

ADDIS ABABA UNIVERSITY
COLLEGE OF HEALTH SCIENCES
SCHOOL OF NURSING & MIDWIFERY

Determinants of multi-drug resistant tuberculosis among patients attending anti-tuberculosis treatment from peripheral districts, Southern Nations, Nationalities and Peoples Region, Ethiopia, 2019

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Dedication

To Almighty God to give me strength throughout this study despite a number of challenges and a long journey.

Statement of the Author

By my signature below, I declare and affirm that this thesis is my own work. I have followed all ethical principles of scholarship in the preparation, data collection, data analysis and completion of this thesis. All scholarly matter that is included in the thesis has been given recognition through citation. I affirm that I have cited and referenced all sources used in this document. Every effort has been made to avoid plagiarism in the preparation of this thesis.

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Acronyms and Abbreviations

ALERT	All Africa Leprosy And TB Rehabilitation, And Training Center
AOR	Adjusted Odd Ratio
BMI	Body Mass Index
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
CSA	Central Statistical Agency
DM	Diabetes Mellitus
DOT	Directly Observed Treatment
DR-TB	Drug resistant Tuberculosis
DS-TB	Drug Susceptible Tuberculosis
ETB	Ethiopian Birr
FMOH	Federal Ministry of Health
MDR-TB	Multi-drug Resistant Tuberculosis
OR	Odd Ratio
RR-TB	Rifampicin Resistant Tuberculosis
SNNPR	South Nation Nationalities and People Region
TB	Tuberculosis
USA	United States of America

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ABSTRACT

Determinants of multi-drug resistant tuberculosis among patients attending anti-tuberculosis treatment from peripheral districts, Southern Nations, Nationalities and Peoples Region, Ethiopia
Lankamo Ena Digesa

Introduction

The emergence of multi-drug resistant tuberculosis (MDR-TB) is a challenge for the global prevention and control of the disease. Ethiopia is one of the 30 MDR-TB burden countries. Addressing underlying risk factors is one of the principal ways to prevent drug resistant TB. Moreover, there is little research evidence of MDR-TB from the peripheral areas of the country.

Objective: to identify determinants of MDR-TB among patients attending anti tuberculosis treatment from peripheral districts, Southern Nations, Nationalities and People Region, Ethiopia, 2019.

Methods: Hospital based case control study was conducted from March to April, 2019 in Southern Ethiopia. Cases were confirmed MDR-TB patients, while controls were those who declared cured or completed first line ant-TB treatment. Stratified random sampling technique was used to recruit study participants. The data were entered into Epi data 4.4.3, cleaned and analyzed by SPSS 24. Bivariate and multivariable analyses were used to identify determinants of MDR-TB. Determinants with P-value <0.05 were declared as having significant association with MDR-TB and OR with 95% CI was used to measure a degree of association.

Result: A total of 180 respondents (90 cases and 90 controls) participated in this study. Uneducated(AOR:4.91,CI:1.63-14.81),rural-residence(AOR:2.36,CI:1.03-5.43),BMI<18.5kg/m² (AOR:3.07,CI:1.42-6.62),pulmonary TB(AOR:4,CI:1.15-13.99),contact history with TB patient (AOR:3.72,CI:1.66-8.30) and history of previous treatment ((AOR:10,CI:4.32-23.16)were found independent determinants of MDR-TB.

Conclusions and recommendations: Uneducated, rural residence, BMI<18.5kg/m², pulmonary TB, contact history with TB patient and a history of previous treatment were associated with MDR-TB. A community level education to enhance public awareness about MDR-TB, nutritional counseling and support; strengthening contact tracing strategies and DOT strategies with treatment adherence interventions were recommended.

Key words: MDR-TB, TB, determinants, case control, SNNPR

1. Introduction

1.1 Background

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*. Commonly, TB affects the lungs but it can affect other parts of body (1, 2) .

Pulmonary tuberculosis refers to any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or tracheobronchial tree. A patient with both pulmonary and extra pulmonary TB should be classified as a case of pulmonary tuberculosis (PTB). Extra pulmonary tuberculosis (EPTB) refers to any bacteriologically confirmed or clinically diagnosed case of TB involving organs other than the lungs. The disease spreads when people with pulmonary TB expel bacteria into the air by coughing, sneezing, shouting, or singing (1-3).

Multidrug-resistant (MDR) refers to TB caused by *Mycobacterium tuberculosis* (M. tuberculosis) that is resistant to at least Isoniazid (INH) and Rifampicin (RIF). Moreover, a drug resistant can be further classified into; resistance to one of anti-tuberculosis drug (mono-resistant), resistance to more than one anti-TB drug other than Isoniazid and Rifampicin(poly-resistance) and resistance to rifampicin(Rifampicin resistant TB) and resistant to both a flouroquilone and at least one of the second-line injectable anti-TB drugs(extensive drug resistant (XDR)(2, 4, 5).

MDR-TB can result from either infection with organisms which are already drug-resistant (primary resistance) or may develop in the course of treatment of a patient (acquired/secondary resistance).Definitive diagnosis of drug-resistant tuberculosis requires to isolate *Mycobacterium tuberculosis* and drug susceptibility test to communicate the results to the clinicians. Rapid laboratory result is a paramount importance in a diagnosis, appropriate treatment and infection control. Drug resistant can be confirmed by a laboratory test called drug susceptibility test (DST). DST is required to make a definitive diagnosis of MDR-TB (5, 6).

A conventional growth-based DST remains the gold standard. Culture provides a definite diagnosis of TB. Culture takes weeks to months and slow growth of *Mycobacterium tuberculosis* for solid culture media. Liquid culture media takes a shorter time for the bacilli but it is at the

higher risk of contamination. However, it is more complex, expensive, requires specific equipment and maintenance cost. Culture-based methods are the current reference standard, they require more developed laboratory capacity and can take up to 12 weeks to provide results(5-7).

Ethiopia has achieved the millennium development goals (MDGs) for TB in 2015. Now adopted the new “END TB strategy”. The aim of the “END TB Strategy” is to end global TB epidemic. END TB strategy is aligned with the national health sector transformation plan and national strategic plan for tuberculosis, TB/HIV, drug resistant tuberculosis (DR-TB) prevention and control. The strategy targets to reduce TB death by 95%. Besides to this, “END TB Strategy” is aimed to cut new cases by 90% from 2015 to 2035. The national TB program has the key strategic interventions to achieve in 2020 after achieving MDG towards the END TB 90-(90)-90 targets. The targets are to ensure 90% of all people with TB and DR-TB diagnosed and treated, 90% of the key populations are diagnosed and treated, and 90% of people diagnosed TB complete treatment successfully with adherence and social support(2, 6).

1.2 Statement of the problem

The emergence of multidrug resistant Tuberculosis (MDR-TB) is a challenge for the global prevention and control of the disease(8).According to WHO 2018 TB report, 160,684 MDR/RR-TB cases were detected and notified in 2017(showed a small rise from 2016 that was 153,119). Of those, a total of 139,114 cases (87%) were enrolled for second-line treatment (1). Also there was a gap between the number of cases notified and started treatment (1, 8).A systematic review and meta-analysis in sub Saharan countries showed that drug resistant TB among previously treated TB patients was highest in East Africa with levels of 29.2% as compared to Southern and central Africa(9).World health organization 2018 global tuberculosis report revealed that Ethiopia is one of the 30 TB-burden countries. The report estimated that the incidence of MDR/RR-TB in 2017 in Ethiopia was 5.2(ranging 3.9–6.6)/100000 populations(1).A systematic review and meta-analysis of multidrug-resistant tuberculosis in Ethiopia revealed that overall prevalence of MDR-TB was 7.24%(10). The reviewers reported that the current prevalence is higher than the previous review in 2017,the overall prevalence among newly diagnosed was 2% and 15% in previously treated patients(11).

The Global Plan to End TB from 2016 to 2020 estimates that the amount for diagnosis and treatment of multidrug-resistant TB (MDR-TB) increases from US\$ 2.0 billion in 2017 to US\$ 3.6 billion by 2020. World health organization 2017 TB report declared by referring Ethiopian national strategic plan for TB, the estimated cost for management of drug-susceptible TB was 59 million dollar, 18 million dollars for MDR-TB and 7.6 million dollars for TB/HIV(7). Moreover, controlling of drug resistant tuberculosis consumes more cost and program implementation is more complicated(6). MDR-TB case management is difficult because it exposes to further economic and social costs that the patients face while seeking help and treatment(12).

World health organization report on drug-resistant tuberculosis shows that poor socioeconomic background, immune-compromising conditions (HIV, under nutrition, smoking, and drug and alcohol abuse), having poor access to diagnosis and treatment, poor adherence due to social and economic constraints, poverty are underlying risk factors and social determinants to drug-resistant TB(1, 12).A systematic review and meta-analysis of 2018 in Ethiopia identified that the risks factors of MDR-TB were mainly associated with a history of previous treatment and

contact history(10). BMI below 18.5 Kg/m², DM and COPD are risk factors for developing of TB. Prisoners and refugees are vulnerable groups of people to MDR-TB(2, 6).Furthermore, smoking, alcohol consumption, smear positivity, history of hospitalization, stigma and poor adherence were identified risk factors of MDR-TB from studies in Addis Ababa(13),in East Shoa(14) and in Jimma(15)

On-going transmission of resistant strains of TB in the community due to late detection of cases and inadequate treatment of patients due to provider/program related factors, drug related factors, and patient related factors are the challenges of controlling MDR-TB. Ethiopian national TB program has prioritized the key strategic intervention with ensuring 90% of people diagnosed drug-resistant TB successfully complete treatment with adherence and social support to achieve in 2020(6). Because of lack of national capacity to perform drug susceptibility testing for all incident TB cases for early identification of drug resistant TB, it is important to prioritize patients based on the risk factors. Moreover, addressing risk factors is one of national MDR-TB implementation frame work through sustained political commitment(6).

