

# Trend and Associated Factors of Mycobacterium Tuberculosis and Rifampicin Resistance in South-west Ethiopia: Institutional Based Retrospective Study

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## Abstract

**Background:** There is scarcity of data on the trends of Mycobacterium tuberculosis and rifampicin resistance in southern part of Ethiopia. This study was aimed to assess the trend of pulmonary tuberculosis and rifampicin resistance and associated factors among patients in South-west Ethiopia.

**Methods:** Health institution-based retrospective cross-sectional study was conducted at Wolkite town Health center from January 2016 to 2020. Data was collected retrospectively from the GeneXpert™ TB registration book using a data extraction checklist and directly entered into SPSS version 21 and analyzed. The results were summarized using descriptive statistics, tables, and figures. Bivariate and multi-variant regression analysis was done to measure the association between dependent and independent variables. P values <0.05 were considered statistically significant.

**Result:** total of 3286 participants had complete Gene X-pert MTB/Rif assay result which included in statistical analysis. The overall detection rate of TB was 27.3 % (899/3286) and the prevalence of TB was higher in males 500 (55.6%) than females 399 (43.4%). From total of confirmed TB cases, 137 (15.2%) participants developed rifampicin resistance. Residence, registration type for TB, reason for diagnosis, HIV status and year of TB diagnosis were independent variables significantly associated with outcome variable (Mycobacterium tuberculosis detection) with  $p < 0.05$ . The significant rifampicin resistance was detected in 2019 which was 70 from total of 137 confirmed rifampicin cases.

**Conclusion:** In this study, the trends of tuberculosis and rifampicin resistance were great in new registered groups, rural residents and HIV positive individuals. Therefore, maximizing early visit to health institutions and detection of Mycobacterium tuberculosis and enhancing active health education and intervention for tuberculosis are forwarded to reduce the threat of disease. There is still need for active health education campaigns and government intervention.

**Keywords:** Pulmonary Tuberculosis; Rifampicin; Associated risk factors; Trend; Ethiopia

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**Abbreviations:** HIV: Human Immunodeficiency Virus; M. tuberculosis: Mycobacterium Tuberculosis; MDR-TB: Multidrug Resistance Tuberculosis; RIF: Rifampicin; TB: Tuberculosis; WHO: World Health Organization

## Introduction

Tuberculosis is still the problematic and kills large number of people globally [1,2]. Despite the availability of chemotherapy, the catastrophic effect of HIV on TB in Africa got global concern to improve TB prevention and control [3]. One-third of world

population is currently infected with TB mainly with latent infection and around 8 million people develop TB disease in every year and from these nearly 2 million death result and Ethiopia is one top Tb burden country in Africa [4]. From 30 countries with high MDR-TB globally, Ethiopia was one of them with estimated 5800 cases in 2016 [5]. Low achievement of global Tb control was due to slow, insensitive diagnostic methods, particularly for the detection of drug-resistant forms and in patients with human immunodeficiency virus infection. Early detection is essential to reduce the death rate and interrupt transmission [6]. Current and

future control of TB relies on the correct use of new diagnostics and new drugs from one side, and on the consistent application of the five core interventions at the programmatic level. In addition, it is mandatory to tackle the social determinants and socio-economic barriers favoring the MDR-TB, otherwise it will not be possible to reach the planned goals as well as TB Elimination [7]. Ethiopia implemented different advanced technologies concordantly with WHO recommendations, including the use of the GeneXpert™ MTB/ RIF assay to achieve the global strategy on TB [8]. Different studies conducted at hospital level and research institutions yielded different results on the trends of TB and rifampicin resistance in Ethiopia [9-12], and most of those were done at hospital level, no researches were done on trends of TB and rifampicin resistance at health center. Globally, almost 0.5 million cases of multidrug resistant TB (MDR-TB) with bacillary resistance to at least isoniazid and rifampicin are estimated to emerge every year. Rifampicin is one of the most potent first-line anti-TB drugs. It inhibits the transcription and elongation of RNA by binding to the  $\beta$ -subunit of RNA polymerase [13]. Detection of rifampicin resistance in *Mycobacterium tuberculosis* isolates use as an initial indicator of multidrug resistance [14]. Even though, Ethiopia is one of the high burden countries, regarding both in TB incidence and MDR-TB [15] there is limited information regarding the trend analysis of mycobacterium tuberculosis and rifampicin resistance in southwestern part of Ethiopia particularly in study area. To the best of our knowledge, there are no studies conducted to identify the trends in Mycobacterium tuberculosis and rifampicin resistance using GeneXpert™ in south-west. Therefore, this study aimed to determine the trends in pulmonary tuberculosis and rifampicin resistance using GeneXpert™ among TB-presumptive cases at Wolkite health center, Southern Ethiopia.

