

DETERMINANTS OF MULTI DRUG RESISTANT TUBERCULOSIS AMONG
TUBERCULOSIS PATIENTS IN SOUTHWEST ETHIOPIA: UNMATCHED
CASE CONTROL STUDY



BY: -SILESHI MESERET GOSHIYE (BSc)

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DETERMINANTS OF MULTI DRUG RESISTANT TUBERCULOSIS
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By: - SILESHI MESERET GOSHIYE (BSc.)

Advisors

1. Lamesa Dube (MPH ass.prof Epidemiology)
2. Solomon Berhanu(MPH ass.prof Epidemiology)

August, 2021
Jimma, Ethiopia

DECLARATION

This is to certify that the thesis prepared by **Sileshi Meseret Goshiye**, entitled with: **determinants of multi drug resistant tuberculosis among tuberculosis patients in south west, Ethiopia** and all the sources of materials used for the thesis have been fully acknowledged.

Name: **SILESHI MESERET** (BSc) Signature: _____ Date: August 2021

Place: Jimma University Faculty of public health Department Epidemiology

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

Advisor

Name: Lamesa Dube (Msc, PhD Candidate.) Signature: _____ Date: August 2021

Name: Solomon Berhanu (MPHE Ass Prof) Signature: _____ Date: August 2021

1. Dr. Gudina Egate

(External Examiner)

Signature

Date

2. Dr. Sahilu Assegid

(Internal Examiner)

Signature

Date

Abstract

Background: Multidrug-resistant tuberculosis (MDR-TB) is caused by Mycobacterium TB a bacterium that is resistant to at least isoniazid and rifampin. There are alarming reports of multidrug-resistant tuberculosis from different parts of the world, including Ethiopia. The multidrug-resistant TB in Ethiopia among new TB cases is estimated at 2.7 % and 14% in previously treated cases. However, Factors leading to development of drug resistance need to be understood to develop appropriate control strategies for national programs. **Objectives:** To identify determinants of multidrug-resistant tuberculosis (MDR-TB) among tuberculosis patients in southwest Ethiopia.

Methods: Unmatched case-control study design was conducted used among 200 study population 134 controls and 65 cases from January13, 2021, to June 30, 2021 in southwest Ethiopia. Using systematic random sampling techniques for controls and for case purposive sampling was used. Data were collected using a structured questionnaire. Data were entered using Epi-Data version 3.4 and SPSS version 24 for analysis. Descriptive statistics was used. Binary logistic regression analyses were conducted to see the association between all explanatory variables and outcome variable and to identify candidate variables with $p \leq 0.20$ for multivariable logistic regression model. Odds ratios along with 95%confidence interval (CI) were estimated to measure the strength of association .Level of Statistical significance was declared at p-value less than 0.05. **Result:** The response rate was 96.7% among cases and 100% among controls. Thirty one (47%) of cases and 63.3% of controls were males. Determinants of MDR TB were Social stigma [(AOR=5.2 95% CI:(1.69, 16.16)] , alcohol consumption [(AOR=4.1,95% CI:(1.04,15.80)], History of previous TB treatment [(AOR=5.3,95% CI:1.72,16.43)], a history of retreatment for TB [(AOR= 13.9,95%CI: (4.44, -40.04)], khat chewing [(AOR=6.2,95% CI:(1.91,20.63)] , Body mass index under nutrition (AOR=3.9 ,95% CI:(1.09,13.92)], and psychological illness [(AOR=9.4, 95% CI:(1.76, 50.17)] and distance from treatment center <25km [(AOR=6.2 ,95% CI:2.00,19.04)] were identified as determinants of developing MDR-TB than their counterparts.

Conclusion: stigma, Alcohol consumption, History of previous TB treatment, History of retreatment, Khat chewing, Body mass index, psychological illness and Distance from treatment center. Therefore better emphasis should be given to the national Prevention and control activities according to the contextual situations so that to avert the increasing problem from the country and moreover, to keep the health of the community.

Key Words: - Determinant, MDR TB, Case-control, southwest, Ethiopia

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Acronomy/Abbreviation

ART	Anti-Retroviral Therapy
BMI	Body Mass Index
CI	Confidence Interval
CEEU	Central and Eastern Europe
DOTs	Direct Observe Therapy
DST	Drugs susceptibility test
ENHRI	Ethiopian Nutrition and Research Institute
FMOH	Federal Ministry of Health
HIV	Human Immunodeficiency Virus
HBCs	High Burden Countries
INR	Isoniazid
TIC	Treatment initiative center
IRB	Institutional Review Board
IUATLD	International Union Against Tuberculosis and Lung Disease
MDR-TB	Multi Drug Resistant Tuberculosis
OR	Odds Ratio
RFC	Rifampicin
SHRE	Streptomycin, Isoniazid, Rifampicin, Ethambutol
TB	Tuberculosis
WHO	World Health Organization
XDR	Extensive Drug-Resistant

1. Introduction

1.1. Background

Tuberculosis (TB) is a major public health problem throughout the world. Approximately a third of the world's population is likely to be infected with tubercle bacilli and hereafter at risk of developing active disease. Recently, treating Tb is a challenge because of widespread resistance to multidrug-resistant tuberculosis and since MDR-TB is life-threatening(1,2).

Multidrug-resistant tuberculosis (MDR-TB) is a particular type of drug-resistant TB caused by Mycobacterium tuberculosis that is resistant to at least two drugs of the most powerful first-line treatment, rifampicin (RFC) and isoniazid (INH) and confirmed through laboratory tests that show that infecting isolates of mycobacterium Tuberculosis grow in vitro in the presence of one or more anti-TB drugs and XDR-TB is MDR as well as any fluoro quinolone, and any of the second-line injectable anti TB drugs (capreomycin, kanamycin, and amikacin)(3,4).

Patients infected with MDR strains are less likely to be cured of TB particularly if they are co-infected with HIV or suffering from other immune-suppressive diseases. MDR-TB is associated with a two to four-fold increase period of treatment, psychological problems, economic wastage, poor treatment adherence, and consequently treatment failure. It is also associated with higher case fatality rates (50 – 80%) as a result of drug toxicity(5).

According to the Global TB Report 2019, 10.0 million people are estimated to have fallen ill with TB in 2018 while an estimated 1.3 million people died of TB. An estimated 3.5% of these new TB cases and 18% of the previously treated cases had Drug-resistant- TB with an estimated 558000 cases of multidrug-resistant TB (MDR-TB) emerging in 2018 and with 8.5% of these being XDR-TB. Among all incident TB cases globally, 4.1% are estimated to have MDR-TB and this caused an estimated 230000 deaths globally, which accounts for 14% in 2017(6–8).

African nations are known to have the peak incidence rate of TB in the world; even at low magnitudes 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 world health organization (WHO) put the number of MDR-TB cases emerging in 2014 in Africa at 69 000(9).In 2019, the estimated incidence rate for TB was 140 per 100,000 populations and the mortality rate were 21 per 100,000 populations. In 2019, 111,039 TB cases were notified. MDR/RR-TB, estimated that 0.7% of new

cases and 12% of previously treated cases. MDR/RR-TB treatment was started in 708 patients, of which 75% were successfully treated in n2017 by WHO(6,10).

Ethiopia is one of the 22 high prevalence of MRD TB in the range of 3.3%-46.3% likewise, two studies reported XDR- TB in the range of 1%-4.4% in Ethiopia previous exposure anti-TB drug treatment was a most powerful predictor of rising MDR TB in Ethiopia this review indicated that MDR TB in Ethiopia is heartfelt open wellbeing issue that is addressed urgently(11).

The Emergency of MDR TB is one of the biggest public health challenges the world has ever seen in recent history. MDR-TB occurs due to different reason like improper management of drug supply, poor adherence, poor infection control practice, poor storage conditions, wrong dose or combination, poor management, lack of information, lack of monitoring treatment, inadequate implementation of DOTS strategy. It is difficult to manage; its treatment involves second-line anti-TB drugs that are more expensive and toxic than first-line drugs. Notwithstanding the emergence of MDR-TB has serious situation particularly in developing countries including Ethiopia(2,6,8).

However; the Regional 2011 EFY/2018-19 24 months cohort evaluation showed that of the total 152 cohorts of DR-TB cases started on long term second-line anti-TB treatment regimen 24 months earlier: one hundred ten(72%) were cured, and 9(6%) were completed with the TSR of 109 (72%). Among these 22 cases were died with a rate of 14%. Besides; the unfavorable treatment outcome registered 1(1%) was failed; 7(5%) were lost to follow up, and 3(2%) were not evaluated(12).

It is known that epidemiologic information on the Determinant of MDR-TB is important for the prevention and control of the spread of the disease in countries where drug resistance is a major threat. The disease is not only a medical problem or a public health problem but is also a critical social problem of great magnitude(13).

1.2. Statement of the problem

MDR-TB is a manmade problem cause of insufficient anti-TB treatment and the emergence of extremely drug-resistant TB further complicates the efforts to tackle the problem especially in developing countries including Ethiopia. MDR-TB remains a public health crisis and a health security threat and the MDR-TB diagnosis and appropriate treatment of the major challenges in Ethiopia(13).

MDR-TB was a gift worldwide in keeping with WHO, 2017 report it's believed that there have been 600,000 new cases with resistance to rifampicin - the foremost effective first-line drug, of that 484,000 had MDR-TB and therefore the international proportion of resistance among all cases was 4.1% and MDR/RR-TB caused 240 000 deaths in 2016. In 2018, an assessed 558 000 new cases of MDR/RR-TB emerge globally. MDR/RR-TB caused 230 000 passes away in 2017.in WHO report 2018, the most recent anti-TB drug resistance surveillance data show that 3.5% of new and 18% of previously treated TB cases in the world are assessed to have multidrug-resistant or rifampicin-resistant tuberculosis(14,15).

Globally, nearly half a million cases of MDR-TB emerge every year, but only 56% of them get treatment,15% of the patient died and treatment failed in 8% of the patient (21% were lost to follow up or not evaluated globally and 251,000 including HIV associated TB die annually in 2018. The MDR-TB burden largely falls on 8 countries: India, China, Indonesia, the Philippines, Pakistan, Nigeria, Bangladesh, and South Africa which together account for 66% of the global cases. About 6.2% of MDR-TB cases had extensively drug-resistant TB (XDR-TB) in 2018(16)(10).

Globally, 187 000 cases of MDR/RR-TB were detected and notified in 2018. A total of 156 000 were enrolled and ongoing on treatment with a second-line regimen. The treatment success rate at 56% remains low globally and more data on drug resistance have become available and estimates of the global MDR-TB burden have been improved(6).

Globally, 206 030 cases of MDR/RR-TB were identified and reported in 2019, signifying a 10% increase from 186 883 in 2018.High MDR-TB burden nations that made mostly good progress in increasing detection and enrolment of MDR/RR-TB cases on treatment included Angola, China, India, Indonesia, Mozambique, Nigeria, Papua New Guinea, and the Philippines. The global number of MDR/RR-TB cases notified in 2019 was 44% of the estimated 465 000 MDR/RR-TB incident cases in 2019(6,8,15).

MDR-TB did not receive main care until newly in sub-Saharan Africa. The TB incidence and risk factors are highest and known. Some of these risk factors are male sex in the young age group, presence of HIV infection, history of diabetes mellitus, history of known contact, alcohol use, malnutrition, socioeconomic status, and patients with history of anti-TB treatment. The odds of developing MDR-TB were higher in those with a history of contact with known TB patients, patients previously treated with anti-TB drugs, those living in a rural situation those with a history of alcohol consumption and those without a job(19).

The detection rate performance for both zones were less than 55 % (Jimma 53% and Illubabor 52%) from the regional annual report of 2011/2018 so that not surprising for emergence of MDR TB and Treatment outcome of confirmed TB were cure rate 86.1% and the highest treatment success rate was reported from West Wellega but, the lowest cure rate was reported from Jimma town which is 59 .8%.from treatment outcome was evaluated, a total of 607 were lost to follow up, while 420(69.2%) were Pulmonary TB cases. Additionally, from the TB case-cohort registered, a total of 903 (2 .23 %) have been reported to have died. Accordingly; of 396 DR-TB cases that have been planned to detect during the reporting period a total of 167(42%) DR- TB cases were detected from the eligible for DST and sent for Gen Xpert site. Among 167 cases detected, 154 were put on second-line treatment(12).

Hence, understanding most dominant determinants of the MDR-TB is urgently required to guide public health interventions that are both specific and effective and also it is used for plan and evaluation strategies on risk factors of MDR-TB is important for prevention and control of the spread of the disease in countries where drug resistance is a major threat. However, there is a lack of information in the study area in spite of incremental of MDR TB cases .Therefore, this study was aimed to identify determinants of MDR TB among tuberculosis patients in Southwest Ethiopia.