A systematic review and meta-analysis published in 2018(10) revealed that almost all studies conducted in Ethiopia focused in main urban centers. This implies that there is little research evidence from the peripheral areas of the country. Therefore, the purpose of this study was to identify socio-demographic, behavioral and clinical determinants of multidrug resistant tuberculosis from peripheral districts in Southern Nations, Nationalities and peoples region, Ethiopia.

2. Literature review

2.1 Introduction

The review was made based on different studies with the same study design (case-control) and other designs such as meta-analysis and systematic review on the topic and related topics, retrospective and cross-sectional study designs. Even though, the study with other designs were reviewed the majority of the reviews were case control studies. The review incorporates a literature from global tuberculosis report, the international and national journals, and Ethiopian national TB, HIV and Leprosy guidelines. It was organized from a global to local sphere. The studies with the titles of risks factors, predictors and determinants of multidrug resistant tuberculosis were included.

The literature was organized into socio-demographic, behavioral and clinical determinants of MDR-TB.

2.2 Socio-demographic determinants

World health organization 2014 tuberculosis report shows that poor socioeconomic background, economic constraints, and poverty were underlying risk factors and social determinants to drug-resistant TB (12).

A case control study done in Serbia on risk factors of MDR-TB among 124 respondents(31cases and 93 controls) revealed that monthly income of the family, stigma associated with TB and subjective feeling of sadness were the identified risk factors(16). Other similar case control study in China(17),Nepal(18),Addis Aba(13) and Jimma (15) showed that fearing of disclosure of TB status because of stigma was significant contributor of MDR-TB.

A systematic review and meta-analysis on prevalence and risk factors for multidrug-resistant tuberculosis in Iran and its neighboring countries depicted that age <45 years and being male were risk factors to develop MDR-TB(19). Another case control study in China(17) and cross-sectional study in India(20) identified being male was risk factor for occurrence of MDR-TB. Besides, age group 26-45 in India (20) and age group (18–25 and 26–45) in Bangladesh(21) were risk factors for development of MDR-TB. Other similar finding in Amhara region(22) divulged that age below 26 years was risk factor of MDR-TB. The findings in Serbia(16) and Iran(23)

were inconsistent with this-age did not contribute for development of MDR-TB. A study in South West Nigeria and Equatorial Guinea in Central Africa(24) revealed that age and gender were not significantly associated with drug resistant TB (25).

According to a case control study in three hospitals in Bangladesh(21) among 250 MDR-TB cases and 750 controls to determine risk factors revealed that lower level of education was predictor of MDR-TB. The finding is in line with finding in China(17). But finding in Serbia(16) showed level of education does not affect occurrence of MDR-TB.

The similar study in Bangladesh revealed that service and business as occupation were predictors of MDR-TB(21).

Finding from case control study in East Shoa in Oromia indicated that those who live in a rural setting acquired MDR-TB than urbanite (14). This was not in line with the finding in Iran(23)- residence did not affect development of MDR-TB.

2.3 Behavioral determinants

World health organization 2014 revealed that smoking, drug and alcohol abuse are determinants for drug-resistant TB (12).

A case control study done in Serbia on risk factors of MDR-TB among 124 respondents reported that the use of sedatives was significant independent risk factor to develop MDR-TB(16). Another study done in Allahabad, India (20) identified that MDR-TB was more common in substance abusers. A Study in Henan province in China among 287 MDR-TB cases and 291 controls identified that smoking was predictor of multidrug resistant TB (17). Similar findings were identified in Bangladesh(21), Nepal(21) and Tanzania(26). According to case control study that was conducted at Amhara regional state among 153 MDR-TB and equal number of non MDR-TB patients alcohol consumers more likely developed MDR-TB than non-consumers(22). Similar finding was identified from case control study in East Shoa in Oromia (14) and in

Jimma(15). But, these findings were inconsistent with other studies in Serbia(16) and Nepal(18) that MDR-TB was not related to consumption of alcohol.

National programmatic management of drug resistant TB in Ethiopia clearly specifies prisoners and refugees are vulnerable groups of people for MDR-TB(6).But, case control study that was conducted in northern Iran among 22 cases and 88 controls on determinant factors of drug resistant tuberculosis revealed that history of imprisonment was not significantly related with development of MDR-TB (23).

A case report on pet dog in Beijing revealed that the pet dog developed mycobacterium tuberculosis that was resistant to isoniazid, ethambutol, and streptomycin. The dog was reported as having pre-multidrug-resistant mycobacterium tuberculosis strain(27).

A review on Bovine tuberculosis infection in animal and human populations in Ethiopia disclosed that bovine tuberculosis mainly occurs due to drinking raw milk and in cervical lymphadenitis form and extra-pulmonary form in close contact(28). Another study in Addis Ababa and its surroundings on prevalence of tuberculosis among dairy farm workers divulged that consuming raw animal products were 4 times developed tuberculosis than consumers of cooked animal products(29).

2.4 Clinical determinants

According to 2014 World health organization report on MDR-TB, immune-compromising conditions such HIV is one of the determinants of drug-resistant TB (12). A report on drug resistance in the United States from 2010 to 2013 revealed that worsening clinical finding with co-morbidity increases risks of drug-resistant TB (5). Another case control study in Henan province, China having an opportunistic infection is predictor of multidrug resistant TB(17). A cross-sectional study in India(20) depicted co-morbidity was risk factor of MDR-TB. Other studies in different countries; case control study in Serbia(16), case control study in Iran(23),case control study in Equatorial Guinea in Central Africa(24), case control study in

Addis Ababa(13) and case control study in East Shoa (14) reported MDR-TB was not related with HIV.

The report on drug resistance in the United States from 2010 to 2013 revealed that a previous history of treatment was strong determinant of MDR-TB(5). Other studies that were conducted in different parts of world are consistent with finding. A review in Iran and neighboring countries(19), case control study in Iran(23), cross-sectional study in India(20), case control study in Nepal(18),case control study in China(17),review in Sub Saharan countries(9), retrospective study in Nigeria(25), Equatorial Guinea in Central Africa(24), case control study in Tanzania(26),case control study in Addis Ababa(13) and case control study in East(14) identified that a previous history of treatment was strong predictor of MDR-TB. However, the finding of case control study in Serbia(16) was inconsistent with previous history of treatment.

The finding on the similar report on drug resistance in the United States from 2010 to 2013 depicted that contact history and exposure to individuals in congregate settings are the most important predictors of drug-resistant TB (5).The similar finding was identified in other studies cross-sectional study in India(20), case control in Equatorial Guinea in Central Africa(24), case control in Tanzania(26),review in Ethiopia(10), case control in Amhara region(22) and case control in East Shoa(14).However, a contact history with TB patient did not have association with MDR-TB in Iran(23)

A case control study done in Serbia on risk factors of MDR-TB among 124 respondents(31cases and 93 controls) revealed that defaulting from treatment was identified risk factor(16). Another case control study in Sheneneh Gibe hospital, Jimma showed that insufficient instruction on how to take anti-TB drug and missing anti-TB drug were identified predictors of MDR-TB(15).A similar case control study in Serbia(16) identified COPD was risk factor of MDR-TB. Another case control study done in Bangladesh revealed DM was one of the predictors of MDR-TB(21). Ethiopia 2015 national wide rapid nutritional assessment report showed, two out of three registered TB patients had low BMI below 18.5 Kg/m².Another a retrospective study in South Korea revealed that underweight status was risk factor for transmission MDR-TB in the community(30). In addition to this, DM patients are at a higher risk of developing TB. Besides,

the patients with diabetes mellitus are more likely to face poor TB treatment outcomes, treatment failure, relapse and even death. Patients with COPD have a three times increased risk of developing active TB compared to the general population(2). A study in Addis(St. Peter TB Specialized and All Africa Leprosy And TB Rehabilitation, And Training Center(ALERT) was inconsistent that a patient with DM less likely develop MDR-TB than drug susceptible TB(13).

A similar case control study done in St. Peter TB Specialized and ALERT showed that patients who had been hospitalized for TB management were 4 times more likely to have MDR-TB than drug susceptible TB. The study also identified that probability of sputum-smear positivity was found to be higher in the cases than the control (13).A retrospective study in South Korean patients with multidrug resistant tuberculosis revealed that a positive sputum smear might be risk factor for transmission MDR-TB in the community(30).

2.5 Conclusion

The review shows that MDR-TB was mainly related to a previous history of treatment and contact history with TB patients. Furthermore, using a substance and comorbidity contributed for the development of MDR-TB.

This study considered other possible determinants associated with MDR-TB incorporating were found the major predictors. Therefore, the study considered socio-demographic, clinical and behavioral determinants that were responsible for occurrence of MDR-TB patients from peripheral districts in Southern Nations, Nationalities and peoples region, Ethiopia.

2.6 Conceptual framework

The conceptual frame work was developed from reviewing the literature and guidelines (2, 6, 13-15, 28, 29). It consists of socio-demographic, behavioral and clinical determinants of MDR-TB.

