ADDIS ABABA UNIVERSITY
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Assessment of multi drug resistant tuberculosis rate and associated factors in public health facilities of Dessie City Administration, North East Amhara, Ethiopia

BY:
GASHAW SHEGAW (B.Pharm)

DECEMBER, 2015
ADDIS ABABA, ETHIOPIA

Assessment of multi drug resistant tuberculosis rate and associated factors in public health facilities of Dessie City Administration, North East Amhara, Ethiopia

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A thesis submitted to the Department of Pharmaceutics and Social Pharmacy, School of Pharmacy, College of Health Sciences, Addis Ababa University for the partial fulfillment of the requirements for the Degree of Masters of Science in Pharmacoepidemiology and Social Pharmacy.

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Abstract

Assessment of multi drug resistant tuberculosis rate and associated factors in public health facilities of Dessie City Administration, North East Amhara, Ethiopia.

Gashaw Shegaw

Addis Ababa University, 2015

The history of TB treatment has observed sequential development of resistance to anti-TB drugs. MDR-TB is defined as an MDR-TB suspect who is sputum culture positive and whose TB is due to *Mycobacterium TB* that are resistant in-vitro to at least INH and RMP.

The emergence of MDR-TB is a threat for the populations of resource limited countries. In Ethiopia MDR-TB is becoming a challenge, because of poor adherence to treatment, TB/HIV co-infection, a few diagnostic and treatment facilities and inadequate trained health professionals. Dessie is densely populated town with high flow of people within the region as well as from neighborhood regions. It is also vulnerable for counterfeit anti-TB drugs through contraband.

The aim of this study is to determine rate of MDR-TB and to identify associated factors in Dessie City Administration, North East Amhara, Ethiopia.

A facility based retrospective cross sectional study design employing medical records review of TB registration books supplemented by key informants' interviews which cover retrospective review period of July 1, 2012 to June 30, 2014.

Prevalence rate of MDR-TB for combined, new and retreated TB cases of all form from public health facilities, were found to be 2.1/100, 0.3/100 and 21.6/100 respectively. Adherence of TB patients to TB treatment (COR=9.0, 95% CI [1.03-78.57]) and previous history of TB treatment (AOR=66.87, 95% CI [6.94-644.10]) were found to be a risk factors for MDR-TB. And related to TB type all MDR-TB cases were dominantly pulmonary TB.

Key words: Tuberculosis, Multi drug resistance, Rate, Associated factors, anti TB drugs.

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List of acronyms/abbreviations

AIDS	Acquired Immune Deficiency Syndrome
AFRO	African Regional Office
AOR	Adjusted Odds Ratio
CI	Confidence Interval
DOTs	Directly Observed Therapy's
DR-TB	Drug resistant tuberculosis
EHNRI	Ethiopian Health &Nutrition Research Institute
EMB	Ethambutol
HIV	Human Immunodeficiency Virus
INH	Isoniazid
MDR-TB	Multi drug resistant tuberculosis
NTP	National tuberculosis program
COR	Crude Odds Ratio
PAS	Para amino salicylic acid
PFSA	Pharmaceuticals Fund and Supply Agency
RMP	Rifampicin
STM	Streptomycin
WHO	World Health Organization

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1. Introduction

Tuberculosis (TB) is an infectious bacterial disease caused by *Mycobacterium TB* that most commonly affects the lungs and despite the recent progress of global control efforts, TB remains a major public health burden (WHO, 2014). In 2014, there were $9.6x10^6$cases and $1.5x10^6$deaths of TB globally (WHO, 2015).

The history of TB treatment has observed sequential development of resistance to anti-TB drugs. Para amino salicylic acid (PAS) and isoniazid (INH) were introduced to reduce the development of streptomycin (STM) resistance, which heralded the era of combination treatment for TB (WHO, 2013). Within 20 years, resistance to both INH and STM was already a challenge in the use of INH, STM and PAS as the standard anti-TB regimens. The discovery of rifampicin (RMP) in 1966 and the expansion of its use between 1970 and 1990 for patients who were already carriers of INH resistant Mycobacterium TB strains also became resistant to RMP and this was the start of MDR-TB (Dhammika, 2013).

MDR-TB is defined as an MDR-TB suspect who is sputum culture positive and whose TB is due to *Mycobacterium TB* that are resistant in-vitro to at least INH and RMP (Kapadia and Tripathi, 2013). And it results from either infection with organisms which are already drug-resistant or might develop in the course of a patient's treatment (WHO, 2013).

Numerous studies have shown that a six month regimen of RMP and INH, supplemented by pyrazinamide (PZA) and STM or ethambutol (EMB) for the first two months will provide a cure in >95% of cases if the medication is taken correctly (WHO, 2010). Each anti-TB drug varies in its ability to kill tubercle bacilli (bactericidal ability), (INH) to deal with persistent organisms which are only occasionally metabolically active (sterilizing ability) (RMP) and to prevent the emergence of drug resistance (EMB) (Abigail *et al.*, 2006). INH is the best bactericidal drug and if monoresistance to this occurs, treatment with RMP and ETB has to be extended for 9 to 12 months, in addition to 2 months initial PZA. RMP is the best sterilizing drug, and monoresistance to this drug requires treatment

with INH and ETB for 18 months with 2 months initial PZA. Therefore loss of response to both the main bactericidal drug and the main sterilizing drug means that patients remain infectious for much longer and the treatment is required for 18 to 24 months, which is less effective and more toxic (Kapadia and Tripathi, 2013).

MDR-TB is a reflection of the mismanagement of TB cases, which includes wrong diagnosis, delay of diagnosis, wrong/interrupted treatment, misuse of TB medicines, and poor adherence to standardized treatment, unregulated supply of anti-TB drugs and utilization of TB drugs of unknown quality (ECDC, 2012). For instance, globally, more than half million new MDR-TB cases are estimated to emerge annually as a result of inadequate treatment and subsequent transmission. Although some individuals who have had previous TB treatment are infected by MDR-TB, many new cases of MDR-TB are also created each year by a combination of physician error and poor patient compliance with treatment and poor quality drugs (WHO, 2010). In countries where drug resistance has been identified, specific measures need to be taken within TB control programs to address the problem through appropriate management of patients and adoption of strategies to prevent the propagation and dissemination of DR-TB (WHO, 2013). This study covered MDR-TB rate and associated factors at public health facilities in Dessie city administration.

2. Statement of the Problem

The global burden of TB and MDR-TB remains enormous. In 2014, an estimated $1.9x10^6$ people died from MDR-TB, relatively high compared with cases of 480,000 MDR-TB and the African region had 28% of the world's MDR-TB cases, 281 per 100,000, more than double the global average of 133 per 100,000 (WHO, 2015). The region of the Americas and the western pacific region have already met the three 2015 targets for reductions in TB and the South- East Asia region appears on track to do so. The other three regions are unlikely to meet the 2015 targets, although incidence, prevalence and mortality rates are falling (WHO, 2014). Globally, in 2014, an estimated 3.3% of new TB cases and 20% of previously treated cases have MDR-TB (WHO, 2015).

Treatment of MDR TB using second line anti-TB drugs has more adverse events, since provided for an extended period of time (WHO recommendation at least 20 months) and is expensive (ECDC, 2012). Globally, in 2014, only 50% of MDR-TB patients were successfully treated and the 2015 treatment success target of ≥75% for MDR-TB patients was achieved only in 43 of the 127 countries (WHO, 2015).

According to the WHO global report on anti-TB drug resistance in the World, MDR TB strains have emerged in all regions of the world despite, the increasing of TB rates in Africa; MDR TB appears to be low from this continent compared to other regional offices like Southeast Asia. The first explanation is the presence of well functioning TB control programs in Africa (DOTS), which is similar to the global average (WHO, 2013). But, each year countries with the lowest case detection and cure rates are clustered in this continent. And the availability of drugs on the open market and a private sector that delivers drugs to the population in an unregulated fashion are also common in Africa. The second explanation is the recent introduction of RMP in Africa. But, still HIV and malnourishment were common which faviour resistance to develop (Yanis *et al*, 2010).

Ethiopia was among the 11 high TB burden countries globally, with an estimated TB mortality, prevalence and incidence of 33, 200 and 207 per 100, 000 persons for all forms of TB respectively (WHO, 2015). And percentages of new and previously treated TB

cases that have MDR-TB were 1.6% and 12% respectively (WHO, 2015). The emergence of MDR-TB is a threat for the populations of resource limited countries. In Ethiopia MDR-TB is becoming a challenge, because of poor adherence to treatment, TB/HIV co-infection, a few diagnostic and treatment facilities and inadequate trained health professionals (Selamawit *et al*, 2013).