1.3. Significance of the study

The benefits of this study are clear, because it will generate comprehensive information on determinants. As one of the top burden countries of MDR-TB, the Ethiopian Federal Ministry of Health and its branches at regional and zonal levels are demonstrating commitments to alleviate the threats posed by MDR-TB in the country. Knowing the determinant factors of MDR TB is fundamental for the program manager and stakeholder for the prevention and management of MDR TB so epidemiological data are useful for the implementation of effective strategies for the prevention and control of MDR TB.

In general, as Ethiopia is one of the developing countries with a limited resource and facing high prevalence of MDR-TB cases, giving an appropriate solution to the developing problem with epidemiological assessment of the possible determinants of MDR-TB is the ultimate goal of the study.

Therefore, this study is aimed to assess the determinants of MDR TB. So the findings of the study helped South west and other similar settings to introduce measures that will contribute to the prevention program of MDR TB and it was utilized by respective program implementers and stakeholders would be benefited. It will also help as a baseline for further study in the area. Moreover, the study will be initiated further research to control MDR-TB.

2. Literature review

This section discusses literature conducted on the determinant of MDR-TB in Ethiopia and elsewhere. This section is assessing a determinant of MDR TB.

2.1. Determinants of MDR-TB

2.1.1. Socio -Demographic determinants associated with MDR-TB

A study conducted in China on Determinant of MDR TB since 2016, age and low family income(24), A study conducted in china 2016 (male sex, high school or lower education degree, unemployment, traveling by foot to reach the health facility and long distance of residence from the health facility(25)), In a study in Georgia, 2009 and 2009-2011years, female gender, (26) , A recent study was done in India also showed that being a female gender and among age, gender, employment, occupational status, and BMI were not significantly risked factors with MDR-TB(27), Study conducted in Croatia unmatched in 2013 years, case control in multiple logistic regressions, the lowest level of education and unemployment(28).

In a study conducted in south India in 2013, being employed in medical wards(29), in Belarus in 2013, age < 35 years(30), In a case-control study conducted in Serbia in 2018; monthly income of the family(31), In a Study Conducted in Pakistan in 2017 years ;Gender, residence(32), Study conducted in Croatia unmatched in 2013 years; the lowest level of education and unemployment(28), In a study conducted in south India in 2013; being employed in medical wards(29), study conducted in Belarus in 2013; age < 35 years(30), In a case-control study conducted in Serbia in 2018; : monthly income of the family(31), In a cross-sectional study design in china 2016, female subjects(33), In a Study Conducted in Pakistan in 2017 years ; Gender, duration of illness, residence(32), a study conducted in Yemen in 2013; place of residence, literacy, travelling time, waiting time, employment(34), A study conducted to in Ethiopia ,2019 years, education(35). A study conduct in Ethiopia, 2015; marital status, male gender, rural residence(36), Study conduct in Ethiopia 2017, age less than 25 year(protective)(37)(38), In a study conducted in Oromia, Ethiopia 2014 years, an occupation of farming, between 18 and 39 years of age(39), A case-control study conducted in the Amhara region, age between 26-45years old(40,41), A study conducted in Ethiopia on and risk factors in; age, sex residence, occupation, income, religion, fasting, education status, marital status were significant factors for MDR TB(42)(43), A study conducted in Ethiopia, Addis Ababa reports, young age being unemployed and monthly income(44)(13), A case-control study in Southern Ethiopia, patients with no formal education, but sex and age, not significant factors for of MDR TB(2)(45), A cross sectional study conduct in Ethiopia, economic status were independently associated with TB treatment non-

adherence(46). Study conducted in Ethiopia a tertiary armed force referral and teaching hospital sex and ages were not significant (21).

2.1.2. Environmental and house hold determinants associated with MDR-TB

A case control study Henan province in China 2016; social stigma not factors(47), A case-control study was conducted in Nepal in 2015; ventilation(not associated), social stigma(48), A Study conducted in Croatia unmatched in 2013 years; poor household equipment(28), study conducted in Belarus in 2013; history of imprisonment and disability sufficient to prevent work(30), In a case-control study conducted in Serbia in 2018; stigma associated with TB(31), In a Study Conducted in Pakistan in 2017 years ; delay, health care system delay, and total treatment delay, respectively(32), A study conducted in Yemen in 2013, living status, family support, stigma travelling time, waiting time, (34), A study a nationwide case-control conducted in Bhutan; frequently travelled in public transport(49), Study conduct in Ethiopia 2017; social stigma (37)(38), A case-control study conducted in the Amhara region, None disclosed tuberculosis-infected to relatives were identified predictors for MDR-TB infection in the study area(40,41), A study conducted in Ethiopia, Addis Ababa reports, Distance more than 25 km from TB treatment health facility(44)(13), A case-control study in Southern Ethiopia, time to reach health facility taking more than three hours significant factors for of MDR TB(2)(45). Distance to clinic >5km [(50)]A cross sectional study conduct in Ethiopia , perceived barriers were independently associated with TB treatment non-adherence(46).

2.1.3. Behavioral determinants associated with MDR-TB

A study conducted in China 2016;alcoholism(24), smoking, poor knowledge, having an opportunistic infection(25), A case-control study was conducted in Nepal in 2015; alcohol drinking habits and knowledge(48), Study conducted in Croatia unmatched in 2013 years contact with tuberculosis; current smoking habits(28), study conducted in Belarus in 2013; alcohol abuse and smoking(30), In a case-control study conducted in Serbia in 2018; subjective feeling of sadness(31), A study conducted in Yemen in 2013, Khat chewing and patients' knowledge of TB(34), A study conducted in Sudan case-control study; water pipe smoking(51), in a study conducted in Brazil in 2015 years, the cross-sectional study design ,smoking(52), in a study conducted in Brazil in 2015 years, the cross-sectional study design ; Among patients with TB, alcohol abuse was found to be a risk factor for the development of MDR-TB(53), A study conducted to in Ethiopia ,2019 years; cigarette smoking history ever(35). A study conduct in Ethiopia, 2015; being a current or past smoker(36), Study conduct in Ethiopia 2017, have depression(37)(38), In a study conducted in Oromia, Ethiopia 2014 years, alcohol use were predictors of MDR-TB(39), A case-control study conducted in the Amhara

region, insufficient instruction on how to take anti-TB drug, alcohol drinking habits were identified predictors for MDR-TB infection in the study area(40,41); A study conducted in Ethiopia on and risk factors in , presence of TB-associated stigma and alcohol consumption(44)(13), A case-control study in Southern Ethiopia , patients who didn't get counseling, patients who didn't hear about MDR-TB, significant factors for of MDR TB(2)(45). A cross sectional study conduct in Ethiopia; alcohol use were independently associated with TB treatment non-adherence(46), A study conducted in china Henan province ; smoking(47). In a study done in Ethiopia social stigma were significant(18).

2.1.4. Clinical features TB and comorbidity illness related determinants of Multi drug resistance TB

A study conducted in China 2016, anti-TB treatment history, retreatment, multiple episodes of treatment, adverse reactions, interrupted treatment and lung cavities(24), A case control study Henan province in China 2016, more than 3 TB foci in the lungs, total time of first treatment was more than 8 months, adverse effects of anti-TB medication and more than 3 prior episodes of anti-TB treatment(25), another study in the years 2013 in china , poor outcomes, a BMI less than 18.5 kg/m², retreatment, diabetes, tumor, decreased albumin and cavitation(54), In a study in Georgia, 2009 and 2009-2011 years: , previous TB treatment, HIV-co-infection(26). A study Conducted in India Smoking(55). A case-control study was conducted in Nepal in 2015; knowledge on DOTS Plus , Study conducted in Croatia unmatched in 2013 years; diabetes, being underweight in the previous year and former(28), In a study conducted in south India in 2013; body mass index (BMI) and having frequent contact with patients(29), study conducted in Belarus in 2013; A history of previous treatment for TB and virus (HIV) infection(30), In a case-control study conducted in Serbia in 2018; defaulting from treatment, use of sedatives and chronic obstructive pulmonary disease(31), In a cross-sectional study design in china 2016, BMI (33), In a Study Conducted in Pakistan in 2017 years; co-morbidity, and past TB treatment(32), A study conducted in Sudan case-control study; history of previous TB treatment, interruption of TB treatment, contact with MDR-TB patients and lower body weight(51), in a study conducted in Brazil in 2015 years, the cross-sectional study design; history of previous treatment, re-entry after abandonment(52). Study conducted in History of previous treatment in the major determinant (20). In a study done in Ethiopia previous history of treatment, history of hospitalization were significant(18).

A study a nationwide case-control conducted in Bhutan, previous TB treatment(49), A study conducted to in Ethiopia ,2019 years, (HIV) positive status, previous contact history with TB patient and body mass index (BMI) of ≤ 18 (35), A study conduct in Ethiopia, 2015; BMI < 18, HIV

infection and a history of worm infestation remained significant independent host-related factors for active PTB(36), Study conduct in Ethiopia 2017, contact history with a known TB, previous history of TB treatment, history of hospitalization, sputum-smear positivity(37)(38), In a study conducted in Oromia, Ethiopia 2014 years, known TB contact history, HIV infection, previous known TB history, and previous TB treatment outcome were predictors of MDR-TB(39), previous history of TB treatment, contact history with MDR-TB, interruption of first-line anti-TB treatment for at list 1 day were identified predictors for MDR-TB infection in the study area(40,41), A study conducted in Ethiopia on and risk factors in; previous history of TB treatment, HIV infection was less common among cases than controls(42)(43). cavitation on chest x-ray ,treatment failure and contact with MDR-TB patients(44)(13), A case-control study in Southern Ethiopia, history of contact with known MDR-TB patients, A cross sectional study conduct in Ethiopia; psychological distress, Antiretroviral Therapy (ART) status and psychological distress were independently associated with TB treatment non-adherence(46). a study conducted in Ethiopia, retreatment factors(13,23,55). A study conducted in Ethiopia retreatment factors(56). Study conducted in Ethiopia a tertiary armed force referral and teaching hospital retreatment cases were identified and BMI not significant (21). A recent study conducted in Ethiopia by 2017, the systematic review and meta-analysis among the new cases was 12.6%, and among previously treated patients was 27.2%(22,23).

2.2. Conceptual framework

There are multiple determinants of multi drug Resistance Tuberculosis. It is not a humble problem with a single and simple solution that causes multi drug Resistance Tuberculosis Various and interrelated determinants are involved in why it develops. The conceptual frame work below shows this inter related factors associated with MDR TB. For this study, the determinant factors are grouped in four classes; namely Socio -Demographic determinants, Environmental and house hold determinants, Behavioral determinants and Clinical features TB and comorbidity illness related determinants. Each of the factors with their constructs are linked with MDR TB as well some of them are related with each other as seen by the direction of relationship.

Mostly, studies reviewed from different countries on determinants of MDR-TB showed that history of previous treatment, gender, age, residence, HIV status, diabetes mellitus, smoking, low BMI, type of TB affect, stigma ,and alcohol drinking showed different findings in a different study conducted so far in various parts of the world. This study used a guiding framework the study which shows factors that are considered to be determinants of MDR-TB (Figure 1).

Conceptual framework for determinants

Socio demographic Determinants

- Age
- Sex
- Education status
- Marital status
- Occupational
- Monthly Income
- Residency

Clinical and morbidity determinants

- History of previous treatment TB
- Contact history of TB/MDR-TB
- History of drug interruption
- Traditional treatment
- History of the Retreatment
- HIV infection
- Hospitalization
- Malnutrition (BMI)
- Psychological illness

MDR TB

ENVIRONMENTAL DETERMINANTS

- Presence of window
- Number of the window
- Numbers of the Rooms
- Open window daily
- Distance (Km)
- Living situation

Behavioral Determinant

- Stigmatized
- Smoking
- Alcoholism
- Chat chewing
- Social stigma
- Counseling and
- Hearing about MDR TB

Figure 1: Conceptual framework for the assessment of determinants of MDR-TB among TB patients in Southwest, Ethiopia, 2021 **Source:** Adapted from more than 25 Literatures

3. Objectives

- ❖ To assess determinants of multidrug-resistant tuberculosis (MDR-TB) among tuberculosis patients in southwest Ethiopia.

Research Question

- ❖ Does Determinant MDR TB among tuberculosis patients increase the risk of MDR-TB?

