Journal of Bioprocessing & Biotechniques

Asfaw et al., J Bioprocess Biotech 2018, 8:5
DOI: 10.4172/2155-9821.1000339

Research Article Open Access

Patterns and Trends of Rifampicin-Resistance *Mycobacterium tuberculosis* and Associated Factors among Presumptive Tuberculosis Patients at Debre Berhan Referral Hospital

Tsegahun Asfaw[1*], Awgichew Terefe[2] and Melkamu Nigus[2]

[1]*Department of Medical Laboratory Science, Debre Berhan University, Debre Berhan, Ethiopia*

[2]*Department of Medicine, Debre Berhan University, Debre Berhan, Ethiopia*

[*]**Corresponding author:** Tsegahun Asfaw, Department of Medical Laboratory Science, Debre Berhan University, Debre Berhan, Ethiopia, Tel: +251 96 729 2745; E-mail: tsegahun.asfaw12@gmail.com

Received date: September 26, 2018; **Accepted date:** October 04, 2018; **Published date:** October 10, 2018

Abstract

In Ethiopia, evidence on rifampicin-resistant *Mycobacterium tuberculosis* is rare. Therefore, this study aims to assess pattern of Rifampicin-resistance *Mycobacterium tuberculosis* (MTB) and associated factors among presumptive tuberculosis patients. A retrospective cross-sectional study design was conducted among presumptive tuberculosis (TB) cases at Debre Berhan referral hospital. Data were collected from registration books using checklist. Data were entered to Epi-data and analyzed using SPSS version 21. Results were summarized using regression statistics and presented with frequency tables and figures. P-value less than or equal to 0.05 was taken as statistically significant. Of a total of 3689 (male=51%, female=49%) presumptive cases screened at Debre Berhan referral hospital Laboratory with gene-x-pert; 34.4% and 65.6% were from urban and rural respectively, with mean age of 33.8 year. 483 (13%) cases were found to be TB positive, of which 25 (5.2%) were with rifampicin resistance. Family member ≥ 3, contact history with TB suspect, previous treatment history and age group 16-30 years were found in 80%, 64%, 28% and 44% of rifampicin resistance cases, respectively. Sero-status of rifampicin resistance cases were statistically significant association (p=0.013, AOR=2.97, CI=1.059-17). The overall prevalence of *Mycobacterium tuberculosis* and Rifampicin resistance *Mycobacterium tuberculosis* was high. Most of the affected study subjects were also productive age group (16-30 years). Therefore, wide range of awareness creation is mandatory. The availability of gene-x-pert should be scaled up and avail at large for early diagnosis and treatment.

Keywords: Gene-x-pert; Rifampicin resistance; *Mycobacterium tuberculosis*; Risk factors; Ethiopia

Introduction

Tuberculosis is a chronic airborne infectious disease caused by the bacillus *Mycobacterium tuberculosis*; affect lungs, pulmonary TB, may also affect any organ or tissue outside of the lungs, extra pulmonary TB [1]. According to a World Health Organization (WHO) 2016 report, it remains a major public health problem, ranking above HIV/AIDS. It is one of the leading causes of morbidity and mortality among infectious diseases worldwide [2].

The emergence of drug-resistant tuberculosis is a critical threat to tuberculosis control and is a major public health concern in several countries. Multidrug-resistant TB (MDR-TB), defined as resistant to at least isoniazid and rifampicin, is emerging as a major clinical and public health challenge in areas of sub-Saharan Africa. Ethiopia is one of the high TB burdened countries in sub-Saharan Africa which ranks 7th among the 22 high TB burden countries in the world [3].

The prevention, diagnosis, and treatment of TB have become more complicated because of HIV-associated TB and multi-drug resistant (MDR) TB. Many people die of TB owing to delayed diagnosis, which makes unable to reduce transmission significantly, and thus the epidemic continues [4]. A global TB report estimated that there were about 230,000 (247 per 100,000 population) incident cases of TB in Ethiopia. In the same report, there were about 16,000 deaths (18 per 100,000) due to TB, excluding HIV-related deaths during the same period [5].