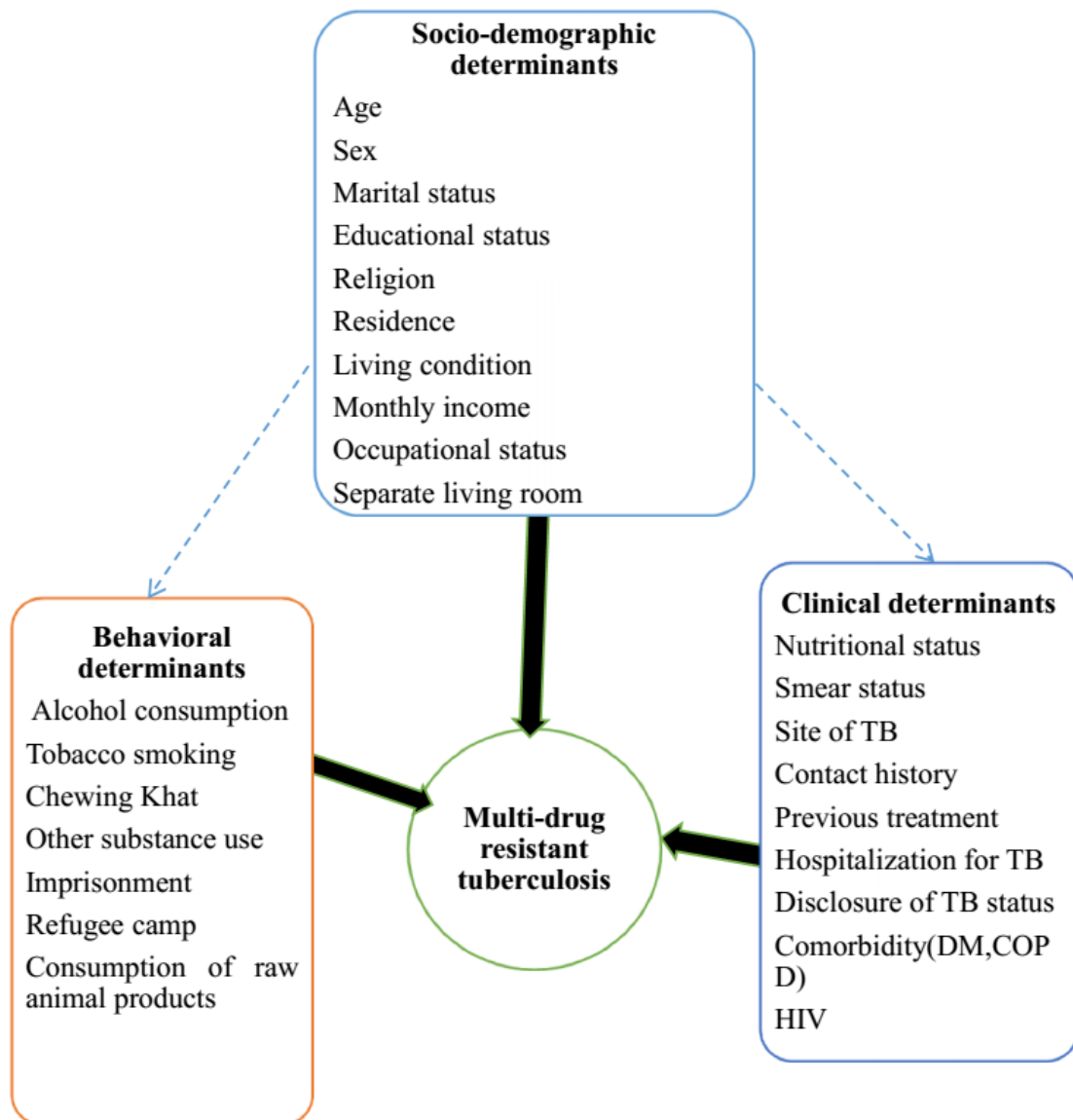


Figure 1: Conceptual framework of socio-demographic, clinical and behavioral determinants of multi-drug resistant tuberculosis of the study hospitals, Southern Nation, Nationalities and Peoples Region, Ethiopia, 2019

2.7 Justification of the study

Ethiopian Federal Ministry of Health set a strategic objective "Improve Equitable Access to Quality Health Services" to achieve from 2015/16-2019/2020 through health sector transformation plan. This strategic objective deals with minimizing disparities between groups and regions with different levels of underlying social advantage/disadvantage in the provision of health services. Equity can be accomplished through absence of preventable differences among groups or populations distinguished economically, socially, demographically and geographically (2, 31). Moreover, little research evidence of MDR-TB determinants from peripheral area of the country. Therefore, this study addressed MDR-TB patients attending MDR-TB treatment initiation centers from peripheral districts in Southern Nations, Nationalities and Peoples Region, Ethiopia.

2.8 Significance of the study

Addressing the factors leading to the development of MDR-TB is one of the national MDR-TB implementation framework(6). The determinants that facilitated for emergence of MDR-TB in peripheral districts were identified in this study. It will also give clue for health care providers working in TB clinics. It helps for public health practitioners to identify the risk differences to prioritize resource in a control and prevention of MDR-TB. The study will benefit the members of the community to educate the population based on the risk factors that is related to the geographic location. Besides, it will provide input for managers and partners to extract the finding in a decision making to halt further emergence of MDR-TB in the TB control program. The study will serve as literature for the future studies and will increase representativeness of the findings of nationwide future review.

3. Objective

3.1 General objective

To assess determinants of multidrug-resistant tuberculosis among patients attending anti tuberculosis treatment centers from peripheral districts, Southern Nations, Nationalities and People Region, Ethiopia, 2019

3.2 Specific objectives

To determine socio-demographic determinants related with multidrug resistant tuberculosis

To identify behavioral determinants associated with multidrug resistant tuberculosis

To determine clinical determinants related with multidrug resistant tuberculosis

4. Methods and Materials

4.1. Study Area

The study was conducted in Southern Nation, Nationalities and Peoples Region (SNNPR). The 2007 population and housing census of Ethiopia revealed that the total population of the region was 14,929,548(32). A population projection figure of 2012 based on 2007 national population and housing census, the population of the region was estimated to be 17,359,008(33).The report on health institutions and services by Aynalem Adugna 2014 showed that 20 hospitals were run by the ministry of health and private entities in the region (34).

According to data of the regional health bureau, Yirgalem, Butajira, Nigist Elen Mohammed Metasebiya, Arba Minch, Dilla, Jinka and Mizan Aman hospitals are MDR-TB treatment initiation centers in the region. Yirgalem general hospital, Nigist Elen Mohammed Metasebiya hospital and Butajira general hospital are the hospitals at which the majority of the cases are managed. Butajira general hospital is one of the hospitals in Gurage Zone and is located 131 km from Addis Ababa. The hospital is MDR-TB drug initiation center for Gurage zone, Yem special woreda and partly Silt zone. Nigist Elen Mohammed Metasebiya hospital is found in Hadiya Zone, Hosaina town, and is located 232 km from Addis Ababa. Queen Eleni Mohammed Memorial hospital is MDR-TB drug initiation center for Hadiya zone, Kambata Zone, Halaba Zone, partly Wolaita and Silt Zones. Yirgalem general hospital is found in Sidama zone. It is located 320 km from Addis Ababa. The hospital is MDR-TB drug initiation center for Sidama zone and Hawassa city administration.

This study addressed the patients from peripheral districts attending Butajira general, Nigist Elen Mohammed Metasebiya hospital and Yirgalem general hospitals.

The hospitals and their catchment areas for populations according to 2012 population projection (33) in the region as mentioned in the following table.

Table 1: Population size of the study hospitals and their catchment area Southern Nations, Nationalities and Peoples Region, Ethiopia, 2019

Hospital	Catchment areas	Population
Yirgalem	Hawassa city administration	328,875
	Sidama zone	3,406,616
Nigist Elen Mohammed Metasebiya	Woliata zone	1,750,079
	Hadiya zone	1433815
	Kambata zone	797,900
	Halaba zone	270,892
Butajira	Gurage zone	1,486,109
	Silt zone	866,565
	Yemi special woreda	93789
Total		10,434,640

4.2 Study Period

The study was conducted from March 18 to April 30, 2019.

4.3 Study Design

Unmatched case control study design was used to identify determinants related to development of MDRTB. This study design was chosen because it allows for assessing multiple risk factors in cases and controls. The study design is also suitable since it allows the study to be conducted within a relatively short period of time and limited resources.

4.4 Source population

All confirmed MDR-TB patients from peripheral districts and Non-MDR-TB patients at the end first line anti-TB treatment attending Yirgalem, Butajira and Nigist Elen Mohammed Metasebiya hospital

4.4.1 Study populations

All confirmed MDR-TB patients from peripheral districts and Non-MDR-TB patients at the end first line anti-TB treatment during study period attending Yirgalem, Butajira and Nigist Elen Mohammed Metasebiya hospital.

4.5 Eligibility criteria

4.5.1 Inclusion criteria

MDR-TB confirmed patients by culture and/or drug susceptibility testing, and patients taking treatment. Drug-susceptible TB patients declared cured or treatment completed at the end of first line ant-TB treatment.

4.5.1 Exclusion criteria

Age below 15 years old

Seriously ill

The patients from main urban centers

4.6 Sample size determination

Sample size was determined by a double population proportion formula. Epi-Info version 7.2.2.6 was used to calculate the number of study participants. Contact with a known TB patient in previous study that was conducted in East Shoa in Oromia(14) was used for sample size determination based on the following assumptions: 95% confidence level at power of 80%, with the ratio of 1:1 case to control, percent of control exposed 39.7 and percent of cases exposed 61.6. The final sample size was 180 (90 cases and 90 controls).

4.7 Sampling technique

Cases were selected by stratified random sampling technique for in-patient (admitted) and on follows up.

Controls were recruited by stratified random sampling technique from the patients completed first line anti-TB drugs.

4.8 Sampling procedure

A total of 135 MDR-TB patients were from peripheral districts and 105 patients were completing first line anti-TB treatment during the study period. A stratum was made based on the hospital the patients attending. A proportional allocation to the size was made by a lottery method (see figure 2).

