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SCHOOL OF PUBLIC HEALTH

DETERMINANTS OF MULTI DRUG RESISTANT TUBERCULOSIS (MDR-TB) AMONG TUBERCULOSIS PATIENTS IN ADDIS ABABA, ETHIOPIA: CASE CONTROL STUDY.

BY

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List of acronyms

AARHB	Addis Ababa regional health bureau
ALERT	All African leprosy and tuberculosis rehabilitation training
AAU	Addis Ababa university
ART	Anti-retro viral therapy
BMI	Body Mass Index
CI	Confidence Interval
CEEU	Central and Eastern Europe
DOTs	Direct observe therapy
ENHRI	Ethiopian nutrition and research institute
FMOH	Federal Ministry of Health
HIV	Human immuno deficiency virus
INR	Isoniazid
IRB	Institutional Review Board
IUATLD	International union Against tuberculosis and lung disease
MDR-TB	Multi Drug Resistant Tuberculosis
OR	Odds Ratio
PhD	Philosophy of Doctor
PI	Principal investigator
RFC	Rifampicin
SHRE	Streptomycin, Isoniazid, Rifampicin, Ethambutol
TB	Tuberculosis
WHO	World health organization
XDR	Extensive drug resistant

Abstract

Background: Tuberculosis (TB) is a major cause of death in developing countries; it comprises of 25% of avoidable adult deaths. Even though the global burden and incidence rates of TB have been declining since 2004, drug-resistant tuberculosis remains a growing threat to public health despite advances made in treatment and diagnosis over the past decade. Multidrug-resistant tuberculosis (MDR-TB) which is resistant to at least two drugs of the most powerful first-line treatment, rifampicin (RIF) and isoniazid (INH) is one of the challenging problem worldwide. Ethiopia ranks 15th among 27 high burden MDR-TB countries in the world with an estimated 5200 new cases of MDR-TB each year.

Objective: of the study was to assess the potential determinants of MDR-TB among tuberculosis patients in Addis Ababa.

Method: A facility based unmatched case control study design was conducted from December 21, 2011 to January 30, 2012. Cases were tuberculosis patients with culture-proved mycobacterium tuberculosis resistant to at least both to isoniazid (INH) and rifampicin (RIF) and controls were Tuberculosis patients with smear positive mycobacterium tuberculosis who turned negative for the recent test after 2nd, 5th or 6th months of treatment course. The case to control ratio was 1 : 2. Cases were selected from two hospitals which give MDR-TB treatment namely St. Peter and Defence Teaching and Referral hospitals. Controls were selected from two hospitals (Federal police and Defence Teaching and Referral hospitals) and seven health centres. Simple random sampling was used to select patients from the register of each hospital and health centres involved. To identify the determinants a multi variate logistic regression was done.

Results: A total of 75 cases and 148 controls were interviewed. Among the respondents 41(54.7%) of cases and 84(56.8%) of controls were males. The mean (standard deviation) age among cases and controls were 30.6(10.4) and 28.6(9.9) respectively. The likelihood of MDR-TB were higher among those who reside out of Addis Ababa (AOR=18.85 (2.21, 161.10), HIV infected (AOR=9.10(1.48, 54.37) and on previous treatment of TB (AOR=65.57(14.21, 302.64) and proved to be statistically significant.

Conclusion: Previous treatment of TB, HIV infection and residence out of Addis Ababa were the independent predictors of MDR-TB and thus needs a better attention of the national TB prevention and control activities according to the contextual situations so that to avert the rising problem from the country and furthermore, to keep the health of the community.

1. Introduction

1.1. Background

Tuberculosis (TB) is one of the most wide spread infections known in the world. Approximately 1.7 billion people or one-third of the world's population is to be infected with mycobacterium tubercle bacilli. Every year, about nine million cases of active TB disease and 2 million deaths occur globally [1]. In 2009, there were an estimated 9.4 million incident cases (range, 8.9 million–9.9 million) of TB globally (equivalent to 137 cases per 100 000 population). The absolute number of cases continues to increase slightly from year to year, as slow reductions in incidence rates per capita continue to be outweighed by increases in population. Most of the estimated number of cases in 2009 occurred in Asia (55%) and Africa (30%); smaller proportions of cases occurred in the Eastern Mediterranean Region (7%), the European Region (4%) and the Region of the Americas (3%). The 22 high burden countries that have received particular attention at the global level since 2000 account for 81% of all estimated cases worldwide [2].

TB affects mostly young adults in their productive years because of the human immunodeficiency virus (HIV) epidemic [3]. Of the 9.4 million incident cases in 2009, an estimated 1.0–1.2 million (11–13%) were HIV-positive, with a best estimate of 1.1 million (12%) and in total, approximately 1.7 million people died of TB in 2009 [2]. Tuberculosis is the major cause of death in developing countries; it comprises of 25% of avoidable adult deaths [3]. Even though incidence rates have been declining since 2004 at the global level [2], drug resistant TB remains a growing threat to public health despite advances made in treatment and diagnosis over the past decade [4, 5].

Multidrug-resistant tuberculosis (MDR-TB) is defined as strains of Mycobacterium tuberculosis that are resistant to at least two drugs of the most powerful first-line treatment, rifampicin (RFC) and isoniazid (INH) [6]. Patients with MDR-TB require treatment for 18–24 months with a regimen of up to six drugs (second-line drugs are expensive and toxic), some of them injectable, and a period of hospitalization to manage their toxic reactions and other complications [7]. Patients infected with MDR strains are not only difficult to cure, but also more likely to remain sources of infection for a longer period of time than those with drug-susceptible organisms [8]. There are alarming reports of raising drug resistance from various parts of the globe which potentially threaten to interrupt the gains achieved in TB control over the last decade [9].

MDR-TB is fundamentally a man-made phenomenon and arises due to inadequate treatment of drug-sensitive TB [10] and the prevalence of this disease mirrors the functional state and efficacy of tuberculosis control programmes in the country [11]. In 2008, an estimated 390 000–510 000 cases of MDRTB emerged globally (best estimate, 440 000 cases). Among all incident TB cases globally, 3.6% are estimated to have MDR-TB and this caused an estimated 150 000 deaths [12]. The 27 countries (15 in the European Region) that account for 86% of all such cases have been termed as the 27 high MDR-TB burden countries [2].

African countries are known to have the highest incidence rate of TB in the world; even at low proportions of drug resistance the caseload of MDR-TB patients becomes very high. As a result, the rates of MDR-TB cases arising per 100, 000 populations in some Southern African countries are 5–6 times higher than those of China and India. Latest estimates of WHO put the number of MDR-TB cases emerging in 2008 in Africa at 69 000 [12].

Ethiopia ranks eighth among the world's 22 countries with a high tuberculosis burden and 15 th among 27 countries with high burden of MDR-TB with an estimated 5200 new cases of MDR-TB in each year [2, 12]. According to the WHO Global TB Report 2010, the country had more than 146, 677 new TB cases in 2009. The country has successfully expanded Directly Observed Treatment Short course (DOTs) with population coverage of 95%. Nevertheless, the incidence of all cases of TB is estimated to be 300/100,000 and MDR-TB rate is 1.8% [2]. The treatment of MDR-TB case is very challenging especially in resource limited settings due to the socio- economic impact and the long duration almost 18-24 months taken for treatment compared to drug susceptible TB [12]. In Ethiopia, MDR- TB treatment was started in 2009 at St. Peter's TB specialized hospital in partnership between the Federal Ministry of Health (FMOH), and Global health committee in limited number of patients [13].

Identifying factors related to drug resistance TB is very crucial to tackle the spread of TB with strengthening the national tuberculosis control program. Several risk factors have been identified in the causation of drug resistant tuberculosis, of which the three most important are previous treatment with anti-tuberculosis drugs which may be inappropriate, incomplete or erratic, high prevalence of drug resistant tuberculosis in the community and contact with a patient known to have drug resistant tuberculosis [14].

In case of MDR-TB various potential demographic and clinical risk factors were also investigated in different countries in the world. However, a virtual consensus among MDR-TB researchers regarding the fact that the number of previous treatment is a risk factor for MDR-TB, variables like sex, age and HIV- status are not still showing clear association with MDR-TB [12].

1.2. Rational of the study

There is scarcity of studies in Ethiopia on determinants of MDR-TB. The implementation of Directly Observed Treatment of Short Course began in 1992 [15] for newly diagnosed smear-positive patients in Ethiopia, by 2009, 84% achieved successful outcomes which is almost close to the expected rate of 85% [2]. However, we are observing MDR-TB among new and previously treated cases.

Adequate study on factors responsible for the occurrence of MDR-TB is still lacking in the local context. Therefore, Identifying factors related to drug-resistance TB in particular to MDR-TB is crucial to halt the spread of TB by strengthening the national tuberculosis control program [14]. Furthermore, it helps to achieve the global target that have been set within the context of the Millennium Development Goals (MDGs) and by the Stop TB Partnership to eliminate TB as a public health problem and, ultimately, to secure a world free of TB [16].

The findings from this study have a significant benefit in strengthening the prevention and control efforts of TB at individual or community level along with treatment care through forwarding valuable recommendations to policy makers and national tuberculosis program implementers. In general, as Ethiopia is one of the developing countries with a limited resource and facing high prevalence of MDR-TB cases, giving a contextual solution to the growing problem with epidemiological assessment of the potential determinants of MDR-TB is the ultimate goal of the study .

2. Literature review

2.1. Global and national epidemiology of MDR-TB.

The first international MDR-TB survey demonstrated that MDR-TB was present worldwide, with 'hot-spots' in Russia, Latvia and the Dominican Republic [17]. According to WHO's anti-tuberculosis drug resistance in the world the estimated finding show that 489,139 MDR-TB cases emerged worldwide in 2006, and the global proportion of resistance among all cases was 4.8% [6]. Among the newly diagnosed TB cases, the total number of MDR-TB cases was 285,718 resulting in the proportion of 3.1%. In previously treated cases, the respective data were 203,230 and resulting in the proportion of 19.0%. Since MDR-TB patients usually require treatment for 2 years or longer, the figures of global MDR-TB prevalence may be three times greater than its incidence [18]. China, India and Russian Federation are estimated to incorporate the highest number of the global MDR-TB cases. China and India account for approximately 50% of the global MDR-TB burden. In these countries 8% and 5% of all TB cases respectively are estimated to have MDR-TB and are thus unlikely to respond to the treatment they currently receive [19]. Studies also show that the cure rates for MDR-TB are lower; typically ranging from around 50% to 70% [16].

A review of 63 surveys conducted between 1985 and 1994 suggested that primary and acquired MDR-TB was between 0-10.8% and 0-48% respectively. In 1994, World Health Organization International Union Against Tuberculosis and Lung disease (WHO-IUATLD) carried out a surveillance which concluded that the problem is global; the median prevalence of primary and acquired multi drug resistance was 1.4% and 13% respectively. A second WHO-IUATLD global project on drug surveillance carried out in 1996-1999 in 58 countries, found that the median prevalence of primary and acquired multi-drug resistance was 1% and 9% respectively [20]. According to the eight year surveillance conducted in France, the annual prevalence of MDR-TB among the total number of patients with culture-positive TB ranged from 0.4–0.9%. A substantial proportion (mean 16%) of the MDR-TB patients were reported during several subsequent years. Consequently, the total number of distinct patients with MDR-TB was 264 during the 8-years surveillance period and the mean annual incidence rate was 0.5%. Among the 264 patients, 174 (65.9%) had been previously treated, and 88 (33.3%) were classified as new patients. Compared with new patients, previously treated patients were more likely to be male, have only pulmonary TB, and smear-positive [21].

Less than 50% of the African Region population is represented in anti-TB drug–resistance surveillance data previously. Experts believed that sub-Saharan Africa had limited prevalence of anti-TB drug resistance, owing to the relatively late introduction of rifampicin- based treatment coupled with expansion of the DOTs strategy. However, the 2006 WHO estimates indicate that nearly 60,000 MDR-TB cases occur annually in the Region (14% of the global burden). South Africa, with a nearly 20% HIV infection prevalence among persons 15–49 years of age, has 10,000 MDR-TB cases annually (2.4% of the global MDR-TB burden). Nigeria and Ethiopia rank second and third, with about 8000 and 5000 cases, respectively [22]. Data on prevalence of MDR-TB among all TB cases collected from various WHO publications and published in peer-reviewed articles of 39 countries showed that 99% of total estimated incident or prevalent TB cases were found in the African Region. The proportion of MDR-TB among all TB cases varies from 5.8% in the Democratic Republic of Congo to virtually 0% in Kenya. The median MDR-TB rate was 1.9% [23].

