2020-01

Ethiopian Field Epidemiology Training Program Proportion and Factors Associated with Rifampicin Resistance Among New Pulmonary Tuberculosis Patients at Gene-Xpert Site Of Hospitals in Eastern Part Of Amhara Region, Ethiopia

Abtew, Abera

BAHIR DAR UNIVERSITY

COLLEGE OF MEDICINE AND HEALTH SCIENCES

SCHOOL OF PUBLIC HEALTH

DEPARTMENT OF EPIDIMIOLOGY AND BIOSTATISTICS

ETHIOPIAN FIELD EPIDEMIOLOGY TRAINING PROGRAM

PROPORTION AND FACTORS ASSOCIATED WITH RIFAMPICIN RESISTANCE AMONG NEW PULMONARY TUBERCULOSIS PATIENTS AT GENE-XPERT SITE OF HOSPITALS IN EASTERN PART OF AMHARA REGION, ETHIOPIA, 2019

BY

ABTEW ABERA (BSc in MLS)

A THESIS RESEARCH SUBMITTED TO THE DEPARTMENT OF EPIDEMIOLOGY AND BIOSTATISTICS, SCHOOL OF PUBLIC HEALTH, COLLEGE OF MEDICINE AND HEALTH SCIENCES, BAHIR DAR UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIRMENTS FOR THE DEGREE OF MASTER OF PUBLIC HEALTH IN FIELD EPIDEMIOLOGY

February, 2020

Bahir Dar, Ethiopia

BAHIR DAR UNIVERSITY

COLLEGE OF MEDICINE& HEALTH SCIENCES

SCHOOL OF PUBLIC HEALTH

DEPARTMENT OF EPIDIMIOLOGY AND BIOSTATISTICS

ETHIOPIAN FIELD EPIDEMIOLOGYTRAINING PROGRAM (EFETP)

PROPORTION AND FACTORS ASSOCIATED WITH RIFAMPICIN RESISTANCE AMONG NEW PULMONARY TUBERCULOSIS PATIENTS AT GENE-XPERT SITE OF HOPITALS IN EASTERN PART OF AMHARA REGION, ETHIOPIA, 2019

NAME AND ADDRESS OF THE PRINCIPAL INVESTIGATOR

ABTEW ABERA (BSC.)

PHONE: 0911066676

EMAIL: ABTABERA03@GMAIL.COM

NAME AND ADDRESS OF THE ADVISORS

1. MR. ZELALEM MEHARI (BSC., M.SC., ASSISTANT PROFESSOR OF BIOSTATISTICS)

PHONE: 0911058918

EMAIL: ZELALEM2011@MAIL.COM

BAHIR DAR UNIVERSITY

2. MR. GETACHEW HAILU (BSC., IN PH, MPH., ASSISTANT PROFESSOR IN EPIDEMIOLOGY)

PHONE: 0936324779

EMAIL:GETACHEWMPH35@GMAIL.COM

BAHIR DAR UNIVERSITY

February, 2020

Bahir Dar, Ethiopia

Acknowledgments

I would like to express my heartfelt thanks to my academic advisors first Mr. Zelalem Mehari, secondly Mr. Getachew Hailu for their unreserved guidance, constructive suggestions and comments, valuable advice, and unrestricted supports in each step of this thesis process.

Thirdly my appreciation also goes to organization officials in study sites, data collectors, supervisors and study participants for their valuable willingness to provide information and support and for their participation in the study respectively.

Fourthly I would like to thank D.r Mehatem Haile for her unrestricted guidance, constructive suggestions and valuable advice in the preparation of this thesis process.

Lastly, I would like to thank Bahir Dar University for providing me to join in Ethiopian Field Epidemiology Training Program and chance to prepare this thesis report.

Abstract

Introduction: - Rifampicin-resistant tuberculosis is caused by bacteria that do not respond to rifampicin. The emergence and spreading of Rifampicin-resistance strains of mycobacterium tuberculosis poses significant challenges to tuberculosis control programs particularly in resource-limited countries like Ethiopia. In Eastern part of Amhara Region rifampicin-resistance also a major challenge for TB control and the available study doesn't show proportion and factor associated with rifampicin-resistance among new pulmonary tuberculosis patients.

Objective: - The aim of this study was to assess proportion and factors associated to rifampicin resistance among new pulmonary tuberculosis patients in Eastern part of Amhara Region, Ethiopia, 2019.

Methods: - A facility based cross-sectional study design was conducted among 570 new pulmonary tuberculosis patients in Eastern Part of Amhara Region, Ethiopia from April to November, 2019. Systematic random sampling technique was used to select the study participants from 8 stratified Gene-Xpert site hospitals. Structured questionnaire and document reviews were used to collect data. Rifampicin resistance was detected by rapid Gene-Xpert assay from sputum specimens. Variables with P-value <0.2 in simple binary logistic regression were included in the multiple binary logistic regressions. Statistical test was reported as significant when p-value < 0.05 in multiple variable logistic regressions. Fitness of goodness was checked by using Hosmer Lemeshow model fitness test.

Results:-A total of 570 new pulmonary tuberculosis patients were participated in this study. Of those, 43 (7.50%) 95% CI: 5-10) was resistance to rifampicin. Persons have contact history with known tuberculosis Patients (AOR 2.5 [95% CI: 1.21-5.11]), persons with human immune virus infection (AOR 2.3 [95% CI: 1.11-4.73]) and persons being diabetic mellitus cases (AOR 4.2[95% CI: 1.51-8.78]) were factors significantly associated with rifampicin resistance.

Conclusions and recommendations: - Proportion of rifampicin resistance among new tuberculosis patients was high. Identified factors significantly associated with rifampicin resistance were: - Persons, who have contact history with known tuberculosis patients, have human immune virus infection and being diabetic mellitus cases. Strengthen prevention of rifampicin resistance tuberculosis transmition, strengthening contact tracing, improve tuberculosis-human immune virus health care services, and screening tuberculosis patient for diabetic mellitus are crucial.

Keywords:-Tuberculosis, Rifampicin resistance, Gene-Xpert, Eastern Amhara, Ethiopia.

Acronyms and Abbreviations

AOR .....Adjusted Odds Ratio
BP.....Base Pair
CDC .....Communicable Disease Control
CI.....Confidence Interval
COR .....Crude Odds Ratio
DM…….. Diabetic Mellitus
DNA.....Deoxyribonucleic Acid
DR…….. Drug resistance
DST.....Drug Susceptibility Test
EMB/E .....Ethambutol
HIV .....Human Immune Virus
IC.....Internal control
INH/H ..... Isoniazid
IUATLD.....International Union Against Tuberculosis and Leprosy Disease
LiPA.....Line Probe Assay
LJM.....Lowenstein-Jensen Medium
MDR .....Multi Drug Resistance
MLS .....Medical Laboratory Sciences
MTB.....Mycobacterium Tuberculosis
MTBC .....Mycobacterium Tuberculosis Complex
OR.....Odds ratio
PCC.....Probe Cell Control
PCR.....Polymerase Chain Reaction
RIF .....Rifampicin
RR .....Rifampicin Resistance
SM.....Streptomycin
SPC .....Sample Processing Control
SSA .....Sub Saharan Africa
TB .....Tuberculosis
UK.....United Kingdom
USA.....United States of America
WHO.....World Health Organization
XDR-TB.....Extensive Drug Resistance Tuberculosis

Table of Contents

Contents page

List of Tables

List of Figures

List of Appendixes

1. Introduction

1.1. Back ground

Anti-tuberculosis (TB) drug resistance (DR) is a major public health problem that threatens progress made in TB care and control worldwide. Essentially, rifampicin resistance (RR/DR-TB) arises in areas with weak TB control programmes and patient who develops active disease with a (RR/DR-TB) strain can transmit this form of TB to other individuals (1).

Tuberculosis (TB) is a chronic infectious disease caused by a group of bacteria called *Mycobacterium tuberculosis* complex (MTBC) that is spread from person to person through the air. *Mycobacterium tuberculosis* (MTB) belongs to the genus Mycobacterium that includes more than 150 species. MTB is aerobic, non-motile, non-spore-forming rod shape bacteria that affects any part of the body and most commonly the lungs (2).

Drug resistance(DR) mainly Multidrug Resistant Tuberculosis (MDR-TB) and Extensively Drug Resistance Tuberculosis(XDR-TB) are caused by genetic mutation of the *MTB* which renders anti-TB agents ineffective against the mutant tubercle bacilli (3). But, according to Caminero, suggestions there are two categories of risk factors for drug resistant tuberculosis. The first category, he describes as 'those facilitating the selection of resistance in the community' and the second as 'specific conditions that appear to increase some patient's vulnerability to resistance (4). The emergence and spreading of MDR and XDR –MTBC strains poses significant challenges to TB control (5). According to the World Health Organization/International Union Against Tuberculosis and Lung Disease (WHO/IUATLD) survey of 20 countries with the highest rates of MDR-TB mostly done in previously treated cases (6).

Even though acid-fast staining has very low sensitivity in detection of MTB, it remains the main diagnostic method in resource-limited settings. On the other hand, culture is the gold standard and the most sensitive method for TB diagnosis and DR; however, its use in clinical practice is limited due to a long turnaround time, biosafety requirements, and high cost (7). In aware of this fact, WHO introduced the wide use of Xpert MTB/RIF assay; which fully automated diagnostic molecular test using real-time polymerase chain reaction (PCR) technology to simultaneously detect MTB and RR mutations in the rpoB gene (8).

1.2. Statement of the problem

Globally, an estimated 10.0 million people fell ill with TB. The burden of disease varies enormously among countries, from fewer than five to more than 500 new cases per 100,000 populations per year. There were an estimated 1.2 million TB deaths among HIV-negative people in 2018 and an additional 251, 000 deaths among HIV positive people. (9)

Globally, 3.4% of new TB cases and 18% of previously treated cases had MDR/RR-TB. And, 51% of people with bacteriologically confirmed TB were tested for RR, up from 41%; Coverage of testing was 46% for new and 83% for previously treated TB patients (9).

Drug-resistance surveillance data show that, 4.1% of new and 19% of previously treated TB cases in the world were estimated to have RR or MDR-TB. There were an estimated 600 000 new cases of MDR/RR- and 240, 000 deaths due to MDR/RR-TB. Most cases and deaths occurred in Asia. And also about 6.2% of MDR-TB cases have additional DR and XDR-TB) (10). Only 55% of the MDR/RR-TB patients who started treatment were successfully treated, while 15% of patients died and treatment failed in 8% of patients. About 8.5% of MDR-TB cases had XDR-TB and treatment success in XDR-TB patients was only 34% (11).The emergence of DR-TB is a critical threat to TB control and is a major public health concern in several countries.

In sub Saharan Africa (SSA) RR/MDR-TB, is an emerging as a major clinical and public health challenge (12). DR-TB in SSA had results for a total of 13,465 new and 1,776 previously treated TB patients through a estimate of any DR-TB prevalence among the new cases was 12.6% (95% CI 10.6-15.0) while for MDR-TB of this was 1.5% (95% CI 1.0-2.3) and among previously treated patients, these were 27.2% (95% CI 21.4-33.8) and 10.3% (95% CI 5.8-17.4%), respectively (13).

Ethiopia is one of the high TB burdened countries in sub Saharan Africa, which ranks ten among the 30 high TB burden countries in the world (9). The National Tuberculosis Reference Laboratory together with seven Regional TB laboratories study in Ethiopia showed the proportion of MDR-TB was 4.3% in new patients, while 6.7% in previously treated patients and the overall proportion of MDR-TB was 11.6% (14). In countries with high burden of TB, continuous surveillance and regular monitoring of DR based on routine drug susceptibility testing (DST) of TB patients is essential to assess the magnitude and trends of DR-TB (15). In Ethiopia, 2.3% of new TB and 17.8% of previously treated TB cases were estimated to have MDR-TB (10).