4. Methods& Materials

4.1. Study area and period

The study was conducted in Jimma Zone, one of the 20 zones found in the Oromia regional state. The capital town of the zone is Jimma Town, located in the South West of Ethiopia with a distance of 352 km from the capital city of Ethiopia, Addis Ababa. Jimma has 3 general hospitals, 5 primary hospitals and 122 health centers. Jimma town has currently public health care setting found in the town includes four health centers, one General hospital and one specialized hospital offering services to the residents of the town and the surrounding community. The hospital was built in 1992. Another study area was conducted in the Illubabor zone, one of the 20 rural zones in Oromia regional state. The capital town of the zone is Mettu town, located in the southwest of Ethiopia with a distance of 600km from the capital city of Ethiopia; .Illubabor has 2 Hospitals and 26 Health centers. The Hospital was referral hospital for the region, including Gambela. It is government-run but built by the German NGO “Menschen fuer Menschen.” It is named after the founder of the NGO, Karl Heinz Boehm. Currently, it serves as a teaching and health care providing center for the region. Mettu, located in the Illubabor Zone of the Oromia Region along the Currently, MDR-TB diagnosis and treatment services were entitled to selected regional hospitals. Accordingly, only four hospitals render these services in the southwest, which are Shenen Gibe General hospital, Mettu Special Hospital, Gambela Referral Hospital, and Mizan tape university teaching hospital respectively. According to data from Oromia regional health bureau, Shenen Gibe General hospital and Mettu Specialized Hospital is found in Jimma town and Mettu town serving as the MDR-TB center for the southwestern part of Ethiopia specifically for the Jimma zone and Illubabor zone. The case of MDR TB emerged in 2004 at the Jimma zone Level and the patient treatment center was in Addis Ababa in Alert Hospital. So that the distance of the Treatment center defaulter is increase. Then it established treatment initiation center southwest July11/2005(2013) by Oromia Health Bureau, ever enrolled 107 and 15 patients are transferred from other and Current MDR TB on Treatment 38 and Mettu specialized Hospital was established 2008(2017) as TIC, current MDR TB patient 32 from them 2 default,30 are on Treatment.

The study was conducted between January 13, 2021, to June 30, 2021, among Shenen Gibe General Hospital and Mettu Special hospital respectively.

Map of Study Area South west Ethiopia 2021

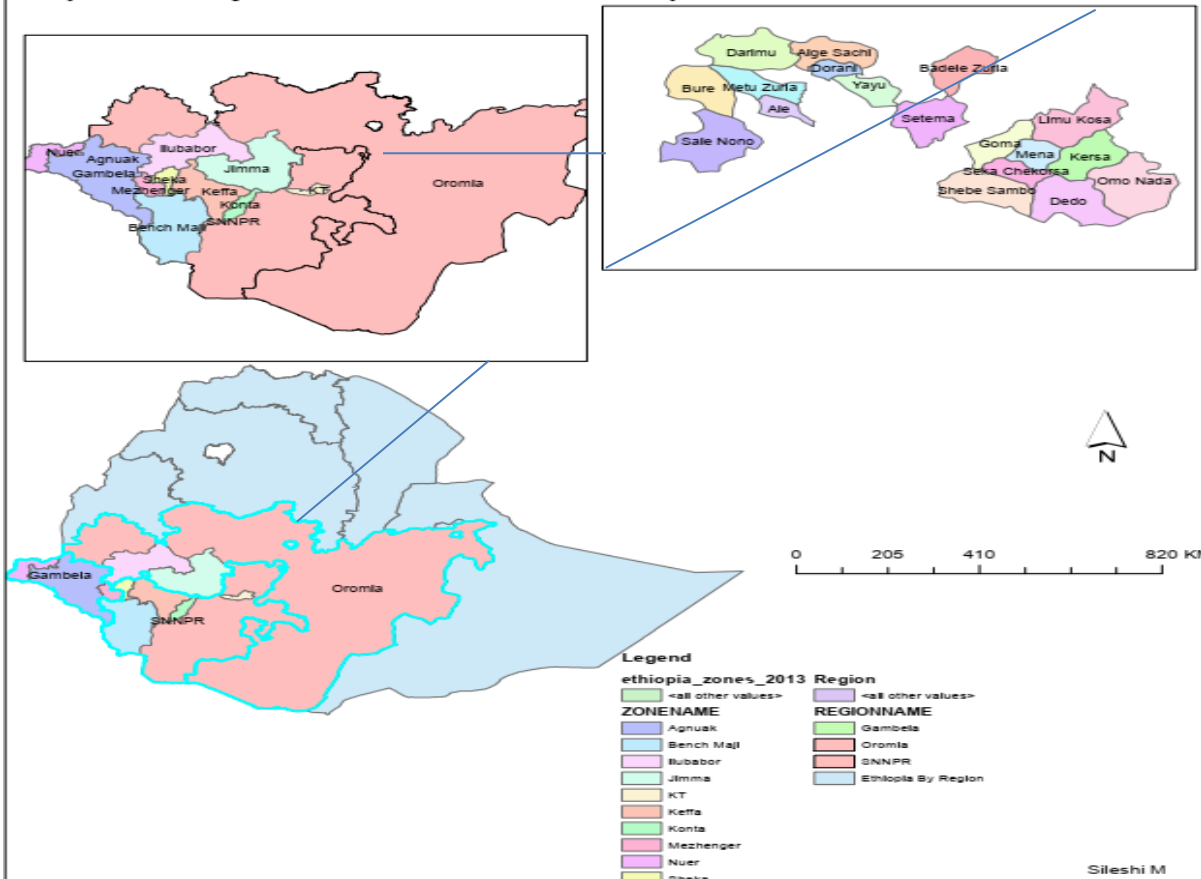


Figure 2:-Map of woreda Report on MDR TB Jimma zone 2021(Arc Gis, 2021)

4.2. Study design

Facility-based unmatched case-control study design was used.

4.3. Population

4.3.1. Source population

The source population for the cases was all MDR-TB patients in Shenen Gibe General Hospital and Mettu Karl special Hospital

The source population for the controls was all TB patients visiting a Health facility, which developing MDR-TB, which means exposure, occurred at Health centers.

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 courses

4.4. Eligibility Criteria for case and control

4.4.1. Inclusion criteria

Cases

- Bacteriologically confirmed pulmonary TB patients for MDR TB enrolled for treatment.
- Registered in the study site and fulfilled the definition of cases were included in the study.
- New patients were included when they were diagnosed with MDR-TB
- Age greater than 15 years

Controls

- Non-MDR-TB patients who were susceptible to first-line TB drugs and registered as cure or treatment completed Using WHO criteria and adopted by FMOH from health facilities selected
- Age greater than 15 years

4.4.2. Exclusion criteria

Cases

- A patient who had documented as a transfer out and with incomplete documentation/registration
- The patient who had completed the treatment 2 years before the data collection period
- Being confirmed XDR patients

Controls

- All health facility controls with the clinical sign or symptom suggestive of TB

4.5. Sample size and sampling procedures

4.5.1. Sample size

The sample size was calculated using Epi Info version 3.4.1 with the application of Fleiss sample size calculation formula for unmatched case-control study; By using the following assumption calculate sample size probability that if two population sample differs to reflect a true difference in the confidence interval of 95%, the probability of two populations differs, the two samples showed a significant difference (Power) of 80%, the ratio of the control to case ratio of 2: 1, percent of control exposed 35.3 and percent of cases exposed 61.2(13).

Table 1:- Sample size determination for the study of determinants of MDR TB among tuberculosis patients in in South west, Ethiopia, 2021

s.n	Variable	Z $\alpha/2$	Power	Ratio of control to case	AOR	Controls exposed	NRR 10%	case	Total
1	smoking (55)	1.96	80%	2	2.56	35.3%	6	61	67
2	Treatment failure (13)	1.96	80%	2	13.5	43.1%	2	14	16
3	Previous treatment(25)	1.96	80%	2	4.51	43.82%	3	28	31
4	Drinking habit (40)	1.96	80%	2	5.1	8.2%	4	37	41
5	Heard about MDR(45)	1.96	80%	2	4.18	66.7%	5	48	53

The sample size was calculated by using two population proportion formulas. Where (55).Therefore, the required sample size was calculated as follows

$$Z\alpha/2 = 1.96$$

$$Z\beta = \text{power } 80\% = 0.84$$

p1 = proportion of exposure among controls 35.3%

r = ratio of controls to cases =2 AOR=2.56(55).

Accordingly, the minimum sample size for cases was 61 and for controls 122 Adding 10 % for possible non-response rate, a sample size of 67cases and 134 controls was computed. Hence, the total sample size was **201**.

4.5.2. Sampling procedures

MDR-TB patients enrolled in second-line drugs at Shenen Gibe General Hospital and Mettu Specialized Hospital from 2020 to 2021 were taken as cases; all cases were used to be included as study subjects from the list of MDR-TB patients register While Controls were also selected from selected health facilities from both zones(from Jimma 14 health facilities from 18 total health facilities encountered with MDR TB in the zone were selected by Simple random sampling and from Illubabor Zone 8 health facilities were selected from 10 total facilities which developing exposure of MDR TB). The exposure MDR TB started from health centers and referred to Shenen Gibe General Hospital TIC and Mettu Specialized Hospital TIC and TB register was adjusted for controls meet inclusion criteria were made.

Finally, controls were randomly selected by a simple random sampling technique method from selected health facility. Most of the MDR-TB cases received their first-line TB treatment in these health centers. The TB patients were selected based on a load of TB cases in the facilities. For each DR-TB case, we selected two controls.

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 before collection of data and the registration books of patients who are diagnosed for MDR-TB and currently on treatment were used as a baseline source of information to prepare the sampling frame in each study facility.(Figure 3).

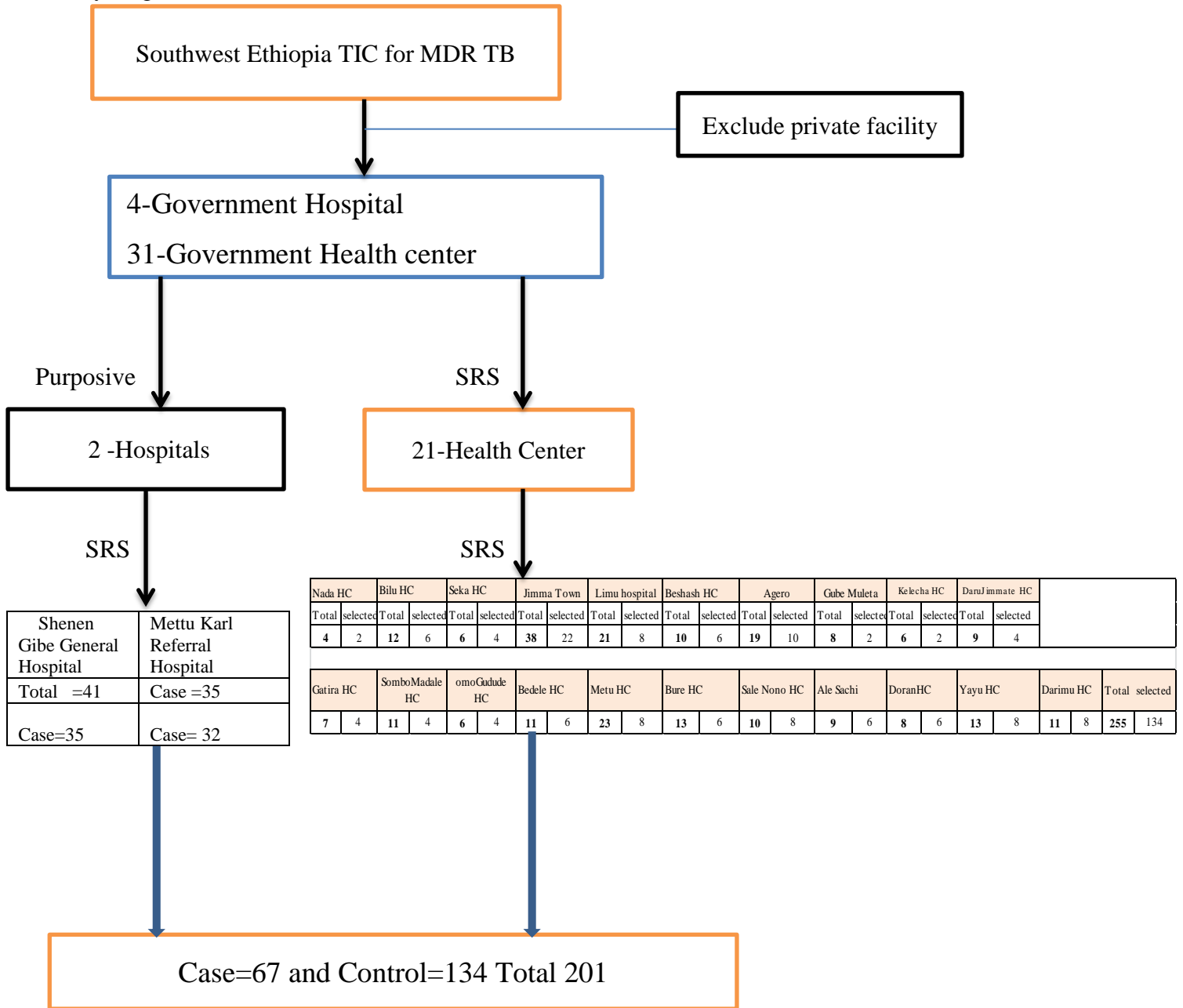


Figure 3: Schematic representation of sampling procedure to assess determinants of multi drug resistant tuberculosis among tuberculosis patients in in South west, Ethiopia, 2021

4.6. Study Variables.

4.6.1. Dependent variables

MDR-TB

4.6.2. Independent variable

Socio-demographic Determinants variables: Age, sex, education status, religion, ethnicity, marital status, income, occupational status and residence

Environmental and household Determinants variables: Living situation, Owner of the House, Numbers of Rooms, Is there a window? Number of window, Open window daily, Wall Type, Distance (Km)

Behavioral Determinants variables: Cigarette smoking, History of alcohol use, History chat chewing, History of illicit drug use, Counseling patients, Hearing about MDR TB and Perceiving stigmatized

Clinical characteristics of TB and Co-morbid illness determinants variables: History of contact TB, Contact of MDR-TB patients, History of previous TB treatment, Number of previous treatment, History of retreatment, Direct observed by health worker while taking anti-TB, If yes, how many months, History of drug interruption at least a day, The first to be infected with TB, History of hospitalization, Cavitation using chest radiography (previou TB), HIV infection, psychological illness and malnutrition status (BMI(kg/m²))

4.7. Operational /standard definitions

- ❖ **New patient:** A patient who has received no or less than one month of anti TB treatment.
- ❖ **History contact with MDR-TB cases-** was measured by asking the respondents if he has ever had contact with MDR-TB patients before.
- ❖ **Primary resistance:** Patients with TB resistant to one or more anti-tuberculosis drugs, but who have never been previously treated for TB, are said to have “primary resistance.”
- ❖ **Acquired resistance:** Patients diagnosed with TB who start anti-tuberculosis treatment and subsequently acquire resistance to one or more of the drugs used during the treatment are said to have developed “acquired resistance
- ❖ **Co-morbid illness:** in this study, it is defined as diseases that have been diagnosed in patients who have TB and these include having HIV AIDS, diabetes mellitus, and experience of any psychological illness(depression, anxiety, and psychoses) encountered in the patient
- ❖ **Alcohol consumption:** taking alcoholic drinks till he/she is drunk at least once in a month.
- ❖ **Smokers:** smoking one or more cigarette per day before the diagnosis of TB.