## Methods and Materials

### Study design, area and period

The study was conducted in Wolkite Town located 158 km southwest of Addis Ababa along the Jimma Road in the Southern Region of Ethiopia. Wolkite town, the capital of Gurage Zone, has a latitude and longitude of 8°17'N37°47'E and an elevation between 1910 and 1935 m above sea level. Based on the 2007 census conducted by the central statistical agency shows a total population of 28,866 of whom 15,704 are and 13,792 women. Institution- based retrospective study design was used to gather existing data from TB patients' registration logbook at Wolkite Town Health Center. Wolkite town Health center is serving the people in wolkite town and catchment areas including provision TB diagnosis using GeneXpert™ and treatment.

### Eligibility

**Inclusion and exclusion criteria criteria:** Participants with complete data in the GeneXpert™ TB registration book were included during the study period of last 5 years (2016-2020) and those cases with indeterminate and/or invalid results were excluded from the study.

**Independent variables:** patients age, sex, residence, year of diagnosis, reason of diagnosis and HIV status.

**Dependent Variable:** Mycobacterium Tuberculosis and

Rifampicin (resistance or sensitivity).

### Sample size, data collection and analysis

The secondary data was collected retrospectively for all presumptive TB patients from a GeneXpert™ TB registration book from February 2016, to January 2020. Laboratory based and Socio-demographic data were extracted from registration logbook by structured questionnaire and checklist by reviewing five years TB results from Wolkite Town Health Center Laboratory. Then, data were recorded from patient's case logbook in well-prepared checklist format containing dependent (outcome) variable and independent variables. After checking its completeness and consistency of data to maintain its quality, it was entered in SPSS version 21 and analyzed. The descriptive data was presented using tables and graphs/figures.

### Data analysis and interpretation

Data obtained through the checklist and laboratory test results were entered to SPSS 21 for statistical analysis. Descriptive analysis, frequencies, and figures were used to explain the findings. Bivariate Logistic regression analysis was conducted primarily to check the association of each independent variable with the dependent variable at P value <0.2. Multivariate logistic regression models were employed to analyze specific associations between variables. Odds ratio (OR) and 95% confidence interval (CIs) were calculated using logistic regression model to measure the strength of an association. In all cases, p-values less than 0.05 were considered statistically significant.

### Ethical consideration

The study was cleared ethically by college of health sciences and medicine, institutional research ethical committee, Wolkite University. Then formal letter of cooperation was written to Wolkite town health center administration. The objective of the study was explained to the health center. The letter of agreement was attached to ensure confidentiality of data. The information taken from patients' recorded data were kept confidential. Only codes were used to identify the study groups.

## Result

### Socio-demographic and clinical characteristics

From a total of 3504 TB clinically suspected patients that have submitted their samples for TB diagnosis in five year, 3286 have complete data in the registration log books. Of the total of study participants, majority were males 1787 (54.4%), majority were found in age group of 35-44 734 (22.3%) followed by 25-34 and 45-55 which both accounted 643 (19.6%). Most of the reason for TB diagnosis was presumptive TB case 2669 (81.2%), while presumptive drug resistant TB reason was 580(17.7%). Among the presumptive TB patients' took diagnosis, majority were new cases 2898 (88.2%). The number of diagnosis of Mycobacterium tuberculosis using the GeneXpert™ have increased between 2016 and 2018 and decreased between 2019 and 2020, whereas between 2018 and 2019, there was no significant change of TB diagnosis. From the total of study participants only 560 (17.04%) know their HIV status, from which 143 (25.5%) were living with HIV, that is TB/HIV co-infection (**Table 1**).

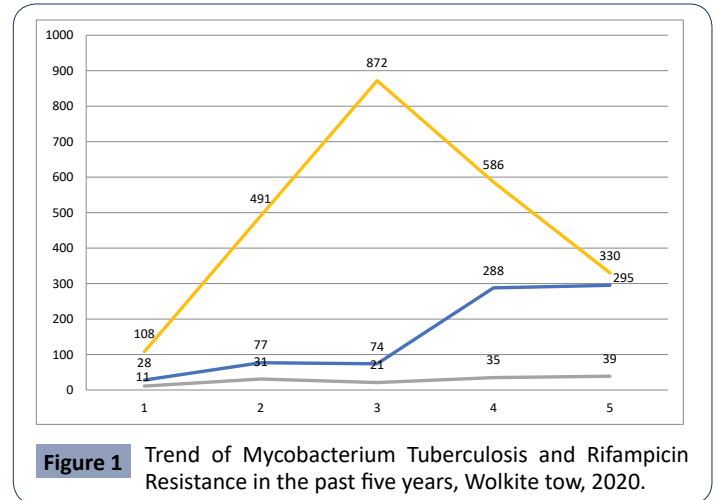
**Table 1** Socio-demographic and clinical characteristics Presumptive TB patients in Wolkite town health center, 2020.

