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TREATMENT OUTCOME OF ADULT PATIENTS WITH RETREATMENT TUBERCULOSIS IN RELATION TO HIV STATUS IN ADDIS ABABA, ETHIOPIA:

A RETROSPECTIVE STUDY

BY: MEKDES BEKELE (BSc)

ADVISOR: WAKGARI DERESSA (PhD)

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Treatment outcome of adult patients with retreatment tuberculosis in relation to HIV status in Addis Ababa, Ethiopia: a retrospective study.

By: Mekdes Bekele (BSc)

Advisor: Wakgari Deressa (PhD)

Approved by the examination board

Dr Wakgari Deressa	_____
(Chairman, dean SPH)	signature
Dr Wakgari Deressa	_____
Advisor	signature
Dr Alemayehu Worku	_____
Examiner	signature
Dr Degu Jereni	_____
Examiner	signature

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List of Acronyms and Abbreviations

AAHB	Addis Ababa Health Bureau
AAU	Addis Ababa University
AFB	Acid-Fast Bacilli
AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Treatment
CNR	Case Notification Rate
CPT	Co-trimoxazole preventive Therapy
DOTS	Directly Observed Treatment, Short Course
EHNRI	Ethiopian Health and Nutrition Research Institution
FMOH	Federal Ministry of Health
HBCs	High Burden Countries
HIV	Human Immuno-deficiency Virus
MDG	Millennium Development Goal
MDR-TB	Multidrug Resistant Tuberculosis
MTB	Mycobacterium Tuberculosis
NTLCP	National Tuberculosis and Leprosy Control Program
IPT	Isoniazid Prophylaxis Therapy
TB	Tuberculosis
WHO	World Health Organization

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Abstract

Background: Retreatment tuberculosis poses a significant threat including drug resistance to tuberculosis control program. However, recurrence and its cause in the era of Human Immuno Deficiency Virus (HIV) have not been well described. Thus, this study was conducted in Addis Ababa to determine recurrent TB treatment outcomes by type of recurrence and HIV status.

Objective: The aim of the study was to assess treatment outcome of retreatment tuberculosis in relation to retreatment TB category and HIV status and investigate factors associated with successful treatment outcome.

Method: A retrospective registered based cohort study design was used to assess the outcome of retreatment tuberculosis category patients above the age of 15 years covering from July 2009 to July 2012 was conducted to determine the treatment outcome of retreatment tuberculosis category in nine health centers in Addis Ababa. Sex, age of TB patients, TB categories, weights, residence categories of treatment regimen, HIV status, ART status, sputum testing and results and documented treatment outcome were extracted from purposively selected three sub-cities that have optimal case in Addis Ababa, Ethiopia.

Results: Five hundred sixty-five retreatment pulmonary TB patients were included in this study. 525 (92.9%) were HIV tested, 192 (36.6%) were HIV positive 105(54.6%) were in antiretroviral treatment, more females were HIV positive 95 (43.4%) compared with male 97 (32.4%), there were 485 (85.5%) with relapse TB, 42 (7.4%) with treatment after default and 40 (7.1%) with failure after treatment TB. The overall treatment success was 65.6%with 11.4% defaulted being the most unsuccessful treatment outcome. Patients who converted sputum at intensive phase had higher treatment success. (Adjusted OR=6.53, 95% CI: 3.059-13.97) and among retreatment TB categories relapse cases had successful treatment outcome (Adjusted. OR= 2.4, 95% CL: 1.017-10.09).

Conclusions: Types of TB and sputum test at intensive phase were significantly associated with treatment success. The treatment success obtained in this study was lower than the global success in 2011 and the small number of drug sensitivity test may hinder the actual number of MDR cases in retreatment tuberculosis. To improve treatment outcome continuous monitoring and follow-up during the course of treatment and further investigation on the cause of the observed finding in lower treatment success will be recommended.

1. Background

1.1. Introduction

Despite the availability of highly efficacious treatment for decades, Tuberculosis (TB) remains a major global health problem (1). In 1993; the World Health Organization (WHO) declared TB a global emergency and subsequently launched the directly observed treatment short-course strategy (DOTS) to control TB (1, 2).

In 2010, 6.2 million people were diagnosed with TB and notified to the national TB control programs. Of these, 5.4 million had TB for the first time and 0.3 million had a recurrent episode of TB after being cured of TB in the past and the remaining 0.4 million had already been diagnosed with TB but had their treatment changed to a retreatment regimen after treatment failed or was interrupted (3).

Currently World Health Organization recommended approach to TB care and control is the Stop TB Strategy, launched in 2006 (1). This approach is recommended to reduce the burden of TB in line with global targets set for 2015. It targets for the reduction in TB cases and deaths that were set for 2015 as part of the Millennium Development Goals (MDGs). The targets are that TB incidence should be falling by 2015 and that prevalence and death rates should be halved compared with their levels in 1990 (4).

Africa has the highest number of both TB cases and HIV infections, with two thirds of TB patients co-infected with HIV (2). About 26% of the incident TB cases occurred in Africa in 2010. The African region accounted for 82% of TB cases among people living with HIV (1). In Ethiopia, TB has long been recognized as a major public health problem since the 1950s and the country has been implementing the WHO recommended DOTS strategy since 1992 (5).

According to the WHO global TB report in 2011, Ethiopia ranked eight among the world's 22 high burden TB countries (6), there were an estimated 220,000 (261 per 100,000) incident cases of TB in 2010.The same report stated that the prevalence of TB was estimated to be 330,000 (394 per 100,000) (1). According to health and health related indicators of the Federal Ministry of Health (FMOH), tuberculosis is the second cause of death in Ethiopia. Retreatment TB are those who default on previous therapy, patients who failed initial treatment and cases who cured and those who had declared completed their treatment without last sputum result and diagnosed

with smear positive TB(7). In 2010 retreatment TB contributes 3.1% of the total notification TB cases. Since 1995 up to 2010 the annual number of retreatment TB in Ethiopia has increased from 343 to 4898 cases. In the same year the estimated proportion of new and retreatment cases that have MDR-TB were 1.6% and 12% respectively (1). Surveillance data suggest that the retreatment regimen is successful in about 70% of the patients but retrospective studies that have evaluated the regimen's efficacy showed variable treatment responses with success rates ranging from 26% to 92% (8).

1.2 Statement of the problem

Retreatment of TB in general is increasing worldwide, especially in sub Saharan Africa and countries with high burden of HIV infection. Ethiopia is one of the 22 high burden countries with TB incidence of 261/100,000 population. In 2011, approximately 4,461(3.1%) cases of retreatment TB were notified (1). Emerging of multi drug resistance tuberculosis (MDR TB) is a challenge for TB control program and patients with recurrent tuberculosis have high risk of MDR TB than newly diagnosed patients. HIV co-infected patients are highly susceptible to pulmonary TB or recurrence of TB; in Ethiopia 15% of TB patients were HIV positive (1, 2).

National survey conducted in 2005 estimated that, proportion of MDR TB from new TB was 3% and 12% from retreatment TB cases. Thus, retreatment cases are becoming a risk for the development of MDR TB cases and become difficult to achieve millennium development goal of TB control program. In general mortality and morbidity related to retreatment TB indicated the seriousness of the problem for individual patients. Furthermore, understanding the specific reasons for unsuccessful outcomes is important in order to improve treatment systems. Therefore, this study aims to assess treatment outcomes of recurrent tuberculosis in relation to HIV status in Addis Ababa, Ethiopia.

1.3. Rationale of the study

High rate of recurrent TB in HIV positive and low treatment success in recurrent TB have been reported from different high burden setting in Sub-Saharan Africa. However, little is known about the treatment success and rate of recurrence in HIV infected patients. In particular, recurrent TB is a high risk for MDR TB. Monitoring the outcome of treatment is one of the TB control in DOTS strategies. Therefore, this study has attempted to identify factor related to poor treatment outcome of retreatment TB in relation to HIV. Moreover, no study has assessed on treatment outcome of retreatment TB. Hence availing scientific sound data on the aforementioned gap will have paramount importance for evaluation of the program and differentiate approaches to retreatment TB.

2. Literature review

2.1 Overview of tuberculosis

Tuberculosis is a major public health problem worldwide. Although, TB deaths are declining the disease continues to pose as one of the world's most urgent health challenges. Nearly one-third of the world is currently infected with the TB bacterium (9). Re-treatment TB cases (TB patients who have been previously treated with anti-TB drugs for at least a month), are a challenge to the primary aim of TB control Program (10). Following treatment with short-course chemotherapy, patients are considered to have a small risk for developing recurrent TB as a result of a relapse or exogenous re-infection (11). However, Retreatment is more likely to harbor and transmits drug resistance TB and is probable to have poor treatment outcomes, including increase risk of death (12). Since the global DOTS framework was launched in1995, up to 2011, the annual number of retreatment notified TB has increased from 59,240 to 575,547 in high burden countries (2, 3).

2.1.1 TB treatment

The aim of TB treatment is to cure the patient, restore quality of life and productivity. Treatment for new cases of drug-susceptible TB consists of a 6 month regimen. The four types of first line drugs: Isoniazid (H), Rifampicin (R), Ethambitol (E) and Pyrazinamide (Z).These drugs are given to patients in two phases, 2 month intensive and 4 month continuation phase. For retreatment TB streptomycin will be added on the above treatment categories, the intensive phase is extended by one month and 5 month of continuation phase so the regimen extends to 8 months (2).

2.1.2 TB prevention

For HIV positive TB patients' secondary Isoniazid prophylaxis has shown to be effective at preventing TB recurrence. A Cochrane review showed that over all IPT (Isoniazid prophylaxis therapy) reduced the risk of active TB by 33% (13)**.** Providing antiretroviral therapy for eligible people living with HIV is an opportunity to reduce the risk of TB transmission to this high risk group. Ensuring infection control in health care facility and in crowded setting are the major prevention activities (7).

2.1.3 Tuberculosis -HIV co-infection

HIV promotes the progression of recent and latent mycobacterium tuberculosis infection to active TB disease; it also increases the rate of recurrent TB (14). People living with HIV who are also infected with TB are about 21-34 times more likely to develop TB disease compared with those who are HIV negative. The co- infection of TB/HIV accounts the highest rates in the African Region, where 44% of TB patients are HIV-positive (ranging between8%–82% among high TB/HIV burden countries) (1) so collaboration of TB /HIV activity are meant to reduce HIV related TB morbidity and mortality (14).

2.1.4 MDR TB treatment

Multi drug–resistance is caused by strain of mycobacterium tuberculosis which is at least resistance to treatment with Isoniazid and Rifampicin (The two most powerful anti-TB drugs). Treatment for MDR-TB is longer, more expensive and toxic to patients with MDR-TB, the current regimens recommended by WHO lasts 20 months (2). Globally in 2009 the proportion of MDR among new and previously treated cases of TB patients were 28.3% and 61.1% respectively (15).

2.1.5 Retreatment TB

Retreatment TB cases are patients who are smear positive for recurrent TB, those who defaulted previous therapy and in cases where initial treatment has failed. However, the case classification and pathogenesis of recurrent TB are still obscure (16). In general terms, recurrence of TB may be a result of relapse in patients previously treated successfully or re-infection with new TB strain (17). Positive sputum culture at 2 months of treatment and HIV infection are independent factors of recurrence. While poor adherence to treatment and substandard regimens have been widely documented as risk factors for recurrence (12).

2.1.6 Tuberculosis in Ethiopia

Ethiopia is one of the highest TB burden countries in the world (6) and TB is among the leading causes of morbidity and mortality in Ethiopia (7). HIV co-infection prevalence was 15% in 2011 (2).The three sub cities (Addis ketema, Arada and Ledeta) which were selected for the study have a high burden of TB cases due to low socio economic, over crowdedness and living in low standard housing condition. According to the 2011/2012 Addis Ababa Health Bureau TB

(AAHB) report a total of 496 retreatment cases were notified, from this 237 cases were notified from the selected sub cities which account 47% of all retreatment cases (18).