The study conducted in Metema northern part of Amhara region among 124, smear positive TB patients the result of RR based on treatment history of participants indicates that, the prevalence of RR/MDR-TB from new smear positive TB cases and who have previously anti TB was 2 (2.3%) and 5(13.9 %) respectively. Seven RR cases were further investigated with LJ medium for growth of MTB and detection of INH resistance as well as confirmation of RR strain , in all seven(100%) of RR isolate were found to be INH resistance cases (16).

Ethiopia is working towards a controlling of transmission dynamics of TB to reduce morbidity and mortality, and preventing emergence and spread of DR in the general population. Despite all these efforts, in Ethiopia, (as well as in eastern Amhara region) there is limited capacity to perform TB culture and DST (12).Due to this reasons there are lack of study on rifampicin resistance among newly pulmonary TB cases in eastern part of Amhara region.

1.3. Justification of the study

Gene-Xpert offers an opportunity for timely and accurate initiation of TB/DR-TB treatment and shortened time to diagnosis in high burden settings. Detection of RR is very important in resource-limited countries since RR is the strongest proxy marker of MDR-TB. Now a day's TB cases which are resistance to rifampicin (RIF) directly treated with second line anti TB drugs as MDR-TB patients (10).

So, detection of RR in early time is detecting of MDR-TB easily and efficiently because there is a limitation of resource to avail culture diagnosis method like Gene-Xpert in every hospitals. In countries with high burden of TB, rapid detection, continuous surveillance and regular monitoring of DR- TB is essential for disease management and earlier treatment initiation.

Conducting a study to detect RR on new cases used to estimate the magnitude and associated factors of primary RR, facilitates early detection of RR and also used to prevent primarily RR transmition to others. However, there is a lack of study on proportion and factors associated with RR-TB among newly pulmonary TB cases. In addition, the available study doesn't show the proportion and factor associated with RR among new pulmonary TB cases in eastern part of Amhara region. Therefore, the aim of this study is to determine the proportion and associated factors of RR -TB among M.TB patients in eastern part of Amhara Region Ethiopia.

2. Literature review

2.1. Proportion of RR-TB

A 2018, WHO report indicates about , 3.5% of new TB cases MDR/RR-TB (11). And study conducted in Peru /Northern America among adults with anew smear-positive pulmonary TB prevalence of RR/MDR-TB cases was 2.3% (17). And in Eastern Uttar Pradesh /Northern India / among new presumptive TB patients showed that 5 (7.6%) were found to be RR/MDR-TB (18).

A study conducted in Iran showed that thirty-seven (32.2%) were resistant to at least one drug and proportion of for RIF mono-DR was 1.7% (19).

In Cameroon Study indicates a 16 (1.6% prevalence of RR-TB with Gen-Xpert diagnosis method but the rate of RR-TB in the regions varied between 0 and 3.3% (20).

A study conducted in Kwazulu-Natal, South Africa RR reported that the proportion of RR varied from a low of 7.3% to a high of 10.0% with the overall RR prevalence of 8.8% (21).

A study conducted in Uganda among 1209 new patients with DST, showed the prevalence of resistance to any of the drugs was (10.3%), resistance to RIF was 1.9%. (22).

A study in Mogadishu-Somalia among patients suspected for MDR-TB showed that prevalence of RR to TB was 71 (51.5%) (23).

A study conducted in Eastern Ethiopia for drug sensitivity test as well as for DR with new smear positive pulmonary TB patients for the first line anti-TB drugs showed that the prevalence of any resistance to one drug among new M.TB cases was 82 (23%). But a resistance to RIF was 10 (2.8%) (24).

In Ambo town, a study employed indicates that prevalence of any resistance to one of the drugs was 23.3%. There was only a single case (1.2%) of MDR/ RR-TB from newly diagnosed pulmonary TB patients (25).

In Amhara region, a study conducted among 606 Presumptive MDR-TB cases the overall prevalence of MDR-TB was 15.3%, RFI and INH mono resistance were 12.8% and 12.5%, respectively. Considering RIF mono resistance as surrogate marker for MDR TB, prevalence of MDR TB/RIF resistance was 11(18.2%) (26).

A retrospective study conducted in University of Gondar hospital on 1,820 TB presumptive cases for the RR detection, the result of RR/MDR-TB shows that from a total of the 24.6% participants TB-confirmed cases, 15.8%, were RR. Of this 13% of RR was among new TB-confirmed cases. (27). A retrospective cross-sectional study conducted on North West Ethiopia in Debre Tabor General hospital and in Felege Hiwot referral hospital from 258 TB positive cases detected by

using Gene-Xpert test and from this TB cases 9.3% of them were found to be RR and the proportion RR cases detected, 41.7% of them were new and 29.2% were relapsed TB cases (28).
Study conducted in East Gojjam zone showed that resistance to RR among newly diagnosed patients was 3.89% and DR to at least one drug was detected in 18 (20.23 %), of the isolates , of which 20.7 % were males and 19.4 % were females (29).
Study conducted in Debre Markos referral hospital showed that from total of 117 confirmed M.TB study participants the overall prevalence for RR was 10.3% and the proportion of RR - M.TB was 17.1% among previously treated TB patients and 6.7% among treatment naïve (new) patients. From new 69 presumptive DR TB patients, RR M. TB detected in 10.7% (30).

2.2. Factors associated with RR

2.2.1. Socio demographic factors with RR

Global surveillance report showed that the load of MDR/RR-TB in children age of less than 15 years old compared to adults aged greater than or equal to 15 years differ widely between countries that was ranging from 0.25 to 5.76. Among the 36 countries included Global analysis reported at least one case of MDR-TB in children aged, <5 years and in children aged 5–14 years. In these countries the odds of harboring MDR-TB was not significantly different between these two groups of children (31).
Study conducted in Uttar Pradesh RR/MDR- TB patients 38 (30.6%) were male while 6 (13.6%) were female and most of them were in the age group of 20-40 years (36.7%). (18).
In Nepal (northern India) the study confirmed that education status of the study participants regarding MDR TB is strongly associated at AOR of 9.643 more times than lower education status (32).
In Uganda the study for factors Associated with DR was done and in urban clusters were more likely (AOR 6.0) to have MDR-TB as compared to those from rural clusters. The study shows also a significant association between age and DR; those greater than 35 years were more likely (AOR=2.0) to have MDR-TB as compared to patients less than 35 years old among new patients (22). A study Kwazulu-Natal, South Africa RR males show a 42% increased odds of being RR as compared to females. RR was 37% more likely to occur in the 25–29 year age category compared to the 50+ age group (21). In Serbia, a study conducted for RR/MDR-TB among TB patients on 124 respondents stigma associated with TB was identified as factors for the occurrence of MDR-TB (33).

Study conducted in Jimma University on MDR-TB from TB study participants whose age was ≤30 years were 7 times more likely to have MDR-TB compared to those whose age was greater than 30 years old (34). Study conducted in East shoa, Bishoftu and Adama hospitals study identified individuals without a job as factors associated with MDR-TB infection those individuals (AOR = 2.4) (35). And study in Amhara region shows individuals young age or ≤ 25 age years old (AOR=2.9) were the other risk factors of MDR-TB (36). Study in Addis Ababa indicates that being female was identified as an independent risk factor (AOR=1.5) for RR-TB as compared to male individuals (37) . Family members living together in crowded area become a risk factors for MDR-TB development and Study done in Nepal showed that size of family members greater than or equal to five was 2.4 times more develop MDRTB compare to family size less than five (38).

2.2.2. Housing condition related factors with RR

In Nepal (northern India) the study confirmed that among study participants regarding MDR TB not association between ventilation of rooms (32). But Study conducted in Jimma University on MDR-TB from TB respondents showed the risk of individuals living in a household with only one room were 5 times at higher risk of having MDR-TB than patients living in a household with two or more rooms (AOR=5.07) (34). In Amhara region, shows among study participants who were living in a house of mud floor was higher in the MDR-TB cases (83.7%) than in the control group (71.2%) (36).

2.2.3. Disease related factors with RR

The study conducted in Peru /Northern America indicates that ,HIV positive status was the only factor that had association to RIF mono-resistance with an odds ratio of 9.43 times than HIV negative individuals (17). A study done in Serbia indicates that study participants that have chronic (asthmatic) pulmonary disease were 4.51 times more likely develop RR/MDR-TB (33).

Meta-analysis study in China indicated significant association between DM and MDR-TB, i.e., patients with DM were more likely to have MDR-TB (AOR =1.71) and another study in china also DM was significantly associated with any DR-TB (AOR=1.30 (39-40). Study conducted in India among patients with confirmed TB, diabetes was associated with 3.0-fold higher risk of rifampicin resistance(41). Study conducted in Sudan shows contact history with TB patients (AOR, 5.40) identified as factors associated with MDR-TB infection(42).

A systematic review studies in Ethiopia Harar from 15 different countries revealed that DM has a significant association with MDR-TB (OR = 1.97) (43). Similarly a study conducted in different parts of Ethiopia shows that in Eastern Ethiopia HIV-positive patients were 3.7 times more likely to develop resistance to any one of anti-TB drugs compared with those HIV negative patients (24).

Study done in Jimma indicates that respondents who had HIV infection were 3 times more likely to have MDR-TB compared to respondents who had no HIV infection (AOR=3.1) (34). Study conducted in Ambo indicates that MDR-TB was detected among HIV positive hospitalized study participant (25). Study conducted in East shoa, Bishoftu and Adama hospitals those have history of contact with known TB patients (OR = 2.1) identified as factors associated with MDR-TB infection (35). And study in Amhara region shows significance associated with MDR-TB infection with individuals have history of close contact with known -TB patients and the odds of contact history with MDR-TB patients were 1.4, times (AOR=1.4) more likely to be MDR-TB patients (36).

2.2.4. Behavioral related factors associated with RR

A study in Nepal revealed that those participants who had smoking habit were 2.350 times more likely to have RR/MDR.TB (32). Other study done in Croatia also shows that a person who had smoking cigarettes 2.3 times more developed MDR TB than non-smoker (44).

In Serbia a study shows that study participants that have a feeling of sadness and that use sedatives were 4.05 and 2,79 times more likely to develop RR/MDR-TB (33).

A study in Mogadishu Somalia showed 67.4% of the study participants had RR/MDR-TB who have a habit of smoking and chewing Khat or both (23).

A surveillance conducted Kenya in refugee camp and non refugee camp DR-TB was 3.7 times higher in the camps than in the non-refugee population (45).

A comparative cross sectional study was conducted on 126 MTBC from prisons and communities in southern and eastern Ethiopia RR/MDR-TB of the community was 2.27% whereas that of prisons was 9.52% (46).And study in East Gojjam Zone among new smear positive prisoners shows that about 0.4% of the prisoners had RR/MDR-TB (47).