Variables	Frequency	Percent (%)
<b>Year of diagnosis</b>		
2016	147	4.5
2017	597	18.5
2018	967	29.4
2019	945	28.8
2020	630	19.2
<b>Sex</b>		
Male	1787	54.4
Female	1479	45.0
Unknown	20	0.6
<b>Age</b>		
0-4	50	1.5
5-14	246	7.5
15-24	431	13.1
25-34	643	19.6
35-44	734	22.3
45-54	643	19.6
≥ 55	505	15.4
Unknown	34	1.0
<b>Residence</b>		
Urban	1503	45.7
Rural	1588	48.3
Unknown	195	6
<b>Reason of diagnosis</b>		
Presumptive TB	2669	81.2
Presumptive DR Tb	580	17.7
Unknown	37	1.1
<b>TB registration type</b>		
New	2898	88.2
Failure	5	0.2
Relapse	170	5.2
Defaulter	3	0.1
Unknown	210	6.4
<b>HIV status</b>		
Reactive	143	4.4
Non-reactive	417	12.7
Unknown	2726	83.0

### Prevalence, trend of mycobacterium tuberculosis and rifampicin resistance

The prevalence of all forms of TB detection was 27.4% (899/3286) in five years of the study. From total positive TB, rifampicin resistance identified among 137 (15.2%). Mycobacterium tuberculosis was reported in all age groups, but the infection rate was higher in the age groups 25-34 years, with a prevalence rate of 209 (23.2%) followed by 45-55 age group with a prevalence rate of 176 (19.6%). From the total confirmed all forms of Mycobacterium tuberculosis cases, 13.5% (121/899) were identified from presumptive TB and 1.8% (16/899) from presumptive drug resistance-TB. Of the total of confirmed positive cases, 14.6% (121/826) and 23.5% (16/68) were rifampicin resistance of presumptive tuberculosis and presumptive drug resistance tuberculosis patients respectively.

The number patients visited to take TB diagnosis increased from 2016 to 2018, whereas it was decreased from 2018 to 2020 as show **Figure 1**.



### Discussion

In this study, five-year retrospective data collected to determine the trend TB among clients visited to TB clinic of wolkite town health center. The overall detection rate of TB in study was 27.4%. This finding was comparable with study done in Eastern zone of Tigray, 24.3% [9] Debre Markos Hospital 23.2% [16], Gambella 20.0% [17] Gondar Referral Hospital (24.6%) [18], Afar (24.5%) [19], South Africa 26% [20], Nigeria 22.9% [21], Southern Sierra Leone 21.3% [22], and report by WHO in Africa 25% [23]. However, our study showed higher overall Mycobacterium tuberculosis prevalence than other studies conducted in Eastern Ethiopia 15.7% [24], Northwestern Tigray, Ethiopia 9.9% [25], Debre Berhan, Ethiopia 13% [26], Felege Hiwot Referral Hospital and Debre Tabor Hospitals 14.6% [27], Addis Ababa 15.11% [28], Nigeria 10.3% [29]. In contrary, our study revealed lower prevalence of mycobacterium tuberculosis compared to other studies conducted in Jigjiga, Ethiopia 65.5% [30], Kenya 32.2% [31], and Congo 79.1% [23]. This difference might be due difference in the method of diagnosis, duration of study period, community characteristics and geographical location, skill of the laboratory personnel to detect TB, study design and other factors that may affect case occurrences in different study areas. The rate of rifampicin resistance was 15.2% in this study among confirmed TB cases. This result was agreed with studies done in Debre Markos Referral Hospital 10.3% [32], Felege Hiwot Referral Hospital and Debre Tabor Hospital 9.3% [27], Addis Ababa 9.9% [28] and India 10.5% [33] and Nepal 10.2% [34]. However, this finding was higher than the study done in Eastern zone of Tigray, Ethiopia 9.1% [9], Eastern Ethiopia 4.1% [24], Northwestern Ethiopia 8.7% [25], Debre Berhan, Ethiopia 5.2% [26]. But higher rifampicin resistance rate was reported in this study than studies done in selected hospitals Addis Ababa 7.8% [28], Nigeria 2.9% [29]. The possible reason for variations could be related to differences in study designs and drug utilization manner of patients. Regarding the age group, 25-34 years were more affected by MTB 209 (23.2%) in the current study followed by 45-55 years 176(19.6%). This was consistent with previous

reports in different part of Ethiopia cited elsewhere above. This might be due to more exposure to the outer environment, high workload and wide range of mobility of young people to acquire the TB bacilli.