Recent study conducted in Ethiopia in 107 isolates subjected to Drug sensitive test (DST) in St. Peter hospital, 41 (38%) were susceptible to all four drugs; streptomycin, isoniazid, rifampicin and Ethambutol, while 8 (7.5%) were mono-resistant and 46 (43%) were MDR or polyresistant (12%). Multidrug resistance was detected in 2.3% of new cases and 71.4% of previously treated patients. Large proportions of the MDR-TB strains (89%) were resistant to all four first-line drugs tested. The overall prevalence of any drug resistance was 60.8% [24].

2.2. Determinants of MDR-TB.

There is virtually consensus among MDR-TB researchers regarding the fact that the number of previous treatment is a risk factors for MDR-TB, but some factors are still controversial according to the study setups. The proportion of MDR-TB among previously treated TB is higher than new TB cases reported globally and from 38 countries and 3 territories providing drug resistance surveillance data stratified by sex, 27 countries and 2 territories reported at least one case of MDR-TB among male and female cases. Overall, combining data from those countries and territories, the odds ratio of harbouring MDR-TB strains for female TB cases compared with male TB cases showed no overall association between MDR-TB and the sex of the patient [12].

In 13 countries of Central and Eastern Europe (CEEUR), the frequency of MDR-TB was higher in all age groups compared with the rest of the countries (all high-income) and peaked in young adulthood. In the high-income non-CEEUR group, frequency of MDR-TB declined linearly with age-group. This pattern suggests that in the countries of the former Soviet Union, where many MDR-TB cases are of local origin, the MDR-TB epidemic is a relatively recent phenomenon and bears the highest toll on young adults [12]. Study done in European country showed that MDR-TB cases were significantly more prone than control patients to the following risk factors: age 40–59 years, male sex, known TB contacts, previous tuberculosis in pulmonary location, living in nursing home, prison, health-care worker or asylum-seeker support as income factor, immuno suppression other than HIV, intravenous drug use, Acquired immuno deficiency disease (AIDS), and pulmonary site of current tuberculosis [25].

According to systematic review conducted in published reports of risk factors associated with MDR-TB in Europe no association was found between the risk of the MDR-TB individual being foreign born and the proportion of patients who were male, younger than 45 years, HIV positive, previously treated, the year the TB occurred, or the study design, but MDR-TB patients were more likely to be HIV positive [11].

A review of the published literature in India also strongly suggested that the most powerful predictor of the presence of MDR-TB is a history of treatment of TB and errors in TB management such as the use of single drug to treat TB, the addition of a single drug to a failing regimen, the failure to identify pre-existing resistance, the initiation of an inadequate primary regimen, the failure to identify and address non adherence to treatment, inappropriate isoniazid preventive therapy, and variations in the bioavailability of anti-TB drugs predispose the patient to the development of MDR-TB [26]. A recent study done in India also showed that being a female is significantly associated with MDR-TB. But, interactions among age, gender, alcohol consumption, smoking, employment, occupational status and BMI were not significantly associated with MDR-TB [27].

However, another study in the same year using retrospective chart review based on positive cultures isolated in 47 extensive drug resistance (XDR), 30 MDR and 117 susceptible controls were examined and in bivariate logistic regression analysis, three variables were associated with MDR compared to susceptible TB. Previous treatment was strongly associated with MDR. Smoking was significantly and negatively associated with MDR as was alcohol use. Residence outside the state of Tamil Nadu demonstrated a trend towards association [28].

A retrospective population-based case-control study conducted in the State of Ceara, Brazil to analyze the risk factors for acquired MDR-TB suggested that lack of home sewer system, alcoholism plus smoking, number of previous treatments, irregular treatment, and lung cavities were important determinants of MDR-TB whereas, gender, age, illegal drug use, Diabetes mellitus, psychiatric illness were not the significant determinants of MDR-TB [29]. However, Study from Korea based on retrospectively reviewed data from the hospital to determine the prevalence of drug resistant tuberculosis and risk factors associated with MDR-TB the multiple logistic regression analysis showed that previous treatment of tuberculosis was a significant independent risk factor for MDR-TB. Whereas military rank, smoking, positive AFB smear and cavity on chest CT were not associated with development of MDR-TB [30].

A prospective cohort study was conducted in Lima Peru from a phase three clinical trial to evaluate rapid diagnostic tests for MDR-TB and the Clinical prediction rule was derived from the data collected and the strongest clinical predictors were previous history of TB (failed or relapsed after the standard regimen) and MDR-TB contact within family [31].

Retrospective study conducted among Patients with MDR-TB in Prague, Czech Republic to evaluate and compare cohorts of patients with MDR-TB, informed that Seventeen patients born inside and four patients born outside of the Czech Republic, had anamnesis of previous TB treatments and had previously used anti-TB drugs for > 1 month, which corresponded to the resistance data obtained [32]. A national Survey conducted in Germany among culture-confirmed TB cases at 27 participating hospitals to assess risk factors and treatment outcomes associated with multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis (TB) as well reviled that Previous treatment mismanagement is the probable cause of M. tuberculosis drug-resistance selection in most of the patients [33].

In line to some studies done in different parts of the world, study done in Madrid Spain also showed that previous treatment for tuberculosis has been consistently associated with MDR-TB. The study found a significantly higher proportion of MDR-TB among the age group 45-64 years. This study suggests that patients with alcohol abuse are less likely to have MDR-TB. The study did not find any association between HIV status and MDR-TB [34].

To date, limited information has been available about the association of HIV and drug-resistant TB at a population level. HIV-positive TB patients in three eastern European countries appear to be more at risk of harbouring MDR-TB strain [12]. In eight year surveillance study of France, HIV co infection and female status were statistically significantly associated with primary resistance [21].

A subsequent survey of 167 consecutive cases of tuberculosis seen at five New York hospitals during 1992 and 1993 demonstrated that HIV-infected persons were significantly more likely to have been recently infected with MDR-TB [35]. A review of the published literature even suggested that, in the early 1990s, several institutional outbreaks of MDR-TB among HIV-infected patients drew attention to the problem. Inconsistent to this some evidence suggests that HIV infection does not appear to be a predisposing factor for the development of MDR-TB. A study has found that MDR-TB is not more common among people infected with HIV [36]. However, increased susceptibility to TB, increased opportunity to acquire TB due to overcrowding, exposure to patients with MDR-TB due to increased hospital visits, and malabsorption of anti-TB drugs resulting in suboptimal therapeutic blood levels despite strict adherence to the treatment regimen potentially increase the chances of MDR-TB occurring in persons with HIV/AIDS, if not adequately addressed [37].

Analysis of cases reported to California from local health jurisdictions showed that large proportion of MDR-TB cases appear to be arising in rural or smaller health jurisdiction with limited resources and expertise; the threat of MDR-TB is exacerbated by a shrinking pool of clinicians experienced in managing these complex patients, who requiring intensive monitoring over an 18 to 24 month period [38].

A systematic review and meta-analysis of 32 studies summarised on the evidence of association between HIV infection and MDR-TB also showed that no clear association was found between MDR-TB and HIV infection across time and geographic locations. Out of all the countries reviewed in Africa, there was no association between MDR-TB prevalence and HIV. In the review, studies in Coted Ivoire, Tanzania, Botswana and South Africa found no statistically significant difference in the prevalence of MDR-TB between HIV positive and HIV negative patients [39]. Based on collected data from 39 African countries on prevalence of MDR-TB among all TB cases from various WHO publication and published peer-reviewed article retreatment failure rate was the most predictive indicator of MDR-TB rates; other variables such as average case detection rate, average TB incidence rate, TB prevalence, and HIV/ TB co infection did not show a linear relationship [23].

A retrospective case-control study was conducted in South Africa among patients with MDR (cases), XDR (cases) and drug-susceptible (controls) TB in a high-HIV-prevalence setting to identify clinical and demographic risk factors for drug resistant TB and in the multivariate analysis MDR-TB was strongly associated with history of TB treatment failure and hospitalization more than 14 days. However, Prior default from TB treatment and HIV infection were not a risk factor for MDR-TB [40].

A national survey conducted in the same country to quantify the extent of anti-TB drug resistance and to identify associated risk factors also clearly suggested that in its multiple logistic regression analysis previous treatment of TB and HIV status were significantly associated with MDR-TB and gender, age and previous imprisonment were not significant determinants [41]. A study conducted in Burkina Faso revealed that the difference between MDR-TB patients and controls showed no significant for sex, alcohol abuse, traditional treatment, HIV infection and centre of origin. After multivariate logistic regression analysis, only TB known contact, previous treatment , and living out of Burkina Faso for a long time were risk factors significantly associated with MDR-TB [42]. Another recent study conducted in this country to compare the drug-resistance patterns of Mycobacterium tuberculosis strains among pulmonary tuberculosis patients, according to their HIV sero status found no significant difference between TB/HIV-negative and TB/HIV-positive patients according to the resistance patterns to anti-TB medications and the study suggested that MDR-TB was not significantly associated with HIV infection [43].

However, in contrary to this finding preliminary result of a survey conducted in Mozambique showed that HIV had significant association with MDR-TB [12]**.** MDR risk is not uniform among retreatment subgroups, with increased prevalence of MDR among patients with initial treatment failure [44, 45]. According to a population-based study conducted among retreatment cases in Morocco, 12.2% had MDR-TB [19]. There are also studies indicating that around 90% of re-treatment cases failing on the standard re-treatment regimen have MDR-TB [46]. Moreover, around 65% of patients with no initial resistance or other types of resistance than MDR will acquire MDR at failure. In general failure cases on 2SRHZ/6HE had a high prevalence of MDR (80%), half of which was primary drug resistance and the remaining half was acquired [47].

A drug resistance study conducted in Ethiopia showed that resistance to first-line drugs was not related to age, gender, or HIV status, ut MDR-TB was seen more in patients who had received a rifampicin-containing regimen. Moreover, all isolates that were resistant to rifampicin were also resistant to isoniazid, indicating rifampicin resistance as a strong predictor of MDR-TB. Of the 13 MDR strains, seven (54%) were isolated from chronic cases, four (30%) from relapse cases, one (8%) from a defaulter and one (8%) from a case who was smear-positive after 5 months of treatment [48].

In the prospective cohort study on TB/HIV interaction in Addis Ababa, resistance to one or more drug was detected in 21(22.3%) participants and multidrug resistance in five (5.3%) participants. The association between resistance and previous TB treatment was significant. Among the five participants with MDR-TB, two had never been treated for tuberculosis, resulting in 2.7% MDR among the 73 new cases [49]. A recent study done in St. Petre hospital also shows that a significant risk factor for presence of resistance was previous anti-tuberculosis treatment; previously treated patients (85.7%) were confronted with resistance compared to new patients(25%) [24].

Generally, studies reviewed from different countries on determinants of MDR-TB showed that history of previous treatment, gender, age, residence, HIV status, diabetes mellitus, smoking and alcohol drinking showed controversial findings in different study conducted so far in various parts of the world. This study used a guiding frame work in the study which shows factors that are considered to be determinants of MDR-TB and it is annexed at the end (Annex -I).

Objective

3.1. General objective

- To assess the potential determinants of multi drug resistant tuberculosis (MDR-TB) among tuberculosis patients in Addis Ababa.

3.2. Specific objectives

- To determine the socio-demographic, environmental and behavioural factors associated with MDR-TB .
- To determine clinical TB characteristics associated MDR-TB.
- To identify the co- morbid illness associated with MDR-TB.

4. Methods

4.1. Study area and period

The study was conducted in Addis Ababa health facilities from December 21, 2011 to January 30,2012 and a total of three hospitals and seven health centres among government health facility were involved in the study.

Addis Ababa is the Capital City of Ethiopia and seat of the African Union & Economic Commission for Africa. Addis Ababa has a population size of over 3 million (3038096) with annual growth rate of 2.1. It was established on November, 1887 by Emperor Menelik II and Empress Taitu. Its average elevation is 2,500 meters above sea level, and hence has a fairly favourable climate and moderate weather conditions.