2.2 Factors associated with the outcome of TB retreatment

A study conducted in Morocco to assess risk factors for unfavorable outcome showed that male patients and continued sputum smear positivity was a strong predictor of poor retreatment outcomes. Use of substance like (tobacco, alcohol or illicit drug use) and missed doses during intensive phase were associated factors for treatment after default TB cases and further exploring of risk factors for treatment default cases was suggested in their study due to the limitation of sample size and independent variable regarding risk factors (19).

Another study done in Uganda to assess challenge of retreatment pulmonary tuberculosis showed that increasing age and male gender were associated with retreatment TB and this implies that more male patients were default their previous treatment or it may suggest that females are poor help seeking behavior with re-treatment TB (16).

A study done in southern Ethiopia showed that risk factors for poor outcome were associated with patient behavior and attitude; this was explained by patients who default initial treatments tend to default in their retreatment regimen. Another reason was patients who acquired drug resistance tuberculosis and sever form of the disease have poor treatment outcome (20).

2.3. Treatment outcome of retreatment TB in relation to HIV status

Successfully treated patients are the sum of patients who are declared cured and those who had a complete treatment (8). WHO global TB report in 2009 from high burden countries showed that, patients who were re-treated under DOTS in 2006 have low cure and success rate compared to new cases of TB patients (4). A Cohort study done in Haiti to assess outcome of HIV infected patients treated for recurrent tuberculosis with the standard retreatment regimen describe that, HIV negative TB patient had good retreatment success rate with 81% compared to the HIV positive control group with 73%. The authors pointed out that lower treatment success was observed in HIV infected patients. Despite the fact, all HIV infected patients having access to ART, there was a high mortality rate (21).

A retrospective study conducted in Nigeria to assess treatment outcome of DOTS for retreatment pulmonary TB assessed that the effect of HIV status and treatment outcome with HIV and without HIV showed that, 63.8% of patients were cured, 10.2% completed their treatment, 17.3% died and 3.1% were defaulted from the treatment. The study also explained that treatment success rate was higher in HIV negative patients compared to HIV positive patients and the higher mortality was observed in HIV positive TB patients (22).

A retrospective cohort study conducted in Zimbabwe to assess treatment outcome of retreatment TB in relation to HIV status showed a treatment success rate of 73% regardless of HIV status the treatment success was similar as well as when stratified by sex and age groups. However, TB treatment success rate was the highest in those with relapse TB (80%) compared to retreatment other (23).

A study conducted in South Africa to assess the description of recurrence of pulmonary tuberculosis reviled the risk factors for unsuccessful treatment outcome were patients older than 46 years which had defaulted from treatment and unemployed patients at the time of treatment. Even though limited information was found on the HIV status of the TB patients, among 41% HIV tested retreatment TB patients 98% were HIV positive. HIV positivity was a risk factor for retreatment TB and the other factor was a lower CD4 counts, as in many study explained that the lower CD4 counts were at a risk of the development of retreatment TB and other opportunistic infection (17).

Another retrospective study done in Nairobi Kenya showed that, from the study units 18.8% cured and 15% completed their treatment without confirmation of cure. The treatment success was very low compared to the other study which is 33.8%; this lowest success rate was observed due to 64.2% of the study patients were found without treatment outcome information however, for patients who had information on treatment outcome the treatment success was 94.5%. The treatment success rate of HIV positive TB patients had significantly lower treatment success compared to HIV negative TB patients with p-value 0.004 (24).

A study done in Zambia to assess HIV infection and outcome of treatment in new and recurrent pulmonary TB in Africa patients showed that factor associated with poor treatment outcome was low CD4 count and it is also a profound cause of death, this was explained by delayed diagnosis

of TB in HIV positive individual. Other factors for poor treatment outcome are low weight, sputum smear positivity and drug resistance TB (25).

2.4. Unsuccessful treatment outcome of retreatment tuberculosis

Unsuccessful treatment outcome of retreatment tuberculosis includes failure, death, default and transfer out. WHO global TB report in 2009 from high burden countries showed that 3.4% death, 5.4% failure, 6.4% default and 11% transfer out rate. This report revealed that there was a high rate of transfer out cases (4). Regarding death as a treatment outcome of TB, a prospective cohort study conducted in Haiti to assess outcome of HIV infected patients treated for recurrent TB with the standard regimen showed that, 18% of patients who took the standard treatment died, 5% defaulted and 4% failed treatment. The relative risk of death during TB retreatment between HIV-infected and non-HIV-infected patients were 4.3. A patient co-infected with HIV more than four times is likely to die than non-infected patients during standard anti-tuberculosis retreatment. High mortality was observed in women during treatment when compared to male patients (21).

Literatures showed that, recurrence retreatment TB has been studied across different settings especially in high burden countries. Although the magnitudes of retreatment cases differ, recurrent TB is a problem in different parts of the world. Most studies showed that risk factors for recurrent TB were male patients compared to female patients and regarding the age of patients, 24-54 age group is the most affected. In some study HIV infection was the common risk factor for patients to develop recurrent TB due to Immuno-compromise and delayed initiation of Anti-Retroviral Treatment (ART). Poor outcome of retreatment was observed in HIV infected patients especially high death rate during their treatment compared with HIV uninfected TB patients. In general the overall treatment success rate of retreatment TB was lower than the standard set by World Health Organization.

2. 5. Conceptual framework

Socio demography is a factor for the occurrence of recurrent TB as well as for the HIV status. HIV positivity is associated with the recurrence TB. Socio demography, HIV states and recurrent TB have an effect on the treatment outcome of individual patients.

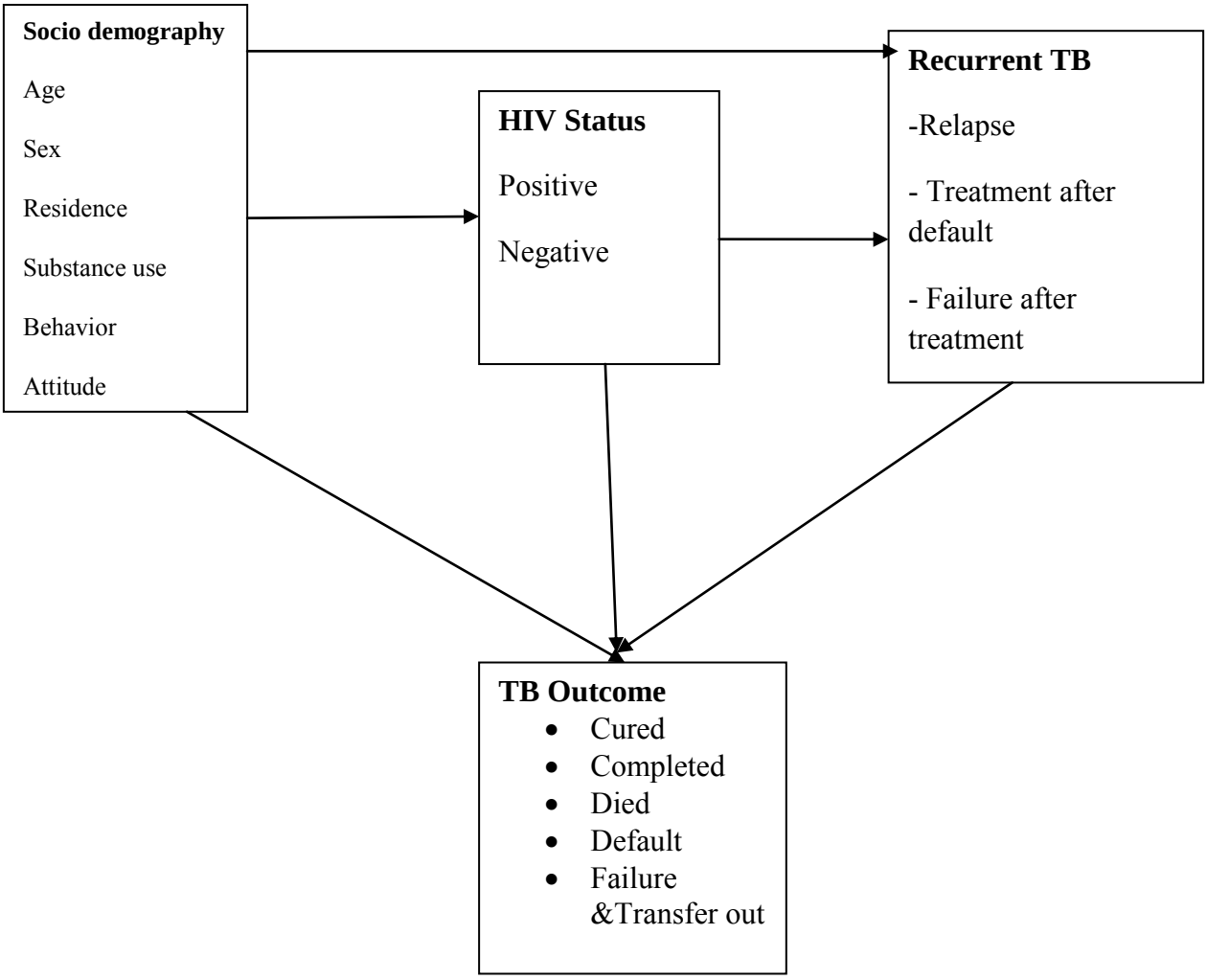

Figure 1 - Conceptual framework analysis of retreatment Tuberculosis.

3. Objectives of the study

3.1. General objective:

- To assess treatment outcome of retreatment tuberculosis in relation to TB category and HIV status of the patients.

3.2. Specific objectives:

- To assess treatment outcome of retreatment tuberculosis.
- To assess treatment outcome of retreatment tuberculosis with their HIV status of the patients.
- To identify factors associated with treatment outcome of retreatment tuberculosis.

4. Methods

4.1. Study area and population

This study was conducted in Addis Ababa City Administration, which is the capital city of Ethiopia. The city comprises of 10 sub-cities and 116 woredas with an area of 540 sq. km. According to Central Statistics Agency 2011, the total population of Addis Ababa was 2,980,001 (26). The health institutions in the city comprise a total of 43 hospitals, 32 health centers, 109 special clinics, 169 higher clinics and 146 medium clinics; among those currently service is provided in 87 health institutions including 19 hospitals, 31 health centers, 27 higher clinics, 3 public Clinics and 7 NGO clinics.

In hospitals and health centers a DOTS clinic is operating under the National Tuberculosis and Leprosy Control Program (NTLCP) of Ethiopia, under which the diagnosis of pulmonary TB is followed by examination of three sputum smears by Zihel -Nielsen staining method for Acid Fast Bacilli (AFB). Chest radiographs and pathological investigations are also used to support the diagnosis (27). Patients diagnosed with tuberculosis are referred to the DOTS clinic where they are registered and treated according to the NTLCP.

All types of re-treatment TB patients are treated in two phase for at least 8 month. The initial intensive phase of treatment which lasts for three month, in the first two months patients are treated with 5 drugs (R, H, Z, E and S) followed by one month of four drugs (H, R, Z and E). The continuation phase is started with three drugs (H, R and E) for 5 months with a three weekly fully-intermittent re-treatment regimen under direct observation (27, 28), Co-trimoxazole Preventive Therapy (CPT) is recommended for the whole duration of TB treatment whilst ART is recommended between 2 and 8 weeks after commencing TB treatment (2, 28).

4.2. Study design

A retrospective cohort study design was used to assess outcome of retreatment tuberculosis patients who completed Directly Observed Therapy; Short-Course.

