30.5)	2.33
	Total	118(100)	472(100)	590(100)	4.00

5.3 Clinical and investigations related characteristics-including HIV test result:

Regarding TB category majority 113 (95.8%) and 447(94.7%) were cases and controls respectively. Related to TB type 48(40.7%) of cases and 198(41.9%) of controls were PTB+, and 38(32.2%) of cases and 141(29.9%) of controls were PTB-

Among 2nd month sputum results majority of cases 32(66.7%) were positive for AFB, but majority of controls 177(89.4%) were AFB negative. Regarding HIV test status of patients, majority of cases 62(52.5%) were HIV positive, But majority of controls 427(90.5%) were HIV negative.

Majority 61.9% weight of cases lies in category of <50Kg But for controls majority 79.4% of weight were lies \geq 50Kg. Regarding nutritional status (BMI) majority 93(78.8) of cases were malnourished but majority 383(81.1) of controls have normal nutritional status

Table 3: Clinical and investigations related characteristics-including HIV test result of the study subjects, Jimma town health facilities, south west Ethiopia, 2013 EC

Variable	Category	Cases No.(%)	Controls No.(%)	Total No.(%)	Control: Case
TB Category	New	113(95.8)	447(94.7)	560(94.9)	3.95
	TI	5(4.2)	25(5.3)	30(5.1)	5.00
	Total	118(100)	472(100)	590(100)	4.00
TB Type	PTB+	48(40.7)	198(41.9)	246(41.7)	4.12
	PTB-VE	38(32.2)	141(29.9)	179(30.3)	3.71
	ETB	32(27.1)	133(28.2)	165(28)	4.16
	Total	118(100)	472(1000)	590(100)	4.00
For PTB+ Smear on 2 nd month?	Negative	12(25)	177(89.4)	189(76.8)	14.75
	Positive	32(66.7)	21(10.6)	53(21.5)	0.66
	Unknown	4(8.3)	0	4(1.7)	-
	Total	48(100)	198(100)	246(100)	4.12

Variable	Category	Cases No.(%)	Controls No.(%)	Total No.(%)	Control: Case
HIV	Negative	56(47.5)	427(90.5)	483(81.8)	7.62
	Positive	62(52.5)	45(9.5)	107(18.2)	0.72
	Total	118(100)	472(100)	590(100)	4.00
Weight in Kg	≥50	45(38.1)	375(79.4)	420(71.2)	8.33
	≤49.9	73(61.9)	97(20.6)	170(28.8)	1.33
	Total	118(100)	472(100)	590(100)	4
Nutritional status(BMI)	Normal	179(14.4)	383(81.1)	400(67.8)	22.52
	Malnourished	93(78.8)	60(12.7)	153(25.9)	0.64
	Unknown	8(6.8)	29(6.2)	37(6.3)	3.62
	Total	118(100)	472(100)	590(100)	4.00

5.4. Treatment related factors

Related to ART treatment, majority 32(51.6) and 45(100) cases and controls respectively starts ART. Among HIV positives only 11(17.7%) of cases initiate cotrimoxazole prophylaxis but 44(97.8%) of controls initiate cotrimoxazole Prophylaxis.

Table 4: Treatment related factors of the study subjects, Jimma town health facilities, south west Ethiopia, 2013 EC

Variable	Category	Cases	Controls	Total	Control:
		No.(%)	No.(%)	No.(%)	Case
ART Started?	Yes	32(51.6)	45(100)	77(72)	1.4
	No	18(29)	0	18(16.8)	-
	Unknown	12(19.4)	0	12(11.2)	-
	Total	62(100)	45(100)	107(100)	
Co- trimoxazole Started?	Yes	11(17.7)	44(97.8)	55(51.4)	4
	No	27(43.5)	1(2.2)	28(26.2)	0.04
	Unknown	24(38.7)	0	24(22.4)	-
	Total	62(100)	45(100)	107(100)	