The City has 48 hospitals. Thirteen are public hospitals of which, five are under Addis Ababa Regional Health Bureau (AARHB) and 5 are specialized referral (central) Hospitals. Two are Defence Forces (military) referral hospitals and one hospital under Police Force. Furthermore, the City has 27 health centres under the Addis Ababa Health Bureau and five newly opened health centres. There are two hospitals, three health centres and 31 different level clinics established by non-government organizations (NGOs). The City also has 33 private hospitals and more than 700 different level private clinics.

Among health facilities, two hospitals, namely St. Peter TB-specialized (which is a central hospital responsible for the care of TB-HIV co-infected patients experiencing TB treatment failure or relapse) and Defence Teaching and Referral hospitals are currently treating centres of MDR-TB. Recently, since this study was initiated the all African Leprosy and Tuberculosis Rehabilitation training (ALERT) hospital was included as one of the treating centre of MDR-TB at national level.

4.2. Study design

A facility based unmatched case control study design, with two controls to each case, was used to identify determinants associated with MDR-TB.

4.3. Population

4.3.1. Source population

All smear positive and/or culture confirmed Tuberculosis patients in three selected hospitals and seven health centres were the source population for cases and controls.

4.3.2. Study population.

Cases (MDR-TB): Tuberculosis patients with culture-proved mycobacterium tuberculosis resistant to at least both isoniazid (INH) and rifampicin (RIF).

Controls (Non-MDR-TB): Tuberculosis patients with smear positive mycobacterium tuberculosis who turned smear negative to the recent result after 2nd, 5th or 6th months of treatment course.

4.3.3. Sample size determination

The sample size was calculated using the methods of "difference between two population Proportions"

$$n1=\frac{[\boldsymbol{Z}\alpha/\boldsymbol{2}\sqrt{((1+1/r)\,(p)\,(1-p))}\quad+\boldsymbol{Z}\beta\sqrt{(p1\,(1-p1)+(p2\,(1-p2))/r)}\quad]2}{(p1-p2)2}$$

$$p1=\frac{p2}{p2+\frac{1-p2}{OR}} \quad , \quad P=\frac{p1+rp2}{r+1} \qquad n_2=n_1 \text{ x } r$$

Where:

Zα**/2** = the percentile of standard normal distribution corresponding to the level of significance

Zβ= the percentile of standard normal distribution corresponding the power of the study

r = ratio of cases to controls

OR= The odds of worth to detecting the difference in the two population.

p1 = the proportion of exposure to HIV infection among the cases

p2 = the proportion of exposure to HIV infection among the controls

n1 = the minimum sample size required for the cases

n2= the minimum sample size required for the controls

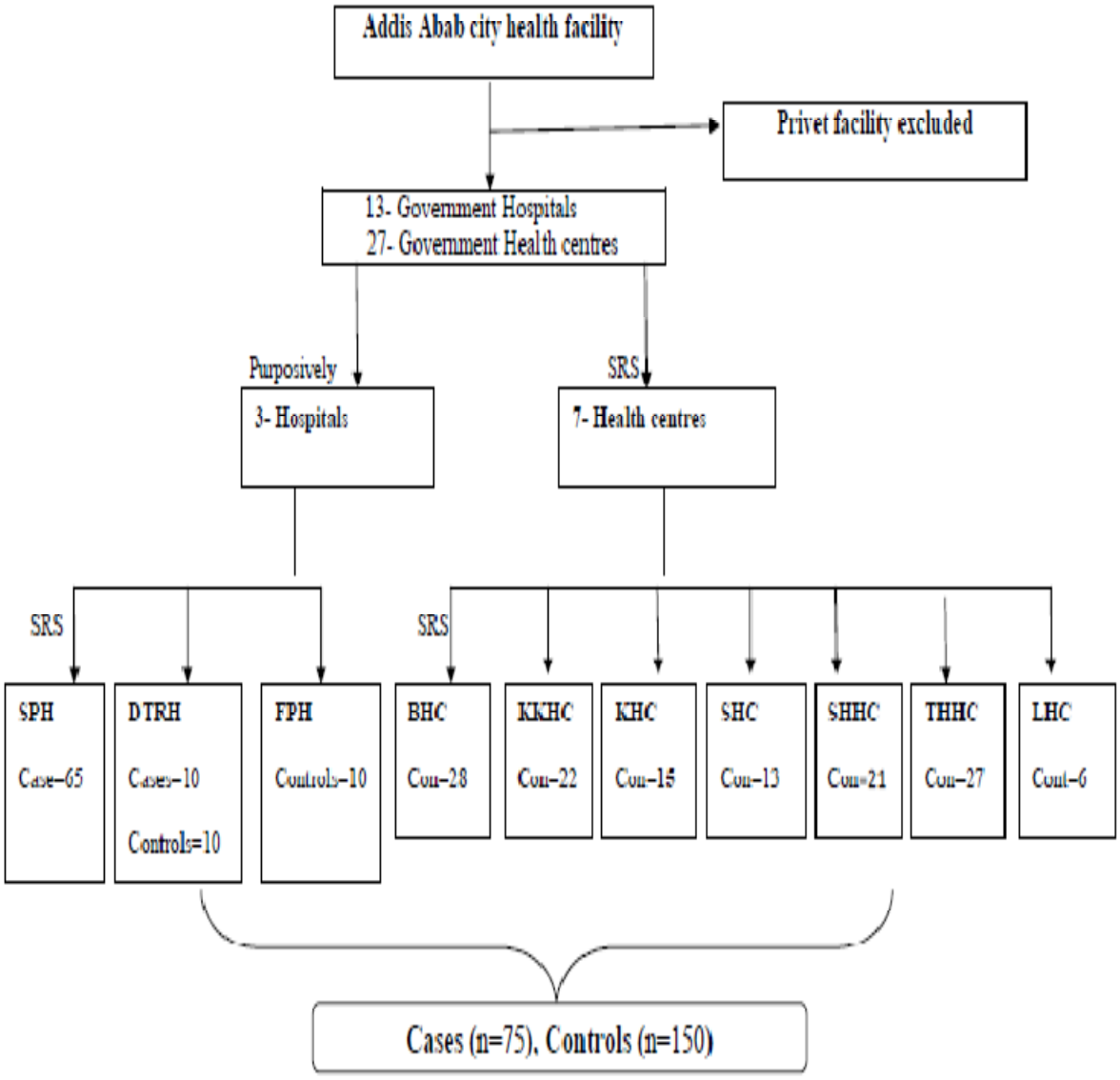
Sample size was calculated based on the following assumption of probability that if the two samples differ this reflects a true difference in the two populations (confidence level) of 95%, probability that if the two populations differ, the two samples will show a significant difference (Power) of 80%, the ratio of case to control of 1: 2, a probable exposure to HIV infection is 28.9% among controls [50] and a sample size of worth determining of difference in the two population of odds ratio 2.46. Accordingly, the minimum sample size for cases was 68 and for controls 136. Adding 10 % for possible non-response rate, a sample size of 75 cases and 150 controls were involved.

4.3.4. Sampling procedures

In this study three purposively selected hospitals namely St. Peter TB-specialized, Defence Teaching and Referral and Federal police hospitals and a randomly selected seven health centres (Bole, Kirkos, Kolfe, Ledeta, Selam, Shiromeda and Teklehaymanot health centres) were involved. Two of the hospitals selected, namely St. Peter TB-specialized and Defence Teaching and Referral hospitals, were selected for recruiting the MDR-TB cases since they are treating centres for MDR-TB patients.

Controls were selected from Federal police hospital and Defence Teaching and referral hospital and seven randomly selected health centres in the city. The Federal police hospital was involved in the study to include police community's to the study sine they have independent hospital and to satisfy the number of controls patients during enrolment of control patients.

Sample size proportionally allocated to each health facility according the flow of TB patients. Finally, a simple random sampling (SRS) technique was used to pick the study subjects. Unit TB registration books of patients currently on treatment with a follow up of 2-6 months prior to collection of data and the registration books of patients who are diagnosed for MDR-TB and currently on treatment were used as a base line source of information to prepare the sampling frame in each study facility.



NB. SPH= St. peter hospital, DTRH= Defence teaching & referral hospital, FPH= Federal police hospital ,BHC= Bole(17) health centre, KKHC=Kirkos health centre, KHC= Kolfe health centre, SHC= Selam health centre, SHHC= shiromeda health centre, THHC=Teklehaymanot health centre , LHC=Ledeta health centre, Con.=control

Fig.1. Diagrammatic presentation of sampling procedure.

4. 4. Data collection procedure

4. 4 .1. Study Variables.

4. 4. 1.1. Dependent variables

- Presence of MDR-TB

4. 4.1. 2. Independent variables

Independent variables	
Socio-demographic variables	Age, sex, education status, religion, ethnicity, marital status, income, occupational status and residence.
Environmental and house hold variables	Living situation, house to live in, family size, number of rooms available, presence of window, daily open the window, wall of the house, floor of the hose, house hold items (Radio, Tv)
Behavioural variables	Smoking, alcohol consumption and illicit drug use.
Clinical characteristics of TB and Co-morbid illness variables	Known MDR-TB patient contact, TB patient contact, prison history, previous treatment and outcome of TB, number of previous TB treatment, type of previous tuberculosis, presence of cavitation in previous TB, DOTs follow up, retreatment history, traditional treatment, treatment regimen taken in previous treatment, hospitalization before diagnosis of TB, diabetes mellitus ,HIV status and CD4 number.

4.4.1.3. Operational definition

Alcohol consumption: taking alcoholic drinks till he/she is drunk at least once in a month.

Co-morbid illness: in this study it is defined as diseases which have been diagnosed in patients who have TB and these include having HIV AIDS, diabetes mellitus and experience of any psychological illness encountered in the patient.

Illicit drug use: is the ever use of drug such as cocaine, heroin, etc, which are under the international control and produced, trafficked and consumed illicitly.

Smoking: smoking one or more cigarette per day before the diagnosis of TB.

4.4.2. Data collection tools

Data collection format consisting of closed and open ended questions were prepared in English and then translated to Amharic and then back to English to check its consistency. During recruitment, information pertinent to the study was imparted to patients and a structured and interviewer administered questioner was used (see appendix-II). In addition to this relevant informations were retrieved from the records. The interview was conducted for MDR-TB patients in their respective in-patient ward and DOTs plus follow up services, and controls were interviewed when they come to the respective health facility for their drug collection.

Data collectors were twelve nurses and health officers recruited from TB clinic of selected hospitals and health centres. Two additional health officers were involved for supervision activities. Training was given for data collectors and supervisors on method of extracting the pertinent data through interview and reviewing the patient's records. How to fill the information on a structured questionnaire, the ethical aspect in approaching the patients and keeping the confidentiality of their information were another focus of the training. The supervisors had monitored the data collection process of the interviewers and taken corrective measures with consultation of principal investigator.

Concerning to the safety precaution to prevent the risk of infection to the data collectors and supervisor they used respirator especially N95, which is a mask that covers the mouth and nose, so that it filter more than 95% of particles. Surgical mask used in patient side, which prevent the spread of microorganism from the wearer to other by capturing the large wet particles near the mouth, was another important precaution measure taken.

4.4.3. Data quality control

Pre-test was carried out on 10-16(3%) study subjects and some modifications were taken according to the findings. During data collection, socio demographic factors, environmental factors, behavioural factors, clinical characteristics of TB status and co-morbid illness were assessed among cases and controls. During data collection, the principal investigator and supervisors monitored the data collection process by checking completeness of the data and took the correction on the spot of data collection site when any problem happened.

Data were cheeked again for its completeness before data entry and the cleaning process was done by running simple frequency after data entry for its consistency. When inconsistency happens to the data, it was checked again referring the hard copy questionnaire. Finally, data analysis were began after completion of the cleaning process.

4.5. Data Processing and Analysis

Data were entered using Epi-info window version 3.4 and analysis were done using SPSS Windows version 16.0. For statistical analysis, Pearson's chi square test or Fisher's exact test were used to analyse the statistical association between dependent and different independent variables. To estimate the magnitude of the association between suspected determinants and MDR-TB, odds ratio (OR) with 95% confidence intervals (CIs) was used.

A logistic regression model was used for both bivariate and multivariate analysis in order to identify determinants of MDR-TB among groups of independent variables. Variables significantly associated ($p < 0.05$) with MDR-TB in the binary logistic regression analysis were entered into the multivariate logistic regression analysis model. Finally, the best model was determined looking the magnitude of -2log likelihood ratio and the standard deviation of two and above for covariates were seen to look multi-Collinearity effect. The model was validated and the Hosmer and Lemenshow test, with p. value of 0.73. The results were expressed in ORs with 95% CIs and a significant threshold was $p<0.05$.