4.3. Source population:

All TB patients who were registered in short term directly observed treatment in Addis Ababa.

4.4 Study population:

All TB patients who were registered in short term directly observed treatment as retreatment TB in selected health centers.

4.5 Inclusion and exclusion criteria

Inclusive: Recurrent TB patients aged 15 and older, who started anti-TB treatment and follow their treatment in the same health center was included in the study.

Exclusive: Previously treated patients recorded as "other" categories (extra pulmonary and smear negative)

4.5 sample size determination

The sample size was calculated by using single population proportion formula. Since there was no study conducted in Ethiopia addressing this issue, proportion of treatment outcome will be used from a study done in 2010, in Uganda.(29)

$$N = \frac{(Z\alpha/2)^2 P(1-P)}{d^2}$$

Where:

N= is source population

Z = Standardized deviation for the normal distribution; =1.96

P = Assuming the prevalence of 44 %

D= Expected margin of error (precision) =5%

	Sample size	
Treatment outcome	proportion	Total sample
Treatment success of HIV negative	44	337
Treatment success of HIV positive	29	316

The calculated sample size from this view was 337 by taking the largest sample size, and considers 10% contingency for incomplete data; the final minimum sample size was 378**.** Since the study was designed to include all retreatment TB patients registered from July 2009 to June 2012 in all health centers found in three purposively selected sub cities, the total sample size used for this study were 565.

4.7. Sampling procedure

Through examining three years reports (from July 2009 to June 2012) of the 10 sub cities and regional hospitals providing TB diagnosis and treatment services, the patient load across the Sub cities were compared based on the number and cases of retreatment patients, the three sub cities were purposefully selected that have optimal cases, a total of 600 patients were registered in the study period from the selected Sub cities, all intake technique was used from nine health centers which is found in the selected sub-cities that provide DOTs treatment. The health facilities are namely, Addis ketema, Weroda7, Arada, Semen, Kebena, Bata, Beletshachew, Ledata and Teklehimanot health centers then the medical records of recurrent TB patients who were taking anti-TB treatment were retrospectively reviewed for the type of TB and their treatment outcomes. All retreatment TB patients with in the study period were included.

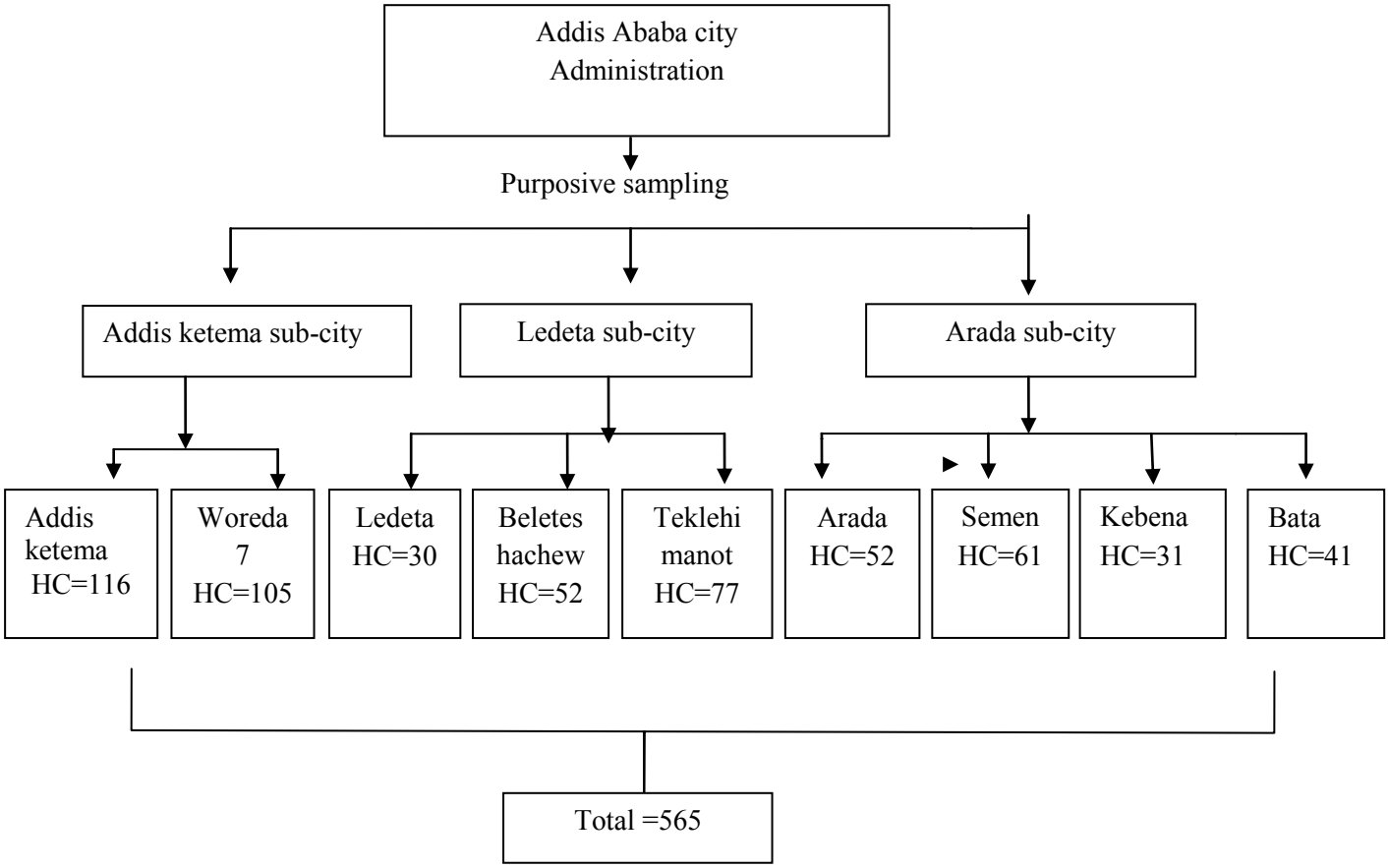

Figure 2 - Sample frame work of the study participant in the nine health centers.

*HC =Health center

4.8. Data collection procedures

Data was extracted from the registers of all health centers found in the selected sub-cities using a structured data sheet developed specifically for this study in order to capture data from the TB registration book. The data sheet was being prepared by reviewing TB registration book from health center. Data was extracted from all adult TB patients registered in the health centers between July 2009 and June 2012. The TB registration book of each heath center contain basic information such as patients' age, sex, address, weight, category of recurrent TB, HIV status, ART and CPT status. AFB smear result at base line, 3rd, 5th and 8th month, treatment regimen, treatment started date, treatment stopped date and treatment outcome. Data extraction was conducted by nurses working at TB clinic of the selected health centers. One-day training was given for all data collectors about how to fill the structured data collection sheet and 5% of sample was taken from randomly selected health center and tested against the registration book to examine the questioner with the existing registration book to captured all available information.

4.9. Study variables

4.9.1: Dependent variable

Treatment success (cure and treatment completed)

4.9.2: Independent variables:

Age, sex, residence, TB category (relapse, return after failed, and return after default), AFB smear result, HIV status, ART, and cotrimoxazole history.

4.10. Operational definition

Pulmonary TB, smear-positive: A patient with at least two sputum specimens which were positive for AFB by microscopy or a patient with only one sputum specimen which was positive for AFB by microscopy and chest radiographic abnormalities consistent with active pulmonary TB.

Patient category

New cases: A patient who has never had treatment for TB before or has been on anti- TB treatment for less than one week.

Retreatment TB

Relapse: A patient who has been declared cure or treatment completed of any form of TB in the past but who reports back to the health service and is found to be AFB smear positive or culture positive.

Treatment after failure: A patient who while on treatment remained smear- positive or become again smear-positive at the end of the five month or later after commencing treatment.

Returned after default: A patient who had previously been recorded as defaulted from treatment and returns to the health facility and found to be smear positive sputum.

TB Treatment categories:

New patient regimen

Previously treated patient regimen

MDR-TB regimen

Treatment Outcome:

Cured: if they completed treatment and had a negative bacteriology result at the end of treatment.

Completed Treatment: if they finished the full 8 month of therapy and were found to be free of TB symptom but no bacteriology result at the end of the treatment.

Treatment failure: Smear positive at five months despite correct intake of medication.

Defaulter: Patients who interrupted their treatment for two consecutive months or more after registration.

Died: If Patients died from any cause during the course of treatment.

Transferred out: Patients whose treatment results are unknown due to transfer to another health facility.

Successfully treated: If patients were declared "cured" and "completed" treatment with no evidence of remaining disease.

Unfavorable treatment outcome: includes failure, death, default and transfer out.

4.11. Data processing and analysis

Data extracted from registration book of patients registered in DOTS were checked for completeness and consistency by the principal investigator. Data was edited, cleaned, coded and entered with EPI-INFO version 3.5 Statistical software. Then it was imported and analyzed using SPSS version 16.0. A descriptive statistical method was used to generate frequencies for categorical variables, to summarize and present frequencies of socio-demographic characteristics of the study participants using text, tables, and graphs. The Chi-squared test was used to compare associations of HIV status and HIV positivity between categorical variables. Significance was attributed to a probability of $p<0.05$. Bivariate logistic regression was used to analyze the association between treatment outcome and potential predictor variables and multivariate logistic regression was used to adjust for potential confounding factor. Variables associated with the outcome with p value <0.05 were included in a step wise multiple logistic regression analysis. Crude and adjusted ORs and 95% CIs were calculated.

4.12. Data quality Control

To ensure quality of the collected data the following measures were taken before starting on the data collection process: all data collectors attended a one-day training provided by the principal investigator on how to fill the structured data collection sheet. To insure data quality, the following measure were taken: one day training was given for data collectors before the start of data collection, the overall activity were monitored by the principal investigator and there was strict supervision during data collection, all data were examined by the principle investigator for completeness during data collection and 5% of sample was randomly selected and tested against the registration book by the principal investigator.

4.13 Ethical consideration

Ethical clearance was obtained from Research and Ethical Committee (REC) of the SPH. Permission was obtained from Addis Ababa City Administration Health Bureau after ethical Board approval; the three Sub-cities health office subsequently were given a written permission to the respected health centers then oral permission was given to the Nurses working in TB clinic from the health center administrator (Medical director) to preserve confidentially.

5. Results

5.1. Socio demographic characteristics of Study participant

In this retrospective document analysis, the socio-demographic information of 565 registered TB patients was summarized (Table 1). The distribution of study participants by residences were 42.8 % from Addis ketema, 22.7 % from Arada, 26.4% from Ledeta and 7.8 % from Gulele sub cities. Out of the total study participants 338 (59.8%) and 227 (40.2%) were males and females respectively. Among all, 61.1% were in the age group of 25-44 years. The mean age of the study participants was 32.88 years with the standard deviation of 11.36 years and a range of 15-90 years. Majority of the study participant 44.3% weight were in 40-49kg.

Table1: Socio demographic characteristics of retreatment TB patients. Addis Ababa, Ethiopia, May 2013.