Particular to study area assessment of MDR-TB is importance because in addition to, TB and MDR-TB detection and treatment gaps in developing countries, Dessie is densely populated area with high flow of people within the region as well as from neighborhood regions. The city is also vulnerable for counterfeit anti-TB drugs because it is one of routes for illegal and poor quality anti-TB contraband drugs. Thus, the aim of this study is to assess the magnitude and possible associated factors for MDR-TB which in turn is vital in order to prevent and treat TB and MDR-TB.

3. Literature Review

3.1 Prevalence rate of MDR-TB

The occurrence of drug resistance has increased since the first drug treatment for TB was introduced in 1943. The emergence of MDR-TB followed the widespread use of RMP since the 1970s (Surendra *et al*, 2011). In terms of prevalence of notified MDR-TB cases in Europe, Baltic States, 22.7% and in Romania, 11.2% (ECDC, 2012). The prevalence of TB patients estimated to have MDR-TB was under 10% in all of the 27 high MDR-TB countries outside the European Region, with the notable exception of South Africa with 81% (Dhammika, 2013). The prevalence of MDR-TB is increasing throughout the world both among new tuberculosis cases as well as among previously treated. Although previous treatment for TB is the strongest risk factor for development of MDR-TB, treatment naive patients are also at risk due to either spontaneous mutations or transmission of resistant strains (Surendra *et al*, 2011). MDR-TB is estimated to be present in 3.7% of newly diagnosed patients with TB and 20% of previously treated patients around the world (WHO, 2012).

In the fourth WHO global report on anti-TB drug resistance in the world, data are reported from eight countries of the Region, and MDR-TB rate in this Region were 2% among new cases, 35.3% among previously treated cases and 5.4% from all or combined cases (WHO, 2010). Study findings in Northeastern China shows, the prevalence of MDR-TB of 8.7% (Qiao *et al*, 2013). Study findings in New Delhi, India, shows from sputum positive pulmonary TB clients enrolled, the prevalence of MDR-TB among newly diagnosed pulmonary TB patients was 1.1% (Surendra *et al*, 2011) and another study in India on the pulmonary TB drug resistant shows 8% MDR-TB (Nagaraja *et al*, 2011). Study conducted in the city of Santos, Brazil also shows MDR-TB rate of 15%, 11.6% of new TB cases and 17.3% of previously treated cases (Andréa *et al*, 2012).

The nationwide anti-TB drug resistance survey conducted in China revealed the proportions of MDR-TB to be 5.7% in primary TB cases and 25.6% in acquired TB cases, which is higher than global levels of 2.7% and 18.5%, respectively (Xin *et al*, 2014).

And a study in Nigeria shows of the 100 participants evaluated MDR-TB was seen in 4% (Akaninyene *et al*, 2013).

According to World Health Organization 2015 report, among newly diagnosed TB cases 1.6% was found to be with MDR-TB and MDR-TB among previously treated TB cases was 11.8% (WHO, 2015). Similarly, Study findings at the Eastern Ethiopia that was conducted between October 2011 and May 2013 shows, from a total of 357 MDR-TB was detected in 1.1% of the patients (Birhanu *et al*, 2014). Another study in Ethiopia also showed that MDR-TB rate was found in the range of 3.3%-46.3% (Fentahun *et al*, 2014).

3.2 Factors associated with MDR-TB

3.2.1 Sociodemographic factors and MDR-TB

In a nationwide survey conducted in China (AOR=1.763, 95% CI [1.060-2.934]) (Qiao *et al*, 2013), in Republic of Georgia (AOR=1.58, 95%CI [1.02-2.32]) and in Mumbai, India, (AOR=1.68, 95% CI [1.02-2.87]) (Sachin *et a*l, 2014).female gender were a risk factors for MDR-TB (Lomtadze*et al,* 2010). But a study finding in Nigeria shows gender was not significantly associated with MDR-TB (Akaninyene *et al*, 2013). And study findings in Thailand also shows male gender as risk factors for MDR-TB (Somsak *et al*, 2010) and in Ethiopia (AOR =2, 95% CI [1.4-5]) showed male gender was a risks factor for MDR-TB (Fikadu, 2015**)**.

Age group at 25-44 years in Ethiopia (AOR=2.8, 95% CI [1.7–6.4]) (Fikadu, 2015**)** and in Bangladesh (AOR=1.72, 95% CI [1.12–2.66]) (Mahfuza *et al*, 2014) and (Flora *et al*, 2013) was a risks factor of MDR-TB.

In Bangladesh urban residence was associated with MDR-TB occurrence (Flora *et al*, 2013) whereas, a study finding in southern Ethiopia shows, there was no significant association between residence and MDR-TB (Gemeda *et al*, 2012).

3.2.2 TB/HIV co-infection and MDR-TB

The high rates of MDR-TB among high burden TB countries are hampering the progress regarding TB care and control. This has been fueled by an increase in the TB incidence, which has been associated with the emergence HIV. Individuals with latent TB are more likely to reactivate and experience rapidly progressive TB and drug resistance when co-infected with HIV (Samuel *et al*, 2013).

The epidemiological impact of HIV on the epidemic of drug-resistant TB is not known and may depend on several factors. The role of HIV infection as a risk factor for the development of drug-resistant TB was not clear. In Kenya, Malawi, Tanzania, Cote d'Ivoire, and France, drug resistance was not associated with HIV infection. In contrast, in a survey of eight metropolitan areas of the United States, HIV infection was associated with resistance to anti-TB drugs (Dhammika, 2013).

Globally, 14.8% of TB patients and 50-80% in parts of sub-Saharan Africa have HIV co-infection. HIV infection increases individuals' susceptibility to TB infection and re-infection, including with DR strains and additionally, it may predispose TB patients to acquisition of drug resistance through gastrointestinal malabsorption of TB medications (Annie*et al*, 2013). Study findings in South Africa shows MDR-TB was more than twice common in HIV patients (27.1% vs 11.9%) (Shaheen *et al*, 2010). The Global Project of DR-TB, which has been gathering data since 1994, included data on the interaction between HIV infection and DR-TB only in its most recent report, from 7 countries, none of which have a high prevalence of HIV infection and there was no association between HIV infection and MDR-TB in 5 of these countries, where as a significant association was observed between MDR-TB and HIV infection in 2 countries in i.e. Latvia (OR=2.1, 95% CI [1.4–3.0]) and Ukraine (OR=1.5, 95% CI [1.1–2.0]) (Haileyesus *et al*, 2010). HIV was a risk factor for TB/MDR-TB accordingly to, WHO report on at California; US during 2011which shows HIV contribute 4.5% MDR-TB cases (WHO, 2012).

Study finding in southern Ethiopia shows there was no statistically significant association of HIV status with MDR-TB (Gemeda *et al*, 2012). Whereas other study shows HIV is associated with increased risk of acquired MDR-TB (OR=1.24, 95% CI [1.04–1.43]) and (OR=2.28, 95% CI [1.52–3.04]) for primary MDR-TB (Yonatan *et al*, 2014). And a study

by Birhanu and his colleagues showed MDR-TB and HIV significant association (OR=3.7, 95% CI [1.90–7.22]) (Birhanu *et al*, 2014).

3.2.3 TB treatment status and MDR-TB

From a nationwide survey conducted in China, the estimated MDR-TB rate was 5.7% for new cases and 25.6% for previously treated cases (Qiao *et al*, 2013). And a study finding in Uganda shows, MDR-TB of 1.4% from new cases and 12.1% from previously treated cases (Deus *et al*, 2013). Study findings in Ahmadabad, shows the prevalence of MDR-TB in pulmonary TB patients were 34.78% (Gupta *et al*, 2014).

Study findings in republic of Georgia shows previously treated for TB were significantly associated more likely to have MDR-TB than patients who were new (OR=5.27, 95% CI [3.75-7.41]). Likewise study in the Community of Madrid shows significant association with a history of previous TB treatment (OR=5.94, 95% CI [1.46-24.18]) (Belén and Teresa, 2010). A study finding in Rio de Janeiro, Brazil shows MDR rates of 3.9% among not previously treated and 17.3% among previously treated male gender (OR=2.3, 95% CI [1.2–4.4]) (Brito *et al*, 2010). Similarly a study in Nepal previously treated TB (AOR=14.94, 95% CI[7.93-28.13]) were found to be independent risk factors of MDR TB (MOH of Nepal, 2011), and nationwide study in China shows previous treatment history had a more than 7 fold increased risk of MDR-TB, compared with those never previously treated (Qiao *et al*, 2013).