5.5 Health care and system-related factors

Related to Health facility 50.8% of cases and 50.8% controls were from Mission of charity 13.6% of cases and 13.6% controls from Jimma HC 9.3% of cases and 9.3% controls from higher two HC. Regarding years of treatment, for cases 35(29.7%) of them from 2010EC, 27(22.9%) from 2011EC and 22(18.6%) from 2012EC, for controls 144(30.5%) of them from 2010EC, 121(25.6%) from 2011EC and 83(17.6%) in 2012EC. Related to the presence of contact person at time of emergency Majority 80.5% of cases were not have contact person but 87.3% of controls have contact person

Table 5: Health care and system-related factors, Jimma town health facilities, south west Ethiopia, 2013 EC

Variable	Category	Cases No.(%)	Controls No.(%)	Total No.(%)	Control: Case
Treatment Facility	MOC	60(50.8)	240(51)	300(50.8)	4
	JHC	16(13.6)	64(13.6)	80(13.6)	4
	H2HC	11(9.3)	44(9.3)	55(9.3)	4
	JUMC	9(7.6)	36(7.6)	45(7.6)	4
	Awetu Hospital	7(5.9)	28(5.9)	35(5.9)	4
	SGGH	7(5.9)	28(5.9)	35(5.9)	4
	MKHC	3(2.5)	12(2.5)	15(2.5)	4
	BBHC	2(1.7)	8(1.7)	10(1.7)	4
	Ethio Africa	2(1.7)	8(1.7)	10(1.7)	4
	Universal	1(0.8)	4(0.8)	5(0.8)	4
	Total		118	472	590
Years of treatment	2008	15(12.7)	53(11.2)	68(11.5)	3.5
	2009	19(16.1)	71(15)	90(15.3)	3.75
	2010	35(29.7)	144(30.5)	179(30.3)	4.11
	2011	27(22.9)	121(25.6)	148(25.1)	4.48
	2012	22(18.6)	83(17.6)	105(17.8)	3.77
	2008	15(12.7)	53(11.2)	68(11.5)	3.53
	Total		118(100)	472(100)	590(100)
Contact person(address)	Yes	23(19.5)	412(87.3)	435(73.7)	17.9
	No	95(80.5)	60(12.6)	155(26.3)	0.63
	Total	118	472	590	

5.6 Test for significance

To evaluate any factors associated with unsuccessful TB treatment outcome for independent variables of Sex, Age and residence, wt., BMI, TB category, TB type, 2nd month AFB, HIV, ART, Cotrimoxazole and years of treatment. As shown in table below Age, Residence, wt., BMI, HIV and contact have statically significant association with unsuccessful treatment outcome with p-value ≤ 0.05

Table 6: Association of sociodemographic factors with Unsuccessful outcome of the study subjects, Jimma town health facilities, south west Ethiopia, 2013 EC

Variable	Category	Cases No.(%)	Controls No.(%)	COR, 95%CI	p-value	AOR, 95%CI	P-value
Sex	Males	75(63.8)	287(60.8)	.889	.583		
	Females	43(36.2)	185(39.2)		1		1
	Total	118(100)	472(100)				
Age in Years	≤34.7	53(44.9)	290(61.4)		1		1
	>34.7	65(55.1)	182(39.6)	2(1.3-2.9)	.001	1.9(1.14-3.2)	.0015*
	Total	118(100)	472(100)				
Residence	Urban	63(53.4)	344(72.9)		1		1
	Rural	55(46.6)	128(27.1)	2.346(1.5-3.5)	.000	1.6(0.9-2.8)	0.77
	Total	118(100)	472(100)				
Weight in Kg	>50	45(38.1)	375(79.4)		1		1
	≤49.9	73(61.9)	97(20.6)	.159(0.1-.25)	0.000	0.55	.165
	Total	118(100)	472(100)				
BMI	Normal	179(14.4)	383(81.1)				
	Malnourished	93(78.8)	60(12.7)	6.2(2.5-15.6)	.000	4.5(1.5-12.9)	.006*
	Unknown	8(6.8)	29(6.2)	.18(0.08-0.42)	.000	.188(0.07-0.5)	.001*
	Total	118(100)	472(100)				