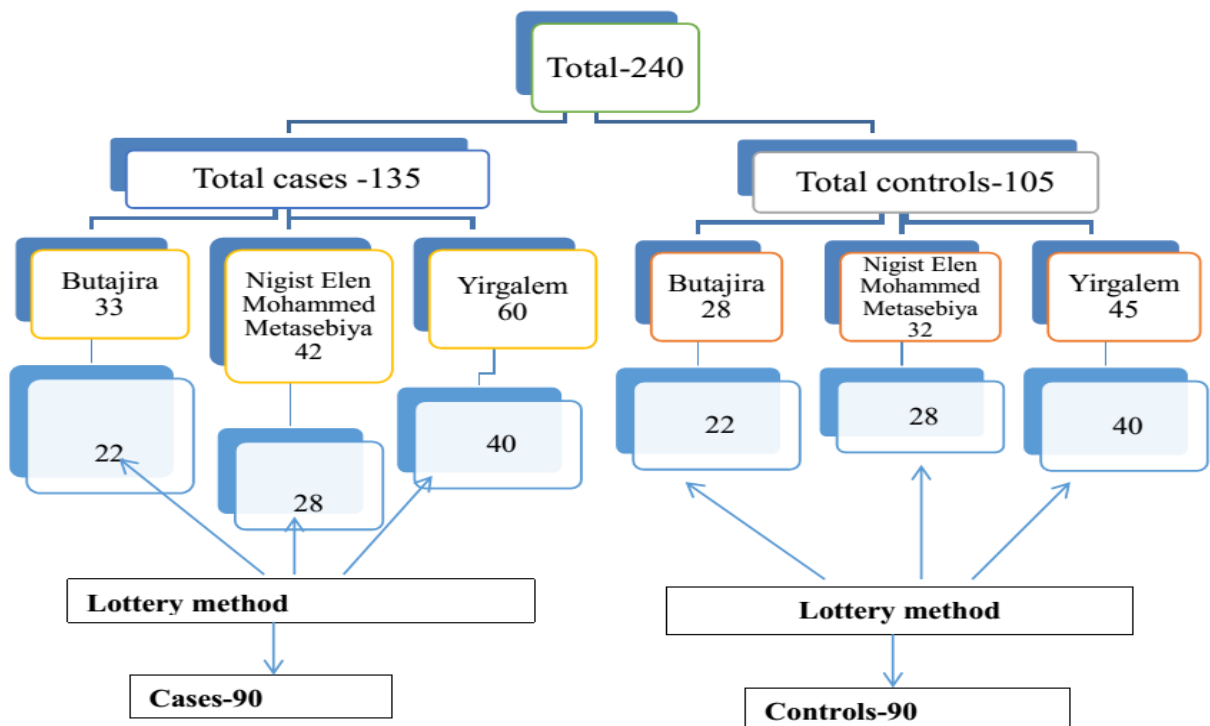


Figure 2: Sampling procedure of case and control in Butajira, Nigist Elen Mohammed Metasebiya and Yirgalem hospitals in SNNPR, Ethiopia, 2019

4.9 Operational definitions

Body Mass Index (BMI)

Nutritional indices that is used to assess and classify malnutrition. A normal if BMI ≥ 18.5 and < 25.0 (Kg/m^2) and malnutrition (underweight) if BMI < 18.5 kg/m^2 (2).

Cured

A pulmonary TB patient with bacteriologically confirmed TB at the beginning of treatment who was smear or culture-negative in the last month of treatment and on at least one previous occasion(2)

Treatment completed

A TB patient who completed treatment without evidence of failure but with no record to show that sputum smear or culture results in the last month of treatment and on at least one previous occasion were negative, either because tests were not done or because results are unavailable(2)

Treatment failure

A TB patient whose sputum smear or culture is positive at month 5 or later during treatment(2)

Lost to follow up

A patient who has been on treatment for at least four weeks and whose treatment was interrupted for eight or more consecutive weeks(2)

Drug susceptible TB

A tuberculosis that is susceptible to Rifampicin and Isonaized (3)

Chronic Obstructive Pulmonary Disease

It is a disease of airway that is characterized by chronic air flow limitation which is not fully reversible(4)

Smear positive

A person who has at least one positive result on AFM microscopy or person whose Xpert MTB/RIF test result detected Mycobacteria with susceptibility to Rifampicin(2)

Smear negative

Pulmonary TB diagnostic method in which two sputum samples are negative(3).

Close contact

A person who is not in the household but who shared an enclosed space(social gathering place, workplace, facility) with the index case for extended daytime periods during the 3 months before the start of the current treatment episode(3)

Household contact

A person who shared the same enclosed living space as the index case for one or more nights or for frequent or extended daytime periods during the 3 months before the start of the current treatment episode(3)

4.10 Study variables

4.9.1 Dependent variable

Multidrug resistant tuberculosis

4.9.2 Independent variables

Socio-demographic variables

Age	Educational status
Sex	Occupation
Ethnicity	Monthly income
Religion	Residence
Marital status	Living condition
	Separate living and sleeping room
	Number of person per room

Behavioral variables

Alcohol consumption

Tobacco smoking

Chewing Khat

Other substance use

Imprisonment

Staying a in refugee camp

Consumption of raw meat

Consumption of raw milk

Living with cattle or domestic animals

Clinical variables

Nutritional status

Type of TB

Smear status

Contact history

Previous treatment

Treatment outcome

Hospitalization for TB

Disclosure of TB status

Comorbidity (DM,COPD)

HIV

4.11 Data collection instrument

Data were collected by using structured questionnaire. Data collection tool was adopted from previously locally conducted studies, national TB, HIV/AIDS guidelines and MDR-TB manual (2, 6, 13-15, 28, 29, 35-37). The data were collected by 6 trained data collectors through interviews from the study participants.

4.12 Data quality assurance

Pre-test was carried out in ALERT hospital before 1 week of main study. Some modifications were made on clarity of questions and lay out of the questionnaire. The time required for interview was fixed (15-20 minutes).

The questionnaire prepared in English was translated to Amharic and retranslated to English for consistency. Training was provided to 6 health professionals who collected data before the beginning of data collection. After completing the interview session, additional data was collected from the MDR-TB and drug susceptible TB registers. To maintain validity of data, regular supervision was made by trained 3 supervisors and principal investigator. The principal investigator and trained supervisors checked the completeness of each questionnaire and data accuracy on daily basis.

4.13 Data processing and analysis

The data were entered into Epi data 4.4.3 then exported to SPSS 24 for cleaning and analysis. The variables were described by frequencies, percentages, presented in tables and graphs. Median for income and age was calculated. Bivariate analysis was done to select the variables for multivariable analysis. The data were analyzed by logistic regression model. Variables with p-value <0.05 in bivariate analysis were entered to multivariable logistic regression to control confounding. Determinants with $P < 0.05$ was considered as having a significant association with MDR-TB and OR with 95% CI was used to measure a degree of association.

4.14 Ethical clearance

Ethical clearance was obtained from School of Nursing and Midwifery, AAU ethical review committee. The ethical clearance was offered to the study hospitals. The purpose of the study was explained to each study participant before data collection. Only those who gave consent to participate in the study was included in the study. Study participant was coded anonymously and confidentiality of information was maintained.

4.15 Dissemination of the result

The study was presented to Addis Ababa University, School of Nursing and Midwifery as partial fulfillment of Master's degree in Adult Health Nursing. Finding of the study will be distributed to study areas and the regional health bureau. The findings will be also presented in different seminars, meetings, and workshops as well as further effort will be made to publish the findings on peer reviewed journals. Hard and soft copies will be made available in the library of AAU, for graduate students as well as for other researchers and readers.

5. Results

5.1 Socio-demographic characteristics of the study participants

A total of 180 patients (90 confirmed MDR-TB cases and 90 drug susceptible TB controls) participated in this study. More male respondents were found in cases 55(61.1%) as compared to controls 48(53.3%). About 43(47.78%) of cases were in age group of 26-45 and 51(56.67%) of controls in the same category of age. The median age for cases was 29 years and it ranged from 16 to 81. The median age for controls was 30.5 years and it ranged from 15 to 66. About 39(43.33%) of cases had average family monthly income 501-1000 Ethiopian birr(ETB) and 43(47.78%) of the control had the same amount. The median income for cases was 700 ETB ranging from 150-4000 ETB, and for the controls was 700 ETB ranging from 200-5000 ETB. Above two third 78 (78.89%) of case participants were from rural and nearly half 49(54.44%) of the controls were from rural. One third (33.33%) of the cases were uneducated as compared to controls 15(16.67%).All of the study participants had a home to live(see table 2).

Table 2: Distribution of socio-demographic characteristics of case and control respondents from Butajira, Nigist Elen Mohammed Metasebiya and Yirgalem hospitals in SNNPR, Ethiopia, 2019

Variables	Category	Case (%)	Control (%)	Total (%)
Sex	Male	55(61.1)	48(53.3)	103(57.22)
	Female	35(38.9)	42(46.7)	77(42.78)
Age	15-25	37(41.1)	30(33.33)	67(37.22)
	26-45	43(47.8)	50(55.56)	93(51.67)
	>=46	10(11.1)	10(11.11)	20(11.11)
Religion	Orthodox Christian	33(36.7)	35(38.9)	68(37.78)
	Protestant	40(44.4)	33(36.7)	73(40.55)
	Muslim	17(18.9)	22(24.4)	39(21.67)
Marital Status	Never married	34(37.8)	35(38.9)	69(38.33)
	Married	56(62.2)	55(61.1)	111(61.67)

Education	Uneducated	30(33.3)	15(16.7)	45(25)
Level	Read and write	12(13.3)	15(16.7)	27(15)
	Primary	30(33.3)	29(32.2)	59(32.78)
	Secondary & above	18(20.0)	31(34.4)	49 (27.22)
Occupation	Employed	14(15.56)	18(20)	32(17.78)
	Unemployed	76(84.44)	72(80)	148(82.18)
Average monthly family income	≤500	29(32.2)	27(30.0)	56(31.1)
	501-1000	39(43.3)	43(47.8)	82(45.56)
	>1000	22(24.4)	20(22.2)	42(23.33)
Residence	Rural	71(78.9)	49(54.4)	120(66.67)
	Urban	19(21.1)	41(45.6)	60(33.33)
Separate room for living and sleeping	Yes	33(36.7)	35(38.9)	68(37.78)
	No	57(63.3)	55(61.1)	112(62.22)

5.2 Behavioral determinants of multidrug resistant tuberculosis

About 34(18.89%) of the study participants were alcohol consumers contributing the same count from the cases and controls. From the cases, 9(10%) were smokers (table 3).