3. Conceptual framework

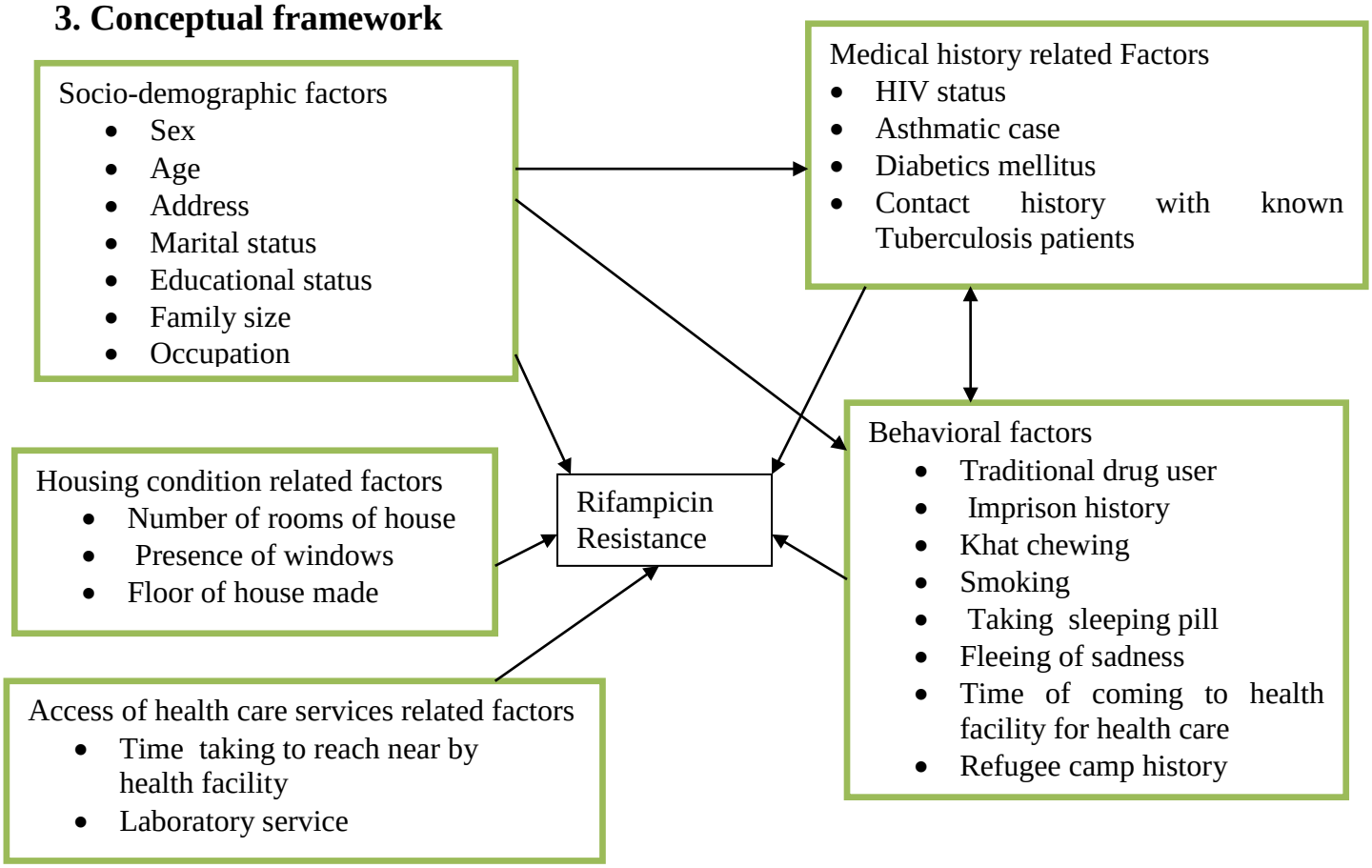

Figure 1: Conceptual framework for RR study among new pulmonary tuberculosis cases in eastern part of Amhara Region, Ethiopia, 2019.

4. Objective

4.1. General objective

- To assess the proportion and factors associated with RR among new pulmonary TB patients at Gene-Xpert site of hospital laboratories in Eastern Part of Amhara Region – Ethiopia, 2019.

4.2. Specific objectives

- To determine the proportion of RR among new pulmonary TB patients at Gene-Xpert site of hospital laboratories in Eastern Part of Amhara Region–Ethiopia, 2019.
- To identify factors associated with RR among new pulmonary TB patients at Gene-Xpert site of hospital laboratories in Eastern part of Amhara Region –Ethiopia, 2019.

5. Methods

5. 1. Study area

The study was conducted in the Eastern part of Amhara Region at eight different Gene-Xpert laboratory sites of hospitals, such as Wolidia general hospital, Borumeda district hospital, Dessie referral hospital, Mekane Selam district hospital, Kemissie general hospital,Ataye district hospital, Shoarobit district hospital and Debrebrehan referral hospital. The Gene-Xpert sites are located in the Northern direction of Addis Ababa in the distance 130 to 581 kilometers far apart and from 250 to751 kilometers from Bahir Dar (capital city of Amhara Regional state) in the Eastern direction. The Eastern part of Amhara Regional States had one metropolitan city administration (Dessie town) and five zones, namely Waghimira (Sekota town), North Wollo (Wolidia town), South Wllo (Dessie town), Oromo special zone (Kemissie town) and North Shoa (Debrebrehan town). According to 2007 censuses projection, the estimated population size of the study area was 7,407,286 million people. Of this, 53.9% were females. The Eastern part of Amhara Region had 75 woredas, 27 hospitals, 339 health centers, 1377 health posts and 198 private health facilities.

5.2. Study design and period

A facility based cross-sectional study was conducted from April to November, 2019.

5.3. Source and study population

The source population for this study was all new pulmonary TB cases in Eastern part of Amhara Region.

The study population was all individuals with new pulmonary TB cases at Gene –Xpert site hospitals.

5.4. Eligibility criteria

5.4.1. Inclusion criteria

- ✓ All new pulmonary TB cases that came to in selected Gene-Xpert sites of hospital laboratories in Eastern part of Amhara region.

5.4.2. Exclusion criteria

- ✓ Persons with new pulmonary TB who were unable to communicate due to severe illness and unable to speak were excluded.

5.5. Study Variables

5.5.1. Dependent variable

- ❖ Rifampicin resistance (primary drug resistant)

5.5.2. Independent variables

Socio-demographic related factors include ---Sex, age, residence, marital status, educational status, family size, occupation status.

Housing condition related factors include-- Number of room of house, presence of windows, and floor of house made.

Access of health care services related factors include--Time of taking to health facility and availability of TB laboratory service in nearby health facilities.

Medical history related factors include **---** HIV status, asthma, diabetic mellitus status, and contact history with tuberculosis patients.

Behavioral related factors include ---Smoking cigarette, traditional drug user, imprison history, chat chewing, taking sleeping pill, fleeing of sadness, delay in visiting health facility, refugee camp living history or live with internally displaced people.

5.6. Operational definitions of terms

New pulmonary TB patients/cases: - Positive result of M.TB patients who were never been treated for TB or received treatment less than one month of therapy.

Presumptive/Suspected:-patients who show sign and symptom of TB and suspected by physicians in outpatient departments send to Gene-Xpert laboratory for the diagnosis of TB/RR/MDR-TB at the same time.

Sign and symptom of TB: - patient of prolonged coughing (≥ two weeks), night sweating, weight loss, chest pain, loss of food desire.

Primary DR:- "New Cases "DR in a patient who has never been treated for TB or received less than one month of therapy, implying they were infected with a resistant TB. This reflects person-to-person transmission of DR- TB bacilli.

Presumptive RR/MDR-TB: - Individuals who have contacted with known TB, MDR/RR-TB, HIV patients and M.TB positive considered to suspect/presumptive to RR/MDR-TB.

Contact: - defined as people from the same household/dormitory/ sharing common habitation rooms/stay.

Rifampicin resistant TB: - TB caused by strains of M. TB that are resistant to RIF.

Non smokers: An adult who has never smoked, or who has smoked less than 100 cigarettes in his or her lifetime.

Smokers: - were an adult who has smoked 100 cigarettes in his or her lifetime and who currently smokes cigarettes

Khat chewer: - person who had chewing Khat for at least 5 years with a frequency of at least once a month and minimum chewing session duration of 3 hours.

Non- Khat chewers: - person who had never chewed khat or those who chewed no more than 5 times in their lifetimes.

Traditional medicine user: - person's practices based on the theories, beliefs, and experiences home-grown to different cultures used in the protection of health as well as in the prevention, diagnosis, improvement for their health problem.

5.7. Sample size determination

The sample size has been determined by using single population proportion statistical formula for prevalence and two-population proportions formula for factors.

5.7.1. Sample size for objective I

Proportion of RR in previous study which has been conducted in East Gojjam zone Amhara Region –Ethiopia 0.0389 was taken (29).

$$n = \frac{(z\alpha/2)^2 \cdot pq}{d^2}$$

Where:-

n=the sample size from single population proportion formula.

Z =Standard normal deviation at 1.96 (which corresponds to 95% level).

p = 3.89% estimated population proportion of RR from a study done in East Gojjam zone Amhara Region-Ethiopia

d = margin of error (2%).

Non- response rate =10%.

Design effect =1.5

Therefore, the final sample size for this study have been =593

5.7.2. Sample size for objective II

Table 1: Sample size determination of factors on RR study among new pulmonary TB patients in eastern part of Amhara region –Ethiopia 2019.

Variables		Outcome variable			Ratio/ unexposed to Exposed	% of outcome in unexposed group	AOR	Assumptions		Sample size
		Cases	Non-cases	Reference group				CI	Power	
HIV Status	positive	6	11		1	16.66	2.76	95%	80%	188
	Negative	12	60	1*						
Age	15-24	4	28	1*	1	12.5	4.2	95%	80%	116
	25-34	10	15							

(29). 1* reference group

The sample size determined based on the proportion of RR was the maximum sample size. Considering 10% non response rate and 1.5 design effect the final sample size for this study was 593 among new pulmonary TB patients.

5.8. Sampling procedure

In Eastern part of Amhara region there are twenty functional governments Gene-Xpert site of hospitals from those, eight (40%) Gene-Xpert sites of hospitals were selected randomly using lottery method and the calculated sample size was proportionally allocated to selected Gene-Xpert sites of hospitals based on average number of new pulmonary TB cases from reviewing survey prior to the study period was used. Systematic random sampling technique was used to select the study participants from each selected Gene-Xpert laboratory sites and sampling interval was conducted to collect study participants by considering the laboratory flow of M.TB cases (figure2).