- ❖ **Stigma** were the mark of disgrace that sets a person apart from others which includes isolation, discrimination, lack of social support, and distress
- ❖ **Illicit drug use:** is the ever use of a drug such as cocaine, heroin, etc., which are under international control and produced, handled, and consumed illegally.
- ❖ **BMI:** is a person's weight in kilograms (kg) divided by his or her height in meters squared before starting MDR Treatment BMI of (17.00-18.49), (16.00-16.99), and (<16) were considered as mild, moderate, and severe malnutrition according to WHO Criteria
- ❖ **Under nutrition :-** The body mass index less than 18.5 kg/m²
- ❖ **Counseling** is a method of professional guidance of the individual that helps the client to use solves the problem–solving process to recognize and manage stress and facilitate interpersonal relationships among the client, family, and health care team.
- ❖ **Distance** from the nearest treatment center from less than 25km and greater than 25km
- ❖ **Others:** which includes single, widowed and divorced in certain cases

4.8. Data collection technique and procedure

Data were collected by using an interviewer-administered structured questionnaire and clinical record review (Variable, like HIV status, Category patient, Types of TB infection, History previous Treatment, Treatment outcome, current episode, and chest radiology). The questionnaire included socio-economic data, history of known MDR TB contact, HIV co Infection, and another determinant with MDR TB.

The interviews were conducted for MDR-TB patients in their particular 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. The English version questionnaire was translated into Afan Oromo and Amharic language and then back-translated to English by language experts to check its consistency. Data collectors were by eighteen health professionals (8 BSc nurses, 6 health officers and 4 Clinical Nurse) recruited from the facility out TB department of selected hospitals and health centers. Two additional supervisions were involved in activities. The training was given to data collectors and supervisors on the method of extracting the relevant data through interviews and reviewing the patient's records. How to fill in the information on a structured questionnaire, the ethical aspect of approaching the patients, and keeping the confidentiality of their information was another focus of the training. The supervisors have monitored the data collection process of the interviewers and taken corrective measures with the consultation of the principal investigator. During recruitment, information pertinent to the study was informed to patients and a structured and interviewer-administered questioner was used (see Annexes).

Concerning the safety precaution to prevent the risk of infection to the data collectors and supervisor, were used a ventilator especially N95, which is a mask that covers the mouth and nose so that it filters more than 95% of particles. A surgical mask was used on the patient side, which prevents the spread of microorganisms from the wearer to others by capturing the large wet particles near the mouth, which was another important precaution measure taken.

4.9. Data quality control

To assure the quality of data, both data collectors and supervisors were given one days of training. Before the actual data collection process, 5% of participants were pre-tested in a similar setting but those were not participating in the study. Accordingly, based on feedback from the pre-test the questionnaires were revised. The Data collectors were submitted the collected data daily to supervisors and principal investigators. Each questionnaire was checked by supervisors on daily basis for completeness and consistency. The Completed questionnaire was rechecked by the principal investigator were followed the overall data collection activities closely and checked for completeness and consistency before data entry. Data were coded before data entry. When inconsistency happens to the data, it was checked again referring to the hard copy questionnaire. Finally, data analyses were begun after the completion of the cleaning process.

4.10. Data Processing and Analysis

The data were checked for completeness, cleaned, coded, and entered using Epi-Data version 3.4 and then exported into SPSS version 24, software used for analysis. Descriptive statistical techniques were used to obtain summary values for cases and controls separately. Bivariable analyses were performed to identify the association of dependent and all independent variables. Those variables, which had a p-value of less than 0.20 in Bivariable analysis, were entered in a back ward stepwise logistic regression procedure for multivariable logistic analyses in order to assess the independent predictors of multidrug-resistant TB among the study participants. Absence Multi Collinearity tests were done using variance inflation factor (VIF) and no Collinearity exists between the independent variables The VIF values of all the variables were less than 10 in the final model suggesting that multi-Collinearity was not a concern in the analysis. The model fitness for variables was assessed by Hosmer Lemeshow Goodness of fit test to for the model adequacy. The test revealed that our model fitted the data well (Pearson's $\chi^2 = 99.976.1$; $p = 0.99$). Level of Statistical significance was declared at P-value < 0.05. Finally, the findings were presented by narration and tables.

4.11. Ethical considerations

Ethical clearance was obtained from the Institutional Review Board (IRB) of the Institute of Health, Jimma University. Permission letter to conduct the research was obtained from Jimma Zone Health Office, Jimma Town Health office, and Illubabor zone health office. Before data collection, the participants were informed about the purpose of the study, their right to refuse participation, and discontinue the interview or measurement. Informed consent was obtained from each participant before the interview to confirm willingness for participation. All the information obtained from each study participant was kept confidential throughout the process of this study. Besides, any identifying information including the name of the participant was being not written on the questionnaire.

4.12. Dissemination of findings

The findings of this study will be submitted to Jimma University, Department of Epidemiology, Jimma Zone Health office, Shenen Gibe General Hospital, and Mettu Karl Special and will be communicated to the local office of the study area. It will be further communicated at different scientific conferences and workshops. Additional efforts will be made to publish the findings in an international journal.

5. Result

5.1. Socio-demographic Characteristics

Of 201 participants selected, 200 study subjects were responded (66 (33%) cases and 134(67%) controls) with over all response rate of 96.7 % (98.5 % for cases and 100% for controls).

Among the respondents 31(47%) cases and 85(63.4%) controls were males and the rest were females. Twenty-three (35%)cases were found between the ages of 25 and 34, followed by the age group of 15 to 24,19(28.7%), the lowest in the age group of cases 10(15%) were greater than 45 age and controls 11(8%) were 15 to 24 and associated age groups 30(15%)For MDR TB ($p = 0.002$). The means (standard deviation) of age among cases 31.5 (13.4) years and 37.2 (12.1) for the controls group were respectively. The mean monthly income of the cases and the controls was 1110 birr and 1385 and with SE of 110 and 593 respectively. There is a statistically significant mean difference between the monthly admissions of the cases and the controls ($p = 0.002$) Religion and occupation that there is no significant difference between case and control. However, there are significant changes in Sex, age, educational level, Residence and income (Table 2).

Table 2:- Socio-demographic characteristics of with MDR-TB, in South west Ethiopia, April 2021.

Variable	Cases		Controls		
	N=66	%	N=134	%	
Age	15-24	19	28.7	11	8
	25-34	23	35	48	36
	35-44	14	21	50	37
	>45	10	15	25	19
Sex	Male	31	47	85	63.4
	Female	35	53	49	36.6
Marital Status	Current married	31	46.9	81	60.4
	Others	35	53.1	53	39.6
Religion	Muslim	30	45.5	67	50.0
	Orthodox	19	28.8	30	22.4
	Protestant	17	25.8	37	27.6
Educational status	Illiteracy	12	18.7	27	20.2
	Read and Write	15	21.1	50	43.9
	Primary school	14	18.2	42	37.8
Occupational status	Secondary school	25	37.8	15	11.1
	Employed /Gov't	10	15	12	9
	Un employed	20	30	75	56
	Daily Labor	12	18	17	13

		Merchant	11	17	20	15
		Student	13	20	10	7
Residence		Urban	37	41.6	52	58.4
		Rural	29	26.1	82	73.9
Monthly family income		<500	19	28.8	68	50.7
		501-1000	33	50.0	56	41.8
		>1001	14	21.2	10	7.5
Living situation		Alone	14	21.2	20	14.9
		With family	52	75.7	114	85

* P value <0.05 Variables that showed significant association during bivariate analysis

5.2. Determinants for MDR-TB

5.2.1. Results of Bivariable analyses on Socio-demographic determinants associated with MDR-TB

The 20(30%) cases and 75(56%) of the controls were the unemployed, 12(18%) of the cases and 17(13%) of controls participant were daily labor and 13(20%) of the cases and 10(7%) of control were students. Forty-two percent of the cases and 58.4% of the controls resided in urban areas and 12.3% of the cases and 26.7% of the controls were illiterate. The odds of being age 25-34 were 4.3 times higher among cases than the controls and this shows a significant association between the two groups (COR=4.3).

Table 3: Results of Bivariable analyses on Socio-demographic determinants associated with MDR-TB

Variables	Case		Control		COR(95%,CI)	P-value	
	N=66	%	N=134	%			
Age	15-24	19	28.7	11	8	1	0.002
	25-34	23	35	48	36	4.3(1.52-12.26)*	0.006
	35-44	14	21	50	37	0.49(1.19-2.90)	0.69
	>45	10	15	25	19	0.7(0.23-1.79)	0.46
Sex	Male	31	47	85	63.4	1	
	Female	35	53	49	36.6	1.9(1.08-3.56)*	0.028
Marital Status	Current married	31	46.9	81	60.4	0.58(0.32-1.05)	
	Others	35	53.1	53	39.6	1	0.072
Religion	Muslim	30	45.5	67	50.0	1	
	Orthodox	19	28.8	30	22.4	1.41(0.69-2.90)	0.34
	Protestant	17	25.8	37	27.6	1.02(0.50-2.10)	0.94
Educational	Illiteracy	12	18.7	27	20.2	0.27(0.11-0.68)*	0.001
	Read and Write	15	21.1	50	43.9	0.18(0.08-0.43)*	0.001
	Primary school	14	18.2	42	37.8	0.20(0.08-0.48)*	0.001

status	Secondary school	25	37.8	15	11.1	1	
	Employed /Gov't	10	15	12	9	1	
Occupational status	Un employed	20	30	75	56	0.32(.12-0.85)*	0.02
	Daily Labor	12	18	17	13	0.84(0.28-2.59)	0.77
	Merchant	11	17	20	15	0.66(0.22-2.05)	0.47
	Student	13	20	10	7	1.6(0.48-5.01)	0.46
Residence	Urban	37	41.6	52	58.4	2.1(1.18-3.90)*	
	Rural	29	26.1	82	73.9	1	0.013
Monthly family income	<500	19	28.8	68	50.7	0.20(0.08-0.52)*	0.001
	501-1000	33	50.0	56	41.8	0.4(0.168-1.056)	0.065
	>1001	14	21.2	10	7.5	1	

NB: *P-value < 0.05 Variables that showed significant association during bivariate analysis

5.2.2. Bivariable on Environmental and household determinants associated with MDR-TB

The study had depicted that 51 (69.6%) of cases and 118 (88.1%) of controls had an owner of the house to live in and among the respondents, 49(82.5%) of the cases and 107(86.9%) of the controls had a presence of window used for refreshment in the household while 14(22.2%) of cases and 12(11.9%) controls were had less than one windows a household. Of these, 21(31.8%) of the cases and 94(72.7%) control had to go greater than 25km distance to take their drugs allocation from the treatment center. Nearly two-thirds of the 52 (75.7%) and 114 (85%) controls and cases lived with their family, and 10 (15.6%) of the cases and 14 (15.1%) lived alone (Table 2).

Table 4:- Results of Bivariable analyses on Environmental and household features associated with MDR-TB in South west Ethiopia, June 2021.