Variable	Category	Cases No.(%)	Controls No.(%)	COR, 95%CI	p-value	AOR, 95%CI	P-value
TB Category	New	113(95.8)	447(94.7)		1		
	TI	5(4.2)	25(5.3)	.79(0.3- 2.1)	0.64		
	Total	118(100)	472(100)				
TB Type	PTB+	48(40.7)	198(41.9)		1		
	PTB-VE	38(32.2)	141(29.9)	.99(0.6- 1.6)	.976		
	ETB	32(27.1)	133(28.2)	.89(0.5- 1.5)	.673		
	Total	118(100)	472(1000)				
For PTB+	Negative	12(25)	177(89.4)				
Smear on 2 nd month?	Positive	32(66.7)	21(10.6)		0.99		
	Unknown	4(8.3)	0		0.99		
	Total	48(100)	198(100)				
HIV	Negative	56(47.5)	427(90.5)		1		1
	Positive	62(52.5)	45(9.5)	10.5(6.5- 16.9)	.000	7.3(3.7- 14.2)	.000*
	Total	118(100)	472(100)				
ART Started?	Yes	32(51.6)	45(100)		1		
	No	18(29)	0		0.999		
	Unknown	12(19.4)	0		1.0		
	Total	62(100)	45(100)				

Variable	Category	Cases	Controls	COR,	p-value	AOR,	P-value
		No.(%)	No.(%)	95%CI		95%CI	
Co-trimoxazole Started?	Yes	11(17.7)	44(97.8)		1		
	No	27(43.5)	1(2.2)		0.998		
	Unknown	24(38.7)	0		1.0		
	Total	62(100)	45(100)				
Years of treatment	2008	15(12.7)	53(11.2)		1		
	2009	19(16.1)	71(15)	1.1(0.51-2.2)	.862		
	2010	35(29.7)	144(30.5)	1.3(0.6-2.6)	.511		
	2011	27(22.9)	121(25.6)	1.2(0.6-2.3)	.662		
	2012	22(18.6)	83(17.6)	1.1(0.5-2.3)	.886		
	Total	118(100)	472(100)				
Have Contact person?	Yes	23(19.5)	412(87.3)		1		1
	No	95(80.5)	60(12.6)	28.4(16.7-48.2)	.000	27(15.8-46.3)	.000*
	Total	118(100)	472(100)				

*significance at $\alpha \leq 0.05$

5.7 Predictors for unsuccessful treatment outcomes

To evaluate any predictors for unsuccessful TB treatment outcome of independent variable Sex, age, Address, presence of contact person, diagnosis category (smear positive pulmonary TB, smear negative Pulmonary TB, Extra Pulmonary TB), treatment category (new vs Transfer in), sputum result at 2nd month after initiation of treatment, HIV sero- status, ART and cotrimoxazole initiation, Nutritional status, and Year of treatment after adjusted for other risk factors multivariate analyses were done for each factors like socio demographic factors, Clinical and investigations related factors, Treatment related and Health care system-related factors. We found that Age, HIV positive, Malnutrition and absence of contact were independent factors associated with poor treatment outcome, but unknown nutritional status was negatively associated with unsuccessful treatment outcome.

The study revealed that Age of >34.7years have 2 times more unsuccessful TB treatment outcome than those age was ≤ 34.7 years with p value 0.0015 (AOR 1.9(95% CI 1.14-3.2)).