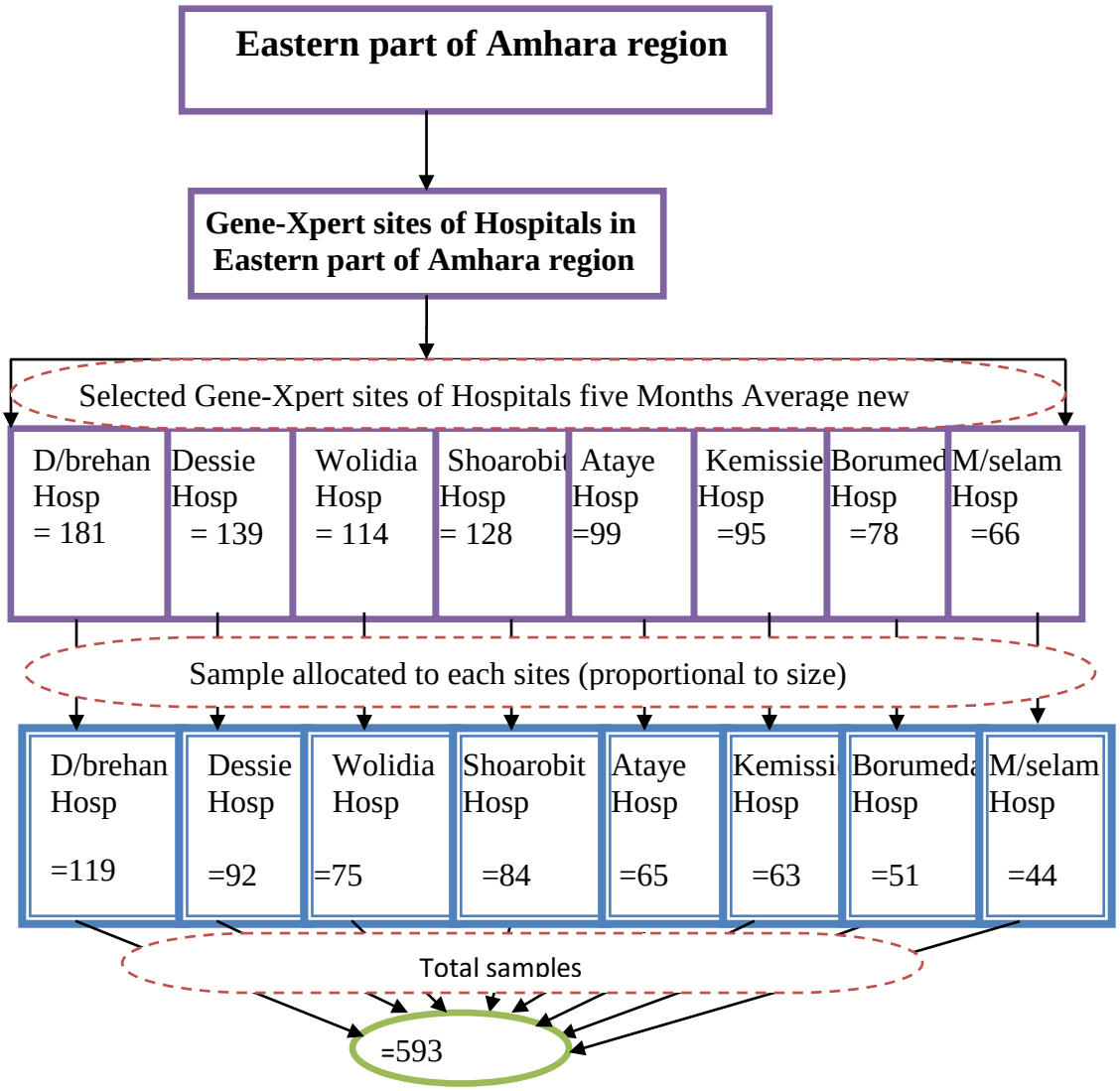

Figure 2:-Diagrammatic representation of sampling procedure of RR and associated factors study among new pulmonary TB cases from Gene-Xpert laboratory sites, in eastern Amhara region Ethiopia 2019

5.9. Data collection procedures

5.9.1. Socio demographic and other related information

Data were collected by face to face interview using a structured questionnaire, document review and laboratory results. The questionnaire developed after reviewing previous similar literatures to include all possible variables that address the objective of the study. The data collection tools (questionnaire) gathered from themes of participants' characteristics, like socio-demographic, clinical related factors housing condition, access of health care service and behavioral related factors. The data were collected by eight medical laboratory technicians and supervised by eight medical laboratory technologists and principal investigator.

5.9.2. Specimen collection and Laboratory investigations

A single sputum specimen was recommended for Gene-Xpert MTB/RIF and 2mL of sputum specimen was collected.

The Gene-Xpert MTB/RIF system is a fully automated nested real-time PCR system, which detects MTB complex DNA in samples. It simultaneously identifies mutations in the rpoB gene, which are associated with RR. The Gene-Xpert MTB/RIF system consists of the instrument, a computer, a barcode scanner and requires single-use disposable Gene-Xpert MTB/RIF cartridges that contain assay reagents. Following a 3-step sample preparation in the laboratory, the specimen was transfer into the MTB/RIF cartridge and entered into the Gene-Xpert instrument.

By starting the test on the system software, the Gene-Xpert automates all following steps, including sample work-up, nucleic acid amplification, detection of the target sequence and result interpretation. The primers in the Gene-Xpert MTB/RIF assay amplify a portion of the rpoB gene containing the 81 base pair “core” region. The probes are able to differentiate between the conserved wild-type sequence and mutations in the core region that are associated with RR.

Furthermore, the assay includes a sample processing control (SPC) to control for adequate processing of the target bacteria and to monitor the presence of inhibitor(s) in the PCR reaction. A Probe Check Control (PCC) verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability. Specimens ware manually transferred to the cartridge, which was loaded into the Gene-Xpert instrument and subsequently processed automatically at Gene –expert sites Laboratory.

5.10. Data management, data quality and data analysis

5.10.1. Data management

Data were coded with unique identification number during data collection and data were entered in to Epi data version 3.1 statistical software. Data entered, cleaned and verifications have been performed to ensure quality of data before analysis. Data confidentiality was ensured by keeping under secured condition using cabinet as well as by allowing access only for authorized persons.

5.11. 2. Data quality

Before data collection the questionnaire was first prepared in English then translated in Amharic (local language) by an expert who is fluent in both languages to maintain its consistency. To enhance the quality of this research pretest was conducted in 5% of the total sample size in Akesta (Hidar 11 hospital) South Wollo Zone, which was out of the study sites. The qualities of the data were assured

by properly designed and pre-tested questionnaire, proper training of the interviewers and supervisors. During the data collection time, regular monitoring and supervision of the overall activity was done by supervisors and principal investigator to ensure the quality of data. All the collected data were checked, cleaned and coded to avoid some inconsistencies and incompleteness before analysis.

5.11.3. Gene-Xpert (laboratory) quality control

The Gene-Xpert System automatically performs internal quality control for each sample. During each test, the system uses one or more of the following controls. Sample-processing control (SPC): Ensures a sample was correctly processed. The sample-processing control is included in the cartridge and is processed with the sample and the DNA is detected by a PCR assay. Internal control (IC)—verifies the performance of the PCR reagents and prevents a false negative result. The internal control PCR assay assesses if there is any inhibition, possibly by components, in the test sample. Internal control is provided in the cartridge and should be positive in a negative sample. Endogenous/inbuilt control (EC): Normalizes targets and ensures sufficient sample is used in the test. Because of its low variability, the endogenous control can also be used to indicate sample-inhibitor contamination. The endogenous control is taking from the specimen sample.

5.10.4. Data analysis

Data were entered into Epi-data version 3.1 and export to statistical Package for Social Sciences (SPSS) software version 20 for analysis. Descriptive analyses (proportions, frequencies, and averages) were used to determine the socio-demographic, disease related and behavioral characteristics.

The possible candidate variables for RR factors have been analyzed first by simple binary logistic regression analysis by using enter method and then variables which have p value < 0.2 were analyzed in multiple binary logistic regression analysis by incorporate backward logistic regression to control the effects of possible confounding variables. Odds ratio, 95% CI was computed to evaluate degree of association between dependent and independent variables to conclude, P-value < 0.05 were consider statistically significant and the goodness of fitness was checked by using Hosmer Lemeshow model of fitness (p-value >0.05).

5.12. Ethical considerations

Ethical clearance was obtained from Institutional Review Board of School of Public Health, College of Medicine and Health Sciences, Bahir Dar University. Co-operation and permission letter were taking from concerned organization. Verbal consent was obtained from each individual after the purpose of the study explained. Anyone who refuses to participate in the study was told as he/she had full right not to participate. Participants were also informed that all the data obtained from them were kept confidential using codes instead of any personal identifiers and locks in file cabinet. Any study participants who were positive for M.TB and RR were linked to TB clinics and treatment initiative center respectively for further follow-up.

6. Results

6.1 Socio demographic characteristics of new pulmonary tuberculosis patients

A total of 570 new pulmonary TB patients were included in the study with a response rate 96.30 % of the study sample size. From those new pulmonary TB patients, 312 (54.7%) of them were males, 380(66.70%) of them married by marital status. The mean age of new pulmonary TB patients found to be 38.91 with a standard deviation $\pm$ 16.74 years old. Three hundred forty seven (60.90%) of them were from rural area. The educational status of new pulmonary TB patients indicates that, 271(47.50%) of them unable to read and write, 171(30%) of them in grade 1-8th plus able to read and write. From new pulmonary TB patients, 193(33.90%) of them were farmer and 144(25.30%) of them housewives by occupational status (Table 2).

Table 2: Socio demographic characteristics of new pulmonary TB patients in Eastern part of Amhara region Gene-Xpert testing sites-Ethiopia, 2019 (n=570).

Variables	Frequency(N)	Percentage (%)
Sex		
Male	312	54.70
Female	258	45.30
Age		
$\leq$30 years of age	218	38.20
$\geq$31 years of age	352	61.80
Address		
Urban	223	39.10
Rural	347	60.90
Marital status		
Married	380	66.70
Single	136	23.90
Divorced	30	5.30
Widowed	24	4.20
Educational status		
Unable to read and write	271	47.50
Read, write and from grade 1-8th	171	30.00
Grade 9-12th	62	10.90
Diploma and above	66	11.57
Occupational status		
Farmer	193	33.90
House wife	144	25.30
Unemployed	116	20.40
Employed	63	11.10
Merchant	54	9.50
Family size		
Less than five	398	69.80
Greater than five	172	30.20

6.2. Housing condition summary of new pulmonary TB patients

From the total new pulmonary TB patients 413(72.50%) them were live in the houses having two and above rooms, 459 (80.50%) of them lives in houses having one and above windows and 352(61.80%) in houses having made of mud.

6.3. Access of health care services profile of new pulmonary TB patients

Of the total new pulmonary TB patients 387(67.90%) of them can access health care services in less than two hours journey and 406(71.20%) of them have got TB laboratory service in nearby living area.

6.4. Clinical profile of new pulmonary TB patients

Ninety four (16.50%) of new pulmonary TB patients were asthmatic cases, 89 (15.60%) of them have HIV infection in their blood, and 39 (6.80%) were diabetic (Table 3).

Table 3 : Clinical characteristics of new pulmonary TB patients in Eastern part of Amhara region Gen-Xpert testing sites -Ethiopia, 2019 (n=570).

Variables		Frequency(N)	Percentage (%)
Asthmatic case			
	No	476	83.50
	Yes	94	16.50
Have HIV status			
	Negative	481	84.40
	Positive	89	15.60
Diabetic disease			
	No	531	93.20
	Yes	39	6.80
Contact history with known TB patients			
	No	476	83.50
	Yes	94	16.50

HIV: Human immune deficiency virus, PT: pulmonary TB, DR: drug resistance, TB: Tuberculosis

6.5. Behavioral assessment of new pulmonary TB patients

Fifty four (9.50%) of new pulmonary TB patients have imprison history, 163 (28.60%) have chat chewing habit, 87(15.30%) take traditional medicines and 55 (9.60%) have history of living in refugee camp (Table4).

Table 4: Behavioral characteristics of new pulmonary TB patients in Eastern part of Amhara region Gen-Xpert testing sites -Ethiopia, 2019 (n=570).

Variables	Frequency(N)	Percentage (%)
Imprisons history		
No	516	90.50
Yes	54	9.50
Khat chewing		
No	407	71.40
Yes	163	28.60
Smoking		
No	531	93.20
Yes	39	6.80
Taking sleeping pill		
No	536	94.00
Yes	34	6.00
Taking Traditional medicine use		
No	483	84.70
Yes	87	15.30
Refugee camp history		
No	515	90.40
Yes	55	9.60
Time of Health facility visit after developing sign and Symptom of TB		
In less 3 weeks	429	75.30
After 3 weeks	141	24.70

TB: Tuberculosis

6.6. Proportion of RR among new pulmonary TB patients

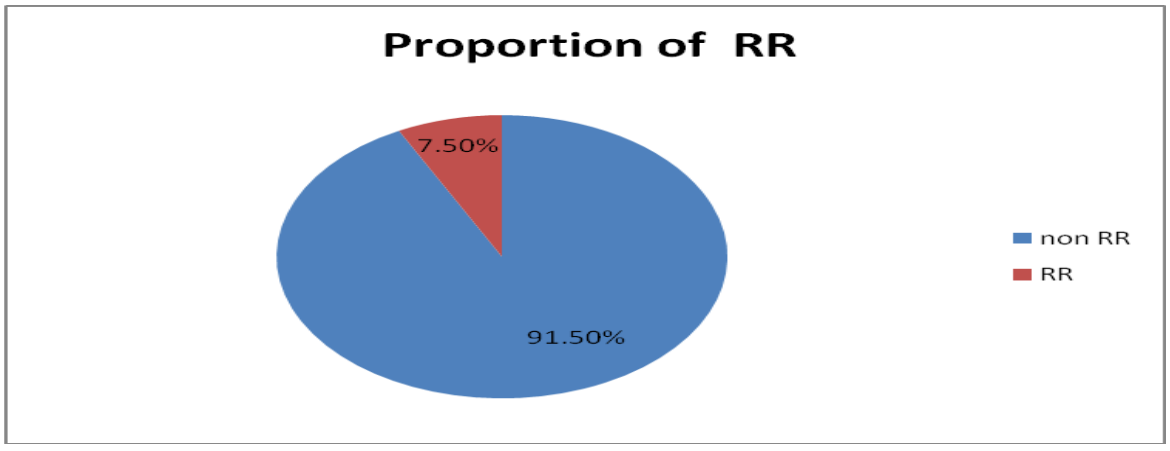

Figure 3:-Proportion of RR among new pulmonary TB cases from Gene-Xpert site hospitals, in eastern part of Amhara region, Ethiopia, 2019.