3.2.4 Causes of inadequate anti-TB treatment and MDR-TB

DR-TB can be prevented by rigorous adherence to the principles of the National TB Control Program (the DOTS strategy) and by consistently building partnerships with patients, their families and communities (FMOH, 2012). Various factors such as adverse effects of drugs, quality of communication between patients and health workers, health culture, beliefs and transportation have been shown to be associated with none adherence (Argiro *et al*, 2013). None adherence to therapy has been cited as the principal obstacle in eliminating TB. Studies indicate that up to half of all of patients with TB do not complete treatment, which contributes to drug resistance (Argiro *et al*, 2013). Cultural beliefs also

lead to TB patients seeking assistance from traditional health practitioners and faith-based healers were reasons for TB treatment none adherence (Maswanganyi *et al*, 2014).

A study finding in, Tomsk, Russian Federation shows, of the 237 patients who were included in the analysis of non-adherence, 30 patients with MDR-TB were more likely illicit drug users (Gelmanova *et al*, 2014). Study in Nigeria, on adherence of TB patients showed of 378 records reviewed 71 interrupted their treatment and interruption of treatment was associated with living > 5 km (AOR=11.3, 95% CI [5.7-22.2]) because of lack of transport fare (40%) and feeling well (25%) and an unfriendly attitude of health care workers was also a barrier for adherence (Mangveep *et al*, 2011).

According to, study findings in Addis Ababa, Ethiopia; factors that were significantly associated with MDR-TB like; drug side effects during first-line treatment (AOR=4.5, 95% CI [1.9 - 10.5]), treatment not being DOTs (AOR=11.7, 95% CI [4–34.3]), interruption of treatment of at least a day (AOR=13.1, 95%CI [3.0-56.6]) (Selamawit *et al*, 2013).

Poor administrative controls on distribution of the drugs with no proper mechanism on quality control and bioavailability tests were factors that play important role in the development of MDR-TB (Marahatta, 2010). Related to regimens, TB treatment regimens in 6 TB hospitals in China showed that only 18% of MDT-TB patients with new cases and 9% of MDR-TB patients with retreatment cases were used standard TB treatment regimens during TB treatment (Guang *et al*, 2011).

3.2.5 MDR-TB detection status

Health education regarding spread of disease, early detection of MDR-TB by strengthened laboratory support, effective therapy, implicating innovative control measures, and applying them specially among immigrants, would interrupt the ongoing transmission and control emerging epidemic (Nirmalya *et al*, 2014). In Eastern Europe, prisons have had to deal with substantial case loads of MDR-TB patients. So close monitoring was mandatory for group of TB patients (WHO, 2013).

4. Objective

4.1 General Objective

- To assess the rate of MDR-TB and associated factors, in Dessie City Administration, Amhara National Regional State, Ethiopia.

4.2 Specific Objectives

- To determine the rate of MDR-TB
- To identify factors associated with MDR-TB

5. Method

5.1 Study Area and period

The study was conducted in Dessie City Administration. Dessie is located at 475 kilo meters South East of Bahir Dar and 401 kilo meters North of Addis Ababa. It has a latitude and longitude of 11' 8°N 39'38°E with an elevation between 2470 and 2550 meters above sea level. Administratively, the city is divided in to 10 sub-cities. According to Bureau of Finance and Economic Development (BoFED) of Amhara National Regional State, the total population for the year 2013/2014 was estimated to be 208,588; of whom 97,821(49%) were males and 110,767(51%) were females.

In terms of health facilities, Dessie City Administration has 5 hospitals (2 public and 3 private), 8 public health centers and 11 private clinics and 23 health posts. During the time of the study, TB service was being provided at 13 health facilities including 2 public and 3 private hospitals, and 8 public health centers. The retrospective review period was, July 1, 2012 to June 30, 2014.

5.2 Study Design

A facility based retrospective cross sectional study design employing medical records review of TB registration books supplemented by key informants' interviews of TB/HIV focal persons and in depth interview of MDR-TB patients was conducted.

5.3 Source population

All TB patients registrations starting from July 1, 2012 to June 30, 2014, all MDR-TB patients and TB unit focal persons of all public health facilities and TB/Leprosy officer of Dessie City Administration Health Department were the source population.

5.4 Study population

All TB patients' registrations starting from July 1, 2012 to June 30, 2014, all MDR-TB patients and TB unit focal persons of all selected public health facilities and TB/Leprosy officer of Dessie City Administration Health Department was the study population.

5.4.1 Inclusion criteria

All TB patients' registrations in the study period with recorded TB treatment outcomes (MDR-TB or non MDR-TB) including those who start at and transfer in, in the selected public health facilities were included.

5.4.2 Exclusion criteria

All TB patients' registrations of those who were transferred out to other health facilities, died and defaulted were excluded from the study.

5.5 Sampling and Sample size determination

All TB patients in the period between July 1, 2012 to June 30, 2014 in all public hospitals and five randomly selected public health centers that provide TB diagnosis and treatment service in Dessie City Administration were considered for quantitative study and all TB unit focal persons and TB/Leprosy officer were taken as key informants in qualitative part of study.

5.6 Data collection procedure

Data was collected from TB registrations books at TB unit of selected public health facilities using structured check list, developed from previous similar studies and TB treatment guideline.

Data collectors were TB trained health professionals who are working in the respective health facilities in order to assure patient confidentiality as well as data quality. A day training was given to seven data collectors on how to use the data collection instruments and collect data; pretest was also done to make data collectors familiar to the instrument

and to assure the feasibility of study. The principal investigator collected the qualitative data.

To interview MDR-TB patients' health professionals working in MDR-TB unit were selected since they are already trained and experienced on the standardized procedures that should be followed during contact with MDR-TB patients.

5.7 Variables

5.7.1 Independent variables

- Socio-demographic variables; Age, Sex, Residence
- TB treatment status
- TB/HIV Co-infection status
- TB treatment Adherence status
- TB type or site of involvement

5.7.2 Dependent variables

- Multi drug-resistant TB

5.8 Operational Definitions

- **New cases of TB:** A new case is defined as a newly registered episode of TB in a patient who, in response to direct questioning denies having had any prior anti-TB treatment (for up to one month).
- **Re-treated cases of TB:** A previously treated case is defined as a newly registered episode of TB in a patient who, in response to direct questioning admits having been treated for TB for one month or more.
- **Relapse:** A patient declared cured or treatment completed of any form of TB in the past, but who reports back to the health service and is now found to be AFB smear-positive or culture positive.
- **Treatment after Failure:** A patient who, while on treatment, is smear-positive at the end of the fifth month or later, after commencing.
- **Return after default:** A patient previously recorded as defaulted from treatment and returns to the health facility with smear-positive sputum.
- **Others:** A patient who does not fit in any of the above mentioned categories.

- **Primary resistance:** Patients with TB resistant to one or more anti-TB drugs, but who have never been previously treated for TB, due to transmission of a drug-resistant strain.
- **Acquired resistance:** Patients diagnosed with TB who start anti-TB treatment and subsequently acquire resistance to one or more of the drugs used during the treatment.

5.9 Data quality management

The structured data abstraction form for review of medical records and guiding questions to key informants' interview were prepared in English language and guiding questions for MDR-TB patients interview which were prepared in English was translated to Amharic. The collected data was supervised and checked for completeness and quality during data collection by principal investigator before data entry.

5.10 Data analysis

Quantitative data were coded before entry and analyzed using Statistical Package for the Social Science (SPSS), version 20.The results were displayed by using table and graphs. Simple descriptive statistics such as mean, SD, frequencies and percentage of different variables were also computed. Statistical inference was made at 95% confidence limit**.** The strength and magnitude of association was estimated for each variable from the corresponding univariate model and was expressed in terms of an odds ratio. And multiple regression analysis was carried out with the set of variables that showed significant association in the univariate analysis. MDR-TB rate was calculated as follows;

$$\text{MDR-TB rate} = \frac{\text{MDR-TB cases of all TB forms}}{\text{TB patients of all forms}} \ldots\text{.and was simplified to per 100}$$

Findings of key informants' interview were summarized by narration according to individual respondents' response as well as for a group of respondents according to commonness of their ideas.

5.11 Ethical considerations

Ethical clearance was obtained from Research and Ethicals Review Committee of the School of Pharmacy, Addis Ababa University, Ethical committee of Amhara National Regional State Health Bureau and Dessie City Administration Health Department. Participants' confidentiality or privacy of information was assured by using staff of the health facility as data collectors and excluding any potential identifiers (names, mobile number and specific residence area) from the medical records review check list. Finally, study findings ought to be disseminated to the respective study sites.

6. Results

6.1 Quantitative findings

6.1.1 Background characteristics of TB patients

6.1.1.1 Socio-demographic characteristics of TB patients

A total of 434 TB cases were found during two years' time period of TB treatment in Dessie City Administration from five public health centers and two public hospitals. And from these TB patients recorded 9 (2.1%) MDR-TB cases were found.