Those have no contact at time of TB treatment initiation was 27 times more unsuccessful TB treatment outcome than those who have contact during initiation with p-value 0.000 AOR 27(95% CI 15.8-46.3)

Those of HIV positive have 7 times more unsuccessful treatment outcome than those of HIV negatives with P-value 0.000 AOR 7.3(95% CI 3.7-14.2)),

Those of Malnourished at time of initiation of TB treatment have approximately 4.5 times more unsuccessful outcome than those of normal nutritional status with p value 0.006 (AOR 4.5(95% CI 1.5-12.9)and those of unknown nutritional status has 81% less unsuccessful TB treatment outcome than those of normal nutritional status p-value 0.001 AOR .188(95% CI 0.07-0.5)

Table 7: Predictors for unsuccessful treatment outcomes among patients on DOTs, Jimma town health facilities, south west Ethiopia, 2013 EC

Variable	Category	Cases No.(%)	Controls No.(%)	COR,95 %CI	p- value	AOR,95% CI	P- value
Age in Years	≤34.7	53	290		1		1
	>34.7	65	182	2(1.3-2.9)	.001	1.9(1.14-3.2)	.0015*
	Total	118	472				
Have Contact person?	Yes	23(19.5)	412(87.3)		1		1
	No	95(80.5)	60(12.6)	28.4(16.7-48.2)	.000	27(15.8-46.3)	.000*
	Total	118(100)	472(100)				
HIV	Negative	56(47.5)	427(90.5)		1		1
	Positive	62(52.5)	45(9.5)	10.5(6.5-16.9)	.000	7.3(3.7-14.2)	.000*
	Total	118(100)	472(100)				
BMI (Nutritional status)	Normal	17(14.4)	383(81.1)				
	Malnourished	93(78.8)	60(12.7)	6.2(2.5-15.6)	.000	4.5(1.5-12.9)	.006*
	Unknown	8(6.8)	29(6.1)	.18(0.08-0.42)	.000	.188(0.07-0.5)	.001*
	Total	118(100)	472(100)				

*significance at $\alpha \leq 0.05$

CHAPTER SIX: DISCUSSION

In the present study, the records of TB cases were extracted from 2015 to 2020GC, a case control study with case to control ratio of 1:4 was conducted by recruiting 590 subjects to determine the predictors of poor TB treatment outcome at Jimma town health facilities, south west Ethiopia. Identifying factors associated with poor treatment outcome could help to evaluate the performance of TB control programs and to design effective interventions.

Although DOTS programs invariably reported treatment outcomes for smear positive PTB, it was recently smear negative PTB and EPTB got a concern. Hence; studies conducted across different populations identify various factors that could affect treatment outcomes of all cases

Finding of this study showed that age group of >34.7years have 2 times more developing unsuccessful treatment outcome than those whose age were ≤ 34.7 years with p value 0.0015 (AOR 1.9(95% CI 1.14-3.2)). It was in agreement with the results of studies conducted in Tigray were AOR 2.50 (1.12-5.59)(25). also different studies done in Ethiopia (10)(14), South Africa(26), Asia(27), China(28), Brazil(29) revealed similar results. Increased risk of death during TB treatment with age was evidenced by different studies (31)(21). A significant association between poor outcome and older age may be partly explained by the reason that older individuals often have concomitant diseases, general physiological deterioration with age, are less able to reach health facilities [18]. The older age group might have much co-morbidity that could result in the high death rate and repeated exposure to treatment may cause for unsuccessful outcome.

In this study the person hasn't contact at time of TB treatment start was 27 times higher unsuccessful treatment outcome than those who have contact person with p-value 0.000 AOR 27(95% CI 15.8-46.3). Study conducted in East Ethiopia depicts lack of registered contact person was also the risk factor associated with unsuccessful treatment outcome (OR=1.37(1.14-2.91, $p < 0.024$) which is less than our study [(14)], also study done in Somalia, Mogadishu(17) shows similar result, The difference might be related with starting of using strategies such as health

extension workers to increase public awareness on the importance of effective completion of TB treatment; use of phone of contact person to ascertain reason for lost follow up are being undertaken so that might contribute to the decreasing of defaulter from TB treatment.