The proportion of primary RR-MTB among newly diagnosed Pulmonary TB patients in eastern part of Amhara region or in this study was 43 (7.50%) (95% CI: 5-10) (Figure3).

6.7. RR status among new pulmonary TB patients and by their socio-demographic characteristics

From RR-MTB confirmed cases 26 (60.40%) of them were females, 23 (53.50%) age greater than 30 years old and 30 (69.80%) of them were from rural area. The proportion of RR was higher in married individuals, 28(65%) and with an educational status who are unable to read and write 23 (53.50 %) (Table5).

Table 5: RR status among new pulmonary TB patients and by their socio-demographic characteristics in Eastern part of Amhara region Gene-Xpert testing sites -Ethiopia, 2019 (n=570) (RR not detected (RR^-) $^=$527, RR detected (RR^+) =43).

Variables	Rifampicin status			
	RR not detected		RR detected	
	N	(%)	N	(%)
Sex				
Male	295	56.00	17	39.50
Female	232	44.00	26	60.40
Age				
≤30 years age	198	37.60	20	46.50
≥31 years age	329	62.40	23	53.50
Address				
Urban	210	39.80	13	30.20
Rural	317	60.20	30	69.80
Marital status				
Married	352	66.20	28	65.10
Single	175	33.20	15	34.90
Educational status				
Unable to read and write	248	47.10	23	53.00
Read, write and from grade 1-8th	161	30.60	10	23.30
Grade 9-12th	54	10.20	8	19.00
Diploma and above	64	12.10	2	5.00
Occupational status				
Farmer	185	35.10	8	18.60
House wife	126	23.90	18	41.90

	Unemployed	107	20.30	9	20.00
	Employed	61	11.60	2	5.00
	Merchant	48	9.10	6	13.90
Family size					
	Less than five	368	69.80	30	69.80
	Greater than five	159	30.20	13	30.20

6.8. Status of RR by housing condition

From RR-MTB confirmed cases 15(34.90%) of them were live in house's with one room, 13(30.20%) in houses which have no windows and 32 (74.40%) live in the house's having floor made of mud.

6.9. Status of RR by acces of health care services

Of the RR-MTB cases 13(30.20%) of them can access health care services in greater than two hours journey and 15(34.90%) of them not get TB laboratory service in nearby living area.

6.10. Status of RR by clinical characteristics among new pulmonary TB patients

The status of RR by clinical characteristics of the study participants indicates that being HIV positives accounted 14 (32.60%) and 9(20.90%) have diabetes mellitus. Similarly, of the total confirmed RR cases, 15(34.90%) of them have history of contact with known TB in the last one year (Table 6).

Table 6: Status of RR by Clinical history characteristics among new pulmonary TB patients in Eastern part of Amhara region Gene-Xpert testing sites, Ethiopia, 2019(n=570).

Variables	Rifampicin status			
	RR not detected		RR detected	
	N	(%)	N	(%)
Asthmatic case				
No	442	83.90	34	79.10
Yes	85	16.10	9	20.90
HIV/AIDS status				
Negative	452	85.80	29	67.40
Positive	75	14.20	14	32.60
Diabetic disease				
No	497	94.00	34	79.10
Yes	30	6.00	9	20.90
Contact history with TB patients				
No	448	85.00	28	65.10
Yes	79	15.00	15	34.90

6.11. RR status by behavioral related factors among new pulmonary TB cases

RR status by behavioral characteristics indicates that, 5(11.60%) of them have imprison history, 13(30.20%) of them were came to health facility after a month for health care follow up and nine (20.90%) of them have history of living in refugee camp or live with internally displaced people camp in the last one year (Table7).

Table 7: RR status by behavioral characteristics among new pulmonary TB patients in Eastern part of Amhara region Gene-Xpert testing sites -Ethiopia, 2019 (n=570).

Variables	Rifampicin status			
	RR not detected		RR detected	
	N	(%)	N	(%)
Imprisons history				
No	478	90.70	38	88.40
Yes	49	9.30	5	11.60
Smoking cigarette				
No	489	92.80	42	97.70
Yes	38	7.20	1	2.30
Khat chewing				
No	376	71.30	31	72.10
Yes	151	25.70	12	27.90
Taking sleeping pill				
No	495	93.60	41	95.00
Yes	32	6.10	2	5.00
Taking traditional medicine use				
No	445	84.40	38	88.40
Yes	82	15.60	5	11.60
Sadness				
No	347	65.80	32	74.40
Yes	180	34.20	11	25.60
Refugee camp history				
No	481	91.30	34	79.10
Yes	46	8.70	9	20.90
Time of coming to health facility after seen sign and Symptom TB				
In less than 3 weeks	399	75.70	30	69.80
After Greater than 3 weeks	18	24.30	13	30.20

6.12. Factors associated with RR among new pulmonary TB cases

In this study the association factors were identified from newly confirmed mycobacterium tuberculosis cases. The candidate variables in simple binary logistic regression for multiple binary logistic regression has been selected based on p<0.2.Then the candidate variable which have been selected from the total twenty four variables in simple binary logistic regression are six such as sex, contact history, HIV status, diabetic's mellitus, refugee camp history, number of windows present.

Then multiple binary logistic regression analysis were carried out on six candidate variables to control potential confounding and to identified predictor variables which have significantly associated with dependent variable.

In multiple binary logistic regressions three predictor variables were identified which associated with dependent variable. Variables in multiple binary logistic regression which have <0.05 p-value consider as significantly associated with rifampicin resistance were:- Persons who have contact history with known TB patients, Persons who have HIV infection in their blood and persons who have diabetic mellitus disease were identified as a factor associated with RR-TB (Table 8).

The odds of RR among newly confirmed MTB cases with persons who have contact history with known TB patients were found to be 2.5 times (AOR 2.5 [95% CI: 1.21-5.11]) higher than those of who have no contact history with known TB patients.

The odds of RR among newly confirmed MTB cases with the persons who have HIV infection in their blood were 2.3 times (AOR 2.3 [95% CI: 1.11-4.73]) higher than from those who have no HIV infection in their blood.

The odds of RR among newly confirmed MTB cases with persons who have diabetic mellitus disease were found to be 3.6 times (AOR 3.6 [95% CI: 1.51-8.78]) higher than from those who have no diabetic mellitus (Table 8).

Table 8: Factors associated with rifampicin resistance among new pulmonary tuberculosis cases in Eastern part of Amhara region Gen-Xpert testing sites, Ethiopia, 2019 (n=570).

Variables	Rifampicin status		COR [95%CI]	AOR [95% CI]
	RR Detected No. (%)	RR not Detected No. (%)		
Sex				
Female	26 (60.50%)	232 (44.00%)	1.94(1.03-3.67)	1.78(0.92-3.44)
Male	17(39.50%)	295 (56.00%)	1	1
Number of windows in the house				
No window	13 (30.20%)	98 (18.60%)	1.89 (0.96-3.77)	1.76(0.85-3.63)
One and above	30 (69.80%)	429 (81.40%)	1	1
Contact history with known TB Patients				
Yes	15 (34.90%)	79 (15.00%)	3.04(1.55-5.94)	2.49(1.21-5.11)*
No	28 (65.10%)	448 (85.00%)	1	1
HIV/AIDS status				
Positive	14 (32.60%)	75 (14.20%)	2.91(1.47-5.76)	2.29(1.11-4.73)*
Negative	29 (67.40%)	452(85.80%)	1	1
Diabetic case				
Yes	9 (20.90%)	30 (6.00%)	4.39(1.93-9.98)	3.64(1.51-8.78)*
No	34 (79.10%)	497 (94.00%)	1	1
Refugee camp history				
Yes	9 (20.90%)	46 (9.00%)	2.77(1.25-6.13)	2.36(0.99-5.58)
No	34 (79.10%)	481 (91.00%)	1	1

1 Reference or control group, * P-value <0.05, RR: Rifampicin resistance, TB: tuberculosis, HIV/AIDS: Human immune deficiency virus, AIDS: acquired immune deficiency syndrome

Notes: - Hosmer and Lemeshow's goodness of model test was done and P-value found to be 0.37.

7. Discussion

Across-sectional study was conducted to assess the proportion and to identify the factors associated with RR/MDR-TB of new pulmonary TB cases in area which the magnitude of RR/ DR-TB is unknown. The study was conducted on 570 new pulmonary tuberculosis confirmed cases. The proportion of RR/MDR-TB in the Eastern part of Amhara region was found to be 7.50% (95% CI: 5-10). it is comparable with the study done in Debremarkos referral hospital 6.7%(30), in Addis Ababa-Ethiopia 7.6% (37) and Uttar Pradesh (Northern India) 7.6% (18). But it is higher when compared to findings in Ambo town 1.2% (25), national surveillance in Ethiopia 4.3% (14), in Cameroon 1.6% (20), in Peru 2.3% (17) and global report 3.4% (9). But This higher value might be due to the existence of active person to-person transmission in this area, the launching of Gene-Xpert diagnosis modality which strengthen the detection of RR/ DR/ bacteria and strong disease surveillance system, as the study conducted from eight different area which makes to higher and life style of the population and geographical difference of study areas in Ethiopia and abroad respectively.

On the other hand , the finding of present study is lower compared to the study conducted in Hitossa district of Arsi Zone, Oromiya Regional State 15.3% (48), in Eastern Ethiopia Dirie Dawa and Jigjiga town 23% (24),in Addis Ababa 8.7% (49), in University of Gondar hospital 13% (27) Debremarkos referral hospital 10.7% among newly RR/MDR suspected cases (30) and in South Africa 8.8% (21),This might be the result of time of study conducted, diagnostic modality and since this study was facility based it depends clients only who visit hospitals. Even if rifampicin resistance-TB is not significantly associated with some factors, finding indicates that, it was higher in rural area 30 (69.8%). This can be related with low awareness about the RR-TB and poor access to TB diagnostic facilities respectively. In individuals who live houses having floor made of mud 32 (74.4%). It is similar indication study in Amhara region (36). This might be due to poor living status or indoor air pollution with aerosols that contain drug resistance bacteria. The proportion of RR-TB was also higher in females 26(60.4%) than males. This is agree with study in Addis Ababa (37). This because females are the one that provide care for the sick of their family members which might make them exposed for the TB illness.