From total TB patients, 250 (57.5%) were males and 184 (42.5%) were females. Among the males, 4 (1.6%) were MDR-TB patients and 246 (98.4%) were non MDR-TB patients, while of the females 5 (3.3%) were MDR-TB patients and 179 (96.7%) were non MDR-TB patients.

From total TB patients 154 (35.5%) were under 25 years, 184 (42.5%) were between 25-44 years, 69 (16%) were between 45-64 years and the remained 27 (6%) were above 65 years. The median age of MDR-TB patients was 35 years.

Among the total TB patients, 349 (80%) were urban residents whereas 85 (20%) were rural residents. Eight of the 9 MDR-TB patients were urban residents (Table 1).

Table 1: Socio-demographic and clinical characteristics of TB patients, in public health facilities, Dessie City Administration, North East Amhara, Ethiopia, December 2014, (N=434).

Characteristics:	Category	Frequency n(%)
Gender:		
	Female	184 (42.4%)
	Male	250 (57.6%)
Age:		
	<25	154 (35.6%)
	25-44	184 (42.4%)
	45-64	69 (16%)
	>65	27 (6%)
Residence:		
	Urban	349 (80.4%)
	Rural	85 (19.6%)
Previous history of TB treatment:		
	Yes	37 (8.5%)
	No	397 (91.5%)
TB type or site of involvement:		
	Pulmonary TB	434 (100%)
	Extra pulmonary TB	0 (0%)
HIV status:		
	Positive	110 (25%)
	Negative	324 (75%)
Total		**434 (100%)**

6.1.1.2 Clinical characteristics of TB patients

From all TB patients, 37 (8.5%) had previous history of TB treatment and 397 (91.5%) were new TB cases. And from TB patients those who had been previously treated for TB 8 (21.6%) were MDR-TB patients and 29 (78.4%) were non-MDR patients. And from new TB cases only one patient had MDR-TB case (Fig.1).

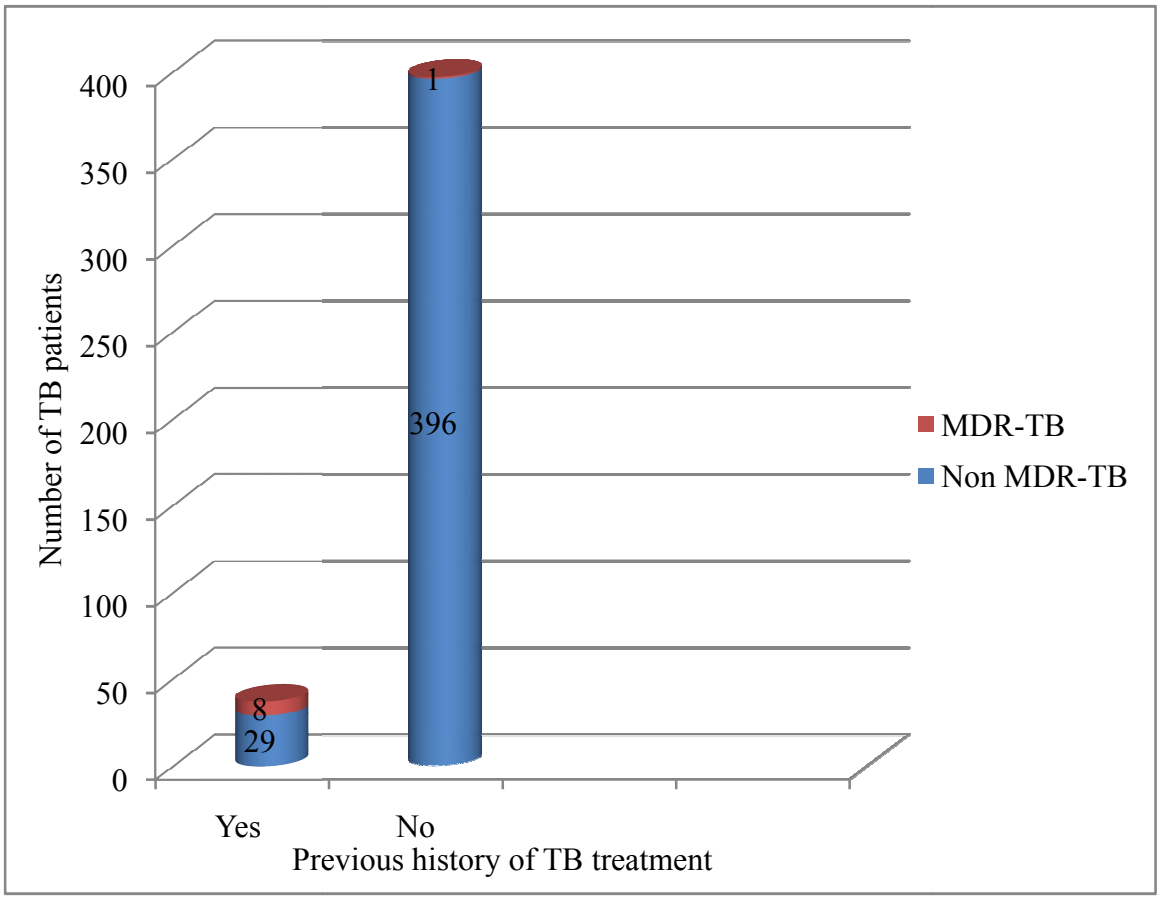

Fig 1: Previous TB treatment history of MDR-TB and non MDR-TB, in public health facilities, Dessie City Administration, North East Amhara, Ethiopia, December 2014.

From reviewed 434 TB patients 273 (62.9%) were pulmonary TB type and 161 (37.1%) were extra pulmonary type. And from pulmonary TB type 264 (96.7%) were non MDR-TB patients and 9 (3.3%) were MDR-TB patients. And compared to pulmonary TB type,

161 (39.2%) of TB patient and none of MDR-TB patient were extra pulmonary TB type (Fig 1).

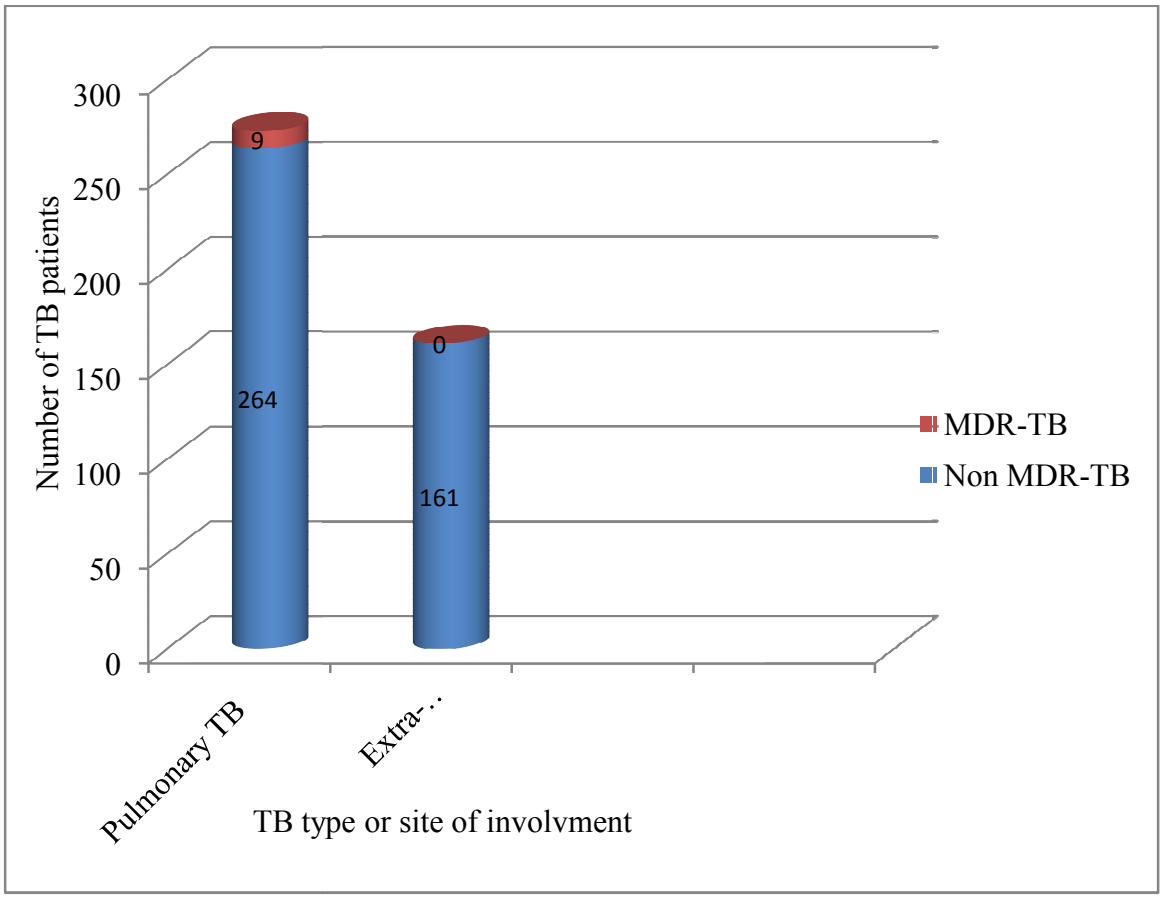

Fig 2: Types of TB among MDR-TB and non MDR-TB patients, in public health facilities, Dessie City Administration, North East Amhara, Ethiopia, December 2014.