Finding of this study showed that HIV positive has 7 times more unsuccessful treatment outcome than those of HIV negatives with P-value 0.000 AOR 7.3(95% CI 3.7-14.2)). Result from study done in East Ethiopia showed that risk of unsuccessful TB treatment outcome was significantly high among patients with HIV positive compared to HIV negative sero status (OR=1.37(1.14-2.91, $p < 0.024$)(14) which less than our result. Also study done in southern region shows HIV positive TB patients have 5 times more unsuccessful than HIV negative AOR 5.47(3.47, 8.63). comparable with many studies that have found that HIV co-infections are associated with poorer outcomes compared to HIV-negative patients(6), a study in Ukraine showed that HIV positive individuals had a 50% higher risk of developing TB treatment failure at their first TB infection(30). The unsuccessful treatment outcome in TB and HIV coinfection patients could be related to pill burden, increase in adverse effect, drug-to-drug interaction, immune reconstitution inflammatory syndrome, risk factor for drug susceptible TB which is related to immune system suppression.

The finding of this study showed those who Malnourished at time of initiation of TB treatment have approximately 4.5 times more unsuccessful outcome than those of normal nutritional status with p value 0.006 (AOR 4.5(95% CI 1.5-12.9)similarly study conducted in Addis Ababa shows that the proportion of persons with a successful treatment outcome was lower among underweight patients compared with normal or overweight patients (85.3% versus 93.4%), The odds of successful treatment outcomes were 2.15 times higher in normal or overweight TB patients versus those that were underweight at baseline(19) also similar result has seen in study done in Malawi(31) and Philippines(32). The unsuccessful treatment outcome in TB with malnutrition could be related to malabsorption of key anti TB drugs, late diagnosis and treatment, malnutrition which implies that their immunity was subsidized and causes difficulty for them to battle the side effects of the drugs and the comorbidities(33).

Also those of unknown nutritional status was 81% less probability of developing unsuccessful TB treatment outcome than Normal nutritional status p-value 0.001 AOR .188(95% CI 0.07-0.5), which was not shown in other studies.

Strength of the study

Study findings are useful to inform policy and programmers that aim to improve management of TB patients in Ethiopia and other comparable settings.

Limitation

First, the retrospective nature of the study is a methodological limitation. Second, we used only routine program data; so that the Ethiopian health institution TB log book might has no enough check list to identify full history of TB patients' characteristics, thus it is possible that there might be another associated factors left to examined. The analysis can only provide evidence of statistical association between those items and unsuccessful treatment outcome and cannot show cause-effect relationships.

CHAPTER SEVEN: CONCLUSSION AND RECOMENDATIONS

Conclusion

In summary, our study has provided with useful insights on factors influencing unsuccessful TB treatment outcomes and has implications for improving treatment success in TB control program. Older age have higher risk for unsuccessful treatment outcome than younger age, Lack of contact person were associated with increased risk of unsuccessful treatment outcome than those who have contact person. HIV positive have increased risk for unsuccessful treatment outcome than those of HIV negative and being malnourished have increased risk of unsuccessful treatment outcome than normal nutritional status,

Recommendations

Based on the results, we recommend for TB patients

- Special attention should be given for older ages.
 - Health care professionals working in TB unit should collect timely and updated cell phone number of contact person to allow the effective tracing of patients during loss to follow-up time and use of health extension workers for TB control program.
 - HIV/AIDS counselling and test should be done routinely as part of patient monitoring while undergoing treatment for DOTs.
 - Nutritional screening and appropriate counselling and management should be done routinely as part of patient monitoring while undergoing treatment for DOTs.
- Lastly, Prospective study is needed in the study area to identify main cause of unsuccessful outcome.