In this study person having contact history with known TB patients (AOR 2.5 [95% CI: 1.21-5.11]) was identified as factor associated with RR- M.TB and this finding is consistence with the study conducted in Sudan (42) , in Dubit Hospital Afar Region (50), East shewa Bisheftu and Adama Hospitals (35), in Amhara region (36). This might be due to the source patients have

DR-TB and associated with direct person to person transmission of primary RR/ DR-TB. Since the spread of TB as well as DR-TB occurs mainly in settings where prolonged contact between people that promotes the transmission from an infectious 'source case' with TB disease to one or several 'contacts (51).

And Being HIV positive (AOR 2.3 [95% CI: 1.11-4.73]) was also the second identified factor for having RR-MTB. This finding was in line with the study done in Peru (17), Eastern Ethiopia Dire Dawa ,Jigjiga (24), and Jimma (34).This might be due to a person with HIV infection have suppressed immunity status that can make them to be easily affected by RR-TB. Similarly, diabetic mellitus cases (AOR 3.6 [95% CI: 1.51-8.78]) were identified as factor for developing RR-TB. This finding was in line with the study finding of south India (41) , China(39-40), Harar Ethiopia (43) . A reasonable explanation for primary RR-TB in diabetes patients might be, due to their impaired immune system and poor glucose control which is often associated with dysfunction of phagocytosis, and T cell reaction that can increase their vulnerability for RR-M.TB (52).

8. Strength and limitation of the study

8. 1. Strengths of the study

This study confirms proportion and factors associated with primary RR-TB among newly diagnosed pulmonary TB patients through Gene-Xpert MTB/RIF diagnostic system/ fully automated molecular technique real-time PCR machine.

8. 2. Limitations of the study

Since the study was facility based it depends on clients who visited the health facilities so, the situation of RR in the community might differ and this study might under estimate the real value of RR-TB in the study area.

9. Conclusions

The proportion of RR/MDR- TB is higher in the study area than the global and national proportion of RR/MDR- TBs. The high prevalence of RR-TB among new TB cases in the current study implies the existence of active person to-person transmission or the existence of undiagnosed primary and new RR-TB cases. Persons who have HIV infection, diabetic mellitus disease, and persons who have contact history with known TB patients were identified factors associated with RR/MDR-M.TB.

10. Recommendations

Based on the study finding the following recommendation is forwarded.

To Amhara Regional Health Beauro/ Hospitals

- Prevention and control strategy of RR /primary DR-TB/ transmission should be strengthening in the study area.
- Strengthen TB-HIV co-infection health care service program in all level health facilities
- Screening TB patient for diabetic mellitus should be conduct to help for proper management of diabetic mellitus and prevention of developing DR-TB.
- Strengthen contact tracing and investigating them should be a main concern because it is an important component of timely case detection of individuals with DR-TB and increases the chance of reducing DR-TB transmission in the community.

References

1. World Health Organization guidelines on drug-resistant tuberculosis update 2019.
2. Murray .P, faller.M, et al. Medical microbiology. Elsevier Health Sciences. 2015.
3. Migliori.B,Lange.C, et al.Emerging epidemic of drug-resistant tuberculosisin Europe, Russia, China,South America and Asia:current status and global perspectives.Curr Opin Pulm Med 2010;16:171-9.
4. JA. C. Multidrug-resistant tuberculosis: epidemiology, risk factors and case fnding.Int J Tuberc Lung Dis. 2010;14:382-90.
5. World Health Organization.Tuberculosis Progress.WHO/HTM/TB.Geneva:WHO; 2015.
6. World Health Organization.Multidrug and extensively drug-resistant TB (M/XDR-TB) - global report on surveillance and Response. Geneva. 2010.
7. Pinyopornpanish. K, CR, Pantip .C, Keawvichit. R, Wongworapat. K, Khamnoi. P, et al. Comparison of Xpert MTB/RIF assay and the conventional sputum microscopy in detecting Mycobacterium tuberculosis in Northern Thailand. Tuberc Res Trea 2015:1-6.
8. Boehme .C, NP, Hillemann D. Rapid molecular detection of tuberculosis and rifampin resistance;. N Eng J Med 2010;363(11):1005–11.
9. WORLD HEALTH ORGANIZATION, GLOBAL TUBERCULOSIS REPORT. 2019.
10. World Health Organization. Multidrug-Resistant Tuberculosis update. 2017.
11. GLOBAL. TUBERCULOSIS REPORT. 2018.
12. World Healt Organization. Global tuberculosis report. 2013.
13. Deus. L, WS, Kenneth. M, et al. Variation and risk factors of drug resistant tuberculosis in sub-Saharan Africa: a systematic review and meta-analysis. BMC Public Health 2015;15.
14. Getu. D, AK, Habteyes.H, Ayinalem.A, Mengistu. T, Epherem. T, et al. Surveillance of drug resistance tuberculosis based on reference laboratory data in Ethiopia. Infectious Diseases of Poverty.2019;8(54).
15. World Health Organization. Anti-tuberculosis drug resistance in the world: Prevalence and trends. 2000.
16. Mekonnen.F, TB, Moges. F, Gelaw. A, Eshetie. S, Kumera. G, et al. Multidrug resistant tuberculosis: prevalence and risk factors in districts of metema and West armachiho Northwest Ethiopia. . BMC Infect Dis 2015;15:461.
17. Leonela .V, LO, Timothy. R, Moises. A, et al. Prevalence, Risk Factors, and Treatment Outcomes of Isoniazid- and Rifampicin Mono Resistant Pulmonary Tuberculosis

in Lima, Peru. PLOS ONE (DOI:101371/journalpone0152933.2016 April 5

18. Praveen.B, Gautam.A, Santosh. et al.Prevalence of rifampicin resistant mycobacterium tuberculosis and associated factors among presumptive tuberculosis patients in eastern Uttar Pradesh: a cross sectional study. Int J Community Med Public Health 2018 Jun,5(6).
19. Farrazi .A, et al. Drug resistance pattern and associated risk factors of tuberculosis patients in the central province of Iran. Caspian J Intern Med. 2013;4(4).
20. Noeske.J, ANY, J, Abena .L, Nguafack.D, and Kuaban .C, et al. Rifampicin resistance in new bacteriologically confrmed pulmonary tuberculosis patients in Cameroon:a cross-sectional survey;. BMC Res Notes (2018) 11:580.
21. Yacoob. M, SM, Melendhran .P, Lise. W, Koleka. M.Rifampicin Mono-Resistance in Mycobacterium tuberculosis in KwaZulu-Natal, South Africa: A Significant Phenomenon in a High Prevalence TB-HIV Region;. PLOS ONE | wwwplosoneorg 2013 1 November 8(11).
22. Deus .L.FA, Kenneth .M, George .W, Willy. W, et al. Anti- Tuberculosis Drug Resistance among New and Previously Treated Sputum Smear-Positive Tuberculosis Patients in Uganda: Results of the First National Survey;. PLOS ONE | wwwplosoneorg 2013 1 Agust;8(8).
23. Ahmed Y. Guled AHE, Bashir Mohamud Abdi,Abdihamid Mohamed Ali Rage, et al. Prevalence of Rifampicin Resistance and Associated Risk Factors among Suspected Multidrug Resistant Tuberculosis Cases in TB Centers Mogadishu-Somalia. Open Journal of Respiratory Diseases. 2016 6 15-24.
24. Berhanu. S, MD, Alemayehu .W, Shiferaw. B, and Abraham. A. Prevalence and Drug Resistance Patterns of Mycobacterium tuberculosis among New Smear Positive Pulmonary Tuberculosis Patients in Eastern Ethiopia Hindawi Publishing Corporation Tuberculosis Research and Treatment , .Volume2014 , Article ID 753492:7.
25. Tilahun. M, AG, Desta K, Zewude A, Yamuah L, Abebe M, et al. Molecular epidemiology and drug sensitivity pattern of Mycobacterium tuberculosis strains isolated from pulmonary tuberculosis patients in and around Ambo Town, Central Ethiopia. . PLoS ONE 2018;13(2).
26. Daniel. M. WM, Bayeh. A., Aschalew. A.,Martha.T., Mulat .Y. Melaku.N. Prevalence of Multi Drug Resistant Tuberculosis among Presumptive Multi Drug Resistant Tuberculosis Cases in Amhara National Regional State, Ethiopia. J Mycobac Dis. 2014; 4(3).
27. Kefyalew. N, MG, Baye. Ge, Habtie. T, Alem .G, et al. Rifampcilin-resistant Mycobacteriumtuberculosis among tuberculosis-presumptive cases at University of Gondar Hospital, northwest Ethiopia;. Infection and Drug Resistance. 2017;10:185–19.

28. Awoke .D, SW, Daniel. M, Yinebeb. M, Abay. T, et al. Xpert MTB/RIF assay for the diagnosis of Mycobacterium tuberculosis and its Rifampcilin resistance at Felege Hiwot and Debre Tabor Hospitals, Northwest Ethiopia: A preliminary implementation research Ethiopian Journal of Health Development .2017 January.
29. Kelemework.A, Shiferaw. B, Markos. A , Abraham.A, et al. Prevalence and drug resistance profile of Mycobacterium tuberculosis isolated from pulmonary tuberculosis patients attending two public hospitals in East Gojjam zone, northwest Ethiopia BMC Public Health 2015;15:572.
30. Wondemagegn .M, Bayeh,A, Mulat. Y, Tadesse. H, Haimanot .A, et al. Rifampicin-resistance pattern of Mycobacterium tuberculosis and associated factors among presumptive tuberculosis patients referred to Debre Markos Referral Hospital, Ethiopia: a cross-sectional study. BMC Res Notes. 2017;10(8).
31. Matteo. Z, CS, Dennis .F, Philippe .G, Masoud .D, et al. Multidrug-resistant tuberculosis in children . global surveillance. 2012.
32. Marahata .S, Kaewkungwal .J, Ramasoota. P, Singhasivanon. P, et al. Risk factors of Multdrug Resistant Tuberculosis in central Nepal: A pilot study. Kathmandu University Medical Journal. 2010;3(32).
33. Maja .S, DV, Dragan .B, Gordana .A, Kristie. L, et al. Risk factors for multidrug-resistant tuberculosis among tuberculosis patients in Serbia: a case-control study . BMC Public Health. 2018;18:1114
34. Abdulhalik .W, WK, Fessahaye .A. Risk factors for multidrug-resistant tuberculosis among tuberculosis patients: a case-control study, Jimma, Ethiopia. Infection and Drug Resistance. 2011; 13 march
35. Fanta .D, TW,Takele. B, et.al. Risk factors for the occurrence of multidrug-resistant tuberculosis among patients undergoing multidrug-resistant tuberculosis treatment in East Shoa, Ethiopia;. BMC Public Health 2018;18: 422.
36. Wondemagegn .M, DM, Mulat. Y, Aschalew. A, Bayeh. A. Risk factors for multidrug resistant tuberculosis patients in Amhara National Regional State. African Health Sciences 2015; 15 (2).
37. Arega B. Prevalence of rifampicin resistant Mycobacterium tuberculosis among presumptive tuberculosis patients in selected governmental hospitals in Addis Ababa, Ethiopia. BMC Infectious Diseases 2019;19(307).
38. Paudel. Risk Factors of Multidruge Resistance Tuberculosis. International Journal of

Applied science and Bio technology. 2017;54:548-54.