Table 3: Distribution of behavioral determinants of case and control respondents from Butajira, Ngist Elen Mohammed Metasebiya and Yirgalem hospitals in SNNPR, Ethiopia, 2019

Variables	Category	Cases (%)	Control (%)	Total (%)
Have you been taking alcohol	Yes	17(18.9)	17(18.9)	34(17.78)
	No	73(81.1)	73(81.1)	146(82.22)
Have you been smoking cigarette	Yes	9(10)	1(1.1)	10(5.56)
	No	81(90)	89(98.9)	170(94.44)
Have you chewing Khat	Yes	13(14.4)	12(13.3)	25(13.89)
	No	77(86.6)	78(86.7)	155(86.11)
Did you have previous imprisonment for any case	Yes	5(5.6)	3(3.3)	8(4.44)
	No	85(94.4)	87(96.7)	172(95.56)
Have you been in a refugee camp	Yes	5(5.55)	8(8.89)	13(7.22)
	No	85(94.45)	82(91.11)	167(92.78)
Have you ever been consuming a raw milk	Not at all	26(28.9)	19(21.1)	45(25)
	Sometimes	64(71.11)	71(78.89)	135(75)
Have you been consuming raw meat	Not at all	21(23.33)	17(18.89)	38(21.11)
	Sometimes	69(76.67)	73(81.11)	142(78.89)
Have you been living with cattle/ domestic	Yes	39(43.3)	48(53.3)	87(48.33)
	No	51(56.7)	42(46.7)	93(51.67)

5.3 Clinical determinants of multidrug resistant tuberculosis

More than half of the cases 55(61.1%) had BMI less than 18.5 kg/m² whereas nearly one third 32(35.6%) of the control had BMI less than 18.5 kg/m². About 85(94.4%) of the cases were pulmonary TB. From the cases, 47(52.2%) had contact history with known TB patients as compared to control only one fourth 23(25.6%) had a contact history. From 73 participants who had a history of previous treatment, 56(76.71%) were from the cases(table 4).

Table 4: Distribution of clinical characteristics of study participants attending Butajira, Nigist Elen Mohammed Metasebiya and Yirgalem hospitals in SNNPR, Ethiopia, 2019

Variables	Category	Cases (%)	Control (%)	Total(%)
BMI(Kg/m ²)	<18.5	55(61.1)	32(35.6)	87(48.33)
	≥18.5	35(38.9)	58(64.4)	103(51.67)
Type of TB	Pulmonary	85(94.4)	68(75.6)	153(85)
	Extra pulmonary	5(5.6)	22(24.4)	27(15)
Sputum smear	Positive	53(62.4)	42(61.8)	95(62.09)
	Negative	32(37.6)	26(38.2)	58(37.91)
Did you have a known contact with TB patients	Yes	47(52.2)	23(25.6)	70(38.89)
	No	43(47.8)	67(74.4)	110(61.11)
Contact level	Household	26(55.32)	11(47.83)	37(52.86)
	Close contact	21(44.68)	12(52.17)	33(47.14)
Were you treated for TB before	Yes	56(62.2)	17(18.9)	73(40.56)
	No	34(37.8)	73(81.1)	103(59.44)
If you were treated TB, were you hospitalized for TB	Yes	17(30.4)	5(29.4)	22(30.14)
	No	39(69.6)	12(70.6)	51(69.86)
If you were treated TB, did you disclose your TB status for the family/relatives	Yes	34(60.7)	11(64.3)	45(61.64)
	No	22(39.5)	6(35.7)	28(38.36)

Comorbidities(DM,COPD)	Yes	4(4.44)	4(4.44)	8(4.44)
	No	86(95.56)	86(95.56)	172(95.56)
HIV status	Positive	1(1.11)	3(3.33)	4(2.22)
	Negative	89(98.89)	87(96.67)	176(97.78)
CD4 count during diagnosis	<500 cells/mm3	1(100%)	3(100%)	4(100)

From the respondents who had a history of previous treatment, the treatment outcome of the majority 43(58.9%) was cured or treatment completed. Only 3(4.1%) was lost follow up.

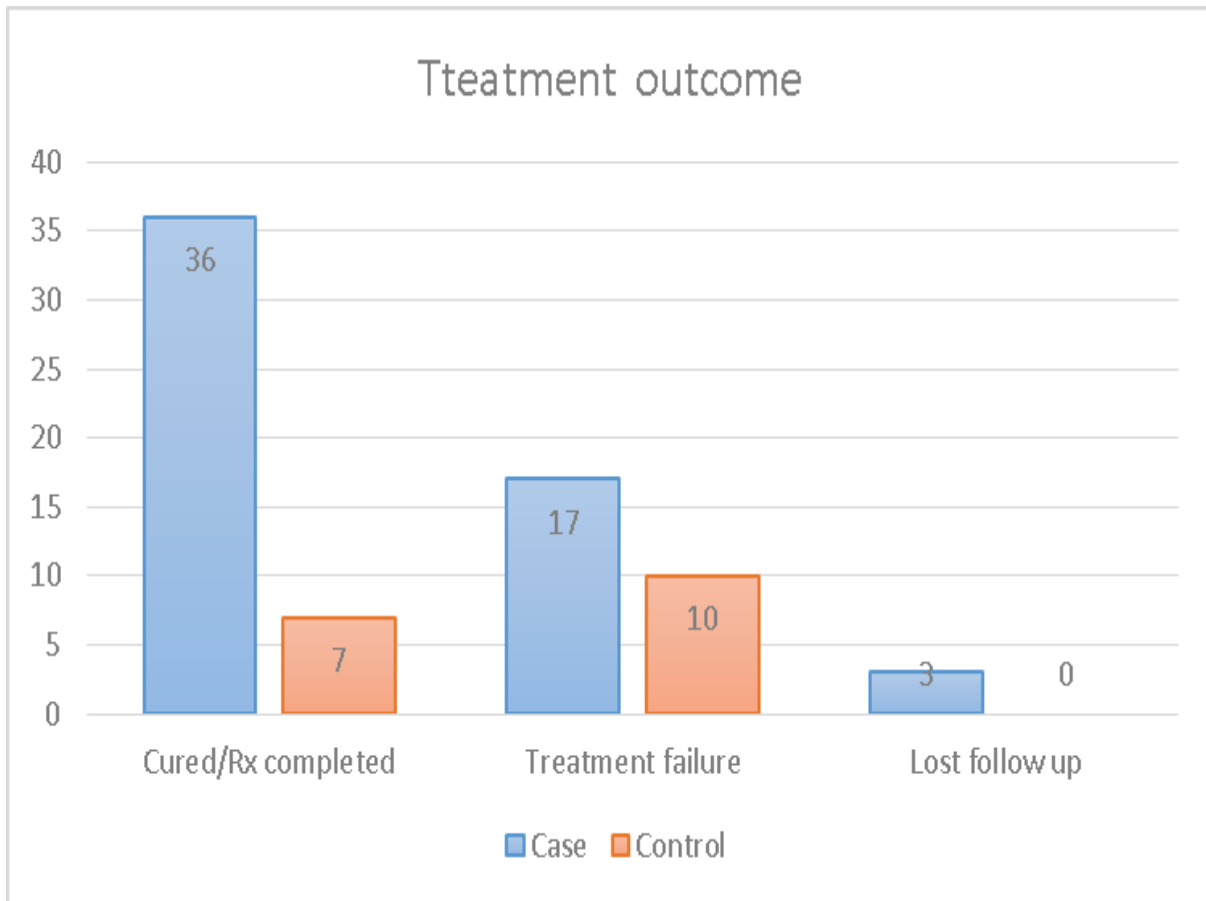


Figure 3: Distribution of treatment outcome of case and control respondents from Butajira, Nigist Elen Mohammed Metasebiya and Yirgalem hospitals in SNNPR, Ethiopia, 2019

5.4 Bivariate analysis

5.4.1. Bivariate analysis of socio-demographic determinants

Uneducated (Crude OR: 3.44(1.47-8.05),P-value:0.004),rural residence(Crude OR:3.127(1.625-6.01), P-value:0.001) were found significant at P-value 0.05(table 5)

Table 5: Bivariate analysis of socio-demographic characteristics of cases and controls respondents from Butajira, Nigist Elen Mohammed Metasebiya and Yirgalem hospitals in SNNPR, Ethiopia, 2019