REFERENCES

1. Democratic F, Of R, Health MOF, Ababa A. FEDERAL DEMOCRATIC REPUBLIC OF ETHIOPIA MINISTRY OF HEALTH NATIONAL COMPREHENSIVE TUBERCULOSIS , LEPROSY AND TB / HIV TRAINING MANUAL for HEALTH CARE WORKERS . PARTICIPANTS ' MANUAL July 2017. 2017;(July).
2. WHO. Global Tuberculosis Control Who Report 1999 World Health Organization. World Health [Internet]. 2000; Available from: <http://www.pbs.org/newshour/rundown/south-africa-still-struggling-with-deadly-tb-hiv-epidemic/>
3. Global Tuberculosis Control (MPCBM 5VCFSDVMPTJT \$ POUSPM. Control. 2010;
4. Hirpa S, Medhin G, Girma B, Melese M, Mekonen A, Suarez P, et al. Determinants of multidrug-resistant tuberculosis in patients who underwent first-line treatment in Addis Ababa: A case control study. *BMC Public Health*. 2013;13(1):1–9.
5. Melese A, Zeleke B. Factors associated with poor treatment outcome of tuberculosis in Debre Tabor, northwest Ethiopia. *BMC Res Notes* [Internet]. 2018;11(1):1–6. Available from: <https://doi.org/10.1186/s13104-018-3129-8>
6. Shaweno D, Worku A. Tuberculosis treatment survival of HIV positive TB patients on directly observed treatment short-course in Southern Ethiopia: A retrospective cohort study. *BMC Res Notes*. 2012;5.
7. Disassa H, Teklu T, Tafess K, Asebe G, Ameni G. Treatment Outcome of Tuberculosis Patients under Directly Observed Treatment of Short Course in Benishangul Gumuz Region , Western Ethiopia : A Ten-Year Retrospective Study *General Medicine : Open Access*. 3(4).
8. Surveillance P. Global Tuberculosis Control. *Tuberculosis*. 2009;17.
9. Wondale B, Medihn G, Teklu T, Mersha W, Tamirat M, Am G. RESEARCH NOTE A retrospective study on tuberculosis treatment outcomes at Jinka General Hospital , southern Ethiopia. 2017;1–7.
10. Hospital G, Dale D, Nega D, Yimam B, Ali E. *Journal of Tuberculosis and Predictors of Poor Tuberculosis Treatment Outcome at Arba Minch*. 2017;2(1):1–8.
11. Fisseha G, Etana B, Hailelassie K, Alemayehu M. Determinant Factors of Treatment Failure among Tuberculosis Patients under Directly Observed Therapy in Tigray Regional State Public Hospitals, North Ethiopia: A Case-Control Study. 2014;14(5).
12. Lee SSJ, Lin HH, Tsai HC, Su IJ, Yang CH, Sun HY, et al. A clinical algorithm to identify HIV patients at high risk for incident active tuberculosis: A prospective 5-year cohort study. *PLoS One*. 2015;10(8):4–13.
13. WANG N, MA Y, LIU YH, DU J, ZHANG H, XIE SH, et al. Risk of Treatment Failure in Patients with Drug-susceptible Pulmonary Tuberculosis in China. *Biomed Environ Sci* [Internet]. 2016;29(8):612–7. Available from: <http://dx.doi.org/10.3967/bes2016.083>