Worldwide incidence of MDR-TB is increasing, with almost half million estimated new cases in 2008. Ethiopia is one of the 27 high MDRTB countries, ranked 15th with more than 5,000 estimated MDR-TB patients each year [6]. Globally, the estimated prevalence of MDR-TB was 3.3% in newly diagnosed patients in the WHO 2015 report [7]. Based on the 2005 nationwide survey in Ethiopia, the prevalence of MDR-TB was 1.6% among new cases and 11.8% in the retreatment cases and rifampicin resistant was lower than 2% in new cases [8].

In Ethiopia, microscopy is widely used for the rapid diagnosis of TB, but it doesn't detect DR-MTB or sensitivity. As results of mycobacterial culture require about 2–8 weeks and not widely available in developing countries, including Ethiopia, create diagnostic delay that hinders disease control, enhances transmission, and increases health-care costs [9,10]. Therefore, Gene-X-pert is an automated real-time polymerase chain-reaction assay designed for the rapid and simultaneous detection of MTB and rifampicin resistance [11-13].

Methodology

Study area and period

A retrospective cross-sectional study was conducted among presumptive TB cases from January, 2014- January, 2018 at Debre Birhan referral hospital.

Sample size determination and sampling procedure

All TB positive and rifampicin resistant cases were included.

Inclusion criteria: Patients presumptive for TB (pulmonary or extra -pulmonary) and who had full documentation in the registration book during the study period were included.

Exclusion criteria: Patients who had incomplete data, e.g., age, sex Gene-X-pert results, were excluded.

Data collection and analysis

Data were collected retrospectively from registration books by using standard check-list. Data were entered to Epi-data and analyzed using SPSS version 21. P-value of <0.05 was considered as Statistical significance association.

Operational definitions

Relapse: are previously treated for TB, were declared cured or treatments completed at the end of their most recent treatment episode and are now diagnosed with a recurrent episode of TB.

Failure: are previously treated for TB and whose treatment failed at the end of their most recent treatment episode.

Contact: are defined as people from the same household sharing common habitation rooms and other known TB cases or chronic coughers.

Defaulter: DR-TB patient whose treatment was interrupted for two or more consecutive months for any non-medically approved reason.

MDRTB: a form of TB caused by bacteria that do not respond to, at least, isoniazid and rifampicin, the two most powerful, first-line (or standard) anti-TB drugs.

Primary drug resistance: Drug-resistant TB in a person with no history of TB treatment, implying they were infected with a resistant TB. This reflects person-to-person transmission of drug-resistant TB bacilli.

Acquired drug resistance: Drug resistant TB in a person with a history of TB treatment. This reflects drug resistance acquired during TB treatment but may also reflect infection or re-infection with resistant TB bacilli.

Rifampicin mono-resistant TB: TB caused by strains of M. tuberculosis that are resistant to only Rifampicin. Rifampicin resistance is a predictor of MDR TB because resistance to RIF, in most instances, co-exists with resistance to isoniazid.

Ethical clearance

Ethical approval was obtained from Debre Berhan University ethical review and research committee.

Results

Socio-demographic characteristics

In our study a total of 3689 {male=51%, female=49%} presumptive TB cases were screened by gene-x-pert, of these 483(13%) cases were found to be positive for TB. Among positive cases 34.4% were from urban and 65.6% were from rural; and majority were within the age group of 16-30 years and the mean age were 33.8 years with minimum and maximum age being 2 and 78 years respectively (Table 1).

Variables		Frequency	Percent	
Sex (n=483)	Male	271	56.1	
	Female	212	43.9	
Residency (483)	Urban	166	34.4	
	Rural	317	65.6	
Marital Status (n=483)	Single	212	43.9	
	Married	267	55.3	
	Widowed	4	0.8	
Age Group (n=483)	<15	24	5.0	Mean=33.8 Minimum=2 Maximum=78
	16-30	226	46.8	
	31-45	144	29.8	
	>=46	89	18.4	

Table 1: Socio-demographic characteristics of TB positive patients who screened for TB at Debre Berhan referral hospital with gene-x-pert from January 2015 to January 2018.