4.6. Ethical consideration

Ethical clearance was secured from institutional review board (IRB) of the Addis Ababa University, College of Health Sciences, IRB of Addis Ababa City Administration Health Bureau and the ethical committee of research in St. peter TB specialized hospital before conducting the study. After securing ethical clearance from those organizations the study facilities were informed to conduct the study through a support letter and permission was obtained from each study facility. Informed consent was obtained from study subjects for their participation. They were told to quit at any time during the interview. To keep the confidentiality of the study subject's their name and any personal identifiers were not included in the data collection format.

5. Results

5.1. Socio-demographic characteristics associated with MDR-TB.

In this study a total of 223 patients (75 cases and 148 controls) were included. Among the respondents 41(54.7%) cases and 84(56.8%) controls were males and the rest were females. Twenty eight (37.3%) cases and 48(32.4%) controls were below age of 24 and 22(29.3%) cases and 61(41.2%) controls were between the age range of 25-34. The mean (standard deviation) of age among cases and controls were 30.6 (10.4) and 28.56(9.9), years respectively.

Forty (53.3%) cases and 65(43.9%) controls were never married or single; while 22(29.3%) cases and 71(48.0%) controls were married. About 29(38.7%) cases and 42(28.4%) controls reported that they attended secondary school, and 23(30.7%) cases and 22(14.9%) controls attended tertiary level, while 5(6.7%) of cases and 20(13.5%) controls were illiterate.

Concerning religion 77.3% and 77.0% of cases and controls, respectively, were Orthodox Christians, and 13.3% of cases and 16.9% of controls were Muslims. Based on ethnic classification, 23(30.7%) cases and 37(25.0%) of controls are Oromo, and 29.3% cases and 37.8% of controls belong to Amahara.

The monthly income of the study participant were asked and 33(44.0%) cases and 70(47.3%) controls earn less than or equal to 500 Ethiopian birr, while 8(10.7%) cases and 20(13.5%) controls earn greater than or equal to 1501 birr.

Fourty five (60.0%) cases and 139(93.9%) controls reside in Addis Ababa, while the rest were living out of Addis Ababa. Almost two third of cases 52(69.3%) and 102(68.9%) controls were living with family, and 18(24.0%) of cases and 40(27.0%) were living alone, while the rest were either homeless or living in camp and prisons (Table 1).

Table 1 also shows that there was no significant difference by sex, age, occupation, monthly income and living situation among cases and controls. However, there is a significant difference in marital status, educational status and residence.

The odds of being married was less likely among cases than the controls and this shows a significant association between the two groups (COR=0.50). Illiterates and education status below primary level were less likely among cases compared to the controls and this was statistically significant. The odds of being out of Addis Ababa was about 10 times higher among cases than controls and this showed that statistically significant association (Table 1).

Table1. Socio demographic factors of MDR-TB in Addis Ababa, April 2012.

Socio demographic characteristics	Cases	Controls	COR, (95%CI)
Sex			
Male	41(54.67%)	84(56.76%)	0.92 (0.53, 1.61)
Female	34(45.33%)	64(43.24%)	1
Age			
≤24	28(37.3%)	48(32.4%)	1
25-34	22(29.3%)	61(41.2%)	0.62 (0.32, 1.21)
35-44	15(20.0%)	22(14.9%)	1.17 (0.52, 2.61)
≥45	10(13.3%)	17(11.5%)	1.01 (0.41, 2.51)
Mean(SD)	30.6(10.4)	28.56(9.9)	
Marital Status			
Single	40(53.3%)	65(43.9%)	1
Married	22(29.3%)	71(48.0%)	0.50 (0.27, 0.94) **
Divorced	11(14.7%)	9(6.1%)	1.99 (0.76, 5.21)
Widowed	2(2.7%)	3(2.0%)	1.08 (0.17, 6.77)
Religion			
Orthodox	58(77.3%)	114(77.0%)	1
Muslim	10(13.3%)	25(16.9%)	0.79 (0.35, 1.75)
Protestant	7(9.3%)	9(6.1%)	1.53 (0.54, 4.31)
Educational level			
Illiterate	5(6.7%)	20(13.5%)	0.24 (0.08, 0.75) **
Read and write	3(4.0%)	14(9.5%)	0.21 (0.05, 0.81) **
Primary school	15(20.0%)	50(33.8%)	0.29 (0.13, 0.65) **
Secondary school	29(38.7%)	42(28.4%)	0.66 (0.31, 1.40)
Tertiary level	23(30.7%)	22(14.9%)	1

Ethnicity				
Oromo	23(30.7%)	37(25.0%)	1	
Amahara	22(29.3%)	56(37.8%)	0.63	(0.31, 1.29)
Tigre	16(21.3%)	11(7.4%)	2.34	(0.93, 5.92)
Guragae	8(10.7%)	30(20.3%)	0.43	(0.17, 1.10)
Others	6(8.0%)	14(9.5%)	0.69	(0.23, 2.05)
Occupational status				
Employed for cash	28(37.3%)	66(44.6%)	1	
Not employed	47(62.7%)	82(55.4%)	1.35	(0.77, 2.39)
Income				
≤500	33(44.0%)	70(47.3%)	1.18	(0.47, 2.953)
501-1000	30(40.0%)	46(31.1%)	1.63	(0.64, 4.17)
1001-1500	4(5.3%)	12(8.1%)	0.83	(0.21, 3.37)
≥1501	8(10.7%)	20(13.5%)	1	
Residence				
Addis Ababa	45(60.0%)	139(93.9%)	1	
Out of Addis Ababa	30(40.0%)	9(6.1%)	10.30	(4.55, 23.31) **
Living situation				
Alone	18(24.0%)	40(27.0%)	1	
With family	52(69.3%)	102(68.9%)	1.13	(0.59, 2.17)
Others	5(6.7%)	6(4.1%)	1.85	(0.50,6.87)

NB.** p< 0.05(variable that shows significant association)

5.2. Environmental and house hold factors associated with MDR-TB

Fifty eight (77.3%) cases and 120(81.1%) controls own house, and 37(63.8%) cases and 89(74.2%) controls houses had less than or equal to two rooms, while the rest had more than two rooms. Thirty four (58.6%) cases and 75(62.5%) controls had less than or equal to four family size and the rest had more than four.

Among study participants who own a house, 48(82.8%) cases and 96(80.0%) controls houses had window. Of those, 45(93.8%) of the cases and 77(80.2%) controls open windows daily, to refresh their rooms. Fifty-three (91.4%) cases and 112 (93.3%) controls had no artificial ventilation in their houses, whereas 53(91.4%) cases and 115(95.8%) controls had electricity connection in their houses.

Among study participants who had a house, the response to the household items also show that 52(89.7%), 38(65.5%), 4(6.9%), 17(29.3%), 3(5.2%) of cases and 99(82.5%), 70(58.3%), 10(8.3%), 22(18.3%), 3(2.5%) of controls had radio, TV, Air conditioner refrigerator, and automobile/car, respectively (Table 2).

The odds of homelessness/ lack of house to live, family size, absence of artificial ventilation and electricity, presence of automobile /car were higher among cases than the controls, but not statistically significant. However, the odds of not open the window at daily (COR=0.27) were less likely among cases than controls and this showed statistically significant association (Table 2).

Table 2. Environmental and house hold factors associated with MDR-TB in Addis Ababa, April 2012.

Environmental Characteristics	Cases	Controls	COR, 95%CI	
Own house				
Yes	58(77.3%)	120(81.1%)	1	
No	17(22.7%)	28(18.9%)	1.26	(0.64, 2.49)
Number of rooms				
≤2	37(63.8%)	89(74.2%)	0.61	(0.31, 1.20)
>2	21(36.2%)	31(25.8%)	1	
Family Size				
≤4	34(58.6%)	75(62.5%)	1	
>4	24(41.4%)	45(37.5%)	1.18	(0.62, 2.23)
Presence of window				
Yes	48(82.8%)	96(80.0%)	1	
No	10(17.2%)	24(20.0%)	0.83	(0.37, 1.88)
Open window daily				
Yes	45(93.8%)	77(80.2%)	1	
No	3(6.2%)	19(19.8%)	0.27	(0.08, 0.96) **
Artificial ventilation				
Yes	5(8.6%)	8(6.7%)	1	
No	53(91.4%)	112(93.3%)	0.76	(0.24, 2.43)
Electricity				
Yes	53(91.4%)	115(95.8%)	1	
No	5(8.6%)	5(4.2%)	2.17	(0.60, 7.82)
Air conditioner				
Yes	4(6.9%)	10(8.3%)	1	
No	54(93.1%)	110(91.7%)	1.23	(0.37, 4.09)
Refrigerator				
Yes	17(29.3%)	22(18.3%)	1	
No	41(70.7%)	98(81.7%)	1.85	(0.89, 3.83)
Automobile /car				
Yes	3(5.2%)	3(2.5%)	2.13	(0.42, 10.88)
No	55(94.8%)	117(97.5%)	1	

NB.** p< 0.05(variables that shows significant association)

5.3. Behavioural factors associated with MDR-TB

The study participants were assessed for certain behavioural factors and the respective results were given accordingly. Nineteen (25.3%) cases and 14(9.6%) controls were smokers. Among those who were smokers 8(42.1%) cases and 8(57.1%) controls smoked 1-4 cigarettes on average per day; and 8(42.1%) cases and 4(28.6%) controls smoked 5-10 cigarette per day on average. The rest consumed between the ranges of 11- 20 cigarettes on average per day. A total of 7(9.3%) cases and 2(1.4%) controls had history of illicit drug use where as 29(39.2%) cases and 32(21.8%) controls had experience of alcohol consumption (Table 3).

The odds of illicit drug use and cigarette smoking were 7.5 times and 3 times higher among cases than controls respectively and these showed statistically significant association. And alcohol consumption was about 2 times higher among cases than controls and statistically significant (Table 3).

Table 3. Behavioural factors associated with MDR-TB in Addis Ababa, April 2012.

Behavioural Characteristics	Cases	Controls	COR, 95% CI.	
History of illicit drug use				
Yes	7(9.3%)	2(1.4%)	7.52	(1.52, 37.13) **
No	68(90.7%)	146(98.6%)	1	
Cigarette smoking				
Yes	19(25.3%)	14(9.6%)	3.21	(1.51, 6.83) **
No	56(74.7%)	132(90.4%)	1	
Cigarette smoke per day(#)				
1-4	8(42.1%)	8(57.1%)	1	
5-10	8(42.1%)	4(28.6%)	2.00	(0.43, 9.42)
11-20	3(15.8%)	2(14.3%)	1.50	(0.21, 11.54)
Alcohol consumption				
Yes	29(39.2%)	32(21.8%)	2.32	(1.26, 4.26) **
No	45(60.8%)	115(78.2%)	1	

NB. ** $p < 0.05$(variables that shows significant association)

5.4. Clinical characteristics of TB and Co morbid illness associated with MDR-TB

Among the study participants only 7(9.3%) cases and 9(6.1%) controls had history of being in prison. Thirteen (18.8%) cases and 11(8.0%) controls had at least one history of contact with medically confirmed MDR-TB patient.

A total of 72(96.0%) cases and 25(16.9%) controls had history of pervious treatment for TB, only 3(4.0%) cases had no history of pervious TB treatment so far, and this was true for 123(83.1%) controls. Among previously treated patients, the outcome of treatment showed that 51(70.8%) of cases had treatment failure, whereas none of the controls had treatment failure. Fourteen (19.4%) cases and 2(8.0%) controls were relapse, 1(1.4%) cases and 2(8.0%) controls were defaulters and 6(8.3%) cases and 3(12.0%) controls completed treatment (fig.2).

The type of TB treated in pervious treatment showed that the majority 69(95.8%) of cases and 23(92.0%) of controls were pulmonary TB, while the rest were extra pulmonary TB. A total of 70(97.2%) cases and 18(72.0%) controls had DOTs follow-up in their previous treatment.

Twenty-one (33.9%) cases and 2(14.3%) controls had pulmonary cavitation in their chest radiography during pervious treatment of TB. Fifty six (77.8%) cases and 16(64.0%) controls had history of retreatment. Fifty nine (81.9%) cases and 3(12.0%) controls were treated in category II regimen.