14. Tariku Dingeta Amante¹, & TAA. Risk factors for unsuccessful tuberculosis treatment outcome (failure, default and death) in public health institutions, Eastern Ethiopia. 2015;8688:1–8.
15. Abebe G, Bensa Z, Kebede W. Treatment Outcomes and Associated Factors in Tuberculosis Patients at Jimma University Medical Center: A 5 - Year Retrospective Study. 2019;35–41.
16. Belachew A, Id M, Kebamo S, Teklie T, Alemkere G. Poor treatment outcomes and its determinants among tuberculosis patients in selected health facilities in East Wollega , Western Ethiopia. 2018;(Ci):1–15.
17. Ali MK, Karanja S, Karama M. Factors associated with tuberculosis treatment outcomes among tuberculosis patients attending tuberculosis treatment centres in 2016-2017 in Mogadishu, Somalia. *Pan Afr Med J.* 2017;28:1–14.
18. Daniel OJ, Oladapo OT, Alausa OK. Default from tuberculosis treatment programme in Sagamu, Nigeria. *Niger J Med.* 2006;15(1):63–7.
19. Sahile Z, Tezera R, Mariam DH, Collins J, Ali JH. Nutritional status and TB treatment outcomes in Addis Ababa, Ethiopia: An ambi-directional cohort study. *PLoS One* [Internet]. 2021;16(3 March):1–14. Available from: <http://dx.doi.org/10.1371/journal.pone.0247945>
20. Democratic F, Of R, Health MOF, Ababa A. FEDERAL DEMOCRATIC REPUBLIC OF ETHIOPIA MINISTRY OF HEALTH NATIONAL COMPREHENSIVE TUBERCULOSIS , LEPROSY AND TB / HIV TRAINING MANUAL for HEALTH CARE WORKERS . PARTICIPANTS ‘ MANUAL November 2016. 2016.
21. Sileshi B, Deyessa N, Girma B, Melese M, Suarez P. Predictors of mortality among TB-HIV Co-infected patients being treated for tuberculosis in Northwest Ethiopia: a retrospective cohort study [Internet]. *BMC Infectious Diseases.* 2013. Available from: <http://www.biomedcentral.com/1471-2334/13/297>
22. Gopi PG, Vasantha M, Muniyandi M, Chandrasekaran V, Balasubramanian R, Narayanan PR. Risk factors for non-adherence to directly observed treatment (DOT) in a rural tuberculosis unit, South India. *Indian J Tuberc.* 2007;54(2):66–70.
23. Elbireer S, Guwatudde D, Mudioppe P, Nabbuye-Sekandi... - Google Scholar [Internet]. [cited 2021 Jul 27]. Available from: [https://scholar.google.com/scholar?q=Elbireer+S,+Guwatudde+D,+Mudioppe+P,+Nabbuye-Sekandi+J,+Manabe+YC+\(2011\)+Tuberculosis+treatment+default+among+HIV-TB+co-infected+patients+in+urban+Uganda.+Trop+Med+Int+Heal+16:+981-987.&hl=en&as_sdt=0,5](https://scholar.google.com/scholar?q=Elbireer+S,+Guwatudde+D,+Mudioppe+P,+Nabbuye-Sekandi+J,+Manabe+YC+(2011)+Tuberculosis+treatment+default+among+HIV-TB+co-infected+patients+in+urban+Uganda.+Trop+Med+Int+Heal+16:+981-987.&hl=en&as_sdt=0,5)
24. Hill PC, Stevens W, Hill S, Bah J, Donkor SA, et... - Google Scholar [Internet]. [cited 2021 Jul 27]. Available from: [https://scholar.google.com/scholar?as_sdt=0,5&q=Hill+PC,+Stevens+W,+Hill+S,+Bah+J,+Donkor+SA,+et+al.++\(2005\)+Risk+factors+for+defaulting+from+tuberculosis+treatment:](https://scholar.google.com/scholar?as_sdt=0,5&q=Hill+PC,+Stevens+W,+Hill+S,+Bah+J,+Donkor+SA,+et+al.++(2005)+Risk+factors+for+defaulting+from+tuberculosis+treatment:)

+A+prospective+cohort+study+of+301+cases+in+the+Gambia.+Int+J+Tuberc+Lung+Dis
+9:+1349-1354.&hl=en