Variables		Cases (N=66) (%)		Controls (N =134) (%)		COR(95%,CI)	P value
Living situation	Alone	14	21.2	20	14.9	1	
	With family	52	75.7	114	85	0.65(0.31-1.39)	0.260
Owner of the House	Yes	51	69.6	118	88.1	1	0.051
	No	15	29.4	16	11.9	2.2 (0.99-4.72)	
Numbers of Rooms	<2	42	67.7	53	43.1	2.8(1.46-5.27)*	0.001
	>2	20	32.3	70	56.9	1	
Is there a window?	Yes	49	82.5	107	86.9	1	0.106
	No	14	17.5	16	13	1.9(0.87-4.22)	
Number of window	0-1	14	22.2	12	11.9	2.6(1.14-6.13)*	0.028
	>2	49	77.8	111	88.1	1	

Open window daily	Yes	49	77.8	110	89.5	1	0.033
	No	14	22.2	13	10.5	2.4 (1.06-5.53)*	
Wall Type	Cement	14	22.2	13	10.6	1	0.036
	Mud	49)	78.8	110	89.4	2.4 (1.06-5.52)*	
Distance (Km)	<25km	45	68.2	38	28.4	1	0.001
	>25km	21	31.8	94	72.7	5.3(2.8610.27)*	

NB: *P-value < 0.05 Variables that showed significant association during bivariate analysis

5.2.3. Bivariable analysis of the Patients health problem and Behavioral factors associated with MDR-TB

The study participants were assessed for convincing behavioral aspects and the relevant results were given consequently. Twenty (30.3%) cases and 70 (52.2%) controls were smokers. A total of 22(33.3%) cases and 10(7.5%) controls had experience of alcohol consumption (Table 3). Of the total 30, (45.4%) of the case and 34(25.4%) controls had been chat chewer. (Table 5)

Table 5:-Results of Bivariable analyses on Patient's health problems and Behavioral determinants associated with MDR-TB in South west Ethiopia, June 2021.

Variables		Cases (n=66)		Controls (n=134)		COR(95% CI)	P value
		n	%	n	%		
Cigarette smoking	Yes	25	37.9	60	44.7	0.39 (0.21- 0.74)*	0.004
	No	41	62.1	74	55.3	1	
History of alcohol use	Yes	22	33.3	10	7.5	6.2(2.73-14.12)*	0.001
	No	42	63.6	124	92.5	1	
History chat chewing	Yes	30	45.4	34	25.4	2.4(1.34-4.56)*	0.001
	No	36	54.6	100	74.6	1	
History of illicit drug use	Yes	12	22.2	10	7.5	2.8(1.12-6.76)*	0.028
	No	54	78.2	124	92.5	1	
Counseling patients	Yes	47	71.2	118	88.8	1	0.004
	No	19	28.7	16	11.9	3 (1.41-6.29)*	
Hearing about MDR TB	Yes	56	84.8	83	61.9	1	0.001
	No	10	15.2	51	38.1	3.7 (1.72-7.81)*	
Perceiving stigmatized	Yes	35	53.1	34	23.4	3.3 (1.76-6.18)*	0.001
	No	31	46.9	100	74.6	1	

NB: *p <0.05 Variables that showed significant association during bivariate analysis

5.2.4. Results of Bivariable analyses on Clinical features of TB and comorbidity /illness related determinants associated with Multi drug resistance TB

Among the study participants 15(22.7%) cases and 12(8.9%) controls had a history of contact with TB patients. Among 66 MDR TB cases, 19(25.7%) and 16(11.9%) controls were in close contact with MDR TB at neighborhoods and in family. A total of 41(62.1%) cases and 27(20.1%) controls had a history of previous treatment for TB. Forty-eight (73.8%) cases and 13(8.9%) controls had pulmonary cavitation in their chest radiography during previous treatment of TB.

The result also indicated 55(83.3%) cases and 33(24.6%) of controls had a history of retreatment. The result also indicated, 18 (26.8%) of cases and 11(8.2%) of controls had a history of drug interruption. Eleven (28.8%) cases and 7(3.7%) controls had a history of experiencing any psychological illness. A total of 16(24.2%) cases, and 17(12.7%) controls had a history of HIV infection (Table 4).A total of 27 (40.9%) cases and 17(12.7%) controls had underweight for their nutritional status (BMI) before starting treatment. (Table 6)

Table 6:- Results of Bivariable analyses on Clinical features of TB and co morbid /illness related determinants associated with MDR-TB in South west Ethiopia, June 2021

Variables		Cases (n=66 %		Controls (n=134) %		COR, (95% CI)	P value
History of contact TB	Yes	15	22.7	12	8.9	2.9 (1.31-6.83)*	0.007
	No	51	77.3	122	91.1	1	
Contact of MDR-TB patients	Yes	19	28.8	16	11.9	2.8(1.12-6.29)*	0.003
	No	47	71.2	118	88.1	1	
History of previous TB treatment	Yes	41	62.1	27	20.1	6.5(3.38-12.48)*	0.001
	No	25	39.9	107	89.9	1	
Number of previous treatment	<2	28	42.4	108	75.4	1	0.001
	>2	38	57.6	25	24.6	5 (2.66-9.46)*	
History of retreatment	Yes	55	83.3	33	24.6	15(7.18-32.63)*	0.001
	No	11	16.7	101	75.9	1	
Direct observed by health worker while taking anti-TB	Yes	51	79.3	123	92.8	1	0.022
	No	15	22.7	11	8.2	3.3(1.42-7.65)*	
If yes, how many months	Weeks	28	42.4	79	58.9	1	0.424
	One month	21	31.8	45	33.6	1.3(0.67-2.58)	

	Two months	17	25.8	10	7.5	4.8(1.96-11.71)*	0.001
History of drug interruption at least a day	Yes	18	26.8	11	8.2	4.2(1.85-9.53)*	0.001
	No	48	74.2	123	92.8	1	
The first to be infected with TB	Yes	35	49.9	120	89.6	1	0.001
	No	31	50.1	14	10.4	7.6(3.64-15.83)	
History of hospitalization	Yes	32	30.3	42	31.3	2.0(1.13-3.78)*	0.018
	No	34	57.6	92	68.7	1	
Cavitation using chest radiography (previou TB)	Yes	48	73.8	13	9.7	26 (11.86-58.24)*	0.001
	No	17	26.2	121	91.3	1	
HIV infection	Reactive	16	24.2	17	12.7	2.2 (1.03-4.70)*	0.038
	No reactive	50	75.8	118	87.3	1	
	Yes	11	28.8	7	3.7	3.6(1.34-9.85)*	0.011
psychological illness	No	55	71.2	127	96.3	1	
BMI(kg/m ²)	Under weight	27	40.9	17	12.7	4.8(2.35-9.66)*	0.001
	Normal	39	59.1	117	87.3	1	

NB: * Variables that show significant association (p< 0.05)

5.3. Determinants of Multi-Drug Resistance TB

All variables which had p value less than 0.20 during the Bivariable analyses. such as Sex, residence, Absence of windows, Number of windows, not opening windows daily, social stigma, Distance, Ever got counseling, Cigarette smoking, Alcohol consumption, Drug Illicit, Hearing about MDR TB, contact of known MDR TB patient, history of drug interruption at least a day, history of previous TB treatment, History treatment under DOTs follow, history of previous retreatment TB, , Directly observed by health worker while taking anti-TB, history of hospitalization, HIV infection, history of any psychological illness, and malnutrition(BMI).

Table 7:- Candidate variable for multivariate logistic regression analysis of factors associated with MDR-TB in Southwest, Ethiopia, and June 2021.

Variables	Case		Control		p. value	
	N=66	%	N=134	%		
Sex	Male	31	47	85	63.4	
	Female	35	53	49	36.6	0.028
Residency	Urban	37	42	52	58.4	
	Rural	29	26	82	73.9	0.013
	Yes	49	77.8	110	89.5	0.033

Open window daily	No	14	22.2	13	10.5	
	<25km	45	68.2	38	28.4	0.001
Distance (Km)	>25km	21	31.8	94	72.7	
	Yes	25	37.9	60	44.7	0.004
Cigarette smoking	No	41	62.1	74	55.3	
	Yes	22	33.3	10	7.5	0.001
History of alcohol use	No	42	63.6	124	92.5	
	Yes	30	45.4	34	25.4	0.001
History chat chewing	No	36	54.6	100	74.6	
	Yes	12	22.2	10	7.5	
History of illicit drug use	No	54	78.2	124	92.5	0.028
	Yes	47	71.2	118	88.8	0.004
Counseling patients	No	19	28.7	16	11.9	
	Yes	56	84.8	83	61.9	0.001
Hearing about MDR TB	No	10	15.2	51	38.1	
	Yes	35	53.1	34	23.4	0.001
Perceiving stigmatized	No	31	46.9	100	74.6	
	Yes	15	22.7	12	8.9	0.007
History of contact TB	No	51	77.3	122	91.1	
	Yes	19	28.8	16	11.9	0.003
Contact of MDR-TB patients	No	47	71.2	118	88.1	
	Yes	41	62.1	27	20.1	0.001
History of previous TB treatment	No	25	39.9	107	89.9	
	Yes	18	26.8	11	8.2	0.001
Drug interruption at least a day	No	48	74.2	123	92.8	
	Yes	55	83.3	33	24.6	0.001
History of retreatment	No	11	16.7	101	75.9	
	Reactive	16	24.2	17	12.7	0.038
HIV infection	No reactive	50	75.8	118	87.3	
	Yes	11	28.8	7	3.7	0.011
psychological illness	No	55	71.2	127	96.3	
	Under weight	27	40.9	17	12.7	0.001
Mal nutrition status BMI(kg/m ²)	Normal	39	59.1	117	87.3	

NB:-Candidate variable that show significant association p Value <0.20

Finally, eight variables were significant in multivariable logistic regression models. From this study the main findings were Social stigmas, being under weight, khat chewing and psychological illness. history of retreatment for TB [(AOR= 13.9,95%CI:(4.44, -40.04)], social stigma [(AOR=5.2 , 95% CI :(1.69-16.16)], Body mass index (being underweight) [(AOR=3.9 ,95% CI: (1.09-13.92)], distance from treatment center (>25km) [(AOR=6.2 ,95% CI:(2.00-19.04)], History of previous TB treatment [(AOR=5.3,95% CI:(1.72-16.43), alcohol consumption [(AOR=4.1,95% CI:(1.04-15.80)], khat chewing [(AOR=6.2,95% CI:(1.91-20.63)] and any psychological illness [(AOR=9.4, 95% CI: 1.76-

50.17)] were found to be independent determinants of the occurrence of MDR-TB after controlling possible confounders.(Table 6)

The odds of MDR-TB was 13.9 times higher among those History of retreatment than none of the retreatment of TB after controlling for all the rest variables in the model (AOR=13.9 (4.44-44.05, P.v 0.001)). Respondents who had a history of previous treatment of TB were 5.3 times more likely to develop MDR-TB compared to those who had no history of previous treatment history TB (AOR=5.3(1.7-16.43, P.v 003). Respondents who had traveling to health facility more than 25km were 4 times more likely to develop MDR-TB compared to those who had no traveling to health facility(AOR; 6.2 (2.00-19.04, P.v 002).The odds of MDR TB were alcohol consumption were 4.1times more likely to develop MDR-TB compared to those who had no alcohol consumption(AOR=4.1,95%,CI 1.04-15.80). Lastly, respondents who had the Body mass index less than 18.5 were 3.9 times more likely to have MDR-TB when compared to respondents who had Body mass index normal measurement(AOR=3.9(1.09-13.92), p.v 0.035).(Table 7)

Table 8:- Results of Multivariable logistic regression analysis on determinants of MDR-TB in Southwest, Ethiopia, and June 2021.

Variables		Cases	controls	COR, (95%CI)	AOR,(95%CI)
Perceive others would stigmatize	Yes	35	34	3.3(1.78-6.18)*	5.2 (1.69-16.16)**
	No	31	100	1	1
Alcohol consumption	Yes	22	10	6.2(2.73-14.12)*	4.1 (1.04-15.80)**
	No	42	124	1	1
History of previous TB treatment	Yes	41	27	6.5(3.4-12.48)*	5.3 (1.7-16.43)**
	No	25	107	1	1
History of retreatment for TB	Yes	11	33	15(7.17-39.63)*	13.9 (4.44-44.05)**
	No	55	101	1	1
Khat chewing	Yes	47	118	2.9(1.41-6.29)*	6.3 (1.91-20.63)**
	No	19	16	1	1
Body mass index(BMI)	<18.5kg	27	14	4.8(2.35-9.66)*	3.9 (1.09-13.92)**
	>18.5kg	39	120	1	1
psychological illness	Yes	8	5	3.6(1.12-11.35)*	9.4 (1.76-50.17)**
	No	58	130	1	1
Distance from treatment center	<25km	45	38	1	1
	>25km	21	94	5.4(2.86-10.27)*	6.2 (2.00-19.04)

NB:-Variables that show significant association (p< 0.05) COR (crude odd ration)* Bivariable analysis, AOR (Adjusted odds ratio) ** Multivariable analysis

6. Discussion

This case-control study identified determinants of MDR-TB in south west Ethiopia. The major determinants of MDR-TB which are identified by this research were stigma, alcohol consumption, History of previous TB treatment, History of retreatment for TB, khat chewing, Body mass index (BMI), any psychological illness and Distance from treatment center.