In the current study, the Mycobacterium tuberculosis detection rate was higher in presumptive TB patients (30.9%) compared to presumptive drug resistance TB patients (11.7%). Our study was consistent with other studies Gondar, Ethiopia 25.2% [18] and Zimbabwe 37.1% [35]. In opposite, this finding showed higher prevalence among Presumptive TB patients than studies conducted in Afar 20.9%(19) Debre Markos Referral Hospital 15.1% [36] and Gambella 19.6% [17]. However, it is much lower than studies conducted in Felege Hiwot Referral Hospital and Debre Tabor Hospital 54.8% [17], The discrepancies might be due to included TB cases, number of study participants.

In this study, sex, age, residence, reason for diagnosis, patient registration group, previous history of TB, HIV status of patients were found to be significantly associated with the disease caused by mycobacterium ( $p < 0.005$ ). In general, most of study participants were new cases as supported many researches referenced in this study. HIV-TB co-infection was identified among 28.8% (41/142) in this study showing for majority of study participants, the HIV status was unknown as shown in **Table 2**.

## Conclusion and Recommendation

In this study, the overall trends of Mycobacterium tuberculosis and rifampicin resistance were found to be significant and with variation each year. Rifampicin resistance is more common in presumptive drug resistance tuberculosis individuals. Therefore, maximizing early detection of drug-resistant and strengthening

**Table 2** the prevalence of mycobacterium tuberculosis Among Presumptive Clients in wolkite town, Ethiopia, 2020.

Variables	M. tuberculosis result by GeneXpert™		COR (95%CI)	p-value
	Detected	Not detected		
<b>Sex</b>				
Male	500	1287	1	P=0.375
Female	394	1085	1.071(0.921,1.244)	
not known	5	15		
<b>Age</b>				
0-4	13	37	.876 (.318,2.413)	p>0.05
5-14	67	179	.822 (.355, 1.905)	
15-24	143	288	.620 (.274,1.403)	
25-34	209	434	.639 (.284,1.435)	
35-44	170	564	1.021 (.454, 2.296)	
45-54	176	467	.816 (.363, 1.837)	
≥ 55	113	392	1.067 (.470, 2.423)	
Unknown	8	26	1	
<b>Residence</b>				
Urban	384	1119	1	P=0.003
Rural	443	1145	.825 (.725, .935)	
Unknown	72	123	x	
<b>Reason of diagnosis</b>				
Presumptive TB	826	1842	.867 (.762, .986)	P=0.03
Presumptive DR TB	68	513	2.696 (2.325, 3.793)	
Unknown	5	32	1	
<b>TB registration type</b>				
New	660	2238	1.453 (1.068, 1.977)	P=0.000
Failure	5	0	X	
Relapse	168	2	0.005 (.001, .21)	
Defaulter	3	0		
Unknown	63	147	1	
<b>Year of diagnosis</b>				
2016	38	109	2,658 (1.780, 3.969)	P<0.01
2017	106	491	4.292 (3.304, 5.576)	
2018	94	873	8.606 (6.609, 11.206)	
2019	358	587	1.519 (1.239, 1.864)	
2020	303	327	1	
<b>HIV status</b>				
Reactive	41	101		P<0.01
Non-reactive	169	248	1.402 (1.216, 1.610)	
Unknown	688	2038	1	

tuberculosis infection control activities are recommended to reduce the burden of this contagious and potentially deadly disease.

### Limitation of the study

As retrospective data was collected from the GeneXpert™ TB registration book, missing and incompleteness of data was faced.

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### Authors' Contributions

AH: Conceived the study, participated in the study design and data analysis, drafted and finalized the manuscript for publication. KH: Participated in the data collection, data processing, and data analysis. SS: Participated in the study design, data acquisition, and data analysis. All authors contributed to the writing of the paper. All authors read and approved the final manuscript.

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### Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### Ethics Approval and Consent to Participate

First ethical clearance was obtained from the Wolkite University ethical review board. Written informed consent was obtained from Health center and any information related to the participants was kept confidential and coded without mentioning their names.

### Consent for Publication

Not applicable.

### Competing Interests

The authors declare that they have no competing interests.

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