Variables	Category	Cases (%)	Control (%)	Crude OR(95% CI)	P value
Sex	Male	55(61.1)	48(53.3)	1.375(760-2.487)	0.292
	Female	35(38.9)	42(46.7)	1	
Age	15-25	37(41.1)	30(33.33)	1.233(0.45-3.35)	0.681
	26-45	43(47.8)	50(55.56)	0.860(0.327-2.261)	0.760
	>=46	10(11.1)	10(11.11)	1	
Religion	Orthodox Christian	33(36.7)	35(38.9)	1	
	Protestant	40(44.4)	33(36.7)	1.28(0.66-2.49)	0.457
	Muslim	17(18.9)	22(24.4)	0.820(0.37-1.81)	0.622
Marital Status	Never married	34(37.8)	35(38.9)	1	
	Married	56(62.2)	55(61.1)	1.048(0.575-1.91)	0.878
Educational Level	Uneducated	30(33.3)	15(16.7)	3.44(1.47-8.05)	0.004
	Read and write	12(13.3)	15(16.7)	1.38(.530-3.56)	0.511
	Primary	30(33.3)	29(32.2)	1.782(.822-3.86)	0.143
	Secondary & above	18(20.0)	31(34.4)	1	
Occupation	Employed	14(15.56)	18(20)	1	
	Unemployed	76(84.44)	72(80)	1.357(0.629-2.93)	0.437
Average family monthly income	≤500	29(32.2)	27(30.0)	0.976(0.438-2.17)	0.953
	501-1000	39(43.3)	43(47.8)	0.825(0.392-1.74)	0.612

	>1000	22(24.4)	20(22.2)	1	
Residence	Rural	71(78.9)	49(54.4)	3.127(1.625-6.01)	0.001
	Urban	19(21.1)	41(45.6)	1	
Do you have separate room for living sleeping	Yes	33(36.7)	35(38.9)	1	
	No	57(63.3)	55(61.1)	0.91(0.498-1.662)	0.759

5.4.2 Bivariate analysis of behavioral determinants

Bivariate analysis of behavior related determinants revealed that cigarette smoking was found significant at p-value 0.05 (table 6).

Table 6: Bivariate analysis of behavioral determinants of case and control respondents from Butajira, Nigist Elen Mohammed Metasebiya and Yirgalem hospitals in SNNPR, Ethiopia, 2019

Variables	Category	Cases (%)	Control (%)	Crude OR(95% CI)	P value
Have you been taking an alcohol	Yes	17(18.9)	17(18.9)	1.00(0.47-.109)	1.00
	No	73(81.1)	73(81.1)	1	
Have you been smoking cigarette	Yes	9(10)	1(1.1)	9.9(1.22-79.77)	0.031
	No	81(90)	89(98.9)	1	
Have you been chewing Khat	Yes	13(14.4)	12(13.3)	1.09(0.47-2.55)	0.829
	No	77(86.6)	78(86.7)	1	
Have you been in a refugee camp	Yes	5(5.55)	8(8.89)	0.63(0.82-1.92)	0.392
	No	85(94.45)	82(91.11)	1	
Have you been consuming a raw milk(P-value=0.419)	Not at all	26(28.9)	19(21.11)	1	
	Sometimes	64(71.1)	71(78.89)	0.66(0.33-1.30)	0.230
Have you been consuming a raw meat	Not at all	21(23.33)	17(18.89)	1	
	Sometimes	69(76.67)	73(81.11)	0.765(0.37-1.57)	0.466
Have you been living with cattle or domestic animals	Yes	39(43.3)	48(53.3)	1.495(0.83-2.7)	0.180
	No	51(56.7)	42(46.7)	1	

5.4.3 Bivariate analysis of clinical determinants

Bivariate analysis of clinical related determinants depicted that BMI <18.5 kg/m², pulmonary TB, contact history and previous treatment were found significant at P-value 0.05 (table 7).

Table 7: Bivariate analysis of clinical determinants of case and control respondents from Butajira, Nigist Elen Mohammed Metasebiya and Yirgalem hospitals in SNNPR, Ethiopia, 2019

Variables	Category	Cases (%)	Control (%)	Crude OR(95% CI)	P value
BMI(Kg/m ²)	<18.5	55(61.1)	32(35.6)	2.848(1.56-5.22)	0.001
	≥18.5	35(38.9)	58(64.4)	1	
Type of TB	Pulmonary	85(94.4)	68(75.6)	5.5(1.98-15.28)	0.001
	Extra pulmonary	5(5.6)	22(24.4)	1	
Sputum smear status	Positive	53(62.4)	42(61.8)	0.975(0.506-1.88)	0.941
	Negative	32(37.6)	26(38.2)	1	
Did you have contact with a known TB Patient	Yes	47(52.2)	23(25.6)	3.184(1.70-5.97)	0.00
	No	43(47.8)	67(74.4)	1	
Contact level	Household	26(55.32)	11(47.83)	1.351(0.49 -3.67)	0.556
	Close	21(44.68)	12(52.17)	1	
Were you treated for TB before	Yes	56(62.2)	17(18.9)	7.073(3.59-13.94)	0.00
	No	34(37.8)	73(81.1)	1	
If you were treated TB, were you hospitalized for TB	Yes	17(30.4)	5(29.4)	1.046(0.319-3.43)	0.941
	No	39(69.6)	12(70.6)	1	
If you were treated TB, did you disclose your TB status for the family/relatives	Yes	34(60.7)	11(64.3)	0.843(0.27-2.61)	0.797
	No	22(39.5)	6(35.7)	1	

5.5 Multivariable analysis

The predictors which were p-value cut point of 0.05 in bivariate analysis were entered into multivariable logistic regression for statistically adjustment. The predictors which were candidate for multivariate analysis were checked for multi-collinearity before statistically adjustment in multivariable logistic regression. All the predictors pass the test of multi-collinearity (Variance inflation factor (VIF) is between 1.022 and 1.093)). Cigarette smoking was not included in multivariable analysis because of small number of observations. A goodness of fit of the model was assessed from the output of the multivariable logistic regression. Overall goodness of fit was 0.462 by Hosmer and Lemeshow test.

The odds of MDR-TB in previous treatment were 10 times higher than were not treated TB (P-value:0.000;95%CI(AOR:10.00(4.32-23.16))). The odds of developing MDR-TB in rural respondents was twice than urban (P value-0.043;95%CI(AOR:2.36(1.026-5.43)))(table 8).

Table 8: Multivariable logistic regression of case and control respondents from Butajira, Queen Elen Mohammed Memorial and Yirgalem hospitals in SNNPR, Ethiopia, 2019

Variables	Case(%)	Control(%)	Crude OR 95% CI	AOR 95% CI	P value
Education level					
Uneducated	30(33.3)	15(16.7)	3.44(1.47-8.05)	4.91(1.63-14.8)	0.005
Read and write	12(13.3)	15(16.7)	1.38(.53-3.56)	2.19(0.61-7.83)	0.229
Primary	30(33.3)	29(32.2)	1.78(.82-3.86)	1.91(0.69-5.34)	0.215
Secondary& above	18(20.0)	31(34.4)	1	1	
Residence					
Rural	71(78.9)	49(54.4)	3.13(1.62-6.0)	2.36(1.026-5.43)	0.043
Urban	19(21.1)	41(45.6)	1	1	

Nutritional status					
BMI <18.5kg/m ²	55(61.1)	32(35.6)	2.85(1.56-5.2)	3.07(1.42-6.62)	0.004
BMI ≥18.5kg/m ² (R)	35(38.9)	58(64.4)	1	1	
Type of TB					
Pulmonary TB	85(94.4)	68(75.6)	5.5(1.98-15.28)	4(1.15-13.99)	0.029
Extra pulmonary	5(5.6)	22(24.4)	1	1	
Contact history TB Patient					
Yes	47(52.2)	23(25.6)	3.18(1.70-5.97)	3.72(1.66-8.31)	0.001
No	43(47.8)	67(74.4)	1	1	
Previous treatment					
Yes	56(62.2)	17(18.9)	7.07(3.6-13.9)	10(4.32-23.16)	0.000
No	34(37.8)	73(81.1)	1	1	

6. Discussion

This unmatched case control study that was conducted on 180 respondents (90 cases and controls) to identify determinants of MDR-TB from patients peripheral districts revealed that illiteracy, rural residence, BMI less than 18.5kg/m^2 , pulmonary TB, contact history and previous treatment were found independent predictors of MDR-TB. The study addressed a number of possible determinants of MDR-TB but only the mentioned were found independent predictors. This might be due to the small number of observations in different predictors related with small sample size. Therefore, the predictors which were found independent will be discussed as follow.

This study indicated that the odds of developing MDR-TB were five times (AOR: 4.91) higher in uneducated than who had education level of secondary and above. The finding was in agreement with study in Bangladesh(21). In contrast, Addis Ababa(13) greater than secondary had a significant association with MDR-TB. However, the studies in East Shoa(14) and Jimma(15), illiteracy were not associated with occurrence of MDR-TB, Serbia(16), a level of education did not affect development of MDR-TB. This may be due to this study recruited the participants from peripheral districts and majority of the respondents were rural dwellers that might have a poor access for education and health literacy.

The current study revealed that rural residents had twice (AOR: 2.36) higher risk of MDR-TB than urban. This was in line with the study that was conducted in East Shoa(14). However, MDR-TB was not associated with residence according to the studies that were conducted in Jimma(15), China(17) and Iran(23). This difference might be due to access of TB services nearby and low knowledge of TB for drug adherence, transportation problem, inadequate social support and fear of stigma to complete anti-TB drugs.

The odds of being BMI less than 18.5kg/m^2 were 3 times (AOR:3.07) higher in cases than controls. The finding was in line with other findings(1, 2, 30). A poor nutritional status decreases a probability of treatment success (response), increases recurrence, decreases smear conversion rate, reduces hosts immunity by enhancing bacilli development and resistance, and a malnutrition is highly common in MDR-TB patients and one of the risk factors for development of MDR-TB(2, 4, 6, 38).

The respondents with pulmonary TB four times(AOR:4.02) more likely developed MDR-TB than extra-pulmonary TB. The finding was in line with study in East shoa(14), Addis Ababa(39),South Korea(30). However, the study in Jimma(15), pulmonary TB had no association with MDR-TB. The possible explanation for this could be higher risk of recurrence of drug resistant dormant bacilli which suppressed by previous TB drug exposure when hosts immunity gets weakened. The patients with pulmonary TB have a higher bacterial load which may not respond to first line anti-TB drugs in a short time. This affects adherence of patients(40).