Sixty seven (89.3%) cases and 136(93.2%) controls had history of traditional treatment. Among study participants co-morbid illness were also assessed and 8(11.1%) cases and 3(2.1%) controls had diabetes mellitus, while 27 (37.0%) of cases and 20 (14.1%) controls were HIV infected. Eleven (15.7%) cases, and 3(2.1%) controls had history of experiencing any psychological illness. A total of 31(41.3%) cases, and 32(21.6%) controls had history of hospitalization before the diagnosis of TB (Table 4).

Table 4. Clinical characteristics of TB and co morbid illness associated with MDR-TB in Addis Ababa, April 2012.

Clinical characteristics	Cases	Controls	COR, 95% CI
Prison history			
Yes	7(9.3%)	9(6.1%)	1.59 (0.57, 4.45)
No	68(90.7%)	139(93.9%)	1
Contact of TB patients			
Yes	30(42.9%)	36(25.9%)	2.15 (1.17, 3.94) **
No	40(57.1%)	103(74.1%)	1
Contact of MDR-TB patients			
Yes	13(18.8%)	11(8.0%)	2.68 (1.13, 6.35) **
No	56(81.2%)	127(92.0%)	1
Pervious TB treatment			
Yes	72(96.0%)	25(16.9%)	118.08 (34.43, 404.94)**
No	3(4.0%)	123(83.1%)	1
Number of pervious treatment			
1	23(31.9%)	16(64.0%)	1
≥2	49(68.1%)	9(36.0%)	3.79 (1.46, 9.84) **
Dots follow up in pervious TB			
Yes	70(97.2%)	18(72.0%)	1
No	2(2.8%)	7(28.0%)	0.07 (0.01, 0.38) **
Type of TB in pervious treatment.			
Pulmonary TB	69(95.8%)	23(92.0%)	2.00 (0.31, 12.72)
Extra pulmonary TB	3(4.2%)	2(8.0%)	1
History of Retreatment			
Yes	56(77.8%)	16(64.0%)	1.97 (0.73, 5.29)
No	16(22.2%)	9(36.0%)	1
History of traditional treatment.			
Yes	8(10.7%)	10(6.8%)	1.62 (0.61, 4.30)
No	67(89.3%)	136(93.2%)	1

History of hospitalization				
Yes	31(41.3%)	32(21.6%)	2.554	(1.41, 4.67) **
No	44(58.7%)	116(78.4%)	1	
Diabetes mellitus				
Yes	8(11.1%)	3(2.1%)	5.71	(1.47, 22.23) **
No	64(88.9%)	137(97.9%)	1	
HIV infection				
Yes	27(37.0%)	20(14.1%)	3.58	(1.83, 6.99)**
No	46(63.0%)	122(85.9%)	1	
Psychological illness				
Yes	11(15.7%)	3(2.1%)	8.83	(2.38, 32.78) **
No	59(84.3%)	142(97.9%)	1	
Pulmonary cavitation (pervious TB)				
Yes	21(33.9%)	2(14.3%)	3.07	(0.63, 15.02)
No	41(66.1%)	12(85.7%)	1	

NB. ** p< 0.05 (variables that shows significant association)

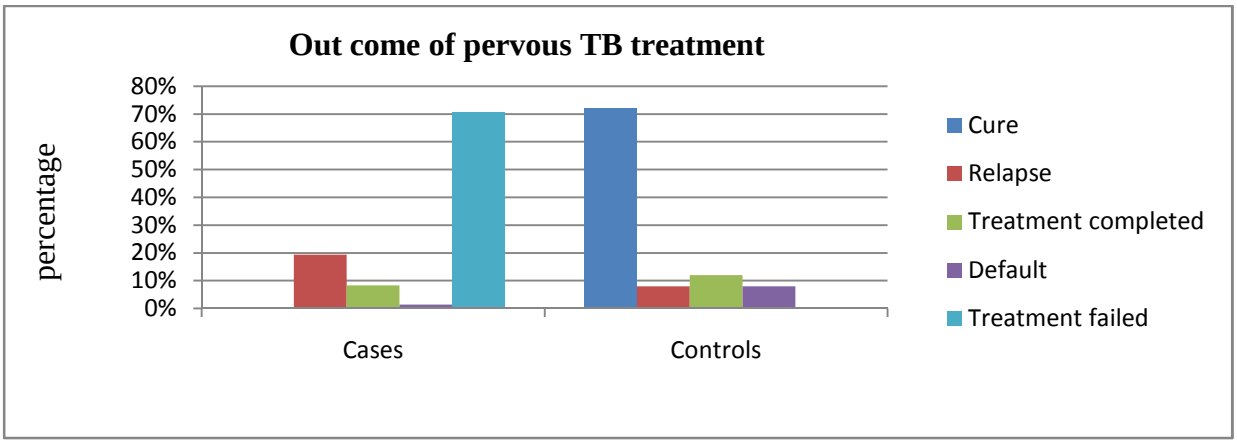


Fig. 2 The outcomes of previous TB treatment among cases and controls in Addis Ababa, April 2012

The odds of being in prison was higher among cases than controls, but it was not statistically significant association (COR=1.59). The odds of pulmonary type of TB, history of retreatment, and presence of cavitation during their pervious treatment were higher among cases than controls, but the results were not statistically significant. The chance of exposure to traditional treatment was also higher (COR=1.62) in cases than controls even though it lacked statistically significant association. However, lack of DOTs follow-up in pervious treatment was less likely (COR=0.07) among cases than controls, it was statistically significant.

The crude association of certain factors like the odds of contact of known MDR-TB patients (COR=2.68), history of pervious TB treatment (COR=118.08), history of hospitalization (COR=2.55), presence of diabetes mellitus (COR=5.71), exposure to HIV infection (COR=3.58) and having any psychological illness (COR=8.83) were higher among cases than their controls, and the differences found to be statistically significant (Table 4).

5.5. Over all determinants of MDR-TB

The variables that showed significant association in binary logistic regression model were residence, marital status, education status, history of pervious TB treatment, number of pervious TB treatment, absence of DOTs follow-up, contact of TB patients, contact of known MDR-TB patients, history of hospitalization, cigarette smoking, illicit drug use, alcohol consumption, presence of diabetes mellitus, HIV infection, history of any psychological illness, have no window and not opening the window daily.

A multiple logistic model including those variables showed that residence, previous TB treatment and HIV infection remained significantly associated with MDR-TB. The odds of MDR-TB were higher among those who were out of Addis Ababa than those who live in Addis Ababa (AOR=18.85 (2.21, 161.10)). MDR-TB was also higher among those who had history of previous TB treatment than those who had no treatment history (AOR=65.57 (14.21, 302.64)). The odds of MDR-TB was nine times higher among those infected with HIV infection than none infected after controlling for all the rest variables in the model (AOR=9.10 (1.48, 54.34)) (Table 5).

After controlling for all the other variables in the model, the odds ratio calculated for, alcohol consumption, contact of TB patients, contact of known MDR-TB patients, history of hospitalization, presence of diabetes mellitus, and experience to any psychological illness, were not significant determinants of MDR-TB (Table 5).

Table 5. Multivariate logistic regression analysis of factors associated with MDR-TB in Addis Ababa, April 2012.

Factors	Cases	Controls	COR, 95%CI	AOR, 95%CI
Residence				
Addis Ababa	45	139	1	1
Out of Addis Ababa	30	9	10.30 (4.55, 23.31)	18.85 (2.21, 161.10) *
Contact of TB patients.				
Yes	30	36	2.15 (1.17, 3.94)	0.65 (0.13, 3.26)
No	40	103	1	1
Contact of MDR-TB				
Yes	13	11	2.68 (1.13, 6.35)	2.48 (0.38, 16.05)
No	56	127	1	1
Pervious TB treatment.				
Yes	72	25	118.08 (34.43, 404.93)	65.57 (14.21, 302.64) *
No	3	123	1	1
History of Hospitalization				
Yes	31	32	2.55 (1.41, 4.67)	0.64 (0.15, 2.81)
No	44	116	1	1
Alcohol consumption				
Yes	29	32	2.32 (1.26, 4.26)	0.69 (0.15, 3.12)
No	45	115	1	1
HIV infection				
Yes	23	25	2.02 (1.04, 3.91)	9.10 (1.48, 54.37) *
No	50	117	1	
Open the window daily				
Yes	45	77	1	1
No	3	19	0.27 (0.08, 0.96)	0.10 (0.01, 1.00)

* variables that shows significant association($p < 0.05$).

6. Discussion

Drug-resistant TB remains a growing threat to public health even with advances made in treatment and diagnosis over the past decade [4]. Concerning to MDR-TB, various potential demographic and clinical risk factors have been investigated in different countries in the world so far; however, the risk factors identified vary based on the types and places (countries) of studies conducted [12].

This study also investigated factors which result in MDR-TB among TB patients in Addis Ababa. Of the factors investigated, we found that previous treatment of TB, HIV/AIDS infection, and place of residence (residence out of Addis Ababa) were the major factors likely to result in MDR-TB.

Previous treatment of TB was one of a strong determinant associated with MDR-TB in this study and it is consistent with studies done in four European countries [25], India [28], Peru [31], Korea and Czech republic [30, 32], Brazil [29], German [33], south Africa and Burkina Faso [40, 42]. However, a systemic review of studies in Europe [11] showed no significant associations. This difference may be due to methodological differences between the studies, such as different referent groups, misclassification of new and previously treated cases.

In this study the finding of previous treatment of TB as independent determinant for MDR-TB may not be a good estimate since it has large variance and which may need a large sample size for further study the association can be explained by looking on factors that help in developing resistance among previously treated TB patients, who were heterogeneous group composed of relapse, and default, treatment completed and cure. Factors such as like frequent inadequate drug therapy, which in turn may be the result of patient non-adherence, incorrectly selected medications, suboptimal drug dosing, or mal-absorption are the likely causes that facilitate developing MDR-TB [51].

A study done in India suggested that errors in TB management such as use of single drug to treat TB, addition of a single drug to a failing regimen, failure to identify pre-existing resistance, initiation of inadequate primary regimen, failure to identify adherence and non adherence to treatment, inappropriate isoniazid preventive therapy, and variations in the bioavailability of anti-TB drugs predispose the patient to the development of MDR-TB [26].

These suggest, the need to have strengthening the management of susceptible TB patients so that to be well diagnosed and adhered to the treatment according to the national TB prevention and control program.

Though the impact of HIV infection on MDR-TB is of great public health importance, their relationship is not yet fully understood [12]. According to this study HIV infection was significant determinant associated to MDR-TB similar to the findings of the studies in Europe [11, 25], France [21], New York [35], Mozambique [39] and south Africa [41] which showed a significant association to MDR-TB. However, this finding was not similar to the findings from review of 39 African countries [23]; studies, Coted' Ivoire, Tanzania, Botswana [39]; two studies in Burkina Faso [42, 43]; South Africa [40] and Madrid [34].

The association between HIV and MDR-TB can be justified in four ways although not yet firmly established. First, people living with HIV, who have weakened immune system, are vulnerable to developing drug resistance as a result of poor adherence to treatment or sub-optimal treatment [12]. However, patients with tuberculosis, with and without HIV infection, can develop drug-resistant tuberculosis strains, Patients co-infected with HIV are more likely and are often the first to progress to active tuberculosis disease and also show active drug-resistant tuberculosis after transmission in an outbreak, whereas HIV-negative individuals may become latently infected and manifest disease years later, if at all [12, 52]. Second, even though HIV infection might not itself be causing an increase in the rate of drug-resistance mutations, it certainly has the potential to increase the number of individuals who select for drug resistance or manifest active disease from resistant organisms, thereby potentially accelerating the propagation and spread of drug-resistant disease [52]. Third, according to WHO 2010 multidrug and extensively drug-resistant tuberculosis global report on surveillance and response, people living with HIV may be more likely to be exposed to MDR-TB patients either due to increased hospitalizations in setting with poor infection control or association with peers who may have MDR-TB [12].

The fourth explanation may be people living with HIV progress more rapidly to TB disease, and especially in our setting (with third prevalent cases of MDR-TB in Africa) and a prevalent cases of HIV/AIDS may lead to rapid development of a pool of drug resistant TB patients as epidemic especially to confected people [12].