Subsequently, After controlling for all the other variables in the model, the odds ratio calculated for sex, residence, opening window, drug illicit, and History of Interruptions drug for at least a day, and ever got counseling were not important determinants of MDR-TB.

In this study, we first recognize social stigma as risk factors for MDR-TB in south west Ethiopia, with no identifiable risk factor reported prior to this. It is identified that bad practices theoretically increase the risks for MDR-TB. Moreover, our study showed that MDR-TB cases are almost 5.2 more regularly skilled stigma associated with TB, used substance (Khat, smoking and alcohol drinking), and felt very miserable compared to without disease TB is known as an extremely stigmatized disease. MDR-TB patients are particularly affected having in mind long (18-20 month) and difficult treatment, regime consisted of potent anti-TB drugs with severe side-effects that can affect mental health, higher case fatality, and lower cure rates are consistent with studies done in Ethiopia [(37),(40)], Ethiopia Addis Ababa(44)] and Patients who did not reveal their TB disease had, in fact, a greater likelihood for developing MDR-TB(13).

This study is in line with Nepal's indicate the stigma was an independent predictor for MDR-TB);(48), But study conducted in china((25), not backing this study. The difference may be population character, living condition, and awareness of patient and handling by the health worker. In this study, we first identify social stigma as risk factors for MDR-TB in Southwest Ethiopia, with no noticeable risk factor reported previous to this. If bad practices develop into misconduct leading to social stigma, their influence becomes a risk factor related to TB. Consequently, our study delivered imperative confirmation that social stigma was a risk factor for MDR-TB. Stigma is harmful in itself since it can lead to feelings of shame, guilt, and isolation of people living with tuberculosis.

Patients who are afraid of social stigma are more likely to lack understanding by their family, friends, or colleagues. Still, the trouble to access sick leaves from their manager and the related possible difficulty to take the recommended drugs regularly strength plays a role. Perceived stigma was typically dominant

in patients with pulmonary tuberculosis when associated with those who had extra pulmonary tuberculosis. In addition to this, there was a significant association between MDRTB-related perceived stigma and the intensive phase of treatment. Public responsiveness and patient education may help to alleviate the isolation and refusal of TB patients and encourage TB suspects to seek initial care(8)(10).

In the current study, alcohol consumption was also one of the risk factors for the development of MDR-TB. In southwest Ethiopia, Personal deeds like counseling of patients and drug illicit were not predictors of MDR-TB on multivariate analysis, while alcohol use, Khat chewing and stigma was associated. Later, it increases the rate of MDR-TB cases. A Study in line with The Studies conducted the Studies from in Ethiopia (40)], East Shoa, Ethiopia (19)],[(39)],[(35)] in Botswana [(53)] and in Belarus[(30)] have also shown alcohol use to be associated with MDR-TB. Some reports, including one from the WHO, shown that the use of alcohol rises the risk of developing MDR-TB in line for to poor adherence to treatment, impaired immune responses and an increased risk of adverse drug effects [(43)]. However, this relationship was not seen in study conducted in china Henan province (AOR; (25)and in Nepal [(48)], in Ethiopia Amhara regional state[(13) and in Sudan[(51)] . suggesting that it may be Situation-related, i.e., associated to local drinking traditions. These changes may be due to different levels of health care provision systems in different nations, living standards, and socio-economic factors. Henceforward, it increases the speed of MDR-TB cases. A poorly working immune system increases the risk of progression, and therefore factors that can impair the immune system (e.g. HIV, under nutrition, diabetes, silicosis, smoking, alcohol abuse, a wide range of systemic diseases and treatments with immunosuppressant) are also risk factors for developing drug-resistant TB disease(1,10).

Having a History of Previous treatment of TB was one of the strong determinants associated with MDR-TB in this study. Patients who had a previous history of treatment for tuberculosis had a 5.3 times higher risk of developing MDR-TB than patients who didn't have a history of previous treatment for tuberculosis. The resistance could be due to repeated and inappropriate ways of taking the medication that made the bacteria mutate and increasing institutions where drug resistance tests can be made to early detect primary resistance is needed. and it is consistent with studies done in Brazil [(52) Belarus[(30)] Georgia[(26)] in Ethiopia [(40)] and in Sudan shows(51)]was strongly associated with MDR TB. This implies consistency with these reports, in the recent study also create that patients with a history of treatment had an increased risk of developing MDR-TB. In our view, poor treatment is likely the main cause of drug resistance in previously treated cases. Due to the increasing burden of drug-

resistant TB, Classifications based on the history of previous TB treatment are the main criteria used to decide on treatment regimen. The results highlight the need to improve the care provided to individuals diagnosed with TB by ensuring the optimal drug dose, effective and authentic drug use, individual-centered care, improved quality of care and access to drug sensitivity testing. In addition, it is vital to consider the monitoring actions of therapeutic interventions with an practiced multi professional team in order to reach greater chances of treatment success(2)(3)(8).It is also described by Federal Ministry of Health of Ethiopia(1).However, this finding was not similar to the findings from in Ethiopia (35)].this might be due to study population(on PTB) and case definition.

According to the current study, the History of the Retreatment of TB patients shows a significant association with developing MDR-TB. The odds of MDR-TB were 13.9 times higher risk of developing MDR-TB than patients who didn't have a history of retreatment for tuberculosis. Similar finding was observed in studies conducted in china (24)],in Ethiopia [(56)] , in Ethiopia [(23)]and Survey conducted in Ethiopia also showed that retreatment cases were 11.8%(18). Strong links of MDR-TB were confirmed in those fails after retreated.

This suggests a requirement for clear drug guide and delivery constant reminders for patients during their DOTs to avoid acquisition of MDR-TB. The countrywide TB control programmed doesn't have the ability to implement DST for all TB patients and for all MDR suspects. With these reports, in the existing study also, we found that patients with a history of treatment, failure had an increased risk of developing DR-TB.A patient with retreatment tuberculosis (TB) signifies those who have been treated previously for one month or further with anti-TB drugs and who have been detected once again with the disease. These patients mainly include relapses, treatment failure, or loss to follow-up on the first-line treatment regimen. Patients qualified for retreatment ought to be referred for a rapid molecular test or drug susceptibility testing to determine at least rifampicin resistance, and rather too isoniazid resistance eminence. On the root of the result of the drug susceptibility test(s), a standard first-line treatment regimen (2HRZE/4HR) can be repeated if no resistance is documented. If rifampicin resistance is present, an MDR-TB regimen should be prescribed according to WHO drug-resistant TB guidelines (2)(8)(10).

Today, the enduring spread of MDR-TB is one of the most vital and difficult challenges facing global TB control. Providing health education to TB cases and their families or friends on appropriate addition and conclusion of TB treatment may help to lower the threat(10).However, significant association but it

is protected study conduct in china retreatment (54)]. The difference may be methodology, infrastructures, and accessibility drugs.

Khat chewing increases the odds of acquiring primary MDR/RR-TB by six times higher risk than those who had no Khat chewing to develop Multidrug-resistant tuberculosis. This discovery was reliable with studies conducted in Yemen [(34)], but in southern Ethiopia [(45)] Khat chewing were protective, these may be living habit of population and no available excessively in this study area.

However, the findings are inconsistent with others(19)(39) (51) . Similar results were not reported Khat chewing treaty in these study conducted in Ethiopia, Addis Ababa[(42)], Ethiopia, Oromia Adama[(39)], in Ethiopia East Shao [(19)] were not in treaty with our study. The possible explanation for this could be the daily chewing Khat leads to poor treatment adherence. Slight kindness has been paid exactly to the effect of Khat chewing on patients' compliance. Maybe Khat chewing is a social habit in few countries. In the present-day study, it was originate that Khat chewing was significantly associated(34). However works of the literature were deficient in this regard, the strong association between Khat chewing and MDR-TB could be because Khat is an endogenous energizing plant in which people have chewed it in groups in an encircled space for altered drives in Ethiopia.

The current study discovered that underweight (BMI <18.5) people were about 3.9 times more common among cases compared to normal nutrition. Previous studies have also learned a high dominance of under nutrition among adult TB people in other countries. The current study shown that underweight (BMI <18.5) people were more likely to develop PTB compared to their counterparts, which is consistent with previous studies conducted at Ambo Hospital, Western Ethiopia(36)] and Croatia[(28)],china[(54)], Sudan [(51)),China [(33)] [(29)] and in Ethiopia (35)). Nevertheless, a study conducted in Ethiopian (21), was not a significant risk factor which conducted armed force and civilians, the difference may study design and area study. In fact weight loss between people with TB can be caused by several causes, including reduced food intake due to loss of appetite, vomiting, and nausea, and abdominal pain.

Similarly, under nutrition weakens the body's ability to fight disease. There is increasing evidence that under nutrition in patients with active TB is associated with an increased frequency and severity of disease and indeed a two to four-fold increase in mortality. Because of the clear link between under nutrition and active TB, nutritional assessment and management are necessary parts of TB treatment and

care for many people with TB. When under-nutrition is identified at the time of TB diagnosis, TB must be considered a key cause that needs to be addressed.

The current study revealed that study participants who had any psychological illness were 9.4 times at higher risk than those who had no psychological illness to develop Multidrug-resistant tuberculosis. Certain drugs used for MDR-TB treatment cause psychiatric disorders. A similar finding was detected by a study in Ethiopia which indicated that Multidrug-resistant TB was significantly associated with Any psychological illness [(46)], in Ethiopia [(38)], and study conducted in Pakistan related MDR-TB patient) (37)], Any psychological illness Patients with TB may undergo from mental disorders as a consequence of long-term treatment, anti-TB drug side effects, and TB relapses. TB treatment is long and a few anti-TB drugs, such as cycloserine, INH, Ethambutol, and fluoro quinolone can cause extraordinary mental wellbeing issues such as sadness, uneasiness, or psychosis. In addition, TB moreover remains extremely stigmatized.

The association between TB and mental health is possibly difficult. Many clarifications for the relation have been suggested in the literature, including the effects of stress on immune functioning and the progression from infection to disease. Stigma experience due to TB is one of the risk factors for common mental disorders. Mental health can be understood by isolating it into two aspects. One is the impact that comes with the diagnosis of the disease—the stigma and loss of social standing—while the other is drug-induced psychosis and side effects.

In this study among patient's health problems and behavioral factors, Distance to reach health facility >25km was risk for MDR-TB, which was consistent in studies conducted with a in Ethiopia Addis Ababa(44), in Bhutan[(49)], study done in China [(25)], and in Uganda [(50)] which travelling long distance to take taking their drugs more than >25km to reach health facility strong predictor of MDR-TB. This is because patients who came to a health facility from a distance more than 25 km are from a somewhat distant area after the health facility and this may generate problems in retrieving a health facility. The results also indicated that those who frequently travel in public transportation such taxis were more likely to develop MDR-TB than those travelling <25km distance, because of long distance, leading to poor adherence(51). The results suggest the free movement of contagious causes in such community transport and late case detection foremost to increased spreading disease. Our finding is in treaty with a study that reported a helpful relationship between public transport and MDR-TB risk. A

Study conducted in southern Ethiopia [(45)], were protective. This may indicate expansion of MDR TB treatment initiated center and strength of DOT (Poor quality of services (hours, wait-time) and Health providers fail to give adequate information) implementation.

In this study, we found that variables such as age, occupation, living situation, contacting TB patients (TB contact), Dots follow up in the previous TB, presence of diabetes mellitus, Hypertension, prior, Type of TB in previous treatment., traditional treatment, prison history, Cigarette smoke per day (#), Owner of the House, Types of the floor of the House, and Family size did not show a statistically significant relationship with MDR TB.

Similar to this study; age, Prison , traditional treatment, Hypertension, Diabetes mellitus, and owner of House did not show a significant association to MDR-TB [(2)(21)(24)(48)(27)]. In difference to this study, variables like Sex, previous treatment, retreatment, interruption drugs, stigma, Khat chewing, psychological illness, known MDR TB contact, BM, smoking, alcohol consumption, were found to be the possible determinants of the likelihood of developing MDR-TB [(13),(37),(48),(31),(28),(30),(35),(36),(51)].

Yet, the deviation in results obtained by this study and others conducted so far in various countries with the search to identify variables that result in MDR-TB arises from the assembly of factors. These include a change in the standard classification of variables used, especially age, occupation, education level, and income; the difference in the study design and therefore the difference in sample size considered which determine effect size (power) of the statistical results, the 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 program.

Finally, this study used a sound study design (Case-control design) which is attractive because it can be performed relatively cheaply and quickly. Also it was conducted on a very relevant and timely issue. It had also tried to control confounding variables. Therefore, as indicated above, in the context of this study, some results are points contrary to some studies, and consistent with other studies, and the existing literature shows controversial findings for the identification of risk factors associated with MDR TB. However, based on the availability of resources, the author considers that study can be further developed to investigate the risk factors that lead to MDRTB at the national level, while takes into account the need to correct the results that they can lead to a preference for getting results.