25. Berhe G, Enquesselassie F, Aseffa A. Treatment outcome of smear-positive pulmonary tuberculosis patients in Tigray Region, Northern Ethiopia. 2012 [cited 2021 Jul 18]; Available from: <http://www.biomedcentral.com/1471-2458/12/537>
26. Azeez A, Ndege J, Mutambayi R. Associated Factors with Unsuccessful Tuberculosis Treatment Outcomes among Tuberculosis / HIV CoInfected Patients with Drug - Resistant Tuberculosis. 2018;
27. Nor N, Nm R, Ns M, Z WM, Sharina D, Nh NR. ORIGINAL ARTICLE FACTORS ASSOCIATED WITH UNSUCCESSFUL TREATMENT OUTCOME OF PULMONARY TUBERCULOSIS IN KOTA BHARU , KELANTAN Study design. 2011;11(1):6–15.
28. Chen C, Zhu L, Yang D, Shao Y, Song H, Li S, et al. Risk factors associated with TB, a case-control study in a Chinese population. *J Public Heal Emerg.* 2017;1(Dm):58–58.
29. Garrido M da S, Penna ML, Perez-Porcuna TM, de Souza AB, Marreiro L da S, Albuquerque BC, et al. Factors associated with tuberculosis treatment default in an endemic area of the Brazilian Amazon: A case control-study. *PLoS One.* 2012;7(6).
30. Aibana O, Slavuckij A, Bachmaha M, Kراسiuk V, Rybak N, Flanigan TP, et al. Patient predictors of poor drug sensitive tuberculosis treatment outcomes in Kyiv Oblast, Ukraine. *F1000Research.* 2018;6.
31. Zachariah R, Spielmann MP, Harries AD, Salaniponi FML. Moderate to severe malnutrition in patients with tuberculosis is a risk factor associated with early death. *Trans R Soc Trop Med Hyg.* 2002 May 1;96(3):291–4.
32. White L V., Edwards T, Lee N, Castro MC, Saludar NR, Calapis RW, et al. Patterns and predictors of co-morbidities in Tuberculosis: A cross-sectional study in the Philippines. *Sci Rep.* 2020;10(1):1–12.
33. Ayele M. Undernutrition and Mortality among Adult Tuberculosis Patients in Addis Ababa , Ethiopia. 2020;2020.

ANNEXES

I. QUESTIONNAIRE

JIMMA UNIVERSITY INSTITUTE OF HEALTH SCIENCE DEPARTMENT OF
EPIDEMIOLOGY; IN PARTIAL FULFILLMENT FOR THE REQUIREMENT OF MASTERS
IN PUBLIC HEALTH (GMPH)

QUESTIONNAIRE ON FACTOR ASSOCIATED WITH UNSUCCESSFUL TB TREATMENT
OUTCOME IN JIMMA TOW HEALTH FACILITIES, 2020

Name of the interviewer _____

Signature _____

Supervisor Name _____

Signature _____

- C. Not done
4. Smear result after 5 month A. Positive B. Negative C. Not done
5. HIV –status A. Negative B. Positive
- C. No result (Unknown)

Section III Treatment related factors

6. If HIV positive ART status A. On HAART B. Not start ART
- C. Unknown ART status
7. Date of Anti TB start Year_____ Month_____ Date _____
8. Date of Rx complete Year_____ Month_____ Date _____
9. Outcome A. Cured B. Rx complete C. Death
- D. Rx failure E. lost to follow-up
10. Treatment category for intensive phase. A. RHZE B. SERHZ
- C. Other specify _____
11. Anti-TB Drug on continuation phase. A. RH B. EH
- C. Other specify
12. If HIV +ve ART status? A. Start B. Not start Unknown
13. IF HIV +ve Cotrimoxazole? A. Start B. Not start Unknown
14. Missed pills in intensive phase # _____
15. Missed pills in continuation phase # _____

Section IV: Individual factors

16. Drink alcohol A. Yes B. No c. Unknown
17. Smoke cigarette A. Yes B. No c. Unknown

Declaration

I, the undersigned, senior General Public health student declare that this thesis is my original work in partial fulfillment of the requirement for the degree of Master of Public health in General public health.

Name: Dereje Teka

Signature: _____

Place of submission: Jimma University Institute of health science department epidemiology

Date of Submission: _____

This thesis work has been submitted with my/ our approval as university advisor(s).

Advisors

	Name	Signature
1.	Dr. Sahilu Assegid	_____
2.	Mr. Mamo Nigatu	_____