Characteristics	Numbers	Percent
Sex (n=565)		
Male	334	59.1
Female	231	40.9
Age (n=565)		
15-24	135	23.9
25-34	212	36.2
35-44	132	24.4
45-54	54	10.0
>=55	8	1.5
Initial Weight (n=544)		
25-40kg	73	12.9
40-50kg	253	44.8
50-60kg	161	28.5
>=60	57	10.1
Sub-cities (n=565)		
Addis ketema	243	43
Arada	128	22.7
Ledeta	146	25.8
Gulele	48	8.5

***Sub-cities**: A second administrative stratum of the city.

5.2 Clinical characteristics of retreatment TB

Five hundred sixty five pulmonary positive tuberculosis patients who presented retreatment TB were identified from retrospective document and were included in this study. Of retreatment cases, 483 (85.5%) had relapse after completing an initial treatment regimen, 42 (7.5%) were return after default cases and 40 (7.1%) were failure after treatment (Table 2). A standard category II retreatment regimen was used in 498 (88.7%) patients in intensive phase and 404 (87.6%) was used in continuation phase. The sputum conversion rate at three, five and eight months were 385/433 (88.9%), 307/329 (93.3%) and 264/288 (91.7%) respectively. Seventy one (19.7%) patients who were not tested for sputum at 8 months declared as treatment completed. All of the retreatment TB cases were ZN smear positive, only 44 (7.8%) retreatment patients had drug sensitivity testing (DST), of which 40 (90.9%) were drug resistance TB.

Table 2 : Clinical characteristics of study participants retreatment TB patients in Addis Ababa, Ethiopia, May 2013

Characteristics	Number	Percent
TB categories (n=565)		
Relapse	483	85.5
Return after default	42	7.4
Failure after treatment	40	7.1
Drug in intensive phase(n=565)		
SRHZE	498	86.8
RHZE	65	11.5
Drug in continuation phase(n=463)		
RHE	400	86.3
RH	36	7.7
EH	17	3.6
Other	10	2.1
Sputum result at three month(n=433)		
Positive	48	11.1
Negative	385	88.9
Sputum result at five month(n=329)		
Positive	22	6.7
Negative	307	93.3
Sputum result at eight month(n=288)		
Positive	24	8.3
Negative	264	91.7
Drug sensitivity test done (n=565)		
Yes	44	7.8
No	521	92.2
Drug sensitivity test result(n=44)		
Sensitive	4	9.1
Resistance	40	90.9

5.3. Patient characteristic in relation to HIV and ART status

From 565 retreatment TB included in this study, 525 (92.9%) patients were tested for HIV. of these 192 (36.6%) tested positive and 333 (63.4%) tested negative. From the total 192 HIV positive patients 158 (82.3%) were initiated co-trimoxazole prophylaxis and 28 (14.6%) were not initiated, among HIV positive patients 105 (54.6%) were on ART, 81 (42.2%) were not on ART and 6 (3%) were not recorded their ART status (Table3).

Table 3: Retreatment TB patients characteristics in relation to HIV and ART status in Addis Ababa, Ethiopia, May 2013.

Characteristics	Numbers	Percent
HIV tested (n=565)		
Yes	525	92.9
No	40	7.1
Client HIV status (n=525)		
Positive	192	36.6
Negative	333	63.4
Co-trimoxazole prophylaxis status(n=192)		
Yes	158	82.3
No	28	14.6
Unknown	6	3.1
ART initiated(n=192)		
Yes	105	54.6
No	81	42.2
Not recorded	6	3.1

5.4 HIV sero-status in relation to type TB, residence, sex and age

Table 4 shows result of HIV status of study subject in relation to type of TB, age, sex and residence. Proportion of HIV tested patients was similar across all categories of retreatment TB; however, there was no association with HIV positivity. Though more females were HIV positive 95 (43.0%) compared to males 97 (31.9%) (P= 0.009). HIV positivity had strong association with sex, though HIV testing was similar between both sexes (Table 4).

HIV testing was perfect in the 45-54year age groups 54 (100%) compared with other age groups, HIV sero-prevalence was higher in the 35-44 year age groups 64 (52.9%) compared to across age groups the difference was statistically significance (p=0.001). More patients who lived in Ledeta sub-city were tested for HIV (96.6%) compared among sub-cities. HIV positivity was similar across sub-cities.

Table4: HIV sero-status of retreatment TB in relation to TB category sex, age and residence in Addis Ababa, Ethiopia, May 2013.

Variable	Number registered	HIV testing n (%)	HIV positive n (%)	p-value
Type of TB				
Relapse	483	447 (92.5)	171 (38.3)	
Failure after treatment	42	39 (97.5)	9 (23.1)	0.110
Treatment after default	40	39 (92.9)	12 (30.8)	
Sex				
Male	334	304 (91.0)	97 (31.9)	**0.009**
Female	231	221 (95.7)	95 (43.0)	
Age group				
15-24	135	130 (96.3)	32 (24.6)	
25-34	212	193 (91.0)	73 (37.8)	
35-44	132	121 (91.7)	64 (52.9)	**0.001**
45-54	54	54 (100)	19 (35.2)	
>=55	8	27 (84.4)	4 (14.8)	
Residence				
Addis Ketema	243	227 (93.4)	86 (37.9)	
Arada	128	112 (87.5)	39 (34.8)	0.951
Gulele	146	45 (93.8)	16 (35.6)	
Ledeta	48	141(96.6)	51 (36.2)	
Total		**525 (92.9)**		

***significance level < 0.05**

5.5. Treatment outcome of retreatment TB in relation to socio-demographic and clinical factors

5.5.1 Treatment outcome of Retreatment TB patients in relation to type of TB, sex, age and residence

A total of 565 retreatment TB patients were registered during 2009 to 2012. Of these 522 retreatment patients were analyzed, excluding 37 (6.5%) patients with MDR-TB and 6 (1%) patients with unknown treatment outcome. Among retreatment cases relapse patients 237 (52.8%) had a better cure rate where as failure after treatment cases 7 (21.9%) had the lowest cure rates and there was no gender difference. Patients in 45-54 age groups had a better cure rate 38 (70.4%) among age groups. Patients living in Gulele sub-city had a lower cure rate of (38.5%) and higher treatment completed rate of 13 (33.8%) compared to higher cure rate in Ledeta sub-city 72 (55%).

Among the 39 (7.4%) death recorded 26 (66.6%) occurred during the intensive phase and 13 (33.3%) during the continuation phase of treatment. Failure after treatment and treatment after default case had higher death rate of (12.2%). There was gender difference, 22 (10.5%) of female died compared to17 (5.4%) of male patients. Among age groups above 55 years 4 (12.9%) had a higher death rate and 11.1% of mortality were in patients living in Addis Ketema sub-city. Failure after treatment cases had a higher failure rate 8 (25%) among the retreatment categories.

All types of retreatment TB categories had the same default rate ranging (11.4-12.5%), there was a high default rate in patients above 55years and 15-24 age groups (16.1%, 13.5%) respectively, patients living in Gulele sub-city had the highest default of 6 (15.4%) than patients living in Addis Ketema. Among TB categories failure after treatment and treatment after default cases had (12%) of transfer out. The overall treatment outcome of retreatment TB was: 262 (50.1%) cured, 75 (14.6%) completed treatment, 39 (7.4%) died, (11.4%) were defaulted, 37 (7.0%) treatment failure and 48 (9.01%) transferred out. Patients who default their treatment 60 (11.4%) constitute the major poor treatment outcome (Table 5).

Table5: Treatment outcome of Retreatment TB patients in relation to type of TB, sex and age and residence. Addis Ababa. Ethiopia, May 2013.

Characteristics	Cured n (%)	Treatment completed n (%)	Death n (%)	Treatment failure n (%)	Default n (%)	Transfer out n (%)	Total (n=522)
Categories of TB							
Relapse	237(52.8)	66(14.7)	30(6.7)	26(5.8)	51(11.4)	39(8.7)	449
Failure after treatment	7(21.9)	5(15.6)	4(12.5)	8(25.0)	4(12.5)	4(12.5)	32
Treatment after default	18(43.9)	5(12.2)	5(12.2)	3(7.3)	5(12.2)	5(12.2)	41
Sex							
Male	155(49.5)	44(14.1)	17(5.4)	24(7.7)	41(13.1)	32(10.2)	313
Female	107(51.2)	32(15.3)	22(10.5)	13(6.2)	19(9.1)	16(7.7)	209
Age							
15-24	50(43.1)	20(17.2)	9(7.8)	10(8.6)	13(11.2)	14(12.1)	116
25-34	93(46.5)	36(18.0)	13(6.5)	17(8.5)	27(13.5)	14(7.0)	200
35-44	68(56.2)	14(11.6)	11(9.1)	6(5.0)	11(9.1)	11(9.1)	121
45-54	38(70.4)	1(1.9)	2(3.7)	4(7.4)	4(7.4)	5(9.3)	54
>=55	13(41.9)	5(16.1)	4(12.9)	0(0)	5(16.1)	4(12.9)	31
Residence							
AKK	126(53.6)	16(6.8)	26(11.1)	23(9.8)	23(9.8)	21(8.9)	235
Arada	49(41.9)	27(23.1)	6(5.1)	8(6.8)	14(12.0)	13(11.1)	117
Gulele	15(38.5)	13(33.3)	3(7.7)	0(0)	6(15.4)	2(5.1)	39
Ledeta	72(55)	20(15.3)	4(3.1)	6(4.6)	17(13.0)	12(9.2)	131
All patient	**262(50.1)**	**76(14.5)**	**39(7.4)**	**37(7.0)**	**60(11.4)**	**48(9.1)**	**522**

5.5.2 Treatment outcome of retreatment TB in HIV positive patients

Out of the 157 HIV positive patients 90 (50%) were cured while 23 (12.9%) completed treatment and among poor treatment outcome 20 (11.2%) died, 21 (11.8%) defaulted during treatment, 10 (5.6%) failed their treatment and patients who transferred out to other health facilities were 14 (7.9%).

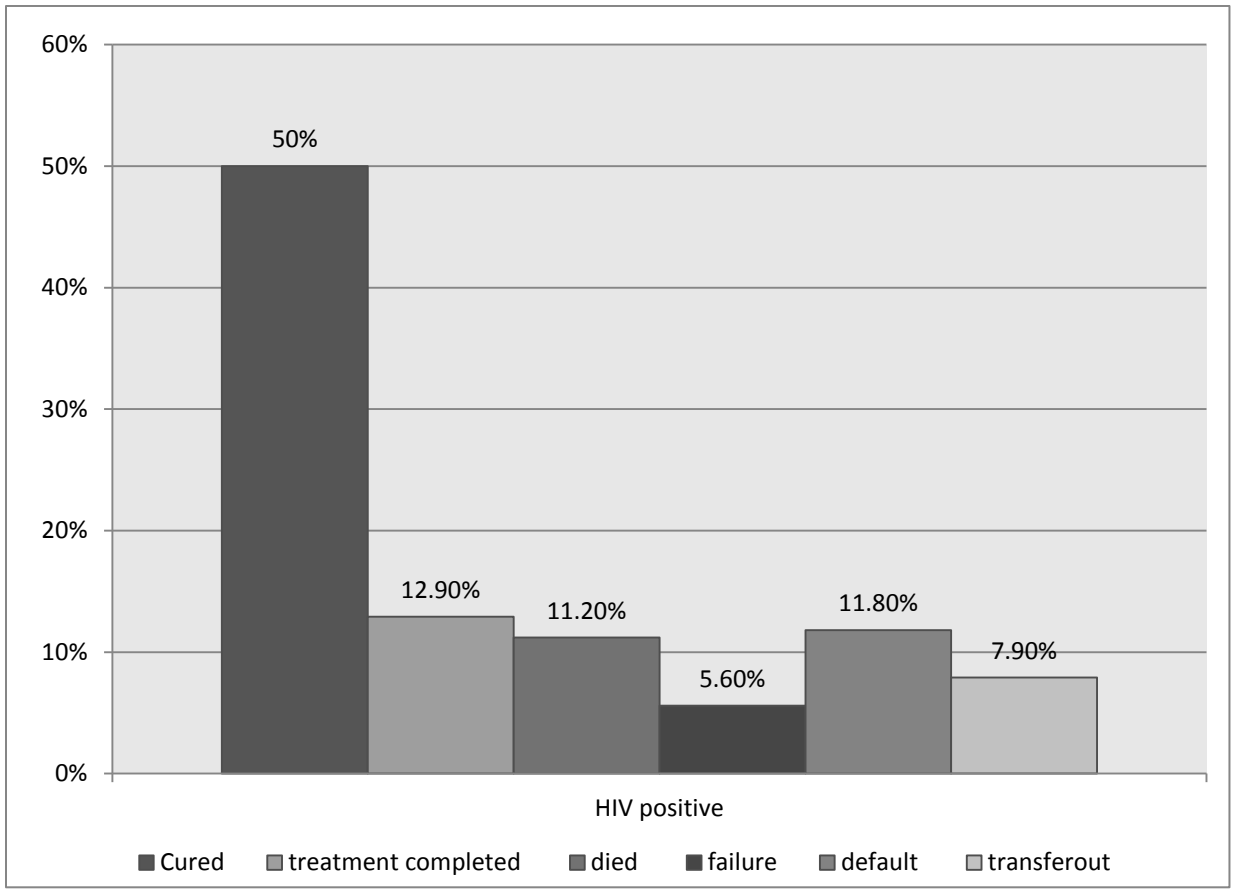

Figure 3 - Treatment outcome of retreatment TB in HIV positive patients in Addis Ababa, Ethiopia, May 2013.