Having a contact history with TB patient had four times(AOR:3.72) higher odds of MDR-TB than non-contact. The similar finding from the studies in East Shoa(14), Amhara regional state(22), Addis Ababa(13), systematic review and meta-analysis in Ethiopia(10), Tanzania(26),Equatorial Guinea(24),Bangladesh(41),India(20),USA(5). This is supported by (2, 6) having a contact is high risk group to develop MDR-TB. A higher chance of acquiring a drug resistant strain by droplets and aerosol from individuals infected with multidrug resistant strain(3, 7). However, a contact history in Iran(23) had no association with MDR-TB .This could be due to a small number of cases in Iran that lacks adequate power to identify association with MDR-TB.

The current study showed that the odds of MDR-TB in previously treated respondents were ten times(AOR:10.00) higher than treatment naïve respondents. And previous treatment was a major predictor of MDR-TB in this study. Similar findings were found in a number of studies from different countries including the Ethiopia, East Shoa(14), Amhara regional state(22), Addis Ababa(13),Iran and neighboring countries(19),Iran(23),Nepal(18),China(17),Sub-Saharan countries review(9), retrospective study in Nigeria(25), Equatorial Guinea(24), Tanzania(26), USA(5). Systematic review and meta-analysis in Ethiopia(10) revealed previous treatment was a major determinant of MDR-TB, systematic review in Europe(42). This is supported by WHO report (43)-previously treated patients are at higher risk of drug resistance and had non adherence(36).The resistance in a history of previous treatment might be due to multiple exposures to first line anti-TB drugs and incorrect methods of taking the treatment regimen that facilitate mutation of bacteria and development of resistance(2). However, the study in Serbia (17): a history previous treatment had no association with MDR-TB. This difference might be due to difference in adherence level, small sample size in Serbia and difference in study setting.

7. Conclusion and recommendations

7.1 Conclusion

This unmatched case control study that was conducted on 180 respondents (90 cases and controls) to assess determinants of MDR-TB from patients peripheral districts in Butajira, Nigist Elen Mohammed Metasebiya and Yirgalem hospitals revealed that illiteracy, rural residence, BMI less than 18.5kg/m², pulmonary TB, contact history and previous treatment had statistically significant association with development of MDR-TB.

7.2 Recommendations

Social mobilization and community level education by health extension workers, religious leaders, and community leaders to enhance public awareness about MDR-TB and quality of life.

Health care workers in TB clinics of the region should assess nutritional status for all TB patients and provide nutritional counseling on proper nutrition. The health institutions in the region should provide nutritional support for patients with malnutrition to prevent MDR-TB.

Health care facilities in the region should intensify contact tracing strategies and address all contacts through the patients, screening all family members to halt further spread of MDR-TB in the community. Public health officials and health extension workers should create a public awareness for early identification and screening for all contacts. .

Public health practitioners should arrange regular TB education session at each community and schools.

Health care workers working at TB clinic should identify the patients most likely relapse and give attention for the patients who have a history of previous treatment by a patient centered care approach, good communication skills and support.

Health care facilities in the region should assure well-functioning DOT strategies with treatment adherence interventions and strengthening laboratory capacity to monitor drug susceptibility based on national recommendation.

The investigator recommends the following evidence based recommendation to strengthen DOT strategies to minimize a previous treatment related MDR-TB:

FMOH and regional health bureau should support the health facilities to provide lay provider DOT other than DOT by health care providers or family.

8. Strength and limitations of the study

8.1 Strength

This study identified the determinants of MDR-TB from the peripheral districts to fill knowledge gap.

The study hospitals were at which the majority of the MDR-TB cases are managed. Therefore, the study identified the relevant regional determinants of MDR-TB.

8.2. Limitations

The study could not identify other known predictors of MDR-TB because of small number of observations related with small sample size.

Since majority of the respondents did not have a fixed amount of monthly income, self-report and estimation of income might affect the finding.

Unavoidable recall bias might affect the finding because some of the information was based on the recall of the study participants.

Since a previous treatment was found a major determinant for MDR-TB in this study and previous studies. This needs a further study to identify factors related to previous TB treatment in MDR-TB patients. As the hospitalized patients are subject to bias, a community based study should be conducted.

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10. Annex

Annex I: Consent form English Version

Addis Ababa University

College of Health Sciences, School of Nursing and Midwifery Graduate Studies

Dear study participant!

I am Lankamo Ena MSc student at Addis Ababa University, College of Health Sciences, School of Nursing and Midwifery. I am conducting research on a topic entitled as determinants of multidrug resistant tuberculosis of patients from peripheral districts in Yirgalem, Nigist Elen Mohammed Metasebiya and Butajira hospitals in Southern Nation, Nationalities and Peoples Region. The purpose of my study is to identify determinants of multidrug resistant tuberculosis from peripheral districts in Yirgalem, Nigist Elen Mohammed Metasebiya and Butajira hospitals in Southern Nation, Nationalities and Peoples Region. You, the client, with tuberculosis of drug resistant and completed tuberculosis treatment are candidate for the study. There are questions that you will be interviewed. The information that you will be interviewed will not be disclosed to anyone else. I assure that no third party can access your information. Your name will not be written in this form. Your information will be used only for the research purpose. The study will not have any risk for you. You can refuse to participate or drop it at any time of the interview. But this study will be successful only if you are voluntary and complete the interview. The interview takes 15-20 minutes. If you feel discomfort and have any question, please feel free to contact the principal investigator by the address mentioned at the end of this page. If you understand the purpose of the study and voluntary to participate for the success of this study, give your consent by the responding **Yes** and signing your signature as the following:

Are you voluntary participate in this study: Yes_____ No_____

Signature_____

Interviewer

Name _____Signature_____Date_____

Address of the principal investigator

Lankamo Ena

Phone: 0916437676

E-mail: lankmoena@gmail.com

Annex II: Questionnaire English version

**Addis Ababa University, College of Health Sciences, School of Nursing and midwifery
Graduate Studies**

Direction: Mark X on the space provided in front of alternatives.

Treatment center _____ Questionnaire ID No _____

Status of the respondent: Case (MDR-TB) _____ Control (Non MDR-TB) _____

S.N	Part I: Socio-demographic factors	Response
101	Sex	1. M _____ 2. F _____
102	Age	_____ years
103	Religion	1. Orthodox Christian _____ 2. Protestant _____ 3. Muslim _____ 4. Others _____
104	Marital Status	1. Single _____ 2. Married _____
105	Education	1. Illiterate _____ 2. Read and write _____ 3. Primary _____ 4. Secondary and above _____
106	Occupation	1. Employed 2. Unemployed
107	Average family monthly income(ETB)	
108	Residence	1. Rural _____ 2. Urban _____
109	Living condition	1. Home _____ 2. Homeless _____ _____
110	Do you have separate rooms for living and sleeping	1. Yes _____ 2. No _____

	Part II: Behavioral factors	
201	Have you been taking an alcohol	1. Yes_____ 2. No_____
202	Have you been smoking cigarette	1. Yes_____ 2. No_____
203	Have you been chewing Khat	1. Yes_____ 2. No_____
204	Did you use any other a recreational substance	1. Yes_____ 2. No_____
205	What is the substance	Specify_____
206	Did you have previous imprisonment for any case	1. Yes_____ 2. No_____
207	Have you ever been in a refugee camp	1. Yes_____ 2. No_____
208	Have you been consuming raw milk	1. Not at all_____ 2. Sometimes_____
209	Have you been consuming a raw meat	1. Not at all_____ 2. Sometimes_____
210	Have been living with cattle or other domestic animals in the same house	1. Yes_____ 2. No_____
	Part III: Clinical factors	
301	Nutritional status	1. Wt.(Kg)_____ Height(m)_____/MUAC(mm)___
302	Site of TB	1. Pulmonary_____ 2. Extra pulmonary_____ If pulmonary, go to Q303
303	Sputum Smear	1. Positive_____ 2. Negative_____
304	Did you have contact with a known TB Patient	1. Yes_____ 2.No_____ If yes, go to Q 305
305	Your contact	1. Close contact_____ 2. Household contact_____

306	Were you treated TB before	1. Yes_____2. No_____	If yes, go to Q 307
307	What was your treatment outcome	1. Cured_____ 2. Treatment completed_____ 3. Treatment failure_____ 4. Lost to follow up_____	If treatment failure, go to Q 308
308	If you treated TB before, were you hospitalized for TB	1. Yes_____2. No_____	
309	If you were treated TB before, did you disclose your TB status for the family/relatives	1. Yes_____ 2.No_____	
310	Did you have diabetes mellitus	1. Yes_____ 2. No_____	
311	Did you have COPD	1. Yes_____ 2. No_____	
312	Di you have any chronic other illness	1. Yes_____ 2. No_____	
313	The illness	Specify_____	
314	HIV status	1. Positive____2.Negative__	If positive, to Q 316
315	The CD4 count	1. During diagnosis_____ 2. Current _____	

Annex III : Consent form Amharic Version

አዲስ አበባ ዩኒቨርሲቲ

የጤና ሳንስ ኮሌጅ፣ የነርቭግና ሚዲዋይሬር ትምህርት ክፍል የድጎረ ምረቃ ፕሮግራም

ውድ የጥናት ተሳታፊ!