7. Strengths and limitations

Strengths:

It used a sound study design and it is the appropriate one and was done quickly and cost-effectively. The data were also enrolled from 22 health care facilities and Two TIC hospitals 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 had been high.

Majority (around 95%) of the total MDR-TB cases were on treatment during the study period.

Limitations:

This study also had some limitations, including those in born to case-control designs. Recall bias may be introduced by respondents since study participants may not remember the condition of the past. 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 types of TB. Environmental and household factors were assessed without observation and this may affect the validity of the findings. Some variables (previous treatment regimen) which were found to be risk factors by other kinds of literature were not included because of incomplete data from patient records.

8. Conclusion and Recommendations

8.1. Conclusion

The major determinants of MDR-TB among the study participants in southwest Ethiopia were Perceive others would stigmatize, Alcohol consumption, History of previous TB treatment, History of retreatment for TB, Khat chewing, Body mass index (being underweight), psychological illness and Traveling to reach the health facility (being more than 25km).

8.2. Recommendations

MDR-TB leftovers' main concerns in TB control. Based on the results of this study the subsequent significant 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:

8.2.1. Federal Ministry of Health

- It is necessary to strengthen the treatment strategy which assures 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 work as main focus.
- To sustain the expansion and early examination of DST of MDR-TB services in south west Ethiopia.
- MOH is reliant on multi-sectorial involvement to address all risk factors and can advocate for these issues to improve control of MDR-TB and the further decreasing problem of the nutritional status patient

8.2.2. For Oromia Regional Health Bureau:

- Strengthening system of the community health services and the early detection and TB treatment in particular in rural areas especially focusing on increasing TB cure rate.
- There is a need for psychosocial support of MDR-TB patients and their caregivers to mitigate the negative effects of stigma, and to manage the associated psychological stressors. Mental health issues control the MDR-TB and hence patients need to be properly evaluated for mental health issues.
- It is better to have strong and functional Zonal or woreda level consultation centers for strengthening the program activities at low or rural setups

8.2.3. For health care providers: Create strong patient and community counseling and Awareness creation during drug allocation to alleviate stigma and psychological problem

8.2.4. Researchers

- Some variables have a weak estimate and the study suggests a need to have a large-scale study produce out normative data for the general population including the possible available number of MDR patients is recommended.

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Appendices

Appendix I

Participant Information Sheet

Good morning/ afternoon?

My name is _____ Currently I am a graduate student at Jimma University, College of Health Sciences, and Department of Epidemiology. And now I am conducting a study to assess determinants of multidrug-resistant tuberculosis (MDR-TB) among tuberculosis patients in southwest Ethiopia in 2021.

Research title: To assess determinants of multidrug-resistant tuberculosis (MDR-TB) among tuberculosis patients in southwest Ethiopia 2021

Name of the investigator: Sileshi Meseret Goshiye

Name of the Organization: Jimma University

Introduction: This information sheet is prepared for Southwest Ethiopia

Purpose of the research: The main aim of this study is to assess determinants of multidrug-resistant tuberculosis (MDR-TB) among tuberculosis patients in southwest Ethiopia in 2021

Procedure: The data for the surveillance system will be collected by using structured questionnaires and Document interviews. The data on MDR TB were collected from Shenen Gibe Hospital and Mettu Special Hospital and Non-MDR TB will be collected from the selected Health center of the case raised.

Risk: No harm to the study participants will happen.

Confidentiality: The information collected from this research project will be kept confidential. It will not be revealed to anyone except the investigator and will be kept locked with a key.

Appendix II:

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. Sileshi Meseret** who is the Master of Public Health student at Jimma University. You are selected as one of the study subjects 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 the evaluation of TB programs and to find out the proper way for the prevention of determinants for MDR in TB patients.

The information that 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 total 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 in 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 the 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 getting any medical services from the hospital. If you have any questions about this study you may ask me or the principal investigator **Sileshi Meseret** (Tel: 0929316169) or **E-mail: silezinu2009@gmail.com**) Are you willing to let your information 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 III: Questionnaire English version

JIMMA UNIVERSITY OF PUBLIC HEALTH DEPARTMENT

Questionnaire related to a determinant of multidrug-resistant tuberculosis (MDR-TB) among tuberculosis patients in Jimma Zone. Date data collection _____ Identification .No ____

Instruction: circle the responses provided by the interviewer or write the appropriate answer on the space provided Status of the respondent: Case (MDR-TB) _____ Control (Non MDR-TB) _____

Section-1 Socio-demographic Information				
S. No	Questions	Option/ answers	Code	Skip to Q
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	Occupational status	1. Farmer		
		2. Housewife		
		3. Merchant		
		4. Military		
		5. Daily laborer		
		6. Student		
		7. Government employ		
		8. Police force		
		9. Refuge Comp		
		10. Others(specify)----- --		
107	Residence	1. Urban		Write woreda name /HC
		2. Rural		

108	Monthly income	Birr		
-----	----------------	------	--	--

Section II: Environmental factors			
S.No	Questions	Option/ answers	Remark
201	Living situation	1. Alone 2. Homeless	
		3. With family 4. Prison	
		5. Other (specify)-----	
202	Do you have a house to live in?	1. Yes	if No skip to 214
		2. No -	
203	How many people living in the house?	-----	
204	What is the Number of rooms in the house?	-----	
206	Do the rooms have windows?	1. Yes	
		2. No	
207	Many windows?	-----	
208	Do you open the window(s) in a sense of refreshing the room?	1. Yes	
		2. No	
209	Do you have artificial ventilation?	1. Yes	
		2. No	
210	Does your house have an electric city?	1. Yes	
		2. No	
211	Which of the listed household items do you have?	1. Radio	
		2. TV	
		3. Air conditioner	
		4. refrigerator	
212	Have you ever got counseling services in ahealth institution?	1) Yes 2) No	
213	Did you perceive others would stigmatize you if they know your disease status?	1) Yes 2) No	
214	Distance from the nearest treatment center	1. < 6hr. 2> 6hr	
215	Have you ever been toa refugee camp	1. Yes,2. No	

Section III: Host related factors			
S. No	Questions	Option/ answers	Remark
301	Do you have a 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 a history of contact with known TB patients?	1. Yes	If no skip to 305
		2. No	
		3. I don't know	
304	If yes to Q. No 303 where is the place you have contact with known TB patients?	1. In the Family	
		2. Workplace	
		3. Health institution	
		4. Transportation service	
		5. School	
		6. Other(specify)----	
305	Do you have a history of contact with known MDR-TB patients?	1. Yes	If the answer no skip to 307
		2. No	
		3. I don't know	
306	If yes to Q. No 305 where is the place you have contact with a known MDR-TB patient?	1. In the Family	
		2. Workplace	
		3. Health institution	
		4. Transportation service	
		5. School	
		6. Other(specify)----	
307	Do you have a history of previous TB treatment?	1. Yes	If the answer is 2 or3 skip to Q312
		2. No	
		3. I don't remember/	
308	How many times do you have a 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 ...Month Back --since now	
310	Do you have a history of treatment under DOTs follow-up for the previous treatment/s?	1. Yes	
		2. No	
311	For how long did you take the treatment for previous treatment?	_____	
312	What was the type of TB you treated for?	1. Pulmonary TB	
		2. Extra pulmonary TB	
		3. Mixed	
		4. I don't know	
313	Do you have a history of retreatment for TB?	1. Yes	
		2. No	
		3. I don't remember	
314	Do you have a history of traditional treatment?	1. Yes	
		2. No	
		3. I don't remember	
315	Do you have a history of	1. Yes	

	hospitalization?	2. No	
		3. I don't know	
316	Do you have a history of illicit drug use that is under control such as cocaine, heroin, hashish, etc?	1. Yes	
		2. No	
		3. No response.	
317	Do you have a history of cigarette smoking at least once a week?	1. Yes	2or3 skip to Q319 If an answer is an option
		2. No	
		3. No response.	
318	How many cigarettes on average do you smoke per day?	1. 1-4	
		2. 5-10	
		3. 11-20	
		4. >20	
319	Do you have a history of Khat chewing at least once a week?	1. Yes	
		2. No	
		3. No response	
320	Do you have a history of alcohol intake till you drunk at least once in Week?	1. Yes	
		2. No	
		3. No response	
321	Do you have a history of experiencing gastrointestinal symptoms with skin lesion manifestation, repeated infection?	1. Yes	
		2. No	
		3. No response	
323	Have you encountered drug side effects of TB?	1. Yes	
		2. No	
324	Suffered the most common drug side effect (vomiting)	1. Yes	
		2. No	
325	For how long did you take the treatment for previous treatment?	2-4 months	
		5-7 months/6month	
		8 months	
		9-13 month	
326	Directly observed by health worker while taking anti-TB	1. Yes	
		2. No	
327	If yes, how many months	1. Daily	
		2. 1-2 weeks	
		3. One month	
		4. Two month	
328	Do you have a history of Interruptions drugs for at least a day?	1. Yes, 2. No	
329	Reason for an interruption for at least a day	1. side effect	
		2. forgot to keep it	
		3. Symptoms were gone and felt good	
		4. shortage of drugs	

330	Do you counsel a health care worker about MDR TB?	1. Yes	
		2. No	
		3. I don't know	
331	Are you heard about MDR TB?	1. Yes	
		2. No	
		3. I don't know	

Section IV: Data reviewed from patients record			
S. No	Questions	Option/ answers	Remark
401	Category of patient	1.New	
		2. Relapse	
		3.Return after default	
		4.Failure	
		5.other (specify)	
402	Presence of HIV infection	1.Yes	
		2.No	
		3.Not known	
403	History of previous TB treatment.	1. Yes	If No Skip to 408
		2. No,	
404	Type of previous TB infection	1. Pulmonary	
		2. Extra pulmonary	
		3. Mixed	
		4. Not known -----	
405	What was the treatment regimen taken in previous treatment? -----	1. Treatment completed	
		2. Default	
		3. Treatment failed	
		4. Transfer out.	
		5. Others(specify)-----	
406	The outcome of previous TB treatment	1 Cure	
		2. Relapse 3. Failure	
407	Presence of cavitation using chest radiography/previous TB/	1.Yes	
		2.No	
		3.Not known	
408	Current episode of TB	1.pulmonary TB	
		2.Extrapulmonary	
		Mixed	
409	Experienced any psychological problem	1.Yes	
		2.No	
410	Do you have a history of other illnesses?	1.Yes 2.No 3.Not known	
411	If Yes list two major disease	-----	
412	Do you have diabetes mellitus?	1. Yes 2. No 3. I don't	

413	Weight measured starting treatment	1. Yes 2. No 3. I don't	
414	Malnourished	1.Yes 2.No	
415	BMI(kg/m2)	Under weight	
		Normal	
		Overweight	

Appendix IV: Translated Amharic version consent form

የታካሚ ስምምነት ቅጽ

ስሜ.....

በሙያዬነርስ/ጤናመኮንንስሆንበዚህየሳንባነቀረሰመድኃኒትንየተላመደየሳንባነቀረሰበሽታመንሴዎችበሚልጥናትላይበጅማዩን ሽርሰቲየሀብረተሰብጤናሁለተኛድግሪተማሪየሆኑትአቶስለሺመሰረትላሚደረገውጥናትመረጃበማሰባሰብላይእገኛለሁ።ዩኒቨር ሲቲ።እርስዎከጥናትምህርቶችእንደበአጋጣሚተመርጠዋል።መረጃዎንበጥብቅምስጢራዊነትለመጠየቅመርማሪቡድኑለዚህ የመረጃአሰባሰብቀጠረኝ።የዚህጥናትግኝቶችየቲቢፕሮግራሞችንለመገምገምእናበቲቢህመምተኞችውስጥለኤም.ዲ.ኤ (MDR) ውሳኔሰጪዎችመከላከልንትክክለኛመንገድለማግኘትከፍተኛሚናደሚኖራቸውእናምናለን።

ለጥናቱአስፈላጊውመረጃክእርስዎይጠየቃልእናምከዚህበተጨማሪምለጥናቱየሚመለከታቸውአንዳንድመረጃዎችከመዝገብዎ ይገመገማሉ።ለተያዙመረጃዎችሁሉምስጢራዊነቱየተጠበቀነው።መረጃሲሰጡትእናመረጃውየሚከናወነውበአጠቃላይበፈቃደ ጃነትላይየተመሠረተነው።በዚህጥናትውስጥጥቅምላይየሚውልመረጃለመስጠትፈቃደኛነትዎየጥናቱተገለጹትንጥቅሞችለማ ሳካትይረዳናል።ስምህእናሌሎችየግልመለያዎችዎበመረጃአሰባሰብቅርጾችላይአይመዘገቡምእናምየሚሰጡንመረጃበምስጢር ይጠበቃልእንዲሁምለዚህጥናትዓላማምጥቅምላይይውላል።ለዚህጥናትየሚጠቅምሚናደሚኖራችንምመረጃየመስጠትሙሉምብ ትአለዎት።ግንየተወሰደውመረጃለጥናቱበጥምጠቃሚይሆናል።ከመዝገብዎላይለመጠየቅወይምለመከለስበተስማሙመረጃ ዎችካልተስማሙእንዲሁምከሆስፒታሉማንኛውንምየህክምናአገልግሎትእንዳያገኙአይከለከሉም።ስለዚህጥናትማንኛውንም ጥያቄካልዎትእኔንወይምዋናውንመርማሪስለሺመሰረት(ቴሌ: 0929316169) ወይምኢ-ሜይል:

silezinu2009@gmail.com መጠየቅያለብዎትመረጃዎለዚህጥናትእንዲጠቀሙበትፈቃደኛነዎት?