5.5.3 Treatment outcome of retreatment TB in HIV negative patients

Among 303 HIV negative patients, 156 (51.5%) were cured whilst 47 (15.5%) completed treatment and the unsuccessful treatment outcomes were 19 (6.3%) died, 25 (8.3%) defaulted during treatment, 29 (9.6%) failed their treatment and patients who transferred out to other health facilities were 27 (8.9%).

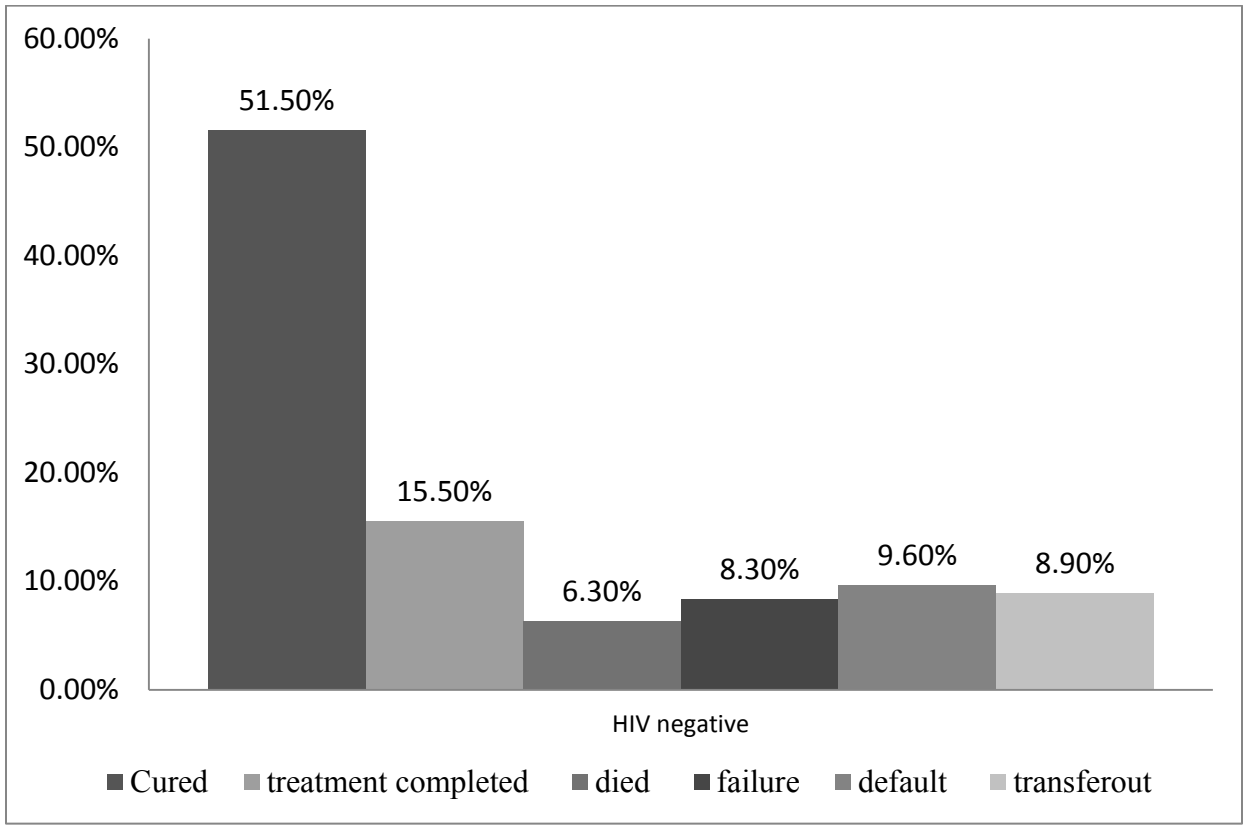

Figure 4 - Treatment outcome of retreatment TB in HIV negative patients in Addis Ababa, Ethiopia, May 2013.

5.5.4 Treatment outcome of retreatment TB in patients with unknown HIV status

Treatment outcome in patients who haven't been tested for HIV in (Figure 5) showed a lower cure rate 16 (39%) compared to patients with known HIV status while 6 (14.6%) were completed treatment. Among unsuccessful treatment outcomes, 10 (24.4%) defaulted and 7 (17.1%) transfer out cases were observed.

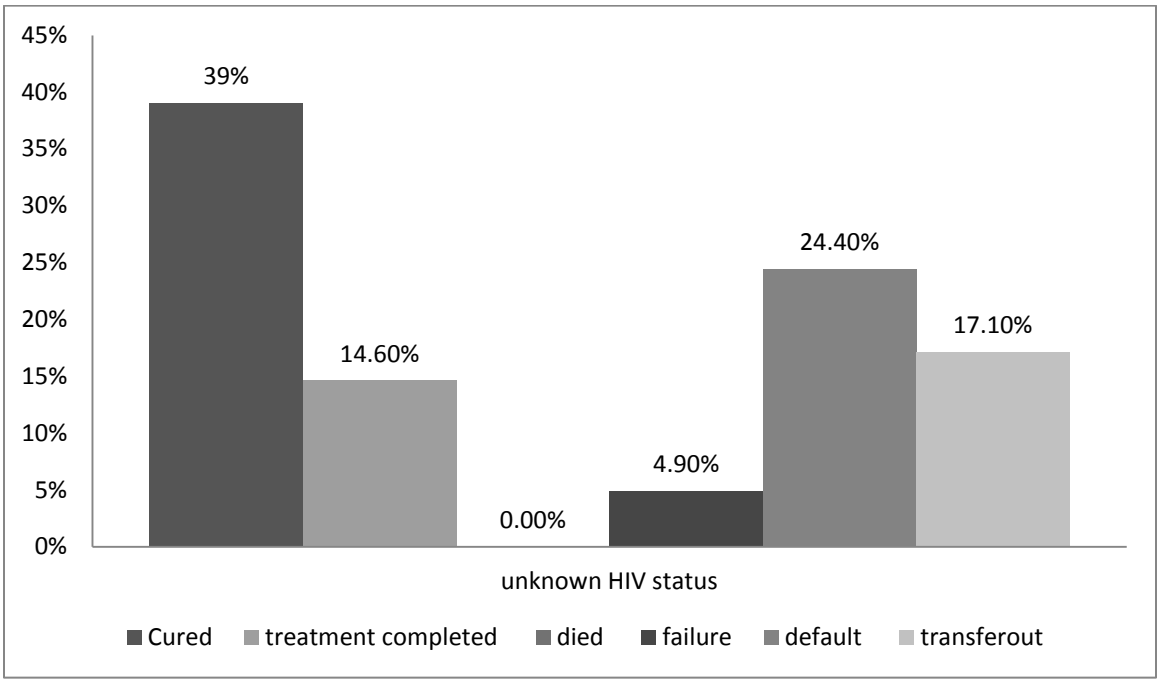

Figure 5 - Treatment outcome of retreatment TB in patients with unknown HIV status in Addis Ababa, Ethiopia, May 2013.

5.5.5 Treatment outcome of retreatment TB in relation to cotrimoxazole status.

Of the 178 HIV positive patients 146 (82%) started cotrimoxazole prophylaxis, among these77 (52.7%) were cured, 22 (15.1%) completed treatment, 17 (11.6%) died, 6 (4.1%) failed, 16 (11%) defaulted and 8 (5.5%) transfer out were observed. Of the 27 (15.1%) patients who were not initiated cotrimoxazole prophylaxis 10 (37%) were cured, 1(3.7%) completed treatment, 2 (7.4%) died, 3 (11.1%) failed, 5 (18.5%) defaulted and 6 (22.2%) transferred out. A lower cure rate, higher default and transfer out were observed in patients who were not initiated cotrimoxazole prophylaxes.

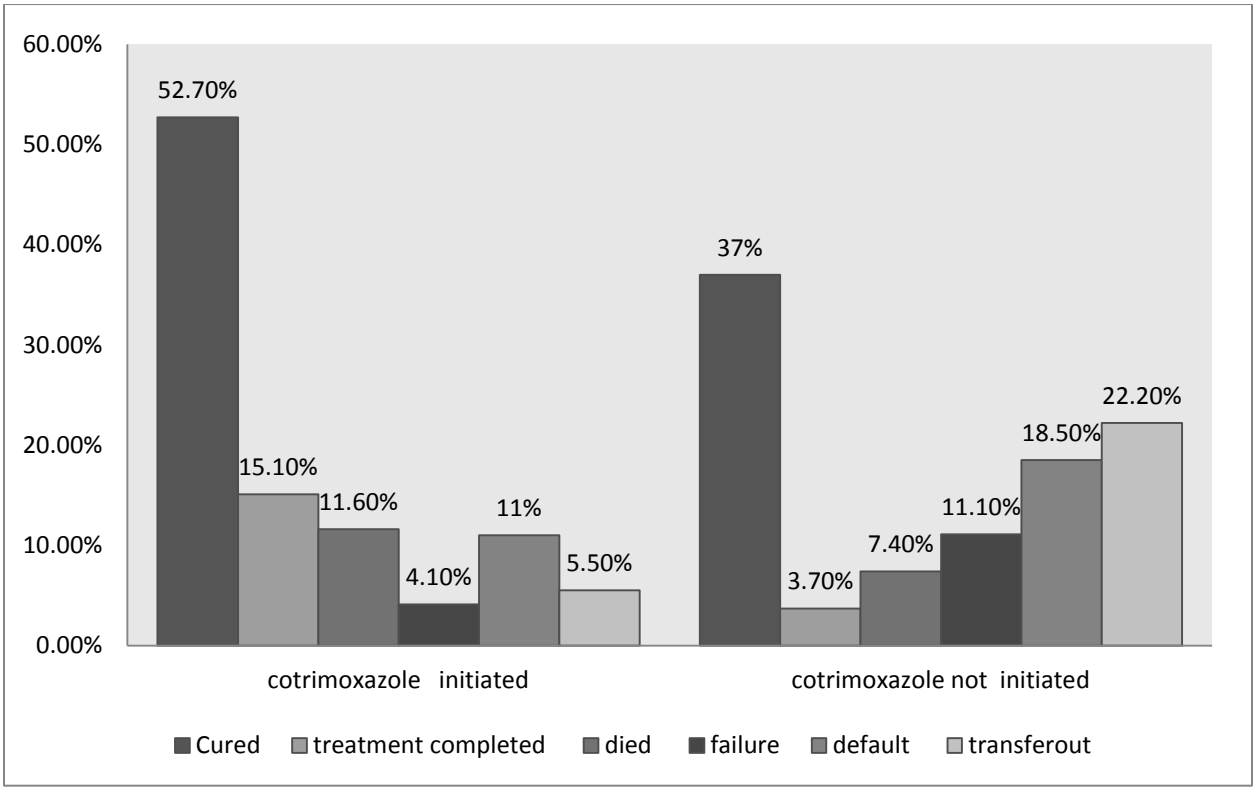

Figure 6- Treatment outcome of retreatment TB patients in relation to cotrimoxazole status in Addis Ababa, Ethiopia. May 2013.