እኔ ላንቃም ኢና የአዲስ አበባ ዩኒቨርሲቲ ጤና ሳይንስ ኮሌጅ፣ ነርቭግና እና ሚዲዋይሬር ትምህርት ክፍል የማስተርስ ተማሪ ነኝ። በደቡብ ብሔር ብሔረሰቦች እና ሕዝቦች ክልል በይርጋዓለም፣ በንግስት እሌን መሐመድ መታሰብያ እና ቡታጅራ ሆስፕታሎች መዳኒትን የተለመደ ቲቢ ያስከተሉ ነገሮች ምርምር በማካሄድ ላይ ነኝ። .

የትጥናቱ ዓላማ በይርጋዓለም፣ በንግስት እሌን መሐመድ መታሰብያ እና በቡታጅራ ሆስፕታል መዳኒትን የተለመደ ቲቢ ያስከተሉ ነገሮችን መለየት ነው። እርሶዎ መዳኒትን የተለመደ ቲቢ ህክምና ሚዲረግሎትና የቲቢ መዳኒትን በመጨረስ ላይ ያሉ የጥናቱ እጩ ነዎት ። ቃለ-መጠይቅ የሚደረግባቸው ጥያቄዎች አሉ። በቃለ መጠይቁ ላይ የሚሳተፉት መረጃ ለሌላ ሰው አይገለጽም። ምንም መረጃ ሶስተኛ አካል ሊደርስበት እንደማይችል እርግጠኛ ነኝ። ስምዎ በዚህ ቅጽ ላይ አይፀፍም። መረጃዎ ለጥናት ዓላማ ጥቅም ላይ ብቻ ይውላል። ጥናቱ ለርስዎ ምንም ጉዳት ወይም አደጋ አይኖረውም። በቃለ-መጠይቁ ከተሳተፉ በማንኛውም ጊዜ መውጣት ይችላሉ። ነገር ግን ይህ ጥናት ስኬታማ ሊሆን የሚችለው በፈቃደኝነት ቃለ መጠይቁን ሲያጠናቀቁ ብቻ ነው። ቃለ መጠይቁ ከ15-20 ደቂቃ ይፈጅባታል። የመከፋት ስሜት እና ማንኛውም ጥያቄ ካለዎት በዚህ ገጽ መጨረሻ ላይ በተጠቀሰው አድራሻ ዋና መርማሪ ማነጋገር ነፃነት ይሰጣዎት። የጥናቱን ዓላማ ከተረዱ እና የዚህ ጥናት ስኬት ላይ ለመሳተፍ በፈቃደኝነት ከፈለጉ፣ አዎ በማለት እና ፊርማዎን በመፈረም የእርስዎን ስምምነት ይስጡ።

በዚህ ጥናት በፈቃደኝነት ይሳተፋሉ: አዎ _____ የለም _____

ፊርማ _____

ቃለ-መጠይቅ አቅራቢ

ስም _____ ፊርማ _____ ቀን _____

የዋና ተቆጣጣሪው አድራሻ

ላንቃሞ ኢና

ስልክ: 0916437676

ኢሜል lankmoena@gmail.com

Annex IV: Questionnaire Amharic Version

የአዲስ አበባ ዩኒቨርሲቲ፣ የጤና ሳይንስ ኮሌጅ፣ የነርቨስ እና የሚዲዋይዲት ትምህርት ክፍል የድጎረ ምረቃ ፕሮግራም

አቅጣጫ: ፊት ለፊት ባለው ቦታ ላይ X ምልክት ያድርጉ

የሕክምና ማዕከል _____ የመጠይቅ መለያ ቁጥር _____

የታካሚ ሁኔታ: መድኒትን የተላመደ ቲቢ(MDR-TB) _____ መድኒትን ያልተላመደ ቲቢ(non MDR-TB) _____

	ጥያቄ	ምላሽ
ተ.ቁ	ክፍል 1 : ማህበራዊ-ተጨባጭ ሁኔታዎች	
101	ጾታ	1. ወንድ _____ 2. ሴት _____
102	ዕድሜ	
103	ሃይማኖት	1. የአርቶዶክስ ክርስቲያን _____ 2. ፕሮቴስታንት _____ 3. ሙስሊም _____ 4. ሌላ (ይግለጹ) _____
104	የጋብቻ ሁኔታ	1. ያላገባ _____ 2. ያገባ

105	ትምህርት	1. ማንበብና መጻፍ የማይችል _____ 2. ማንበብ እና መጻፍ _____ 3. አንደኛ _____ 4. ሁለተኛና ከዛ በላይ _____	
106	የስራ ሁኔታ	1. የተቀጠረ 2. ያልተቀጠረ	
107	የተቤተሰብ አማካይ ወርሃዊ ገቢ (ETB)		
108	መኖሪያ	1. ገጠር _____ 2. ከተማ _____	
109	የኑሮ ሁኔታ	1. ቤት ዉስጥ _____ 2. ቤት አልባ _____	ቁ109 ቤት ዉስጥ ከሆነ ወደ 110
110	መኖሪያና እና መኝታ ክፍል የተለየ ነዉ	1. አዎ _____ 2. አይደለም _____	
	ክፍል ሁለት- ባህሪያት		
201	አልኮል ይጠጡ ነበር	1. አዎ _____ 2. አይደለም _____	
202	ሲጋራ ያጩሱ ነበር	1. አዎ _____ 2. አይደለም _____	
203	ጫት ይቅማሉ	1. አዎ _____ 2. አይደለም _____	
204	ከተጠቀሰዉ ዉጪ ሌላ ነገር ይወስዱ ነበር	1. አዎ _____	ቁ204 አዎ ከሆነ ወደ 205

		2. አይደለም _____	
205	የሚወስዱት ምን እንደሆነ	ይግለፁ _____	
206	በማንኛውም ጉዳይ ታራሚ ሆነው ያዉቃሉ	1. አዎ _____ 2. አይደለም _____	
207	በስደተኞች መጠለያ ካምፕ ውስጥ ገብተው ያውቃሉ	1. አዎ _____ 2. አይደለም _____	
208	ያልፈለ ወተት ይጠጡ ነበር	1. ችረ በጭራሽ _____ 2. አንዳንዴ _____	
209	ጥሬ ሥጋ ይወስዱ ነበር	1. ችረ በጭራሽ _____ 2. አንዳንድ ጊዜ _____	
210	በአንድ ቤት ውስጥ ከእንስሳት ወይም ከሌሎች የቤት እንስሳት ጋር ይኖሩ ነበር	1. አዎ _____ 2. አይደለም _____	
	ክፍል ሦስት፡ ክሊኒካዊ ምክንያቶች		
301	የአመጋገብ ሁኔታ	1. ክብደት (ኪ.ግ) _____ ቁመት (ሜ) _____ ወይም MUAC (mm) _____	
302	የቲቢ አይነት	1. የሳንባ _____ 2. ከሳንባ ዉጪ _____	ቁ302 የሳንባ ከሆነ ወደ 303
303	የአክታ ዉጤት	1. ፖሰትቭ _____ 2. ነገትቭ _____	
304	ከታወቀ የቲቢ ታካሚ ጋር ግንኙነት ነበረዎት	1. አዎ _____ 2. አይደለም _____	ቁ304 አዎ ከሆነ ወደ 305

	የት ነዉ ግንኙነት ያደረጉት	1. የስራ/የአምልኮ ስፍራ/ሕዝብ ቦታ _____ 2. የቤት ውስጥ ግንኙነት _____	
306	ከዚህ በፊት ቲቢ ታክመዉ ያዉቃሉ	1. አዎ _____ 2. አይደለም _____	ቁ306 አዎ ከሆነ ወደ 307
307	ውጤቱ	1. የዳነ _____ 2. ሕክምናውን የጨረሰ _____ 3. ሕክምናዉ ያልተሰካ _____ 4. አቀርጦ የተመለሰ _____	ቁ307 ሕክምናዉ ያልተሰካ ከሆነ ወደ 308
308	የታዘዘሎትን መድኃኒት በትዛዝ መሰረት አይወስዱም ነበር	1. አዎ _____ 2. አይደለም _____	ቁ308 አዎን ከሆነ ወደ 309
309	ቲቢን ታክመዉ ከሆነ በቲቢ ምክንያት ሆስፒታል ገብተዋል	1. አዎ _____ 2. አይደለም _____	
310	ቲቢን ታክመዉ ከሆነ ለቤተሰብ / ዘመዶች የቲቢ ሕመምዎን አሳዉቃልን?	1. አዎ _____ 2. አይደለም _____	
311	የስኳር ህመም አለቦዎት	1. አዎ _____ 2. አይደለም _____	
312	ስር የሰደደ ትንፋሽ የሚያሳጥር የሰንባ ህመም አለቦዎት	1. አዎ _____ 2. አይደለም _____	
313	ሌላ ዓይነት ሕመም አለቦዎት	1. አዎ _____ 2. አይደለም _____	ቁ313 አዎ ከሆነ ወደ 314

314	ህመሙ ምንድነው	ለይግለፁ _____			
315	የደመዎ HIV ዉጤት	<table border="1"> <tr> <td>1. ፖስት-ቫ _____</td> <td rowspan="2">ቁ 315 ፖስት-ቫ ከሆነ ወደ 316</td> </tr> <tr> <td>2. ነገት-ቫ _____</td> </tr> </table>	1. ፖስት-ቫ _____	ቁ 315 ፖስት-ቫ ከሆነ ወደ 316	2. ነገት-ቫ _____
1. ፖስት-ቫ _____	ቁ 315 ፖስት-ቫ ከሆነ ወደ 316				
2. ነገት-ቫ _____					
316	CD4	<table border="1"> <tr> <td>1. በምርመራው ወቅት _____</td> </tr> <tr> <td>2. የአሁኑ _____</td> </tr> </table>	1. በምርመራው ወቅት _____	2. የአሁኑ _____	
1. በምርመራው ወቅት _____					
2. የአሁኑ _____					