Patients who were living out of Addis Ababa were more likely to have MDR- TB compared to those who were living in Addis Ababa. Similar finding was reported by study done in India which showed that the residency out of the state of Tamil Nadu had trend towards association [28]. Study done in California [38] revealed that large proportion of MDR-TB cases appear to be arising in rural or smaller heath jurisdictions and a study done in Burkina Faso also showed that living out of Burkina Faso had a significant association to MDR-TB [42].

However, the finding estimate between the association of residency as independent factor for MDR-TB is may not be good since it has large variance which need further study with large sample size as recommendation the association can be explained by People living out of Addis Ababa was found to be more likely to MDR-TB since they may have weak health seeking behaviour for the treatment, this in turn creates opportunity for transmission. That is, patients infected with resistant strain and reside in setups where infection control system was poor have a great opportunity to transmit this drug resistant disease to other community members. In addition, even if the effect of education level has been found unclear in this study, it is reasonable to guess that people who reside in rural settings, may have lack of awareness with regard to adherence of the medication and hence contagious spreads to more number of people who reside in the same locality and often involve in common social activities. Most importantly, relative difference living standards, especially difference in the quality of housing material, and family size also the availability and accessibility of the treatment facility may espouse the difference in exposure to MDR-TB between those who live in Addis Ababa and out of Addis Ababa. Because of the later are less advantaged in access for socio-economic infrastructure compared to their counterparts. This suggests that the implementation of national tuberculosis prevention and program has to give due emphasis to reach the less disadvantaged areas and expand its outreach in creating awareness with regard to mechanisms that help stop the spread of TB and MDR-TB.

In this study, we found that variables such as age, sex, income, living situation, contacting TB patients (TB contact), contacting patient with MDR-TB (Known MDR-TB contact), smoking, alcohol consumption, presence of diabetes mellitus, prior hospitalization, retreatment history, traditional treatment, prison history, psychological illness, illegal drug use and presence of cavitations on chest radiography did not show statistically significant relationship with MDR-TB.

Similar to this study; age, gender, alcohol consumption, smoking, occupational status, alcohol consumption, traditional treatment, smoking, cavitation on chest radiography, illegal drug use, Diabetes mellitus and psychiatric illness did not showed a significant association to MDR-TB [12, 27, 29, 30, 42]. In contrast to this study, variables like age, sex, known TB contact, income, prison history, hospitalization, smoking, alcohol consumption, cavitation on chest radiography were found to be the possible determinants of likelihood of developing MDR-TB [11, 21, 25, 29, 34]. However, the variation in results obtained by this study and others conducted so far in various countries with the quest to identify variables which result in MDR-TB emanates from multitude of factors. These include difference in the standard classification of variables used, especially age, occupation, education level and income; difference in the study design and hence difference in sample size considered which determine effect size (power) of the statistical results, difference in or (lack of) controlling confounding factors in some studies, heterogeneity of the study participants in terms of living standards, and differences in the national tuberculosis prevention and control programme.

Thus, as it has been elaborated above, within the context of this study, some of the results go against some studies and conform to others and also the existing literatures are showing controversial findings in identification of risk factors associated with MDR-TB. Nonetheless, based on the availability of resources, the author believes that, the study can be further developed in order to investigate the risk factors leading to MDR-TB at the national level, while taking into account the need to remedy possible factors which tend to bias the results obtained.

7. Strengths and limitations

Strengths: It used a sound study design and it is appropriate one and was done in quickly and cost effective way. The data were also enrolled from 10 health care facilities and culture for MDR-TB cases confirmation was done in a reference laboratory that follows the standard WHO guides line. The response rate among the study participant was high.

Limitations: Recall bias may be introduced by respondents since study participants may not remember condition of the past. Selection bias may be introduced during enrolment of cases by involving only those who was on treatment. In controls also selection bias may be introduced since we included only patients with positive AFB smear and turned to negative or responding to the treatment due to logistic reason to do the test for other type of TB. The incompleteness of data on CD4 count for co-infected patients and not addressing immuno suppression other than HIV were another limitation of the study. Environmental and house hold factors were assessed without observation and this may have effect in the validity of the findings. Finally, some variables have weak estimate and the study suggest a need to have large scale study with including the possible available number of MDR patients.

8. Conclusion

Previous treatment of TB, HIV infection and residency out of Addis Ababa were independently associated significant determinants of MDR-TB.

Factors like, age, sex, income, occupation, prison history, traditional treatment, retreatment history, prison history, TB contact, known MDR-TB contact, alcohol consumption and history of hospitalization were proved to be not significantly associated determinants of MDR-TB.

9. Recommendation

Based on the findings of this study the following important recommendations are forwarded for the respective body starting from national to grass route TB prevention and control program implementers, policy makers and researchers who are engaged on TB area as of one main public health concern:

- It is necessary to strengthen the treatment strategy which assure the direct observation of treatment taking to ensure better treatment adherence.
- Prevent creation of drug resistant by ensuring that all TB patients are rapidly diagnosed, and appropriately treated .
- a need to have appropriate and timely monitoring and supervision activities in prevention and treatment of TB.
- It is better to strengthen TB/HIV collaborations
- It is better to have strong and functional regional or zonal level consultation centres for strengthening the program activities at low or rural setups
- Finally, it is better to do further large scale epidemiological research, in the largest possible number of available MDR-TB patients to identify the potential determinants of MDR-TB to the local setup at large.

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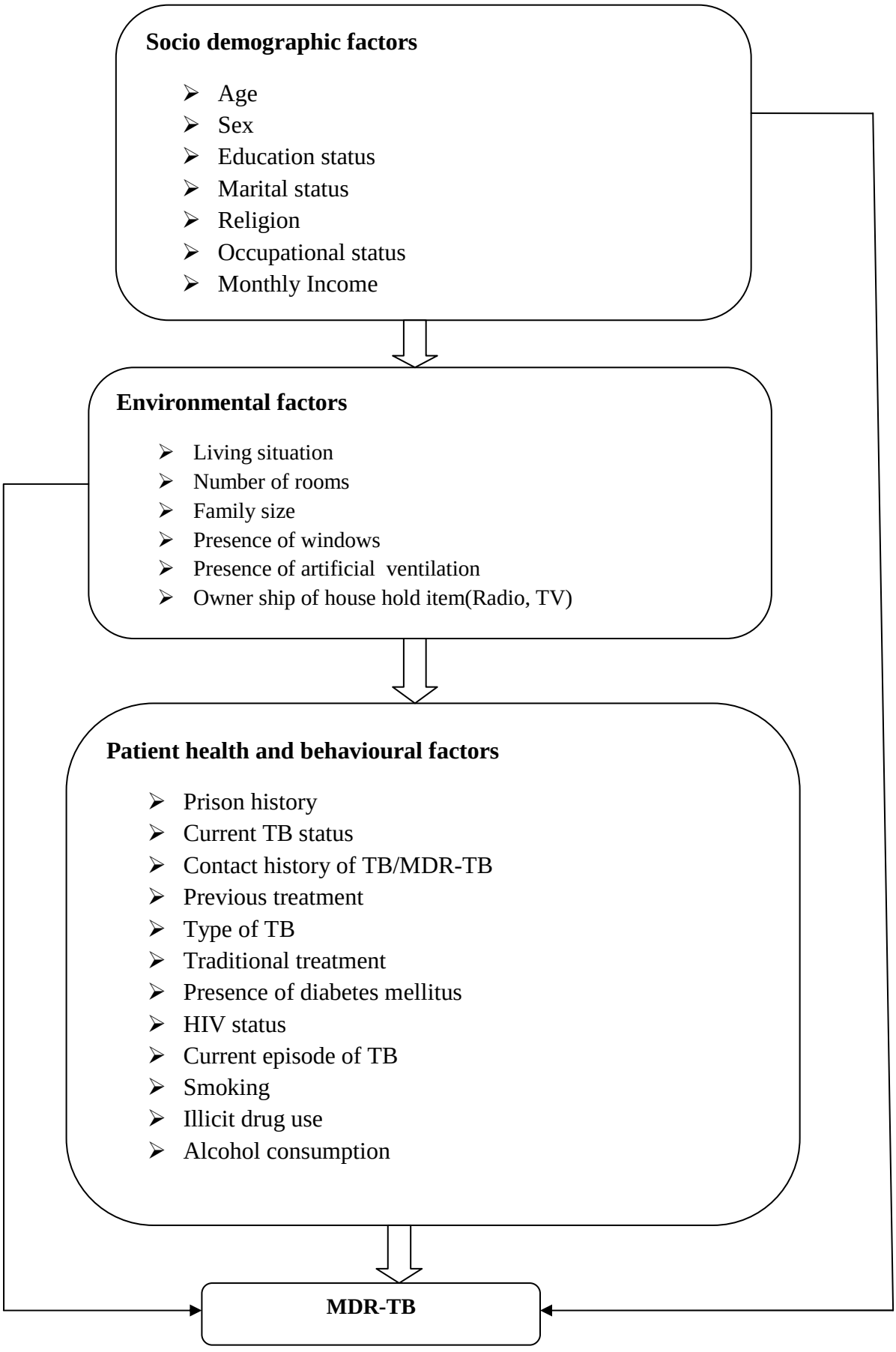
Appendix-I Conceptual frame work for determinants of MDR-TB



Appendix-II Information sheet

Description of the study

Title of the study: Determinants of multi drug resistant Tuberculosis (MDR-TB) among tuberculosis patient in Addis Ababa: case control study.

- **Objective of the study**: To identify determinants of multi drug resistant tuberculosis (MDR-TB) among tuberculosis patients in Addis Ababa.

Introduction: Rationale of the Study and its benefits

Multi drug resistant tuberculosis which result from strains of mycobacterium tuberculosis resistant to at least the two power full first line drugs isoniazid and rifampicin to tuberculosis treatment were the global problem. The situation is increasing from time to time. Ethiopia is also facing the challenge to the problem in recent time. Patients infected with MDR strains are not only difficult to cure but also more likely to remain sources of infection for a longer period of time than those with drug-susceptible organisms. studies show that multi drug resistant is a manmade phenomenon arises due to inadequate treatment of drug-sensitive TB and there are reports showing raising of multi drug resistance from various parts of the globe which potentially threaten to interrupt the gains achieved in tuberculosis control. Concerning to the determinant factors several countries in the world have shown different factors which are associated with multidrug resistance. However, there is inconsistency of finding in certain factors in study conducted so far.

Knowing country specific factor is very important to have successful management of the problem. However, there is deficiency of literatures in Ethiopia concerning to determinants of multi drug resistant tuberculosis. This study is there for, designed to assess the potential determinant factors for MDR-TB among tuberculosis patients in three hospitals. I hope this study will contribute in bridging the gaps in literature to the local context and it may also help for policy makers to make right decision in prevention and control of multi drug resistant tuberculosis. Information which is necessary for the study will be interviewed and in addition information relevant to the study will be reviewed from their records. The study will be conducted in full agreement of informed consent and no one patients will be subjected to any harm. To keep the confidentiality of the patients, personal identifiers will not be included in the data collection form.

Appendix-III Patient Consent Form

My name is _____, I am Nurse professionally and now I am collecting data from the patients for the research being conducted to identify the determinants of MDR-TB among tuberculosis patients, by Mr. Sefonias Getachew who is the Master of public Health student in Addis Ababa University. You are selected as one of study subject by chance. The investigator employed me for this data collection to maintain your data strictly confidential. We believe that the findings of this study will have paramount for evaluation of TB programs and to find out proper way for prevention of determinants for MDR in TB patients.

Information which is necessary for the study will be asked from you and in addition to this some information relevant to the study will be reviewed from your record. For all information taken the confidentiality is kept. The information will be taken when you give permission and participation is totally volunteer based.

Your willingness for giving information to be utilized in this study will help us to achieve the stated benefits of the study. Your name and other personal identifiers will not be recorded on data collection format 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 give any information to be consumed for this study. But the information that would be taken will be quite useful for the study. You will not face any problem if you do not agree to the information to be asked or reviewed from your record and you will not be also denied of getting any medical services from the hospital. If you have any questions about this study you may ask me or the principal investigator Sefonias Getachew (Tel: 091204 9682 or E-mail: safoget@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 _____

Appendix-IV

ADDIS ABABA UNIVERSITY SCHOOL OF
PUBLIC HEALTH
QUESTIONNAIRE FORM

Questionnaire related to determinant of multi drug resistant tuberculosis (MDR-TB) among tuberculosis patients in Addis Ababa.