5.5.6 Treatment outcome of retreatment TB in relation to ART status

Of the 178 HIV positive patients 96 (53.9%) started ART. Among these 47 (49%) were marked cured, 17 (17.7%) completed treatment, 8 (8.3%) died, 6 (6.2%) failed, 12 (12.5%) defaulted and 6(6.2%) were transferred out. From the 77 (43.2%) patients who did not start ART 40 (51.9%) were cured, 6 (7.8%) completed treatment, 11 (14.3%) died, 3 (3.9%) failed, 9 (11.7%) defaulted and 8 (10.4%) were transferred out. The higher number of mortality was observed in patients who did not start ART however there was no difference in treatment success of both groups.

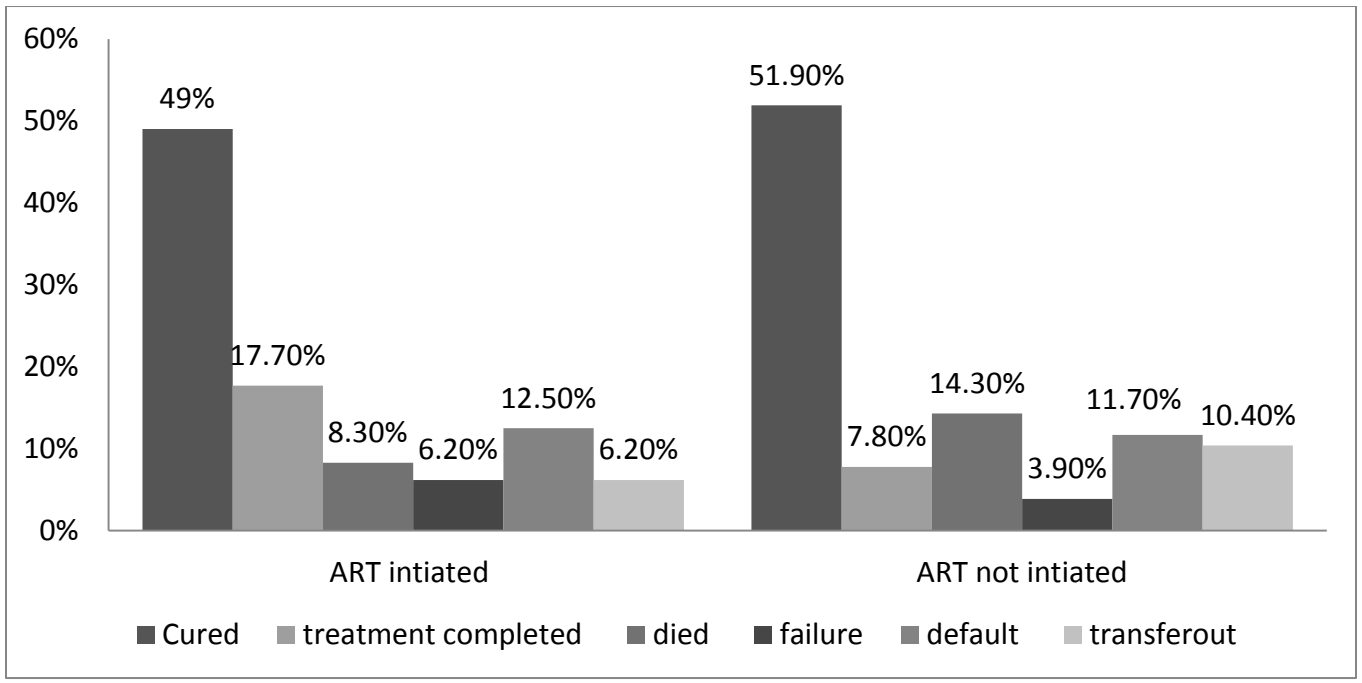

Figure 7- Treatment outcome of retreatment TB patients in relation to ART status in Addis Ababa, Ethiopia, May 2013.

5.6 Successful retreatment TB outcome in relation to category of TB and HIV status

The relation between the variable and successful treatment outcome was analyzed using Bivarate logistic model, Socio demography and clinical characteristics when compared with the dependent variable, the analysis showed that treatment success of retreatment TB were significant association with patient residence and sputum result at three month. Patients living in Ledeta sub-city were 1.72 (CI: 1.03-2.89) times more likely to have treatment success than patients living in Addis Ketema with p= 0.037 statistically significant. The crude odds ratio shows that patients whose sputum result were negative at three month 7.241 (CI: 3.53-14.86) times more likely to have treatment success than those whose sputum result was positive with p=0.001, this was statistically significant. Characteristics such as age, sex, TB categories, HIV status did not show any association with successful treatment outcome.

The result among the retreatment categories showed that the highest treatment success was 303 (73.9%) among relapse patients followed by return after default 23 (63.9%) and the lower treatment success was 12 (42.9%) among failure after treatment cases. There was no gender difference in treatment success; patients older than 45years had a good proportion of treatment success 57 (75%) and younger patients with age group 15-24 had the lowest treatment success of 70 (68.6%). It was also found that HIV negative patients respond better to treatment 203 (73.6%) than patients with unknown HIV status at all 22 (64.7%) with p=0.393 though not statistically significant. Retreatment patients who were initiated cotrimoxazole and ART had a better treatment success than those not initiated (Table 6).

Table 6: Bivarate logistic regression analysis of factors associated with successful treatment outcome of retreatment patients. Addis Ababa, Ethiopia, May 2013.

Variable	Treatment success			
	Yes, n (%)	NO, n (%)	COR(95%CI)	p-value
TB categories				
Relapse	303 (73.9)	107 (26.1)	1.60 (0.78-3.27)	0.197
Failure after treatment	12 (42.9)	16 (57.1)	0.42 (0.154-1.17)	0.096
Return after default	23 (63.9)	13 (36.1)	1.00	
Sex				
Male	199 (70.8.5)	82 (29.2)	1.00	
Female	139(72.0)	54(28.0)	1.061(0.71-1.59)	0.776
Age				
15-24	70(68.6)	32(31.4)	1.00	
25-44	211(71.3)	85(28.7)	1.14(0.70-1.85)	0.612
>=45	57(75.0)	19(25.0)	1.37(0.70-2.67)	0.353
Residence				
Addis ketema	142(66.4)	72(33.6)	1.00	
Arada	76(73.1)	28(26.9)	1.38 (0.820-2.31)	0.227
Gulele	28(75.7)	9(24.3)	1.58 (0.77-3.52)	0.266
Ledeta	92(77.3)	27(22.7)	1.728 (1.03-2.89)	***0.037**
Sputum result at3month				
Positive	16 (44.4)	20 (55.6)	1.00	
Negative	307 (85.3)	53 (14.7)	7.24 (3.53-14.86)	***0.001**
Not done	13 (65.0)	7 (35.0)	2.321(0.75-7.19)	0.144
HIV status				
Positive	113 (68.9)	51(31.1)	1.00	
Negative	203 (73.6)	73 (26.4)	1.25(0.82-1.92)	0.295
Cotrimoxazole prophylaxis				
Initiated	99 (71.7)	39 (28.3)	2.31(0.91-5.87)	0.079
Not initiated	11(52.4)	10 (47.6)	1.00	
ART status				0.881
ART initiated	64 (71.1)	26 (28.9)	1.07(0.46-2.47)	
ART not initiated	46 (66.7)	23 (33.3)	1.00	

N=number of observation, COR =crude odds ratio and CI= confidence interval

***** Significance level < 0.05

*The total number of patients of evaluated across age group add up to 474 excluding the 48patients who were transfer out to other health facilities.

5.7 Factors associated with successful treatment out come

Multivariate logistic regression analysis was carried out for selected socio demographic and clinical risk factor including age, sex. Residence, TB categories, HIV status and sputum result after 3 month. After adjusting for a pre-specified selected risk factors, Relapse patients were 2.5 (CI: 1.07-6.16) times more likely to be successful with p=0.34, compared to treatment after default cases and patients with negative sputum result after 3 month were 7.6 (CI: 3.37-17.39) times more likely to have a successful treatment outcome than those whose sputum result was positive with p=0.001. These two variables were independently associated with treatment success. Patients who did not have tested their sputum were 2 times more likely to have successful treatment outcome compare to patients with positive sputum result but statistically not significant. Patients residence had significant association in Bivariate analysis however after adjusting did not show association, in addition age, sex and HIV status of patients also did not show any association with successful treatment outcome (Table 7).

Table 7: **Multivariate logistic regression analysis of factors associated in treatment outcome of retreatment TB patients. Addis Ababa, Ethiopia, May 2013.**

Variable	Treatment success		AOR(95%CI)	p-value
	Yes, n (%)	NO, n (%)		
TB categories				
Relapse	303 (73.9)	107 (26.1)	2.57 (1.02-10.09)	***0.034**
Failure after treatment	12 (42.9)	16 (57.1)	0.82 (0.23-2.86)	0.758
Return after default	23 (63.9)	13 (36.1)	1.00	
Sex				
Male	199 (70.8.5)	82 (29.2)	1.00	
Female	139(72.0)	54(28.0)	0.90(0.50-1.62)	0.713
Age				
15-24	70(68.6)	32(31.4)	1.00	
25-44	211(71.3)	85(28.7)	1.44(0.73-2.86)	0.286
>=45	57(75.0)	19(25.0)	1.37(0.54-3.42)	0.501
Residence			1.00	
Addis ketema	142(66.4)	72(33.6)	1.00	
Arada	76(73.1)	28(26.9)	0.92(0.47-1.82)	0.822
Gulele	28(75.7)	9(24.3)	2.10 (0.55-8.02)	0.276
Ledeta	92(77.3)	27(22.7)	1.91(0.88-4.15)	0.098
Sputum result at3month				
Positive	16 (44.4)	20 (55.6)	1.00	
Negative	307 (85.3)	53 (14.7)	7.66(3.37-17.39)	***0.001**
Not done	13 (65.0)	7 (35.0)	2.29(0.62-8.42)	0.209
HIV status				
Positive	113 (68.9)	51(31.1)	1.00	
Negative	203 (73.6)	73 (26.4)	1.13(0.62-2.05)	0.68

N=number of observation; COR =crude odds ratio; AOR Adjusted odds ratio; CI confidence interval

***** Significance level < 0.005

6. Discussion

This study provides information on the treatment outcome of retreatment TB in relation to HIV status in Addis Ababa, also revealed certain associations between treatment outcome of retreatment TB and some predictor variables. Retreatment TB categories differed considerably by group: 85% of the patients were relapse TB cases, 7.6% of patients were return after default and 5.9% of patients were failure after treatment cases. The high number of relapse cases observed in this study was in agreement with the previous study conducted in Addis Ababa (30).This high number of relapse might be new strain of TB infection of mycobacterium tuberculosis to previously treated patients or relapse of previous infection.