39. Qianqian L. YC, et al. Diabetes mellitus and the risk ofmultidrug resistant tuberculosis: a meta-analysis. wwwnaturecom/Scientific Reports. April 24 2017.
40. Wan-mei. S, YS, et al. Primary drug resistance among tuberculosis patients with diabetes mellitus: a retrospective study among 7223 cases in China. Infection and Drug Resistance. 2019;12:2397-407.
41. Saurabh. M, EAY. S, Wesley. B, John. K . Rifampin resistance and diabetes mellitus in a cross-sectional study of adult patients in rural South India. BMC Infectious Diseases. 2015.
42. Adel. H,EM, Abbas. R,Hamdan. M, Hamdan. A, et al. Assessment of the risk factors associated withmultidrug-resistant tuberculosis in Sudan:a case-control study. epiH EPIDEMIOLOGY AND HEALTH. 2019;41.
43. Balewgizie. S, Andreas. A, Mamaru. A, et al. Association between diabetes mellitus and multi-drug-resistant tuberculosis: evidence from a systematic review and meta-analysis in Ethiopia, . BioMedCentera. 2018;7(161).
44. Savicevicetal J. Risk factors for pulmonary tuberculosis in Croatia:a matched case–control study. BMC Public Health. 2103;13(991).
45. Githui .W, HM, Juma. E, et al Surveillance of drug-resistant tuberculosis and molecular evaluation of transmission of resistant strains in refugee and non-refugee populations in North-Eastern Kenya. Int J Tuberc Lung Dis. 2000;4(10):947-55.
46. Solomon. A, PB, Abraham. H , et al. Drug Resistance and Population Structure of M.tuberculosis Isolates From Prisons and Communities in Ethiopia. BMC Infect Dis. 2016;16(1):687.
47. Mucheye. G, Beza. E,Moges. T. Prevalence and Associated Factors of Tuberculosis in Prisons Settings of East Gojjam Zone, Northwest Ethiopia;. Hindawi International Journal of Bacteriology. 2017.
48. Shallo. D, DT, Mohammed. S, Meaza. D, Bernt L. Primary and secondary anti-tuberculosis drug resistance in Hitossa District of Arsi Zone, Oromia Regional State, Central Ethiopia. BMC Public Health. 2016.
49. Waganeh. S, AK, Adane. B, Ephrem. T, Mengistu. T, et al. Prevalence of tuberculosis, multidrug resistant tuberculosis and associated risk factors among smear negative presumptive pulmonary tuberculosis patients in Addis Ababa, Ethiopia. BMC Infectious Diseases. 2019;19(641).
50. Gebremedhn. B, AG, Letemichael. N, Amlsha. K, Getahun. K, et al. Rifampicin resistant

tuberculosis in presumptive pulmonary tuberculosis cases in Dubti Hospital, Afar, Ethiopia. Jornal of Infection in Developing Countries. 2019;13(1).

51. Management of contacts of MDR-TB and XDR-TB patients. Stockholm. European Centre for Disease Prevention and Control. ECDC. 2012.

52. Nijland HMea. Exposure to rifampicin is strongly reduced in patients with tuberculosis and type 2 diabetes. Clinical infectiousdiseases: an official publication of the Infectious Diseases Society of America. 2006;43:848–54.

11. Appendixes

11.1. Appendixes 1:-Client's information sheet and consent form

1.1.1. English Version

My name is Abtew Abera and I am MPH student in Field Epidemiology at Bahir Dar University. I am doing a research entitled "----------among pulmonary Tuberculosis patients in Eastern part of Amhara Region, Northeast Ethiopia, 2019."

Purpose: - The objective of the study is to assess proportion and associated factors of RR/MDRTB in newly presumptive for pulmonary Tuberculosis. The knowledge gained from this work is believed to help to know the magnitude, the factor associated with RR and to design appropriate strategies to reduce the transmission as well as development of MDR TB**.**

Study procedures: -The data collector team member, will explain the details of the study to you and will ask you, your consent to participate in the study. If you are willing to participate in this study, you will be asked again to sign a consent form. Data collectors will then ask you some questions to capture relevant socio-demographic information, and other related factors to RR/MDR TB.

Benefits: - The findings of this study will assist health care professionals to assess the burden of RR and its associated factors, and it also will help to policy makers, program planners and service providers for decision making and to design appropriate control strategy.

Confidentiality:-Your name will not be mentioned on the s questionnaire. Code will be used in the study as an identifier .The results of the study will only be used for the purpose of this study.

Sharing the result:- The results of the study will be shared through presentation at the conference and publication. The reports will not disclose any information relevant to your personality.

Right to refuse:-Since participation in this study is voluntary; you can refuse to participate in this research at any time. Refusal to participate in the study did not affect any benefits you get from health facilities.

Freedom to ask question or raise concerns:-If you have any question(s) or concern(s) regarding the study; you can forward to the study principal investigator with the name and address indicated below. Abtew Abera Phone: - +251911066676, E-mail:- abtabera03@gmail.com

Consent form

Title of the study Proportion and associated factors for RR-DR-TB in new Pulmonary TB clients/patients in Eastern part of Amhara region Gene-Xpert sites.

Dear participant, my Name is ----------, professionally I am _____ and I am a worker of ---------- hospital and I am collecting data for research project intended to assess proportion and associated factors for RR-DR –TB in newly Pulmonary TB clients/patients. Now, I want to ask you, your willingness to participate on this research by your full interest. The research is important for you and for general community to increase curability of TB disease and to prevent medication resistant types of TB germ by assessing magnitude of RR/DR and avoiding/decreasing factors that help to minimize DR problem. I would like to tell you that you have the full rights to participate or not participate in this study and as you have right to stop participation at any time on the process of study duration. Additionally, all information you will give for us are will be kept confidential and used only for this study.

Dear participant, thank you for your cooperation in advance; and now I will read to you or you can read this written consent form; and you will sign for me as you agreed to participate in this study with your full willingness , after you understand the objective of the study, all procedures will be taken, and your benefits and right.

11.1.2.መገለጫ (Amharic Version)

በጥናቱለሚሳተፉግለሰቦችመገለጫየሚሰጥበትአማርኛቅፅ

ስሜ አብተው አበራ ይባላል በባህርዳር ዩኒቨርሲቲ የህክምና ጤና ሳይንስ ትምህርት ክፍል የፊልድ ኢፒዲሚዮሎጅ የማስተርስ ዲግሪ ተማሪስሆን፡- መድኃኒትየተለመደቲቢስርጭትና አጋላጭ ምክንያቶች በሚል ርእስ በ2019 እእአ በአማራ ክልል ምስራቁ ክፍል ጥናትና ምርምር እያካሄድን ሲሆን።

የጥናቱዓላማ፡- መድሀኒት የተላምደ ቲቢ እና አጋላጭምክንያቶችንመለየትነው፡ከጥናቱ የሚገኘው እውቀት መድኃኒት የተላመደ ቲቢ መጠንና አጋላጭ ምክንያቶች ለይቶ በማወቅ ለመከላከልና ለመቆጣጠር ይረዳል።

የጥናቱሂደት:-ስለ ጥናቱ ዝርዝር ሁኔታ በጥናቱ ቡድን አባል(ላት) ገለፃ ያደርግሎታል።በጥናቱ ዉስጥ ለመሳተፍ ፍቃደኝነትዎን ይጠየቃሉ።ፈቃደኛ ከሆኑ የስምምነት ቅፅ ላይ ይፍርማሉ።ስለዚህ ስነህዝብ እና ማህበራዊ እንዲሁም ለምርመራ የሚጠቅሙ ጥያቄዎችን የጤና ባለሙያ ይጠይቆታል።ለጥያቄዎቹም የሚሰጡትምላሽበተዘጋጀውመጠይቅላይይሞላ።

የጥናቱጥቅሞች:በዚህ ጥናት ዉስጥ ለሚሳተፉ በቀጥታ የሚያገኙት ጥቅም ባይኖርም ጥናቱ ለጤና ባለሙያዎች ለተመራማሪዎች እንዲሁም በበሽታዉ የሚያዙ ህሙማን የስርጭቱ መጠን እና አጋላጭ ምክንያቶች እንዲያዉቁት ክትትል እና ቁጥጥር እንዲደርግ እንዲሁም ሁሉም የበኩሉን ድርሻ እንዲዎጣ ያግዛል።

ሚስጥራዊነት፡-ከዚህ ጥናት የሚገኘው ውጤት ለጥናቱ አላማ ብቻ እንደሚውል በመጠይቁ እና ከጥናቱ በሚገኘው ማንኛውም ውጤት ላይ ስምዎት አይጠቀስም። ለጥናቱ ብቻ የሚውል ልዩ መለያ ቁጥር እንጠቀማለን። ይህ መለያ ቁጥር ከስሞት ጋር ማገናኘት የሚችለው ዋና ተመራማሪው ብቻ ይሆናል።

የጥናቱንዉጤትስለማሳወቅ:የዚህ ጥናት ዉጤት በተለያዩ የህትመት ውጤቶች የሚቀርብ ሲሆን ይህ ከማንነትዎ ጋር የተያዘ ምንም አይነት መረጃ አያካትትም።

ከጥናቱስለመውጣትናስለማቋረጥ:ይህ ጥናት በፈቃደኝነት ላይ የተመሰረተ ሲሆን በማንኛዉም ስዓት በፈቃድዎ ከጥናቱ መውጣት ይችላሉ።ከጥናቱ ቢወጡም በየትኛውም ጊዜ የሚያመጣብዎት ተፅኖ አይኖርም።

ጥያቄዎችንመጠየቅነጻነት፡ጥናቱን በተመለከተ ጥያቄ ካሎት በማንኛውም ጊዜናሁኔታ ዋና ተመራማሪውን በሚቀጥለው አድራሻ ማግኘት ይችላሉ።

የተመራማሪው ስም፡- አብተው አበራ

አድራሻ ፡- ስልክቁጥር፡0911066676 E-mail:abtabera03@gmail.com

የስምምነትቅፅ

የጥናቱ ርእስ፡- መድሀኒትየተለመደ ቲቢ መጠንና መንስኤዉ ምንድን ነዉ?

የጥናት ቦታ፡- ምስራቅ አማራ

የተከበራችሁየጥናቱተሳታፊወች ስሜ----------ይባላል

ሞያየ----------ሲሆን በ----------ጤና ተቋም እየሰራሁ እገኛለሁ።በአሁን ስዓት መድሀኒት የተላመደ ቲቢ መጠኑንና መንስኤዉን ለመለየት ጥናት ለማድረግ ታስቦ የተዘጋጀ ፅሁፍይዣ ቀርቢያለሁ። ስለዚህ አሁን እርሶ በዚህ ጥናት ለመሳተፍ በሙሉ ፈቃደኝነትዎ ብቻ መሳተፍ የሚችሉ ይሆናሉ ።የሚፈጀው ግዜ ከ30 ደቂቃ አይበልጥም።

የዚህ ጥናት ዋና አላማ ለእርሰወ እንዲሁም በአጠቃላይ ለማህበረሰቡ ቲቢ መድሀኒት ፈዋሽነት እንዲሁም መድሀኒት የመለመደ ቲቢን ለመከላከል ብሎም ስርጭቱንና መንስኤወችን በደንብ አዉቆ ለመስራት ይረዳንዘንድ ነዉ፡ውድ የጥናቱ ተሳታፊዎች አሁን የጥናቱን የስምምነት ቅፅ አነብልዎታለሁ ከተስማሙ ፊርማዎንያስቀምጣሉ።

1. የዚህ ጥናት አላማ ካነበቡኩ በኃላ ወይም ከተነበበልኝ በኃላ ለእኔ እንደሚጠቅም አስቤ ተሳትፊያለሁ።
2. በዚህ ጥናት ስሳተፍ በፈቃደኝነት ሲሆን የግሌን ሚስጥሬ እንደሚጠብቅ አውቄ እንዲሁም ባልሳተፍም በምርመራው ምንም የሚጎድልብኝ እንደሌለ በማሰብነው።
3. በማንኛውም ጊዜ ከጥናቱ መውጣት እንደምችል እና መደበኛ ምርመራየን እንደማይስተጓጉል አውቃለሁ፡
4. መረጃ ሰብሳቢው ስለቲቢ ህመምና ህክምና መጠየቅ ጥቅሙን ከገለፀልኝ በኃ ጥቅሙን ተረድቻለሁ።
5. ቃለ መጠይቅ አድራጊው ቃለ መጠይቅ በማድረጉ ምንም አይነት አደጋ ወይም አለመመቸት እንደማያጋጥመኝ ነግሮኛል።
6. ይህ የሚሰበሰበው የጥናት ጥያቄ ሚስጥሩ በጥብቅ የሚያዝ እና የጥናቱን ፀሁፍ ሪፖርት የሚያደርጉት የግል ማንነቴ በማይጋለጥ መልኩ መሆኑን ተረድቼ ስምምነቴን ሰጥቻለሁ።