Date_____

Identification .No ____

Instruction: circle the responses provided by the interviewer or write the appropriate answer on the space provided.

Section-1 Socio-demographic Information			
S. No	**Questions**	**Option/ answers**	**Remark**
101	sex	1.Male 2.Female	
102	Age	----------(in years)	
103	Marital Status	1. Single 2. Married 3. Divorced 4. Widowed	
104	Religion	1. Orthodox 2. Muslim 3. Protestant 4. Catholic 5.Others(specify)_____	
105	Educational level	1.Illiterate 2.Read and write 3.Primary school 4. Secondary school 5. Tertiary	

106	Ethnicity	1. Oromo 2. Amahara 3. Tigeri 4. Guragae 5. Others (specify)----------	
107	Occupational status	1. Farmer 2. House wife 3. Merchant 4. Military 5. Daily labourer 6. Student 7. Government employ 8. Police force 9. NGO 10. Others(specify)----------	
109	Residence	1. Addis Ababa 2. Out of Addis Ababa	
1010	Monthly income	----------(Birr).	

Section II: Environmental factors

S. No	Questions	Option/ answers	Remark
201	Living situation	1. Alone 2. With family 3. Other (specify)----------	
202	Do you have house to live in?	1. Yes 2. No -if No skip to ⟶	Q 301
203	How many people living in the house?	----------	

204	What is the Number of rooms in the house?	----------	
205	What is the type of the wall of the house?	1. Cement 2. Mud 3. Wood 4. Other(specify)	
206	What is the type of the floor of the house?	1. Cement 2. Mud 3. Wood 4. Other(specify)	
207	The rooms have windows ?	1. Yes 2. No /if No skip to →	Q2010
208	What is the average number of windows to the rooms?	----------	
209	Do you open the window in sense of refreshing the room?	1. Yes 2. No	
2010	Do you have artificial ventilation?	1. Yes 2. No	
2011	Does your house has electric city?	1. Yes 2. No	
2012	Do you have latrine to use?	1. Yes 2. No	
2013	Which of the listed house hold items do you have?	1. Radio 2. TV 3. Air conditioner 4. refrigerator 5. automobile /car	

Section III: Host related factors			
S. No	**Questions**	**Option/ answers**	**Remark**
301	Do you have history of being in prison?	1. Yes 2. No 3. No response	
302	Is it the first to be infected with TB??	1. Yes 2. No	
303	Do you have history of contact with known TB patient?	1. Yes 2. No 3. I don't know	
304	If yes to Q. No 302 where is the place you have contact to known TB patient?	1. In the Family 2. Work place 3. Health institution 4. Transportation service 5. School 6. Other(specify)----------	
305	Do you have history of contact with known MDR-TB patient?	1. Yes 2. No 3. I don't know	
306	If yes to Q. No 304 where is the place you have contact to known MDR-TB patient?	1. In the Family 2. Work place 3. Health institution 4. Transportation service 5. School 6. Other(specify)------	

307	Do you have history of previous TB treatment?	1. Yes 2. No 3. I don't remember/ If answer is 2 or3 skip to →	Q 3012
308	How many times do you have history of previous TB treatment?	---------- ---(in number)	
309	When it was the previous treatment of TB?(if more than once fill the last one)	----------years back or ---- ----------months back since now	
3010	Do you have history of treatment under DOTs follow up for the previous treatment/s	1. Yes 2. No	
3011	For how long did you take the treatment for previous treatment?	----------(in month)	
3012	What was the type of TB you treated for?	1. Pulmonary TB 2. Extra pulmonary TB 3. Mixed 4. I don't know	
3013	Do you have history of retreatment for TB?	1. Yes 2. No 3. I don't remember	
3014	Do you have history of traditional treatment?	1. Yes 2. No 3. I don't remember	
3015	Do you have history of hospitalization since birth?	1. Yes 2. No 3. I don't know	

3016	Do you have history of illicit drug use which are under control such as cocaine, heroin, hashish etc ?	1. Yes 2. No 3. No response.	
3017	Do you have history of cigarette smoking at least once in a week?	1. Yes 2. No 3. No response. If answer is option 2or3 skip to	Q 3019
3018	How many cigarette on average you smoke per day?	1. 1-4 2. 5-10 3. 11-20 4. >20	
3019	Do you have history of khat chewing at least once in a week?	1. Yes 2. No 3. No response	
30120	Do you have history of alcohol intake till you drunk at least once in a month?	1. Yes 2. No 3. No response	
3021	Do you have history of experiencing gastro intestinal symptom with skin lesion manifestation, repeated infection?	1. Yes 2. N o 3. No response	
3022	Do you counteract diabetes mellitus?	1. Yes 2. No 3. I don't know	

Section IV: Data reviewed from patients records			
S. No	**Questions**	**Option/ answers**	**Remark**
401	Category of patient	1. New 2. Relapse 3. Return after default 4. Failure 5. Others(specify)----------	
402	Presence of HIV infection	1. Yes 2. No 3. Not known	
403	If yes to Q 402 what is the base line CD4 count?	----------(specific number)	
404	History of previous TB treatment.	1. Yes 2. No If No Skip to ⟶	Q 409
405	Type of pervious TB infection	1. Pulmonary TB 2. Extra pulmonary 3. Mixed 4. Not known	
406	What was the treatment regimen taken in previous treatment ?	----------	
407	Outcome of pervious TB treatment	1. Cure 2. Relapse 3. Treatment completed 4. Default 5. Treatment failed 6. Transfer out. 7. Others(specify)----------	
408	Presence of cavitation using chest radiography/previous TB/	1. Yes 2. No 3. Not known	
409	Current episode of TB	1. Pulmonary TB 2. Extra pulmonary 3. Mixed	
4011	Experienced any psychological problem	1. Yes 2. No 3. Not known	
4012	History of other illness	----------	

Appendix-V: Translated Amharic version of information sheet

የአዲስ አበባ ዩንቨርስቲ የህብረተሰብ ት/ቤት

የሳንባ ነቀርሳ መድኃኒትን የተላምደ የሳንባ ነቀረሳ በሽታ መንሴዎችን ለማናት የተዘጋጀ ፎርም

መረጃ መስጫ ቅፅ

የጥናቱ መግለጫ

የጥናቱ ርእስ; የሳንባ ነቀረሳ መድኃኒትን የተላምደ የሳንባ ነቀረሳ በሽታ መንሴዎች በሚል በሳንባ ነቀረሳ በሽታ በተያዙ ሰዎች ላይ የሚደረግ ጥናት ነው፡፡

የጥናቱ ዳራ; የሳንባ ነቀርሳ መድኃኒትን የተላምደ የሳንባ ነቀረሳ በሽታ መንሴዎችን በሳንባ ነቀረሳ በሽታ ከተያዙ ሰዎች ላይ ማጥናት፡፡

መግቢያ ; የጥናቱ ዓለማና ጥቅሞቹ

የሳንባ ነቀረሳ መኃኒትን የመላምደ የሳንባ ነቀረሳ በሽታ ማለትም በእንግሊዘኛው “multidrug resistance(MDR-TB) የተባለው በሽታ በአሁኑ ሰዓት በዓለም አቀፋ ደረጃ የሚታወቅ በሽታ ነው፡፡ የበሽታው ችግር ከግዜ ወደ ጊዜ እየጨመር የመጣ ሲሆን ኢትዮጲያም በበሽታው ከሚጠቁ አገሮች አንዱ ናት፡፡ ይህ በሽታ ለመዳን ረጅም ጊዜ ከመውሰዱም ውጭ በበሽታው የተያዙ ሰዎች ከማንኛውም የሳንባ ነቀረሳ በሽታ ይልቅ ለረጅም ጊዜ በሽታውን ለሌላው ወገን የማስተላለፍ ምንጭ ሆነው ይቆያሉ ፡፡ የተለያዩ ጥናትቶች እንደሚጠቀሙት ይህ መድኃኒቱን የመላመድ ኃይል ያለው በሽታ ሰዎች ለህመማቸዉ ከሚያደረጉት ጉድለቶች ሲሆን መለትም ለሳንባ ነቀረሳ በሽታ በቂና አግባብ ያለው ህክምና ካለመውሰድ የመነጨ ይሆናል፡፡ እንደ ጥናቶች መረጃ ችግሩ እየጨመረ በመሆኑ የሳንባ ነቀረሳ በሽታን ለመከላከል የሚደረጉ ጥረቶችን ሊያደናቅፍ ይችላል፡፡ የዚህን የበሽታ መንሴዎች በተመለከተ የተለያዩ የዓለማችን ሀግሮች ላይ የተሰሩ ጥናቶች የተለያዩ መንሴዎችን ያሳዩ ቢሆንም እንደያገራቱ አንዳዶቹ መንሴዎች የተለየ መረጃ ያሳያሉ፡፡ የበሽታውን ሁኔታ በተገቢው ለመከላከልና ለመቆጣጠር ብሎም ለማከም የየሀገሩን የበሽታ መንሴ ማወቅ በጣም ጠቃሚ ነው፡፡ በዚህ በሽታ መንሴዎች ዙሪያ ኢትዮጲያን በተመለከተ የጥናቶች እጥረት ያለ ሲሆን የዚህ ጥናት አላማም ይህን መድኃኒት የመላመድ አቅም ያለውን የበሽታ መንሴዎች በአዲስ አበባ በተመረጡ ጤና ተቐማት ማጥናት ነው፡፡ እንደኔ እምነት ይህ ጥናት በሀገራችን ያለውን የበሽታውን መረጃ እጥረት ከመቅረፍም አልፎ በሽታውን የመከላከልንና የመቆጣጠረ ብሎም ለፖሊስ አውጭዎች ውሳኔ እንዲሰጡ እጅጉን ይጠቅማል፡፡

Appendix-VI Translated Amharic version consent form

የፈቃደኝነት መጠየቂያ ቅጽ

ስሜ …… በሙያዬ ነርስ/ጤና መኮንን ስሆን በዚህ የሳንባ ነቀረሳ መድኃኒትን የተላመደ የሳንባ ነቀረሳ በሽታ መንሴዎች በሚል ጥናት ላይ በአዲስ አበባ ዩንቨርስቲ የህብረተሰብ ጤና ሁለተኛ ድግሪ ተማሪ የሆኑት አቶ ሰፎኒያስ ጌታቸው ለሚደረገው ጥናት መረጃ በማሰባሰብ ላይ እገኛለሁ፡፡ እረሶ በዚህ ጥናት እንዲሰተፉ የተመረጡት በእጣ ነው፡፡ እኔን ተመራማሪው/ የጥናቱ ባለቤት የቀጠረኝ የእርሶን መረጃ ሚስጥራዊነት በጥንቃቄ እንድጠብቅ ነው፡፡ እኛ እንደምናምነው የዚህ ጥናት ውጤት የሳንባ ነቀረሳ ፕሮግራምን አሰራረ በተመለከተ ምርመራ ለማደረግ ብሎም የዚህን የሳንባ ነቀርሳ መድኃኒት የተላመደ የሳንባ ነቀርሳ በሽታ መንሴዎች ለማወቅና ትክክለኛውን መፍትሄ ለመስጠት እገዛ ያደረጋል፡፡ለጥናቱ የሚጠቅሙ መረጃዎች ከእረሶ በቃለ መጠይቅ መልክ እና በተጨማሪ ከእረሶ መረጃ ሪከርድ ላይ የሚወሰድ ይሆናል፡፡ መረጃው የሚወሰደው በእረሶ ሙሉ ፈቃድ ሲሆን የሚወሰደውም መረጃ መስጥራዊነት እጅግ በጣም የተጠበቀ ነው፡፡

ከዚህ ጥናት ለሚገኘው ጠቀሜታ መረጃን በመስጠት የእረሶ በጎ ፈቃደኝነት እጅግ ጠቃሚ ሲሆን የሚሰጡት መረጃ ሚስጥራዊነቱ እንደተጠበቀ ሆኖ መረጃው ለዚህ ጥናት ብቻ የሚውል ነው፡፡ መረጃን ላለመስጠት ሙሉ መብት አሎት ግን የእረሶ በዚህ ጥናት መሳተፍዎ እጅግ በጣም ጠቃሚ ሲሆን ማንነትዎን የሚገልፅ ስም ወይም ሌላ ገላጭ ነገሮች በመጠየቂያ ወረቀቱ ላይ አይሞላም፡፡ በዚህ ጥናት አልሳተፍም ካሉ ምንም ዓይንት ችግር አይገጥሞትም፡፡ በተጨማሪም ከሚገለገሉት የህክምና አገልግሎትም አይታገዱም ወይም አይስተጓጉሉም፡፡ በመጨረሻም ይህን ጥናት በተመለከተ ጥያቄ አለኝ ካሉ የዚህን ጥናት ባለቤት የሆኑትን አቶ ሰፎንያስ ጌታቸውን በዚህ አድራሻ ስልክ 0912049682 ኢ-ሜል safoget@yahoo,com መጠየቅ ይችላሉ፡፡

ለዚህ መረጃ ጥናት እንዲውል መረጃ ለመስጠት ፈቃደኛ ነዎት

አዎ 2. አይደለሁም

በዚህ ጥናት ላይ መረጃ ሰጭው ፈቃደኛ ሆነው ሰለመሳተፋቸው የሚያረጋግጥ

የመረጃ ጠያቂው ፈረሚያ _____

Appendix-VII Translated questioner/Amharic version/.