Of all TB patients 110 (25%) were HIV positive and 324 (75%) were HIV negative. And nearly half of, 4 (44.4%) of MDR-TB and quarter of, 106 (24.9%) of non MDR-TB patients were HIV positive. Whereas 5 (1.5%) of MDR-TB patients and 319 (98.5%) non MDR-TB patients were HIV negative (Fig 3).

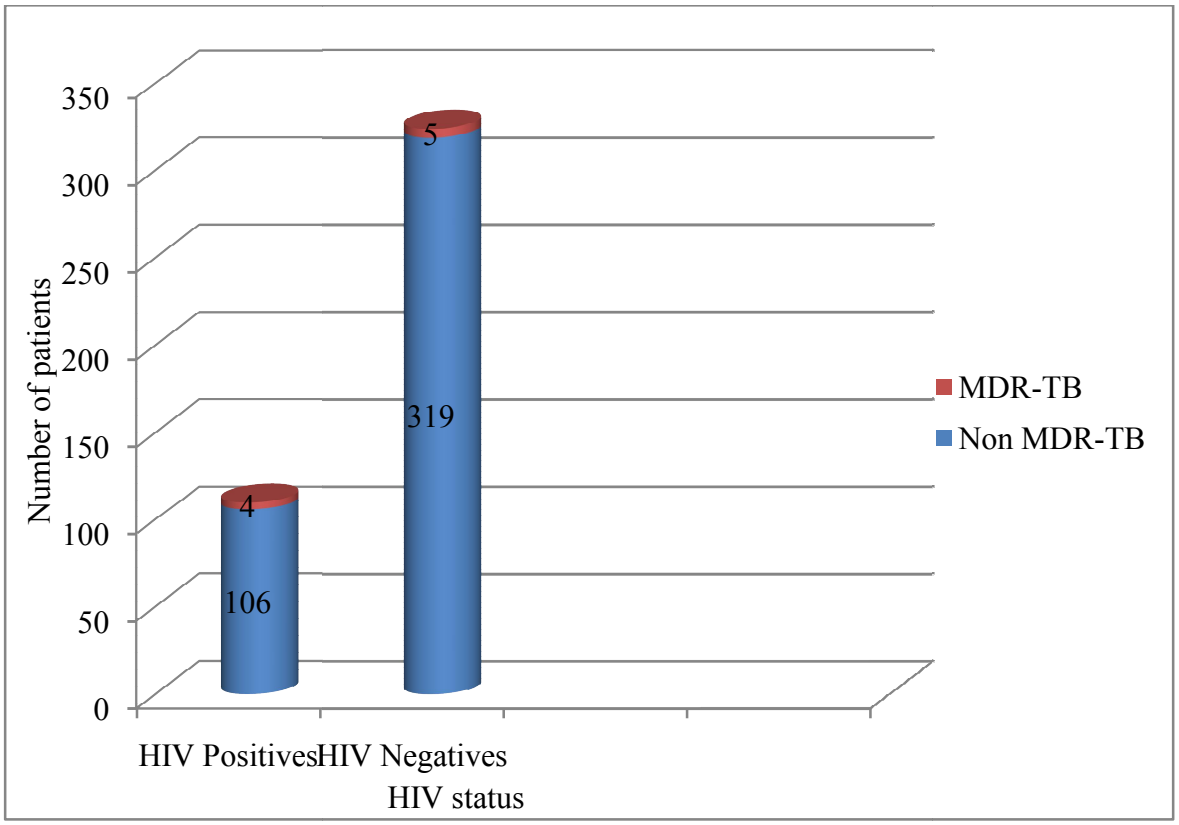

Fig 3 HIV status among MDR-TB and non MDR-TB patients, in public health facilities, Dessie City Administration, North East Amhara, Ethiopia, December 2014.

During intensive phase treatment 1 MDR-TB and 396 non MDR-TB patients who were under new TB treatment, none of MDR-TB and 40 (10%) of the non MDR-TB patients missed a dose of anti-TB drug. And 1 (100%) of MDR-TB patients and 86% (341) of non MDR-TB patients did not miss even a dose of anti-TB drug.

Among 8 (21.6%) MDR-TB and 29 (78.4%) none MDR-TB patients who had previous history of TB treatment, 6 (75%) of MDR-TB and 7 (24%) of none MDR-TB patients missed at least a dose of anti-TB drug during intensive phase of TB treatment (Table 3).

6.2 Factors associated with MDR-TB

Gender and age were not associated with MDR-TB. Even though the proportion of urban resident MDR-TB patients was much greater than the rural residents, residence didn't show association with MDR TB occurrence (AOR=1.67, 95% CI [0.196-14.254]).

The logistic regression analysis indicated that there was strong association between previous history of TB treatment and MDR-TB In this regard those with history of previous TB treatment were 66.87 times more likely to become ill with MDR-TB in comparison to those who did not have previous history of TB treatment (AOR =66.87, 95% CI [6.94-644.10]). In addition, non adherence to previous treatment was found to be a risk factor for development of MDR TB. Presence of HIV showed no significant association with MDR-TB (Table 3).

Table 2: Analysis of socio-demographic and clinical factors for MDR and non MDR-TB patients, in public health facilities, Dessie City Administration, North East Amhara, Ethiopia, December 2014.

Characteristics	MDR-TB patients	Non MDR-TB patients	COR (95% CI)	AOR (95% CI)
Gender:				
Female	5 (56%)	179 (42%)	1.72 (0.45-6.49)	1.69 (0.45-6.41)
Male	4 (44%)	246 (58%)	1.00	1.00
Age:				
<25	2 (22%)	152(36%)	0.33 (0.03-3.76)	0.30 (0.03-3.49)
25-44	5 (56%)	179 (42%)	0.70 (0.08-6.22)	0.54 (0.06-5.16)
45-64	1 (11%)	68 (16%)	0.36 (0.02-6.01)	0.32 (0.02-5.47)
>65	1 (11%)	26 (6%)	1.00	1.00
Residence:				
Urban	8 (89%)	341(80%)	1.97 (0.24-15.97)	1.67 (0.20-14.25)
Rural	1 (11%)	84 (20%)	1.00	1.00
Previous history of TB treatment:				
Yes	8 (89%)	29 (7%)	109.2 (13.2-903.6)	66.87 (6.9-644.1)
No	1 (11%)	396 (93%)	1.00	1.00
HIV status				
Positive	4 (48%)	106 (24.9%)	2.408 (0.64-9.13)	2.212 (0.56-8.65)
Negative	5 (52%)	319 (75.1%)	1.00	1.00
Total	9	425		

Table 3: None adherence status of retreated TB patients during intensive phase treatment, in public health facilities, Dessie City Administration, North East Amhara, Ethiopia, December 2014.

Non adherence status of retreated TB patients during intensive phase	MDR-TB cases	Non MDR-TB cases	COR , 95% CI
>10 days	2	1	10.0 (0.44-228.70)
5-10 days	3	3	10.0 (1.15-86.88)
1-5 days	1	3	3.3 (0.23-49.09)
Fully adhered	2	22	1.00
Total	8	29	

6.3 Prevalence rate of MDR-TB

Prevalence rate of MDR-TB from new TB cases, retreated cases and combined of all were found to be **0.3/100, 21.6/100 and 2.1/100** respectively from all forms of TB cases. The prevalence rate of acquired MDR-TB was similar to the combined prevalence rate above since all MDR-TB cases were acquired whereas, primary MDR-TB rate was null.

6.4 Findings of key informants interview

Key informants interviews were held with all the focal persons of TB units in the public health facilities and health institutions included in the study. Among the eight respondents interviewed; five of them were clinical nurses, two BSc nurses and one health officer. Five of eight key informants interviewed were males. The mean year of work experiences of respondents was eight.

6.4.1 Causes of inadequate anti-TB treatment

All TB-unit focal persons said that TB is a major health problem in their respective locality and three added that MDR-TB is their major concern as it shows increasing trends.