According to WHO, the targets of TB programs for new patients for smear positive cure rate is 85%.Whilist no specific targets for the outcome of retreatment TB have been set, it is logically assumed that they should not be less than new TB cases. The overall cohort analysis of treatment success rate among retreatment TB patients were 64% which was higher than the study conducted in South Africa 49.1% (17) and Nigeria 53.9% (22) and lower compared to the NTLCP reported in 2008 75% (6), in Pakistan (31), Turkey (32) and Zimbabwe (23). The possible elucidation for the observed low retreatment success in our study had a higher number of defaulted and transfer out patients compared with the previous study.

In this study, the treatment success rate of relapse and treatment after default patients were (73.9%, 63.9%) respectively, this is lower than the study done in Pakistan (83%, 70.6%) (31) and in Zimbabwe (80%, 68%) (23) respectively. However, our study corresponds well with previous finding from southern Ethiopia (74%, 65%) (20). In this study the lower success rate in relapse TB case might be due to the higher number of default patients, the lower success in default after treatment TB cases might be explained by higher mortality and default rate during treatment. Poor default tracing mechanism in the health facilities and undiagnosed MDR TB during or prior to treatment might be the reason for high death found in return after default TB category. some study observed defaulters of previous treatment were potential defaulters during retreatment (33) however, it is not related to our study since all types of retreatment TB have the same default rate.

The sputum conversion rate is an important indicator for efficacy of treatment regimen and also the effectiveness of program implementation. In this study, we found that patients who converted sputum at three month had successful treatment outcome, even after controlling for confounders. Patients who had negative smear result were 6.4 times more likely successful than patients with smear positive result and this could be explained by smear positivity after intensive treatment was a strong predictor of poor treatment outcome.

Patients who were treated in health centers found at Ledeta sub-city had (75%) of treatment success compared with patients treated in Addis ketema and Arada sub city, this might be explained by the heterogeneity of service provision among sub-Cites. For example, the quality of follow up of patients on anti-TB treatment under DOTS might be better in Ledeta sub-city resulting in increased likelihood of better treatment outcome, some evidence shows that human resources for health in TB control is unsatisfactory and there is a significant variability in workload and productivity of staff within and between sub-cities as well as major factors contributing to this are patient load, organization of services and Human Resource Management activities all will be different in different settings (34).

The main factor for treatment failure reported in literature are drug resistance and poor treatment adherence (35). The proportion of unsuccessful treatment outcome in treatment after failure TB cases in this study was very high (57.2%) among retreatment TB categories. This result was higher than the study conducted in Addis Ababa Ethiopia (46.1%) and in southern Ethiopia (50%) (20, 30). while it was lower than the study done in India (67%) (36). This high rate could be due to the higher frequency of drug resistance as the prevalence of multi drug-resistance TB in Ethiopia was estimated to be 12% among retreatment cases.

Of the study participant more than one-third of the retreatment TB patients (36%) were HIV positive, there was a significance association of HIV positivity with age and sex of the patients but there is no association with TB categories. The TB-HIV co-infection in this study is higher than the study done in Kenya of 29.4% (11) and lower than the study done in Nairobi Kenya which was 41.8%, in Malawi 41% and in Zimbabwe 85% (23, 37, 38), this lower rate of co-infection found in our study might be due to that HIV positive patients tend to develop pauci-bacillary TB, often presented with negative smear results and HIV infection contributed to the

increasing of smear negative cases. In addition this study was addressed only smear positive retreatment TB patients.

When outcome is assessed in relation to HIV status, a successful outcome was obtained in 203 (73.6%) HIV negative patients who were higher than HIV positive TB patients who had 113 (68.9%), however the difference in the retreatment success rate of the two groups was not statistically significant. A study done in Kenya (24) and Haiti (21) also revealed similar result with this study but a study done in Zimbabwe and South Africa showed that there was no difference in treatment success in relation to HIV status. High rate of unsuccessful treatment outcome in HIV positive patients in this study might be explained due to high number of death compared to HIV negative patients.

Although HIV positive TB patients who started ART (71.1%) had a good retreatment success rate, which was lower than the study conducted in India 89.3% (39). In Bivarate logistic regression analysis, patients who were on cotrimoxazole prophylaxis and ART had 2.51 (CI: 0.91-5.87) times more likely to have a successful treatment outcome than those who were not initiated cotrimoxazole prophylaxis and ART. A study conducted in India showed that concurrent treatment of ART during TB treatment increases treatment success, decrease mortality and lower failure rate. The better treatment outcome found in TB patients who were initiated ART might be due to a decreased opportunistic infection in patients who were on cotrimoxazole prophylaxes and patients who start ART may have an increased CD4 which boosted immunity.

Among patients with poor treatment outcome, the majority (12.7%) had defaulted their treatment, which was lower than the study done in the southern region of Ethiopia (13.5%) (20) , turkey (13%) (32) and higher than the NTLCP 4% (28) and the study done in India (6.7%) (36). Some study observed defaulters of previous treatment were potential defaulters during retreatment (33). However, in our study we observed that all TB categories have almost the same default rate, to minimize default rate for all type of retreatment TB patients treatment adherence is the main solution apart from the patient's attitude and behavior towards the disease (19).

Higher rate of defaulted patients is observed in male (14.6%) than females (9.8%). This finding is consistent with the study done in Morocco (40) and the study done in Turkey also showed that

relatively large proportion of male patients defaulted from the treatment (32).This might be explained females were eager to come into the center and receive their treatment than males and they used their medication regularly.

HIV positive TB patients were twice more likely to die than HIV negative TB patients, Similar with a study done in India and Haiti (21, 22) this might be due to difficulty of diagnosis TB in HIV positive patients, which may lead to late initiation of anti TB treatment and could end up with poor prognosis of TB treatment. Multidrug-resistant TB at enrollment and a low CD4count was also common risk factor for death during follow-up regardless of HIV status (8). However, we could not be certain if the death was due to the consequence of advanced HIV disease, TB or both.

Furthermore, there is a high death rate of 15.9% in patients who didn't start ART compared to 8.9% of patients who started ART. The study done in India also showed a high death rate in a group that had not started ART, this may be explained by the emergence of drug resistance TB strain and delayed initiation of antiretroviral therapy. Studies in different countries showed that early initiation of ART among co-infected patients can decrease mortality (36).

As expected, treatment failure was higher (28.6%) among failure after treatment cases which is higher than the study done in Pakistan (31) and in Southern Ethiopia (20). This might be due to patients who failed initial treatment were at higher risk of harboring MDR strain plus small number of DST tested patients causes poor treatment outcome in failure after treatment cases.

The present study showed that drug susceptibility testing is underutilized; it was performed only for 44 (7.7%) of retreatment patients and 37 (6.5%) were developed MDR-TB, from the total tested (90.9 %) were found to be drug resistance TB. Despite WHOs policy of DST for all retreatment cases only few patients were tested. This lower proportion of DST test might Cause delaying diagnosis and treatment of MDR-TB, which increase the risk of mortality and expose the community where this patient reside to MDR-TB strain. Furthermore, MDR TB treatment is very expensive to treat and needs longer treatment duration, which makes it difficult for patients to adhere to treatment (41).

7. Strengths and limitations of the study

7.1. Strengths

The study was conducted at primary health centers, where majority of retreatment TB patients were treated and different type of service were integrated with TB clinics. All health facilities had a good HIV testing, a better integration of ART and cotrimoxazole prophylaxis for retreatment TB patients.

7.2. Limitations

The study was limited by the design, which is retrospective in nature. The study relies on previously collected data and information in the patient file. Not all information was found on patients TB registration while some had no data about weight on continuation phase and sputum results on TB treatment schedule. An incomplete data and lost registration was the main limitation since, the study relies on the registered based data analysis.

8. Conclusions

Persistent monitoring of treatment outcomes for relapse, failure and default cases is crucial for improving TB control programs. The mean treatment success rate of retreatment TB was 64.5% and types of TB and sputum result in intensive phase were significantly associated with treatment success. During the study period there were a significant number of defaulted patients and the rate of defaulted patients was similar in all type of recurrent TB. Based on this finding it is important to implement continuous adherence counseling and monitoring of DOTs at health facility during the course of treatment and conducting further research on the reasons of default in health centers.

HIV co-infection was lower compared to other studies, this may be due to difficulty to diagnosis smear positive pulmonary TB in HIV infected patients and mortality was doubled in HIV positive patients compared to HIV negative patients thus, to reduce recurrence of TB and mortality in HIV infected patients, INH prophylaxis and early initiation of ART is an important prevention strategy.

9. Recommendations

In order to improve the treatment success of retreatment TB patients, drug sensitivity test should be done for all retreatment TB to address MDR-TB .A high proportion of defaulters 11.4% were noticed and this is the main cause of the MDR TB, continuous transmission disease and under achievement of treatment success rate. Therefore default tracing, continuous health education and strengthen counseling of retreatment TB patients during the intensive and continuation phase of TB treatment is important to achieve 85% of target. The high relapse requires further investigation to distinguish relapse TB cases from endogenous reactivation or exogenous re-infection, in order to address new infection and true relapse TB.

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11. ANNEX

ANNEX I. Data collection format

Data collection format for Addis Ababa University MPH research project on outcome of recurrent tuberculosis in adult patient.

No	Variables	Descriptions	Remark
Part I: Socio demographic characteristic			
Questionnaire No---------- Registration number----------		Name of Health facility ----------	
101	Age (years)	-	
102	Sex	1. Male 2. Female	
103	weight (KG)	-	On diagnosis
104	Residence	Sub city_____ Woredas _____	
Part II: TB related information			
2o1	Sputum results	1. Positive 2 .Negative 2. Others, specify----------	
202	Sit of TB or TB category	1. Relapse after treatment 2. Return after Default 3. Failure after treatment	
203	TB treatment category		
204	Intensive phase start date (DD./MM/YY).	 ____/_____/_____EC	
205	1. Drug in intensive phase	1. SRHZE 2. RHZE	

206	2. Dose	----------	
207	Continuation phase Start date (DD./MM/YY).	_____/_____/_____EC	
208	Drug in continuation phase	1. RHE 2. RH 3. EH 4. other	
209	Dose		
210	Weight in continuation phase		
211	Sputum result at the end of 3nd month	1. Positive. 2. Negative 3. Not done	
212	Sputum result at the end of 5th month	1. Positive. 2. Negative 3. Not done	
213	Sputum result at the end of 8th month	1. Positive. 2. Negative 3. Not done	
214	Treatment Outcome(circle)	1. Cured 2. Treatment completed 3. Died 4. Failure 5. Default 6. Transfer out 7. MDR	
215	DST done for MDR	1. Yes 2. No	

216	If yes to question number 208 the result of DST	1. Sensitive 2. Resistance	
	Part III HIV related information		
217	HIV Tested	1. yes 2. No	
218	HIV test result	1. Positive. 2. Negative 2. Unknown/not done	
219	Co- trimoxazole Prophylaxis Initiated	1. Yes. 2. No	
220	ART initiated	1. Yes 2. No	

ANNEX II. መረጃ መሰብሰቢያቅጽ፡

በአዲስ አበባ ዩንቨርሲቲ ማሰትረስ ትምህረት ፕሮግራም ሪከረንት ቲቢ ህክምና ውጤት ጥናት መረጃ መሰብሰቢያ ቅጽ፡

ተ.ቁ	መርጃዎች	መግለጫ	ምርመራ
ክፍልአንድ : መሰረታዊመረጃ			
የጥያቄ ቁጥር----------		የጤና ጣቢያው ስም ----------	
የመዝገብ ቁጥር ----------			
101	እድሜ (በአመት)		
102	ፆታ	3. ወንድ 2 ሴት	
103	ክብደት (ኪ.ግ)		መድሃኒት ሲጀመር
104	መኖሪያ	ክፍላከተማ_____ ወረዳ_____	
ክፍልሁለት: ከቲቢ ጋር የተገናኘ መረጃ			
201	የአክታ ምርመራ ውጤት	1. አለበት 2.የለበትም 4. የተለየ ካለ ይግለፁ----------	
202	የቲቢ ዓይነት/ ክፍል	1. ከህክምና በኃላ ያገረሸ ቲቢ 2. የቲቢ ህክምና ካቋረጡ በኃላ በድጋሚ የተከሰተ ቲቢ 3. ህክምና ጨርሰው ያልዳነ ቲቢ	
203	የቲቢ ህክምና ምድብ		
204	የጽኑ ህክምና ወቅት የተጀመረበት ቀን፤ወር፤ዓ.ም	___/_____/_____ዓ.ም	
205	የጽኑ ህክምና ወቅት መድሃኒት	1.SRHZE 2. RHZE	
206	የክኒን መጠን በቀን		
207	ተከታታይ የህክምና የተጀመረበት ቀን ፤ወር፤ ዓ.ም	____/_____/____ዓ.ም	