የተሳታፊ ፊርማ_____

11.2. Appendixes 2:- Data Collection tools

11.2.1 (English Version)

Data collection Questionnaire, code of respondent----------

Part-I Socio-demographic data collection Questionnaire				
S.No	**Questions**	**Answer**	**Code**	**Skip to**
101	What is the Sex?	Male Female	1 2	
102	What is your age in year?	----------		
103	Address	Urban Rural	1 2	
104	What is your current marital status?	Single Married Divorced Widowed	1 2 3 4	
105	What is your educational Level?	Illiterate Read & write 1-8 9-12 Diploma Degree and above	1 2 3 4 5 6	
106	Occupation status	Farmer House wife Employed Merchant Others -------	1 2 3 4 88	
107	Do you live with Your Family?	Yes No	1 0	If no go to question 201
108	If your answer to question 107 is yes, how many people live with you (Family size)?	<5 ≥5	1 0	
Part - II Housing condition related data collection questionnaire				
201	How many rooms are there in the house you live?	1 ≥2	1 0	
202	How many windows are there in the room you live?	No windows 1 ≥2	1 2 3	

203	Do you open the windows?	yes No	1 0	
204	Floor of house made you live?	mud Cemented	1 0	
Part - III - Health access related data collection questionnaire				
301	Distance of health facility from you live?	5-10km >10Km	1 0	
302	How much time you travel to reach nearby health facility?	<2 hours > 2 hours	1 0	
303	Is the health facility which you get health seeking nearby has laboratory service?	Yes No	1 0	
Part - IV - diseases related data collection questionnaire				
401	Do have Asthma	Yes No	1 0	
402	HIV/AIDS status (document review)	Negative Positive Unknown	0 1 2	If negative/2 go to question 205
403	If your answer for question 402 is 1, how much is CD4 test result? (document review)	----------		
404	If your answer for question 402 is 1, how much is viral load status; (document review)	>1000copies/m <1000copies/ml	1 0	
405	Diabetic disease /cases/ (document review)	Yes No	1 0	
406	Do you have any other diseases?	Yes No If yes specify ----	1 0	
407	Do you have contact history with known tuberculosis patients? (document review)	Yes No unknown	1 2 3	If no go to Question 409
408	Where was your contact?	Home Work-place Otherplaces------	1 2	
409	What were the symptoms that you had been experiencing before you were diagnose as having TB.	ProlongedCough Chet Pain Coughing up blood Shortness of breath Sweating at night	1 2 3 4 5	

410	How long stay to visit a Health facility or doctor?	in less than 3 Weeks > 3 Weeks	1 2	
Part –V- Respondents behavioral related data collection questionnaire				
501	Have you Ever been in prison?	Yes No	1 0	
502	Smoking status?	Yes No	1 0	If no go to question 504
503	How frequent you smoke	Daily Someday	1 2	
504	Have you ever live with someone smoking cigarettes?	Yes No	1 0	
505	Do you take sleeping pill	Yes No	1 0	
506	Do you have sadness feeling in your life now?	Yes No	1 0	
507	Chewing Khat?	Yes No	1 0	If no go to question 509
508	If your answer yes for question 507, how frequent you chewing?	Daily Weekly Occasionally	1 2 3	
509	Do you live with displaced people camp	Yes No	1 0	
Part- VI- Sputum specimen Laboratory result related data collection questionnaire				
601	M.TB status	M.TB detected	1	M.TB Detected
602	RR status	RR not detected RR detected	0 1	

11.2.2.መጠይቅ (አማርኛ ክፍል)

መረጃ መሰብሰቢያ መጠይቅ፣ መለያ ቁጥር ----------

ቁጥር	ጥያቄ	መልስ	ኮድ	ማለፍ
ክፍል 1 የጥናቱ ተሳታፊዎችን የስነህዝብና ማህበረዊ አኗኗር ሁኔታ መርጃ መስብሰቢያ ጥያቄ				
101	ፆታ	ወንድ ሴት	1 2	
102	እድሜ በዓመት?	----------		
103	መኖሪያ ስፍራ?	ከተማ ገጠር	1 2	
104	የጋብቻ ሁኔታ ምን ላይ ነወት ?	ያላገባ/ች ያገባ/ያገባች የትዳርአጋርየሞተበት/ባት የፈታ/ች	1 2 3 4	
105	የትምህርት ሁኔታ ?	ያልተማሩ ማንበብናመፃፍ 1-8 ክፍል 9-12 ክፍል ድፕሎማ ድግሪና ከዚያ በላይ	1 2 3 4 5 6	
106	የስራ ሁኔታ በምን ላይ ነው የተሰማሩት ?	ገበሬ የቤት እመቤት የመንግስት ስራ ነጋደ ሌላ	1 2 3 4 88	
107	ከቤተሰብወ ጋር ነው እሚኖሩት?	አዎ አይደለም	1 0	መልሱ 0 ከሆነ ወደ ጥያቄ 201 ይለፉ
108	ለጥያቄ 107 መልሰወ አወ ከሆነ ከርሰዎ ጋርምንያህል ሰዉ በቤት ይኖራሉ?	ከ5 ያነሱ 5 እና ከዚያ በላይ	1 0	
ክፍል 2 የመኖሪያ ቤት ሁኔታ				
201	የሚኖሩበት ቤት ስንት ክፍሎች አሉት?	አንድ ሁለትናከዛበላ	1 0	
202	የሚኖሩበት ቤት በቁጥር ምንያህል መስኮቶች አሉት?	መስኮት የለውም 1 ≥2	1 2 3	መልሱ 1 ከሆነ ወደ ጥያቄ 204 ይለፉ
203	መስኮቶች በየቀኑ ይከፈታሉ?	አዎ አይከፈቱም	1 0	

204	የቤትወ ወለል የተሰራው ከምንድን ነው?	ከጭቃ ከሲምንቶ	1 2	
ክፍል 3 የጤና አገልችሎት ሁኔታ				
301	ባቅራቢያዎ ወደ ለው ጤና ተቋም ሂደው ለመታከም ቢፈልጉ ምን ያክል ኪሎ ሜትር ይረቃ?	5-10ኪሜ >10ኪሜ	1 2	
302	ታመው ህክምና ለማግኝት ቢፈልጉ ስንት ሰዓት ተጉዘው ጤና ተቋም ያገኛሉ ?	2 ሰዓት ከሁለት ሰዓት በላይ	1 2	
303	በአቅራቢያዎ የሚገለገሉበት ጤና ተቋም የቲብ ምርመራ የላብራቶሪ አገልግሎት ይሰጣል?	አወ የለም	1 0	
ክፍል 4 ተሳታፊዎች የበሽታ ሁኔታን መርጃ መስብሰቢያ ጥያቄ				
401	አስም አልብዎት?	አዎ የለብኝም	1 0	
402	የ ኤች አይቪ ሁኔታ HIV/AIDS status (document review, testing)	Negative (የለም) Positive (አለ) የማይታወቅ	0 1 2	መልሱ 0/2 ከሆነ ወደጥያቄ 405
403	የ ኤች አይቪ ቫይረስ መጠን ስንት ነው (document review)	>1000copies/ml <1000copies/ml	1 2	
404	የ CD4 መጠን ስንት ንው(document review)	----------		
405	የስኪር ህመም /Diabetic disease /cases/ (document review)?	አለ የለም	1 0	
406	ሌላ የቆየ በሽታ አለዎት ?	አዎ የለም አለ ካሉ ይገለፅ----	1 0	
407	ቲቢ ከተያዘ ሰው ጋር ግንኙነት/አብሮ መቆየት አጋጣሚ/ ነበረዎት?	አዎ አልነበረኝም የማይታወቅ	1 2 3	
408	የተጋለጡበት ቦታ የት ነበር?	ከቤተሰብ/አስታማሚ ከስራቦታ ሌላ ይገለፅ------	1 2 3	
409	ቲቢምርመራከማድረጎበፊትምንአይነትምልክትይታ ይበዎትነበር?	ከሁለትሳምንትበላይ ሳል ደረተወላይህመም ደምየቀላቀለአክታመ የእስትንፋስመቆራረጥ ለሊትለሊትማላብ	1 2 3 4 5	
410	ወደ ጤና ተቋም በስንት ቀን ዉስጥ ሄዱ/መጡ?	3 ሳምንትእናበታች ከ3 ሳምንት በላይ ቆይቶ	1 2	
ክፍል 5 የጥናቱ ጠሳታፊዎች ባህሪ ሁኔታን መርጃ መስብሰቢያ ጥያቄ				
501	ማረሚያቤትቆይተዉያዉቃሉ?	አዎ አላዉቅም	1 0	
502	ሲጋራ ያጨሳሉ?	አዎ	1	መልሱ 0 ከሆነ ወደ ጥያቄ

		አላጨስም	0	504 ይለፉ
503	ለጥያቄ ቁጥር 502 መልሱ አወ ከሆነ በየስነት ጊዜ ነው እሚያጨሱት ?	በየቀኑ አልፎአልፎ	1 2	
504	ሲጋ ራየሚያጨስ ጋር አብረዉኖረዉያዉቃሉን?	አዎ አላዉቅም	1 0	
505	የእንቅልፍ ከኒን ወስደው ያውቃሉ?	አዎ ወሰጀአላውቅም	1 2	
506	የባህል መድሃኒት ወስደው ያውቃሉ?	አወ አልወሰድኩም	1 2	
507	በኑሮህ /ሽ/ ደስታን እንዳታገኝ የሚያደርጉህ ነገሮች አሉ?	አወ የለም	1 0	
508	ጫት ቅመው/ጫት/ ይቅማሉ ?	አወ አልቅምም	1 0	መልሱ 0 ከሆነ ወደ ጥያቄ ይለፉ 510
509	ለጥያቄ ቁጥር 508 መልስወ አወ ከሆነ ከቃሙ እንደትነው እሚቅሙት?	ቀንበቀን በሳምንትአንድጊዜ አልፎአልፎ	1 2 3	
510	በተፈናቃዮች ካምፕ ተጠልለው(ኑረው) ያውቃሉ ?	አዎ አላውቅም	1 0	
ክፍል 6 የላብራቶሪ ውጤት መርጃ መስብሰቢያ ጥያቄ				
601	ቲቢ ውጤት?	ፖዘቲቭ	1	ፖዘቲቭ
602	መድሃኒት የተላመደ ቲቢ ሁኔታ(RR) ?	መድሀኒት የተላመደ ቲቢ(RR)የለም መድሀኒት የተላመደ ቲቢ (RR)አለ	0 1	

አመሰግናለሁ

Declaration form

Declaration

I, the undersigned, declare that this is my original work and has never been presented by another person in this or any other University and that all the source materials and references used for this thesis have been duly acknowledged.

Name: Abtew Abera Signature: _____, Date _____

Place: Bahir Dar University, Date of Submission: _____

Name of advisors:

1. Mr. Zelalem Mehari Signature: _____, Date: _____

2. Mr. Getachew Hailu Signature: _____, Date: _____

Name of examiners:

1. Mr. Anemaw Asrat Signature: _____, Date: _____

2. Mr. Fentaw Fetene Signature: _____, Date: _____