Regarding the cause of MDR-TB, all respondents suggested that poor adherence of patients particularly, during continuation phase of TB treatment as major reason for its occurrence. One of the seven key informants also mentioned that poor professional adherence to standardized treatment guidelines as a cause for MDR-TB. .

Related to TB treatment regimens; none of respondents mentioned gaps about availability of standardized guidelines and appropriateness of guidelines. But respondents mentioned problem was adherence of professionals to TB treatment guidelines, TB or MDR-TB trained human resource and Professional commitment. For example, one respondent said;

.... "*There is poor adherence of health care providers to standardized TB treatment regimens and he/she mentioned a scenario of MDR-TB case which was committed by health professional that missed combinable drug during TB treatment.*"

All respondents mentioned *pharmaceuticals fund and supply agency* as sole supplier of anti-TB drugs. And almost none of respondents had complained anti-TB drugs shortage. Two respondents said there was occasion of drug shortage in their facility.

Related to quality of anti-TB drugs, all respondents said the only ways we maintained the quality of anti-TB drugs were through checking *expire date* at any time of receiving and

dispensing to patients and by storing at *room temperature*. Regarding quality of laboratory reagents they are checked by, internal and external quality assurances.

About adherence all respondents said; almost all TB patients collected their anti-TB medications every month during continuation phase of TB treatment without any complain particularly, related to *transportation*, *drug side effect*s and *stigma/discrimination*. But still all respondents added their suspect ion as follow;

...."still we fear adherence of TB patients to right drug, right dose and right time of drug taking at home, during continuation phase of anti-TB treatment since there is no strong monitoring as intensive phase treatment."

6.4.2 MDR-TB detection status

As *risk factors of MDR-TB*, all key informants described TB treatment history, HIV/AIDS co-infection, geographical location of residence and repeated failure results of pulmonary TB outcomes and direct contact to MDR-TB patients. Almost all key informants said we were constantly aware of the risk factors for drug resistance TB and all sorted out TB Patient groups who should be prioritized for culture and drug sensitivity test (DST) as follows: *Failure or relapse after re-treatment regimen with first line drugs, Symptomatic close contacts of a proven MDR-TB case, Failure or relapse after new patient treatment regimen, Retreatment patients sputum smear positive at end of intensive phase (month 3), New patients sputum smear positive at end of month 3, All HIV positive patients diagnosed with active TB*. And all respondents said MDR-TB screening takes place at different outpatient department units of their health facilities together with screening of other different cases. And those patients who were suspected for MDR-TB detected at *GeneXpert sites* and *culture sites*.

As MDR-TB detection gaps, five of eight key informants mentioned, *Low TB trained human resource, Low professional commitment and capacity* in MDR-TB detection. Particularly, to detect those clients with symptomatic close contact with MDR-TBs it need strong professional commitment because other MDR-TB risks are already

constantly monitored during their laboratory follow up examination. But the remained three respondents mentioned low professional commitment as a gap for MDR-TB detection. As challenge, in MDR-TB detection key informant from Dessie city administration said;

...."*We highly suspect private clinic or hospitals commitment in MDR-TB detection. For example, in 2006 fiscal year private health facilities TB treatment outcome was 60% and patients with unknown outcome were 28% but none of them report either MDR-TB suspect or MDR-TB case so far."*

And related to all health facilities he/she added;

...."*There is low professional commitment in MDR-TB detection at different units of outpatient department, health extension workers and private clinics weak screening of either TB or MDR-TB, fear of health care providers of MDR-TB cases and lack of regular assessment of highly risky areas (churches and mosques and prisons) for both TB and MDR-TB."*

Lastly, two key informants said;

.... "*Referral system from private health facilities is not clear or it does not contain all necessary information so this may probably add risk for MDR-TB development."*

6.5 Findings of MDR-TB patients in depth interview

From total MDR-TB patients recorded, seven of them were alive and among these five were females and six of them were urban dwellers'. The mean age of respondents was thirty three.

Two of in depth interview participant patients said that they used holly and they admitted that while on holly water, anti-TB treatment with drugs was interrupted.

None of in depth interviewees was herbal traditional medicine user while they were under anti-TB treatment and no interruption TB treatment as well.

All respondents mentioned as, none of them took any anti-TB drugs from other sources other than starting/recommended health facility. And related to drug handling, five of seven MDR-TB patients said we;

"We *handled according to health care providers advice; that means we put to cool and pest free area."* But the remained two respondents said; *"we put to any accessible place and no special care of how to handle."*

And one respondent said; "*I sometimes chew chat while taking anti-TB drugs."*

None of in depth interview respondent mentioned; transport inaccessibility, getting up-to-date information/monitoring/, negative community perception towards TB patients i.e. stigma and discrimination and supply of anti TB drugs as a possible cause for being MDR-TB patient.

Related to smear examination follow-up and adherence to anti-TB treatment unlike their health care providers expected or said, three of seven respondents said we were not well adhered to the treatment and they interrupted taking of drugs but none of them remember for how much days they interrupted.

Finally, as MDR-TB cause, two of seven respondents said; "*while we took, anti-TB drugs there was vomiting and appetite lose so we suspect such conditions as a cause for MDR-TB*." On the other hand three of the rest five respondents said; "*we complain our right time and right dose of drug taking as a cause of MDR-TB."*

7. Discussion

The combined MDR-TB rate documented in this study was found to be 2.1% for all form of TB cases which is much lower compared to what other studies showed in eastern European countries (ECDC, 2012) and 27 high MDR-TB countries outside the European Region (Dhammika, 2013). And studies in Northeastern China (Qiao *et al*, 2013), in Rio de Janeiro, Brazil (Brito *et al*, 2010), in the Community of Madrid, Spain (Belen and Teresa, 2010) and in the city of Santos, Brazil (Andréa *et al*, 2012) show MDR-TB rate of 8.7%, 7.4%, 4.5% and 15% respectively which were much higher compared to this study finding. This low figure may be due to better patient counseling during intensive phase of TB treatment, better pharmaceutical supply, no patients adherence complain related to transportation, side effects of drugs. E.g. study in Addis Ababa, Ethiopia shows, drug side effects was significantly associated with MDR-TB (Selamawit *et al*, 2013). Besides above mentioned, this may also be related to availability of standardized TB treatment regimens. E.g. study finding in TB hospitals in China showed that only 18% of patients from new cases and 9% of patients from retreatment cases were used standard TB treatment regimens (Guang *et al*, 2011).

On the other hand, this study finding was slightly higher compared to a study, at Eastern Ethiopia (Birhanu *et al*., 2014) and southern Ethiopia (Gemeda *et al*, 2012) with 1.1% and 1.5% respectively. And this difference may be related to gaps mentioned from both key informants and MDR-TB patients like; poor TB patients adherence during continuation phase of TB treatment particularly, related to taking right drug, right dose, at right time and chewing chat , vomiting without dose adjusting and chosen another option of treatment like holly water. E.g., study in Addis Ababa, Ethiopia shows interruption of treatment of at least a day were a risk factor for MDR-TB (Selamawit *et al*, 2013). In addition to above gaps, inadequate TB/MDR-TB trained health professionals, low professional commitment, and fear of MDR-TB resistant strain and poor adherence to standard treatment regimens by professionals and lack of regular assessment of highly risky areas of MDR-TB could compromise the result.

The new cases MDR-TB rate of this study was found to be 0.3 for all form of TB cases, which was extremely lower compared to other studies. E.g. MDR-TB rate of 1.1% in Newdelhi, India (Surendra *et al*, 2011), 1.4% in Uganda (Deus *et al*, 2013), 11.9% in South Africa (Shaheen *et al*, 2010), 3.6% in Bangladesh (Flora *et al*, 2013) and 5.7% from nationwide survey in China (Qiao *et al*, 2013) were much higher. In addition a WHO report of 2015 in Ethiopia showed MDR-TB rate of 1.6% among new TB cases was also much higher than this finding (WHO, 2015). And possible reason for this low figure finding could lie on, low MDR-TB detection status.

The previously treated TB cases MDR-TB rate of this study was 21.6% from all form of TB. And other studies revealed somewhat higher figures like; MDR-TB rate of, 35.5% in Middle East (WHO, 2010), 25.6% from nationwide survey in China (Qiao *et al*, 2013), 34.78% in Ahmadabad (Gupta *et al*, 2014) and 27.1% in South Africa (Shaheen *et al*, 2010). Whereas, this study finding was a little bit higher compared to, 12.1% in Uganda (Deus *et al*, 2013), 12% in Ethiopia (WHO, 2015) and 20% study by WHO around the world (WHO, 2015).