Patterns of TB positivity with /without RIF resistance

Of a total of 483 confirmed TB positive cases 25 (5.2%) cases were with rifampicin resistance. The prevalence of all confirmed TB cases screened with gene-x-pert is 13%. The prevalence of rifampicin resistance TB from all presumptive TB cases and confirmed TB cases is 0.68% and 5.2%, respectively (Table 2).

Variables	Screening Result					
	T		RR		Total	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
Year screened						
2014	2	50	2	50	4	0.8
2015	77	97.4	2	2.6	79	16.4
2016	254	93.7	17	6.3	271	56.1
2017	125	96.9	4	3.1	129	26.7
Total	458	94.8	25	5.2	483	100.0

Table 2: Patterns of MTB positive patients, who screened at DBRH laboratory with gene-x-pert from January, 2014 to January, 2018.

Variables		RIF-R cases		ODDs Ratio (95% CI)		P-value
		Yes	No	COR	AOR	
Family member (n=483)	Two	5	53	1.86 (0.56-6.12)		0.3
	Three	13	267	1.04 (0.37-2.46)		0.93
	> four	7	138	1		
Contact history (n=483)	Yes	16	206	2.17 (0.94-5.02)		0.069
	No	9	252	1	1	
Those had contact history (n=222)	Family member on anti-TB	1	3	8.2 (0.72-93.46)	9.38 (0.80-109)	0.09(0.074)
	Other TB pt.	9	77	2.87 (0.93-8.89)	2.54 (0.77-8.39)	0.067(0.126)
	With MDR pt.	1	3	8.2 (0.72-93.46)	5.5 (0.37-81)	0.09(0.214)
	Chronic cougher	5	123	1	1	
Age group (n=483)	<=15	1	23	0.60 (0.069-5.25)		0.646
	16-30	11	215	0.72 (0.25-1.97)		0.509
	31-45	7	137	0.70 (0.23-2.18)		0.545
	>=46	6	83	1		

Table 3: Binary and multivariate regression test between number of family member and contact history, with Rifampicin resistant TB patients who screened at DBRH laboratory with gene-x-pert from January 2014 to January 2018.

Figure 1 shows of a total of 25 RIF resistance TB cases majority of them (17) were documented in the year 2016, and the lowest (2) were in 2014 and 2015.

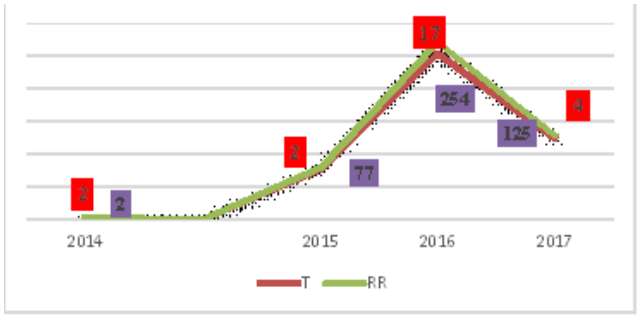

Figure 1: Patterns of confirmed TB cases and Rifampicin resistance TB among patients who screened for TB at DBRHL with gene-x-pert from January, 2014 to January, 2018.

Associated factors

Family member, contact history and age group with RIF resistant TB patient: Those associated factors listed in the table below were analyzed with binary logistic regression, then factors with p-value <0.25 were considered to be analyzed further by multivariate logistic regression to control the confounding effect of different variables while assessing the effect of each variable on the likely hood of RIF-RTB development. There was no significant association with Rifampicin resistance MTB cases and factors listed in Table 3.

Previous treatment history and sero-status with RIF resistant TB patient: A statistical signi icant association was found between sero-status and RIF-resistance MTB (p=0.013, AOR=5.8, CI=1.46-23) showing almost six fold more likelihood to develop RIF-resistance MTB in patients with sero-reactive than non-reactive (Table 4).