የአዲስ አበባ ዩንቨርስቲ የህብረተሰብ ት/ቤት

የሰንባ ነቀረሳ በሽታ መደኃኒትን የተላመደ በሽታ (MDR-TB) መንሴዎችን ለማጥናት የተዘጋጀ የመጠየቂ ያፎረም፡፡

የመጠየቂያ ፎርም

ቀን---------- መለያ ቁጥር----------

መመሪያ: መላሹ የሰጡትን መልስ በማክበብ ወይም በክፍት ቦታ ላይ መልሱን ይፃፉ፡፡

ክፍል -1 የመሃበራዊ ሁኔታዎች መርጃ			
ተ.ቁ	ጥያቄዎች	መልስ/ምረጫ	ምርምራ
101	ፆታ	1. ወንድ 2. ሴት	
102	ዕድሜ	----------(በዓመት)	
103	የጋብቻ ሁኔታ	1. ያገባ 2. ያላገባ 3. የፈታ 4. ባል/ሚስት ሞተዋል	
104	ሃይማኖት	1. ኦረቶዶክስ 2. ሙስሊም 3. ካቶሊክ 4. ፕሮቴስታንት 5. የተለየ/ይጥቀሱ……..	
105	የትምረት ደረጃዋ እስከምንድነው?	1. ያልተማረ/ች 2. ማንበብ እናመፃፍ 3. የመጀመሪያ ደረጃ 4. ሁለተኛ ደረጃ 5. ከፍተኛ ደረጃ	
106	ጎሳዎት ምንድነው?	1. ኦሮሞ 2. አማራ 3. ትግሬ 4. ጉራጌ 5. የተለየ/ይጥቀሱ……..	
107	የስራ ሁኔታ	1. ገበሬ 2. የቤት እመቤት 3. ነጋዴ 4. መከላከያ 5. የቀን ሰራተኛ 6. ተማሪ 7. የመንግስት ሰራተኛ 8. የፖሊስ ሃይል 9. መንግስታዊ ያልሆን ድርጅት 10. የተለየ/የጥቀሱ……	
108	የመኖሪያ ቦታ	1.አዲስ አበባ 2.ከአዲስ አበባ ውጭ	
109	ወረሃዊ ገቢ (በብር)	_____(ብር)	

ክፍል 2- የአከባቢ ሁኔታዎች መረጃ			
ተ.ቁ	**ጥያቄ**	**ምረጫ/መልስ**	**ምረመራ**
201	የኑሮ ሁኔታ	1. ለብቻ 2. ከቤተሰብ ጋር 3. የተለየ (ይጥቀሱ)----------	
202	የመኖሪያ ቤት አልዎት?	1. አዎ 2. የለኝም___(የለኝም ከሆነ ወደጥያቄ ⟶	301 ይለፉ
203	የሚኖሩበት ቤት ስንት ክፍል አለው?	_____(በቁጥር)	
204	የሚኖሩበት ቤት የሰው ብዛት ስንት ነው?	---------- (በቁጥር)	
205	የመኖርያ ቤትዎ ግድግዳ አናት ምንድ ነው?	1. ስሚንቶ 2. ጭቃ 3. እንጨ ት 4. የተለየ/ይጥቀሱ----------	
206	የመኖሪያ ቤትዎ ወለል ምንድ ነው?	1. ስሚንቶ 2. ጭቃ 3. እንጨት 4. የተለይ/የጥቀሱ----------	
207	የመኖሪያ ቤትዎ መስኮት አለው?	1. አዎ 2. የለውም/ ከሆነ ወደ ⟶	ጥያቄ 2010ይለፉ
208	በአማካኝ የመኖረያ ቤትዎ መስኮቶች ስንት ናቸው?	----------	
209	የቤቶን መስኮት አየረ እንዲገባ በሚል ይከፍታሉ	1. አዎ 2. አይደለም	
2010	በመኖሪያ ቤቶዎ ሰው ሰራሽ የሆነ አየር ማቀዝቀዣ(ventilation)አልዎት?	1. አዎ 2. የለኝም	
2011	የመኖሪያ ቤትዎ መብራት አለው?	1. አዎ 2. የለውም	
2012	የሚጠቀሙበት መፀዳጃ ቤት አለዎት?	1. አዎ 2. የለኝም	
2013	በቤቲዎ ውሰጥ ከምከተሉት የትኛዉ ይገኛል?	1. ሬድዮ 2. ቴሌቭዝን 3. ኤር ኮንድሽነር 4. ፍሪጅ 5. አዉቶሞቢል/መኪና	

ክፍል-3 በበሽታ ተያዥ ሁኔታ በተመለከተ/Host related factors				
ተ.ቁ	ጥያቄ	ምረጫ/መልስ	ምረመራ	
301	እስር ቤት ታስረው ያውቃሉ?	1.አዎ 2.አላውቅም 3.መልስ የለም		
302	በሳንባ ነቀረሳ በሽታ ሲያዙ የመጀመሪያዎት ነው?	1.አዎ 2.አይደለም		
303	በሳንባ ነቀረሳ በሽታ ከተያዘ ሰው ጋ ኖረው/በቅርብ ተገናኝተዉ አሳልፈዉ ያውቃሉ?	1.አዎ 2.አላውቅም 3.አላስታውሰም		
304	ለጥያቄ303 አዎ ከሆነ የት ነው አብረው የኖሩት ወይም ያሳለፉት?	1.ቤተሰብ ጋ 2.ስራ ቦታ 3.ጤና ተቋም 4.በህዝብ ማመላለሻ 5.ት/ቤት 6.የተለየ(ይጥቀሱ)….		
305	በሳንባ ነቀረሳ መድኃኒት ከተለመ በሽታ የተያዘ ሰው ጋ ኖረው/በቅርብ ተገናኝተዉ አሳልፈዉ ያውቃሉ?	1.አዎ 2.አላውቅም 3.አላስታውስም		
306	ለጥያቄ 305 መልስ አዎ ከሆነ የት ነው አብረው የኖሩት ወይም ተቀራረበዉ ያሳለፉት ?	1.ከቤተሰብ ጋር 2.ስራ ቦታ 3.ጤና ተቋም 4.በህዝብ ማመላለሻ 5.ት/ቤት 6.የተለየ(ይጥቀሱ)_____		
307	ከዚህ በፊት የሳንባ ነቀረሳ ህክምና ታክመዋል?	1. አዎ 2. አልታከምኩም መልሱ አልታከምኩም ከሆነ →	ወደጥያቄ 3013ይሻገሩ	
308	ለያቄ 307 አዎ ከሆነ ስንት ጊዜ ታክመዋል?	----------		
309	የሳንባነቀርሳ ህክምና ከዚ በፊት የታከሙት መች ነበር? ከአንድ በላይ ከሆነ የመቸጨረሻውንይሙሉ።	----- አመት በፊት/---------ወር በፊት		
3010	በመጀመሪያ ህክምናዎ ላይ በተመላላሽ መልክ በጤና ባለሙያ ወይም በተወከለ ሰው ክትትል ታክመዋል/መዳኒቶን ዉተዋል?	1. አዎ 2. አልታከምኩም		
3011	የመጀመረያውን ህክምና የወሰዱት ለምን ያህል ጊዜ ነው?	_____(በወር)		

3012	የመጀመሪያ የታከሙት በሽታኣይነት ምን ነበር?	1. የሳንባ ቲቢ 2. ከሳንባውጭ የሆነ የቲቢ በሽታ 3. ከሁለቱ የሆነ 4. አላውቅም		
3013	ለሳንባ በሽታ ሲታከሙ በመጀመሪያ አልድን ብሎ ለሁለተነኛ ጊዜ መድኃኒትወስደው ያውቃሉ?	1. አዎ 2. አላውቅም 3. አላስታውስም		
3014	የባህላዊ ህክምና ተጠቅመው ያውቃሉ?	1. አዎ 2. አላውቅም 3. አላስታውስም		
3015	ከተወለዱ ጀምሮ ሆስፒታል ተኝተው ያውቃሉ?	1. አዎ 2. አላውቅም 3. አላስታውስም		
3016	በህግ የተከለከለ እፅተጠቅመው ያውቃሉ ? እንደ ሀሽሽ ኮኬይን ማርጅዋና የመሳሳሉ።	1. አዎ 2. አላውቅም		
3017	ሲጋራ ቢያንስ በሳምት አንድ ቀን አጭሰዉ ያዉቃሉ?	1. አዎ 2. አላጨስም 3. መልስ የለም	መልሱ2ወይም3 ከሆነ ⟶ ወደጥያቄ3019 ይሻገሩ	
3018	በቀን በአማካይ ስንት ሲጋራ ያጨሳሉ?	1. 1-4 2. 5-10 3. 11-20 4. >20		
3019	ጫት ቢያንስ በሳምት አንድ ቀን ቅመው ያውቃሉ?	1. አዎ 2. አላውቅም 3. መልስ የለም		
3020	አልኮል ቢያንስ በወር ዉስጥ አንድ ጊዜ እስኪሰከሩ ድረስ ተጠቅመው ያውቃሉ?	1. አዎ 2. አላውቅም 3. መልስ የለም		
3021	አብዛኛዉን ጊዜ የሆድ ዕቃ ችግር(ማስመለስ፡ማስታወክ) ; የሰዉነት ቆዳ መላላጥ/መቁሰል እና ተደጋጋሚ የሆነ እፊክሽን ይታይቦታል ?	1. አዎ 2. አይታይም 3. መልስ የለም		
3022	የስካር በሽታ አለብዎት?	1. አዎ 2. የለብኝም 3. አላውቅም		

Section IV: Data reviewed from patients records			
S. No	Questions	Option/ answers	Remark
401	Category of patient	1. New 2. Relapse 3. Return after default 4. Failure 5. Others(specify)----------	
402	Presence of HIV infection	1. Yes 2. No 3. Not known	
403	If yes to Q 402 what is the base line CD4 count?	----------(specific number)	
404	Presence of diabetes mellitus	1. Yes 2. No 3. Not known	
405	History of previous TB treatment.	1. Yes 2. No	
406	Type of pervious TB infection	1. Pulmonary TB 2. Extra pulmonary 3. Mixed 4. Not known	
407	What was the treatment regimen taken in previous treatment ?	----------	
408	Outcome of pervious TB treatment	1. Cure 2. Relapse 3. Treatment completed 4. Default 5. Treatment failed 6. Transfer out. 7. Others(specify)-------- ----	
409	Presence of cavitation on chest radiography	1. Yes 2. No 3. Not known	
4010	Current episode of TB	1. Pulmonary TB 2. Extra pulmonary 3. Mixed	
4011	Experienced any psychological problem	1. Yes 2. No 3. Not known	
4012	History of other illness	---------- ----------	

DECLARATION

I, the undersigned, declare that this thesis is my original work and has never been presented for a degree in this or any other university and all the sources of materials used for the thesis have been fully acknowledged.

Name: **Sefonias Getachew (Bsc. PH)**

Signature: _____

Date :_____

Place : Addis Ababa university school of public health

This thesis work has been submitted for the examination with my approval as a university advisor

Name: **Fikre Enquselasie (Msc, PhD, Associate prof.)**

Signature: _____

Date: _____