This study shows MDR-TB of all from acquired TB cases and no primary MDR-TB. But nationwide survey in China shows MDR-TB of 5.7% in primary TB cases and 25.6% in acquired TB cases (Xin *et al*, 2014) and 2.7% of primary and 18.5% acquired MDR-TB cases globally. No primary MDR-TB case from this study may be relate to low commitment and fear of professional in MDR-TB detection or screening.

There was no statistically significant association between age groups and MDR-TB occurrence from this study and it was similar to study finding in southern Ethiopia (Gemeda *et al*., 2012). A study finding in Bangladesh at age group of 25–44 years (AOR=1.72, 95% CI [1.12–2.66]) (Mahfuza *et a*l, 2014) and nationwide survey in China at age group of 25–44 (AOR=2.224, 95%CI [1.158-4.273]) showed significant association with MDR-TB (Qiao *et al*., 2013).

Gender is not significantly associated with MDR-TB according to, this study finding. Similarly, a study in Nigeria also shows gender was not significantly associated with

MDR-TB (Akaninyene *et al*, 2013). And other studies like; nationwide survey in China (AOR=1.763, 95% CI [1.060-2.934]) (Qiao *et al*, 2013), a study in Republic of Georgia (AOR=1.58, 95% CI [1.02-2.32]) (Lomtadze*et al,* 2010) and a study in Mumbai, India (AOR=1.68; 95% CI [1.02-2.87]) (sachin *et al*, 2014) shows female gender was a risk factor for MDR-TB. And studies in Rio de Janeiro, Brazil (AOR=2.3, 95%CI [1.2–4.4]) (Brito *et al*, 2010), a study in Ethiopia (AOR=2, 95% CI [1.4-5]) (Fikadu, 2015**)** shows male gender was a risk factor for MDR-TB.

Geographical location of residence of TB patients was not significantly associated with MDR-TB from this study. But a study in Bangladesh shows urban residence of TB patients was significantly associated with MDR-TB occurrence (Flora *et al*, 2013).

This study (AOR=9.0, 95% CI [1.03-78.57]) shows non adherence of TB patients significantly associated with MDR-TB and was analogous with study findings in Addis Ababa, Ethiopia, none adherence due to interruption of treatment of at least a day (AOR=13.1, 95% CI [3.0-56.6]) was significantly associated with MDR-TB (Selamawit *et al,* 2013). Again this study shows significant association of previous TB treatment history and MDR-TB occurrence (AOR=66.87, 95% CI [6.94-644.10]) and it was much higher compared to, in Nepal (AOR=14.94, 95% CI [7.93-28.13]) (MOH of Nepal, 2011), in Addis Ababa, Ethiopia (AOR =5.7, 95% CI [1.82 - 8.32]) (Meseret and Meaza, 2014), in the community of Madrid, Spain (AOR=5.94; 95% CI [1.46-24.18]) (Belen and Teresa, 2010), in Ethiopia (AOR=14, 95% CI [1.3-9]) (Fikadu, 2015**)** and in Republic of Georgia (AOR=5.47, 95% CI [3.87-7.74]) (Lomtadze *et al,* 2010) which were also significantly associated with MDR-TB.

HIV/AIDS did not show significant association with MDR-TB occurrence according to, this study finding. And this was analogous to other studies like; in Uganda (Deus *et al*, 2013), in southern Ethiopia (Gemeda *et al*, 2012) and study in Kenya, Malawi, Tanzania, Cote d'Ivoire, and France. In contrast, other studies in Ethiopia shows HIV was a risk factor (AOR=1.24, 95% CI [1.04–1.43]) for acquired MDR-TB and (AOR=2.28, 95% CI [1.52–3.04]) for primary MDR-TB (Yonatan *et al*, 2014). Again in Ethiopia (AOR=2.66, 95% CI [1.32-5.6]) and in Eastern Ethiopia (AOR= 3.7, 95% CI [1.90–7.22]) (Birhanu *et*

al, 2014) show significant association. Whereas, Global Project of drug resistance-TB study findings from 7 countries shows no significant association in 5 of these countries, and significant association were observed in remained 2 countries (Haileyesus *et al*, 2010).

Finding of this study shows all of MDR-TB cases were from pulmonary TB type and another study in Ethiopia also shows pulmonary TB type was a risk factor for MDR-TB (Fikadu, 2015**).**

8. Conclusion

Prevalence rate of MDR-TB for combined, new and retreated TB cases of all form from public health facilities, in Dessie City Administration were found to be 2.1/100, 0.3/100 and 21.6/100 respectively.

Adherence of TB patients to TB treatment with (AOR=9.0, 95% CI [1.03-78.57]) and previous history of TB treatment with (AOR=66.87, 95% CI [6.94-644.10]) were found to be significantly associated with MDR-TB. And related to TB type all MDR-TB cases were dominantly pulmonary TB type.

9. Limitations of the study

More or less this study findings were discussed as stated above, but still it was subjected some limitations;

- A few number of MDR-TB patients which compromise risk factors association analysis findings particularly, Sociodemographic and HIV positivity.
- Recall bias as it is true to retrospective cross sectional study design,
- Being cross-sectional design and
- Use of secondary data.

10. Recommendations

- Organized and regular assessment of MDR-TB at risky areas should be strengthened.
- Strong counseling related to TB patient adherence to anti-TB drugs, even while taking holy water is mandatory.
- There should be regular regulation of private clinics, drug stores and pharmacies related to supply and quality of anti-TB drugs.
- Strengthening early case detection and proper treatment of drug susceptible TB in accordance with WHO treatment guidelines and professional adherence to these protocols to ensure adequate treatment success rates is critical.
- Even though there were not significant association of HIV/AIDS with MDR-TB and urban residence with MDR-TB, still there were higher proportions of MDR-TB cases from HIV/AIDS patients and urban residents so that further studies should be done for these factors.

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12. Annexes

Annex 1: Data collection tool for Socio-demographic variables, TB detection and treatment outcomes with drug resistance from TB patients' medical records in selected public health facilities, Dessie, Ethiopia, December 2014.

Addis Ababa University

School of Pharmacy

Department of Pharmaceutics and social pharmacy

Health facility code----------

Purpose: this study is aimed to determine rate of MDR-TB cases, to assess the pattern of MDR-TB case rate and the associated risk factors at Dessie city administration. So data of your facility is vital and valuable to the successful completion of the study.

Please be honest in filling this check list, since it will be only used for research purposes. This study will be confidential and data will be analyzed in aggregates.

For any questions or comments please contact

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Dr Teferi Gedif (Advisor), Mobile +251911684854, **E-mail**, tgedif@gmail.com

Socio demographic variables				TB Detection status									Adherence	Drug resistance	
				TB treatment history(√)											
				New (√)	Re-treatment						Extra pulmo nary TB(√)	Co-morbidity (HIV/AIDS)		Acquired	primary
MRN	Age	Sex /**M**/**F**/	Residence (**U**/**Ru**)		Failure (categ. 1)	Relapse (categ. 1)	Return after Default	Failure (categ 2)	Relapse (categ 2)	Others			Adherence status of intensive phase TB treatment in **days**	Resistant to (**R, I,**	Resistant to (**R, I, S, E, P** others)

Key:

Rifampicin=**R**, Isoniazid=**I**, Ethambutol=**E**, Streptomycin=**S**, Male=**M**, Female=**F**, Urban=**U**, Rular=**Ru,** Medical Record Number **=MRN,** (USAID, 2010).

Name or code of health facility----------, year ----------

Annex 2: Interview guiding questions for key informants' interview of **TB unit focal persons**, **TB/Leprosy officer** and **MDR-TB patients** about MDR-TB causes/risks in public health facilities of Dessie city administration, Dessie, Ethiopia, December 2014.

Addis Ababa University

School of Pharmacy

Department of Pharmaceutics and social pharmacy

Health facility code: _____

Verbal consent form:

Greeting, my name is _____I am Pharmacoepidemiology and social pharmacy postgraduate student at School of Pharmacy, Addis Ababa University. Currently, I am undertaking my research on "MDR-TB rate and associated factors in Dessie city administration" and I would like to interview you some questions regarding multidrug resistant TB (MDR-TB) causes; on TB treatment regimens, supply/quality of anti-TB drugs and laboratory reagents and adherence status of TB patients in your facility or institute. The interview will take 10 to 15 minutes. The aim of this study is to assess types and degree of factors that cause MDR-TB in Dessie town. And this will be important in preventing and treating of TB as well as MDR-TB through prioritizing the more alarming factors. Your participation is vital and completely voluntary based. You can refuse to answer any questions or withdraw from the study at any time without a problem to you or to your family. Your privacy will be kept strictly at any time. For any questions or comments please contact

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Dr Teferi Gedif (**Advisor**), **Mobile** +251911684854, **E-mail**, tgedif@gmail.com

Do I get your permission to proceed?