208	ተከታታይ የህክምና ወቅት መድሃኒት	1. RHE 2. RH 3. EH 4. ሌላካልይገለፅ	
209	የከኒን መጠን በቀን	.	
210	የተከታታ ይህክምና ወቅት ክብደት		
211	የአክታ ውጤት በሶስተኛው ወር	1.አለበት2. የለበትም3. አልተሰራም	
212	የአክታ ውጤት በአምስተኛ ወር	1.አለበት 2. የለበትም 3. አልተሰራም	
213	የአክታ ውጤት በስምንተኛ ወር	1.አለበት 2. የለበትም 3. አልተሰራም	
214	የህክምና ውጤት	1. ከቲቢ የዳነ 2. የቲቢ 3. የሞተ 4. የመከነ 5. የቋረጠ 6. ወደ ሌላ ህክምና ማዕከል የተዘዋወረ	
215	ለተለማመደ ቲቢ (DST) ተሰርቷል?	1. ተሰርቷል 2. አልተሰራም	
216	ለ215 ጥያቄ መልሱ ተሰርቷል ከሆነ የምርመራ ውጤት	1. ያልተለማመደ 2. የተለማመደ	
ክፍል ሶስት፤ ከኤች አይ ቪ ጋር የተያያዘ መረጃ			
217	ለ210 ጥያቄ መልሱ ተመርምሯል ከሆነ የኤች አይ ቪ ምርምራ ውጤቱ	1. አለበት 2. የለበትም 3. አልተሰራም/አይታወቅም	
218	ኤች አይ ቪ ኤድስ ተመረምረዋል	1. ተመርምረዋል	

		2. አልተመረመሩም	
219	ኮትሪሞክዛዞል መከላከ ያተጀምሯል?	1. ተጀምሯል 2. አልተጀመረም	
220	የፀረ ኤች አይ ቪ መድሀኒት ተጀምሯል	1. ተጀምሯል 2. አልተጀመረም	

ANNEX III: patient information sheet English version

Participant information sheet

Description of the study

Title of the study: Treatment outcome of recurrent tuberculosis in adult patients in relation to HIV status in Addis Ababa, Ethiopia.

Objective of the study: To evaluate outcome of recurrence pulmonary tuberculosis patient under DOTS.

Introduction: Anti- TB treatment is used to reduce morbidity, mortality, relapse, treatment failure and increase cure rate when appropriately addressed. However, TB control program set by WHO is not attained by many countries with high death, default and low cure rates primarily due to HIV infection according to many studies conducted abroad.

Rationale of the study and its benefit

TB on patients in relation to HIV status on the survival treatment outcome and type of recurrence emerging of multi drug resistance tuberculosis is a challenge for TB control program. Moreover, no study has assessed on recurrent outcome except few studies. Therefore availing scientific sound data on the aforementioned gap will have paramount importance for evaluation of the program and differentiate approach to recurrence TB in HIV patients. This study is designed to assess the out of recurrence TB.

ANNEX IV: ***ለጥናቱ ተሳታፊዎች መረጃ የመስጫ ቅጽ***

የጥናቱ ርዕስ - የሪከረንት ቲቢ ውጤቶች እና የኤች.አይ .ቪ ውጤቶች

የጥናቱ ዓላማ፡ የቲቢ ዓይነቶችንና የቲቢ ሕክምና ውጤቶችን ከኤች. አይ. ቪ ጋር በሚኖሩና ከኤች. አይቪ ነጻ በሆኑ በአዲስ አበባ ጤና ጣቢያዎች ቲቢ ታካሚዎች መካከል ያለውን ልይነት ማጥናት፡፡

መግቢያ

ፀረ ቲቢ መደረሃኒቶች በትክክል ከተሰጡ ሞትንና በሽታን በመቀነስ ትልቅ አስተዋፅኦ አላቸው፡፡ ሆኖም ግን የአለም ጤና ድርጅት ያስቀመጣቸውን የቲቢ መቆጣጠሪያ ግቦች ብዙ አገሮች አላሳኩትም፡፡ ለዚህም ዋነኛው ምክንያት የኤች.አይ. ቪ/ኤድስ ተፅእኖ መሆኑን ከአገር ውጭ የተሰሩ የተለያዩ ጥናቶች ያመለክታሉ፡፡

የጥናቱ አስፈላጊነት

ጥናቱ ካስፈለገባቸው ምክንያቶች መካከል ኢትዮጵያ ቲቢንና ኤች .አይ. ቪ/ ኤድስን ለማከም ጥረት እያደረገች ባለችበት በአሁኑ ሰዓት የኤች .አይ. ቪ/ኤድስ በሪከረንት ቲቢ ሕክምና ላይ ያለውን ተጽእኖ የሚያሳይ ምንም አይነት መረጃ ያለመኖርና ይህንን ጉዳይ የሚዳስስ ጥናት ያለመደረጉ ናቸው፡፡ እነዚህ ነገሮች ላይ ሳይንሳዊ ሂደትን የተከተለ መረጃ ማ ቅረብ የቲቢና የኤች. አይ. ቪ መከላከያና መቆጣጠሪያ ፕሮግራሞችን ለመገምገምና በኤች. አይ. ቪና ቲቢ ታካሚዎች የተለየ ጥንቃቄ እንዲደረግ አስተዋጽአው የጎላ ነው፡፡

ስለዚህ ለጥናቱ አስፈላጊ የሆኑ መረጃዎች አዲስ አበባ ጤና ጣቢያዎች የቲቢ ታካሚዎች ቲቢ ህክምና መዝገብ ላይ ይወስዳሉ፡፡ ጥናቱ የሚደረገው የቲቢ ህክምናን የጨረሱ ያቋረጡ እና የሞቱ ሰዎች መረጃ ላይ ስለሆነ ግለሰቦቹን የሚጎዳ ምንም ነገር አይኖርም፡፡ ምስጥራዊነቱን ለመጠበቅ እዚያው የቲቢ ህክምና የሚሰጡ የጤና ባለሙያዎች መረጃ ከመዝገብ እንዲሰበስቡ ይደረጋል፡፡ በመረጃ ስብሰባ ወቅት ለሚመጡ ታካሚዎች ፈቃደኝነታቸውን በመጠየቅ መረጃ ይወሰዳል፡፡ በተጨማሪም የቲቢ ታካሚንነት የሚገልጽ ምንም አይነት መረጃ በመጠየቅ ላይ አይሞላም፡፡ የተወሰደው መረጃ ምስጥራዊነቱ ተጠብቆ ሙሉ በሙሉ ጠቀሜታው ለምርምር ሥራ ብቻ ይውላል፡፡

ANNEX V: Consent Form

My name is _____, I am a TB clinic nurse working here in health center TB clinic and I am now collecting data from our patients TB logbook for the research being conducted to determine the treatment outcome of recurrent TB , by Mekeds Bekele Who is a public Health student in Addis Ababa University . The health center is selected as one of the study area. The investigator employed me (from this TB clinic) for this data collection to maintain your data strictly confidential, I am not to let others outside of this clinic to access your name and other identifiers. We believe that the finding of this study will have paramount importance for evaluation of recurrent TB.

Information which is necessary for the study will be taken from your TB log book. As the study will be conducted through review your medical records alone, it will not inflict any harm as far as the confidentiality is kept. The information will be taken when you give permission, participation is totally voluntary.

Your willingness for your TB record information to be utilized in this study will help us achieve the stated benefits of the study. Name and personal identifiers will not be recorded on data collection form and the information that you give us will be kept confidential and will also be used for this study purpose alone. You have full right not to let your information on TB log book to be consumed for this study. If you have any questions about this study you may ask me or the principal investigator Mekdes Bekele (tele : 0911607622 or E-mail: mekdtati @yahoo.Com.)

Are you willing to let your information to be utilized for this study?

1. Yes 2. No

Signature of the interviewer which shows that the respondent has consented (verbally) to take part in the study _____

ANNEX VI ለጥናቱ ተሳታፊዎች የፍቃደኝነት መጠየቂያ ቅጽ

ስሜ----------ይባላል፡፡

በዚህ ጤና ጣቢያ ቲቢ ክሊኒክ ውስጥ የምሰራ የጤና ባለሞያ ስሆን አሁን የ Recurrent TB ህክምና ውጤት ከኤች አይቪ ጋር ያለው ግንኙነት በሚል ርዕስ ላይ በአዲስ አበባ ዩኒቨረሲቲ የድህረ ምረቃ ተማሪ የሆኑት ወ/ሮ መቅደስ በቀለ ለሚሰሩት ጥናት ከቲቢ ታካሚዎች መ□ገብ ላይ እየሰበሰብኩ ነው፡፡ ጤና ጣቢያው የጥናቱ አካል በመሆን ተመርጧል፡፡ አጥኝው እዚህ ቲቢ ክፍል ላይ የምሰራውን እኔን ለመረጃ ሰብሳቢነት ሲመርጠኝ የመረጃውን ሚስጥራዊነት ለመጠበቅ ብሎ ነው፡፡

የጥናቱ ውጤት ሳይንሳዊ ሂደትን የተከተለ መረጃ በማቅረብ መከላከያና መቆጣጠሪያ ፕሮግራሞችን ለመገምገምና ለኤች አይቪና ቲቢ ታካሚዎች የተለየ ጥንቃቄ እንዲደረግ አስተዋጾው የጎላ እንደሚሆን ይታመናል፡፡ በመሆኑም ለጥናቱ አስፈላጊ የሆኑ መረጃዎችን ከጤና ጣቢያው ካሉ የቲቢ ታካሚዎች መዝገብ ላይ ይወሰዳል፡፡ የጤና ተቋሙ መረጃው እንዲወሰድ መፍቀድ ለተጠቀሰው የጥናቱ ዓላማ መሳካት የጎላ አስተዋፆ ይኖረዋል፡፡ ከህክምና መዝገቡ ላይ ሲዎሰድ የታካሚዎች ስምና ማንነት ዓይገለፅም፡፡ የተወሰ□ው መረጃም ሚስጢራዊነቱ ተጠብቆ ሙሉ በሙሉ ለምርምር ስራው ብቻ ይሆናል፡፡

ጥናቱን በተመለከተ ጥያቄ ካለዎት አጥኝዋን ሲ/ር መቅደስ በቀለን በስልክ ቁጥር 0911607622 ወይም በኢሜል አድራሻ mekdtati@gmail.com መጠየቅ ይችላሉ፡፡

መረጃው ለምርምር ቢውል ጤና ተቋሙ ፈቃደኛ ነው፡፡

1.አዎ 2.አይደለም

መረጃቸውን ለጥናቱ ስራ እንዲውል ፈቅደዋል

የጤና ተቋሙ ሀላፊ/ተወካይ ስምና ፊርማ_____

የመረጃ ሰብሳቢው ስምና ፊርማ_____