1. አዎ፣ 2. የለም

መልስሰጪውአመሌካችሊወስንእንደፈቀደሚያሳየው (በቃለም)

በጥናቱውስጥአንድክፍል _____

የሰንባነቀረሰበሽታመድኃኒትንየተላመደበሽታ (MDR-TB) መንሴዎችንለማጥናትየተዘጋጀየመጠየቂያደረገው።የመጠየቂያደርገው-----

----- መለያቁጥር-----

መመሪያ: መላሹየሰጡትንመልስበማክበብወይምበክፍትበታላይመልሱንይፃፉ።

ክፍል -1 የመሃበራዊሁኔታዎችመርጃ			
ተ.ቁ	ጥያቄዎች	መልስ/ምረጫ	ምርምራ
101	ፆታ	1. ወንድ 2. ሴት	
102	ዕድሜ	----- (በዓመት)	
103	የጋብቻሁኔታ	1. ያገባ 2. ያላገባ 3. የፈታ4. ባል/ሚስትሞተዋ	
104	ሃይማኖት	1. ሙስሊም2. ኦሪቶዶክስ 3. ካቶሊክ 4. ፕሮቴስታንት 5. የተለየ/ይጥቀሱ.....	
105	የትምህርትደረጃዎ እስከምንድነው?	1. ያልተማረ/ች 2. ማንበብእናመፅፍ 3. የመጀመሪያደረጃ 4. ሁለተኛደረጃ 5. ከፍተኛደረጃ	
106	ጎሳዎትምንድነው?	1. ኦሮሞ 2. አማራ 3. ትግሬ 4. ጉራጌ 5. የተለየ/ይጥቀሱ.....	
107	የስራሁኔታ	1. ገበሬ 2. የቤትአመቤት3. ነጋዴ 4. መከላከያ 5. የቀንሰራተኛ 6. ተማሪ 7. የመንግስትሰራተኛ 8. የፖሊስሃይል 9. መንግስታዊያልሆንድርጅት 10. የተለየ/ይጥቀሱ.....	

ክፍል II የአካባቢሁኔታዎች

ጥያቄዎች/ምረጫዎች / መልሶች/ምልክት/የድርጊቶች			
201	የኑሮሁኔታ	1. ብቸኛ 2. ከቤተሰብጋር	
202	የምትኖሩበትቤትአላችሁ?	3. ሌላ (ይግለጹ) ----- 1. አዎ	
203	እቤትወስጥስንትሰዎችአሉ?	2. No -if የለም -----	እስከቁ 301 ድረስመዝለል
204	በቤቱወስጥያሉትክፍሎችስንትናቸው?	----- 1. ሲሚንቶ 2. ጭቃ 3. እንጨት 4. ሌላ (ይግለጹ)	205 የቤቱግድግዳምንዓይነትነው?
206	የቤቱወለልምንዓይነትነው?	1. ሲሚንቶ 2. ጭቃ 3. እንጨት 4. ሌላ (ይግለጹ)	
207	ክፍሎቹመስኮቶችአሏቸው?	1. አዎ 2. የለም / የለምካለወደ -----	Q210
209	ክፍሉንበማደስስሜትመስኮቱን (መስኮቱን) ይከፍታሉ?	1. አዎ 2. የለም	
210	ሰውሰራሽአየርአለዎት?	1. አዎ 2. የለም	
211	ቤትዎየኤሌክትሪክከተማአለው?	1. አዎ	

		2. የለም	
2012	ለመጠቀም የመጠቀሚያ ቤት አለዎት?	1. አዎ	
		2. የለም	
2013	ከተዘረዘሩት የቤት ዕቃዎች ውስጥ የትኛው ነው ያለዎት?	1. ሬዲዮ	
		2. ቴሌቪዥን	
		3. የአየር ማቀዝቀዣ	
		4. ማቀዝቀዣ	
		5. መኪና / መኪና	
2014	በጤና ተቋም ውስጥ የምክር አገልግሎት አግኝተው ያውቃሉ?	1) አዎ	
		2) የለም	
2015	የበሽታዎን ሁኔታ ካወቁ ሌሎች ሊያሳዝኑዎት እንደሚችሉ አስተውለዎታል?	1) አዎ	
		2) የለም	
2016	የርቀት በአቅራቢያው ከሚገኝ የሕክምና ማእከል	1. ሁለት ሰዓታት።	
		2. አራት ሰዓታት 3. 6 ሰዓታት	

ክፍል III ከአስተናጋጅ ጋር የተዛመዱ ምክንያቶች

ጥያቄ የለም አማራጮች / መልሶች ምልክት ያድርጉበት			
301	በእስር ቤት ውስጥ ታሪክ አለዎት?	1. አዎ 2. የለም	
		3. ምላሽ የለም	
302	በቲቢ የተለከፈው የመጀመሪያው ነው??	1. አዎ	
		2. የለም	
303	ከሚታወቁ የቲቢ ሕመምተኞች ጋር የመገናኘት ታሪክ አለዎት?	1. አዎ	
		2. የለም	
		3. አላውቅም	
304	መልስዎ አዎ ከሆነ ጥ. 302 ከሆነ ከታወቁ የቲቢ ሕመምተኞች ጋር የመገናኘት ታሪክ አለዎት?	1. በቤተሰብ ውስጥ	
		2. የሥራ ቦታ	
		3. የጤና ተቋም	
		4. መጓጓዣ	
305	ከሚታወቁ MDR-TB ሕመምተኞች ጋር የመገናኘት ታሪክ አለዎት?	1. አዎ	
		2. የለም	
		3. አላውቅም	
306	መልስዎ አዎ ከሆነ ጥ. ቁ. 304 ከሆነ ከሚታወቁ MDR-TB ሕመምተኞች ጋር	1. በቤተሰብ ውስጥ	
		2. የሥራ ቦታ	
		3. የጤና ተቋም	
		4. መጓጓዣ አገልግሎት	
		5. ትምህርት ቤት	
		6. ሌላ (ይግለጹ) ----	
	የመገናኘት ታሪክ አለዎት?	1. አዎ 2. የለም	
		3. አላስታውስም / መልሱ 2 ወይም 3 ለ	Q3012 መዝለል ከሆነ
308	ያለፈው የቲቢ ሕክምና ታሪክ ስንጊዜ አለዎት?	ቁጥር _____	
309	ከዚህ በፊት የቲቢ ሕክምና መቼ ነበር? (የመጨረሻው ንክክን ድንገት ከሆነ)	ከሞሉ) - መመለስ ወይም	
		... ወር ተመለስ	
		- ከዘፈጀምሮ	
3010	ለቀድሞው ሕክምና / ዎች በክትትሎች ቁጥጥር ስር በሕክምና ታሪክ ታሪክ አለዎት?	1. አዎ	
		2. የለም	
3011	ለቀዳሚ ሕክምናው ለምን ያህል ጊዜ ወስደዋል? _____		

3012	የታከሙበት የቲቢዩይንት ምን ድንገት?	1. የሰምባነቅርሳ	
		2. ተጨማሪ የሰምባነቅርሳ	
		3. የተቀላቀለ 4. አላውቅም	
3013	ለቲቢዩመልሶማቋቋም ታሪክ አለዎት?	1. አዎ	
		2. የለም	
		3. አላስታውስም	
3014	ባህላዊ ሕክምና ታሪክ አለዎት?	1. አዎ	
		2. የለም	
		3. አላስታውስም	
3015	የሆስፒታሎች ታሪክ አለዎት?	1. አዎ	
		2. የለም	
		3. አላውቅም	
3016	እንደ ኮከብ ደን፣ ሄሮይን፣ ሃሽሽ፣ ወዘተ ያሉ ቁጥጥር ስር ያለ ሕገ ወጥ የአደንዛዥ ዕፅአጠቃቀም ታሪክ አለዎት?	1. አዎ	
		2. የለም	
		3. ምላሽ የለም::	
3017	ቢያንስ በሰላም ንት አንድ ጊዜ የሲጋራ ማጨስ ታሪክ አለዎት?	1. አዎ	
		2. የለም	
		3. ምላሽ የለም:: መልስ አንድ አማራጭ ከሆነ	
3018	በአማካይ ስንት ሲጋራዎች ያጨሳሉ?	1. 1-4 2. 5-10 3. 11-20 4. > 20	
3019	በሰምንት ውስጥ ቢያንስ በሰላም ንት አንድ ጊዜ የአደንዛዥ ታሪክ አለዎት?	1. አዎ 2. የለም 3. ምላሽ የለም	
3020	ቢያንስ በሰላም ንት አንድ ጊዜ እስኪጠጡ ድረስ የአልኮል መጠጦች ታሪክ አለዎት?	1. አዎ	
		2. የለም	
		3. ምላሽ የለም	
3021	በቆዳ የቆዳ ቁስለት፣ በተከታታይ ኢንፌክሽኖች የጨዋራና የሆድ ህመም ምልክቶች የታዩበት ታሪክ አለዎት?	1. አዎ	
		2. No	
		3. ምላሽ የለም	
3023	የቲቢዩን የንጥረ ነገሮች አጋጥሞ ዎታል?	1. አዎ	
		2. የለም	
	በጣም የተለመደው መድሃኒት የንጥረ ነገሮች (ማስታወስ)	1. የታመመ 2. የለም	
3024	ለቀዳሚ ሕክምናው ለምን ያህል ጊዜ ወስደዋል?	ከ2-4 ወራት ከ7-7 ወራት	
3025	ፀረ-ቲቢዩን ሚዲካሊክ ስርዓት ጊዜ በጤና ባለሙያው በቀጥታ ታዩ::	1. አዎ 2. የለም	
3026	አዎ ከሆነ፣ ስንት ወር 1-2 ሳምንቶች	አንድ ወር	
		ሁለት ወር	
3027	ቢያንስ ለአንድ ቀን የንጥረ ነገሮችን የሚያቋርጥ ምክንያት ለማቆየት	ረሳሁ	
		ምልክቶቼ ኔደው	
		ጥሩ ስሜት ተሰማቸው	
		የአደንዛዥ ዕፅአጥረት	
3028	ስለ MDR ቲቢዩን ጤና አጠባበቅ ባለሙያው ይመክራሉ?	1. አዎ	
		2. የለም	
3029	ስለ MDR ቲቢዩን ሰማዎታል?	1. አዎ 2. የለም	
		3. አላውቅም	

Curriculum Vitae (CV)

Mr. SILESHI MESERET

Personal Information

Full name: Sileshi Meseret Goshiye

Sex: Male

Date of birth: 12/011/1987 G.C

Arsi Jeju, Ethiopia

+251929316169

Email:silezinu2009@gmail.com

Work Experiences

A. From July 2018 up to now:

Title/Position: NTD and CDC coordinator beside class

Place of work: Jimma zone Southwest Ethiopia

B. .From September 2015 to June 2017:

Title/Position: CDC coordinator at Woreda Level and NTD focal

Organization Name: Jimma zone Southwest Ethiopia

C. From June 2013 to August 2015:

Title/Position: Maternal and child health coordinator at woreda level and HMIS.

Organization Name: Chora Botor Jimma Zone Oromia Regional State, Southwestern Ethiopia

D. From March 2010 to May 2013:

Title/position: Plan and Evaluation Public Health emergency management, Health Extension Coordinator

Organization Name: Chora Botor Jimma Zone Oromia Regional State, Southwestern Ethiopia

Educational Background

1. From September 2018 to Present

Name of Institution: The Department Epidemiology, Public Health Faculty, Jimma University.

Field of Study: Masters of Science in Epidemiology

2. from September 2008 to July 2010:

Name of Institution: The Department of Nursing, Institute of Public Health, Rift valley university college Adama branch

Field of Study: Nursing

Award: Bachelor of Science in Nursing

3. from September 2005 to July 2008:

Name of institution: Arbenyoch secondary and Abomsa preparatory school

Field of study: high and preparatory school (Natural science stream)

Award: ESLCE and EHEEC certificate

Skills

Communication and Interpersonal skills

Organizational/managerial skills

Computer skills:

- Microsoft Office (Word, Excel, PowerPoint),
- Statistical analysis Software SPSS, EPIDATA, EPI Info, and ATLAS

Other Certification and Recommendation Letters

- Community Service Certificate from the Mana Woreda Health Office, Southwest Ethiopia
- Master TOT on Health Extension Insertion of Implanon and removal
- Two recommendation letters on Community service, and teamwork approaches from the Health Office Mana, southwest Ethiopia