Yes ☐ No ☐

If Yes, Continue to the Next Page

If No, Skip to the next participant

Date of Interview ----------

Time Started----------Time Finished ----------

Annex 2.1: Interview guiding questions to health facilities **TB unit focal persons** in public health facilities, Dessie City Administration, North East Amhara, Ethiopia, December 2014 (WHO, 2012).

Background information of respondents;

Age----------sex--------Profession----------Work experience----------

1. Adherence of TB patients and MDR-TB detection status.

1.1 Is TB and TB MDR major problem in your health facility?

1.2 How do you describe the trend? Is it increasing, decreasing or become stable?

1.3 How do you see adherence status or DOT strategy of TB patients related to; transportation, any adverse effects, social barriers etc?

1.4 Do you encounter MDR-TB case so far in your facility? If yes, how many and what do think the possible causes/risk factors?

1.5 How do you see MDR-TB detection status in your health facility?

1.6 What group of TB patients are MDR-TB suspects?

1.7 Where and who do screening of MDR-TB suspects?

1.8 What gaps/weaknesses available in your facility related to MDR-TB detection?

2. Supply or quality of drugs/laboratory reagents;

2.1 Where do you get anti-TB drugs or laboratory reagents?

2.2 Do you encounter shortage of anti-TB drugs or laboratory reagents/instruments in your facility/institution in previous two years?

2.3 How do you assure quality of

2.3.1 Anti TB drugs?

2.3.2 Laboratory reagents of TB?

3. Health care providers or Regimens;

3.1 How do you see the regimens related to TB control program in your facility?

3.1.1 Appropriateness of guidelines?

3.1.2 Availability of guidelines?

3.1.3 Adequacy of TB or MDR-TB trained human resource?

3.1.4 Commitment of professional in MDR-TB detection?

Annex 2.2: Interview guiding questions to Dessie city administration health department **TB/Leprosy officer,** Dessie City Administration, North East Amhara, Ethiopia, December 2014 (WHO, 2012).

Back ground information of respondents;

Age----------Sex----------Profession----------Work experience----------

1. How do you describe TB control program in your city administration?
2. How do you see trend of TB or MDR-TB in Dessie city administration?
3. How do you see MDR-TB detection service in Dessie city administration?
4. Where do you get anti TB drugs or laboratory regents?
5. How do you see TB/MDR-TB trained human resource adequacy in Dessie city administration?
6. Is there regular assessment of high MDR-TB risky areas in Dessie city administration?
7. Is there regular regulation of private clinics or pharmacies/drug venders related to TB treatment services or holding anti-TB drugs?

Annex 3: Interview guiding questions to **MDR-TB patients**, Boru Meda General Hospital, Dessie City Administration, North East Amhara, Ethiopia, December 2014 (WHO, 2012).

1. Do you take any traditional medicine or holly water during TB treatment? If yes, what do you get? Do you proceed with TB treatment or interrupt?
2. Do you use smoking, chat chewing and alcoholic drinking while you were under TB treatment
3. Do you take any anti TB drug from other sources during TB treatment?
4. Accessibility of anti TB drugs at health facilities?
5. How do you store your medications during TB treatment?
6. What seems your adherence status during TB treatment?

6.1 Transportation accessibility to health facility?

6.2 Getting up-to-date information from health professionals/monitoring?

6.3 Community perception towards TB patients/stigma and discrimination?

6.4 Your commitment to medication intake, while feeling better prognosis, side effects/adverse drug reactions during TB treatment?

7. What do you think the reason you develop MDR-TB?

መጠይቅ2:በደሴከተማብዙመድሃኒትየተላመደቲቢመነሻምክንያቶችንአስመልክቶየሚደረግ ቃለመጠይቅ፣ደሴ፣ 2006::

አዲስአበባዩንቨርስቲ

ፋርማሲ ትምህርት ቤት

የፋርማስዩቲክስና ሶሻል ፋርማሲ ትምህርት ክፍል

የሆስፒታል/ተቋም መለያ ቁ, ----------

የቃል ፍቃደኝነት ቅጽ

ሰላምታ

ሰላም፤ስሜ----------ይባላል፣እኔ በአዲስ አበባ ዩንቨርስቲ ፋርማሲ ትምህርት ቤት የፋርማስዩቲክስና ሶሻል ፋርማሲ ትምህርት ክፍል የፋርማኮኢፒዶሞሎጂ እና ሶሻል ፋርማሲ ፕሮግራም የሁለተኛ ዲግሪ ተማሪ ነኝ። እኔ በሆስፒታላችሁ/በተቋማችሁ ላይ ብዙ መድሃኒት የተላመደ የቲቢ በሽታ ምክንያቶች ዙሪያ ማለትም በቲቢ ማከሚያ ሪጅሜን የቲቢ መድሃኒቶች የመመርመሪያ ሬጀንቶችና መሳሪያዎች አቅርቦትና ጥራት እንዲሁም የቲቢ በሽተኞች ህክምና ላይ እና መድሃኒት አወሳሰድ ላይ ያላቸው የክትትል ሁኔታ በተመልከተ በተወሰኑ ጥያቄዎች ላይ ቃለ መጠይቅ ማድረግ እፈልጋለሁ። ቃለ መጠይቁ ከ 10 እስከ 15 ደቂቃ ይወስዳል። የዚህ ጥናት ዋና አላማ በደሴ ከተማ ብዙ መድሃኒት የተላመደ ቲቢ መነሻ ምክንያቶች አይነትና ቁርኝት ዙሪያ ጥናት ማድረግ ነው። ስለዚህ የጥናቱ ውጤትም ይበልጥ አሳሳቢ የሆኑ ምክንያቶችን በማስቀደም ቲቢን እንዲሁም ብዙ መድሃኒት የተላመደ ቲቢን ለመከላከልና ለማከም ይጠቅማል። ተሳትፎህም እጅግ አስፈላጊና ፈቃደኝነት ላይ የተመሰረተ ነው። ስለሆነም ምንም አይነት ችግር በራሶና በቤተሰቦ ላይ ሳይደርስ በፈለጉት ስአት ጥያቄ አለመመለስና ከጥናቱ አቋርጦ መሄድ ይችላሉ። የግል ደህንነቶም ሁሌም የተጠበቀ ነው። ፍቃደኛ ኖት?

አዎ ☐ አይደለም ☐

ፍቃደኛ ከሁኑ, ወደ ሚቀጥለው ገጽ አሄዳለሁ

ፍቃደኛ ካልሆኑ, ወደ ሚቀጥለው ተረኛ ተጠያቂ እሄዳለሁ

ቃለ መጠይቁ የተካሄደበት ቀን----------

የተጀመረበት ሰአት----------

የተጠናቀቀበት ሰአት----------

መጠይቅ 3:ለመድሃኒት ለተላመደ ቲቢ ህመ·ማን የሚቀርቡ መነሻ መጠይቅ ቦሩ ሜዳ ሆስፒታል ደሴ ኢትዮጵያ፡ 2007፡፡

1. ቲቢ ህክምና በመከታተል ላይ እያሉ የባህል መድሃኒት ወይም ጠበል ይጠቀሙ ነበር? መልሱ አዎ ከሆነ ምን አይነት ውጤት አገኙ? ከዛ በኃላስ ህክምናውን ቀጠሉ ወይስ አቋረጡ?
2. የቲቢ ህክምና በመከታተል ላይ እያሉ በተለያዩ ሱሶችን ማለትም፤ጫት፣ሲጋራ፣ እንዲሁም አልኮል ይጠቀሙ ነበር?
3. የቲቢ ህክምና ላይ ሁኖ ከሌላ ምንጭ የቲቢ መድሃኒት ይጠቀሙ ነበር?
4. የቲቢ መድሃኒቶች አያያዝ እንዴት ነበር?
5. ቲቢ ህክምና በመከታተል ላይ እያሉ የቲቢ ምርመራ/ህክምና ክትትሉ እንዴት ነበር?

5.1 ከትራንስፖርት አገልግሎቱ?

5.2 ከባለሙያዎች ክትትልና መረጃ አሰጣጥ?

5.3 ከማህበረሰቡ በሽተኞች ላይ ያለው አመለካከት?

5.4 ከቲቢ መድሃኒቶች አቅርቦት?

5.5 የእርሶ ቲቢ ምርመራና ህክምና ወይም መድሃኒት አወሳሰድ ላይ የነበሩት ቀረቤታ/መድሃኒት አወሳሰድ በሽታው የመሻል ስሜት ሲሰማ መድሃኒቶች ጎነዮሽ ጠንቅ ሲሰማ?

5.6 በመድሃኒት የተላመደ ቲቢ የተያዙበት ምክንያት ምን ይመስሎታል?