Variables		RR-Cases		ODDs Ratio (95% CI)		P-Value
		Yes	No	COR	AOR	
Treatment History (n=483)	Yes	7	65	2.35 (0.94-5.85)	0.82 (0.20-3.31)	0.066 (0.775)
	No	18	393	1	1	
Patient had Treatment History (n=72)	Relapse	4	39	0.92 ()0.16-5.51		0.93
	Defaulter	1	8	1.13 (0.89-14.28)		0.92
	Re-treatment	2	18	1		
Sero-status of Patient (n=483)	Reactive	9	24	11.34 (4.48-28.94)	5.8 (1.46-23)	0.00 (0.013)
	Non-Reactive	2	9	6.74 (1.33-34.16)	2.97 (1.059-17)	0.021 (0.999)
	Unknown	14	425	1		

Table 4: Binary and multivariate regression test between previous treatment history and sero-status with Rifampicin resistant TB patients who screened at DBRH laboratory with gene-x-pert from January 2014 to January 2018.

Discussion

The prevalence of MTB case is 13% which is low as compared to the previous report done in Debre Markos Referral hospital 23.2% [14] and University of Gondar Hospital 24.6% [15], but higher than the study done in Debre Berhan and Dessie 2.6% [16]. This discrepancy might be as a result of the difference in threshold for TB suspicion in the clinician, duration of study period, community and geographical location and might be due to study population difference and time.

The burden of DR-TB is increasing in an alarming pace with function of time particularly in the poorest countries. In this study the prevalence of Rifampicin resistant is 5.2% which is lower than the study done in West Armachiho and Metema district 5.6% [16], and Debre Markos Referral hospital, 10.3% [14], but higher than study done in Amhara national regional state [17]. This difference could be due the fact that this study was conducted at the site where TB patients less likely served for medical attention and presumably they have familiarized to visit relatively advanced health institutions.

In this study, the detection rate of *M. tuberculosis* was significantly higher in males than females. Likewise, reports from Debre Markos Referrel hospital [14], and Amhara national regional state [17] supports this finding. The reason for this might be due to social and health seeking behavior difference and higher exposure of males to outer environment, smoking and alcoholism.

The highest proportion of Gene-x-pert positive *M. tuberculosis* cases were seen in the age group of 16-30 years. This is consistent with previous reports in other part of Ethiopia [16,17]. This might be due to more exposure to the outer environment, high work load and wide range of mobility of young people to acquire the TB bacilli.

This study showed that there is a significant association between sero-status and RIF- resistance MTB (p=0.013, AOR=5.8, CI=1.46-23), which is consistent with study done in three major towns in the eastern part of Ethiopia (Dire Dawa, Haraar, and Jigjiga) [17], Amhara national regional state [18], Debre Markos referral Hospital [14] and University of Gondar Hospital [15]. It also showed that 6.25% of Rifampicin resistant cases had history of contact with MDR-TB suspect at some point in time, which is lower than the study done in Amhara national regional state (28.8%) [18]. This variation could be due to difference in study design, Sero-status and MDR-TB prevalence.

As it is outlined by the study, 28% of RIF-resistant TB cases had previous treatment for TB; relapse being 57%, re-treatment 28.5% and

defaulter 14.5%. This result is higher than the study conducted in University of Gondar Hospital (16.4%) [15] and DebreMarkos Referral Hospital (17.1%) [14]. It might be due to low sample size that leads to unnecessary percentage.

Conclusion and Recommendation

The overall prevalence of *Mycobacterium tuberculosis* was 13%. From these, 5.2% was account for Rifampicin resistance *Mycobacterium tuberculosis*. Most of the affected study subjects were productive age group (16-30 years). Most Rifampicin resistant TB patient had contact history with TB suspect and those had previous treatment history for TB suggested that wide range of awareness creation and improved monitoring of treatment is mandatory. The availability of gene-x-pert should be mounted for early diagnosis and treatment.

Conflicts of Interests

The authors declare that they have no conflict of interests.

Funding

This research is funded by Debre Berhan University.

Author's Contributions

TA, AT and MN: Collect and analyzed the data; TA: Analyze the data and wrote the manuscript. AT and MN: Reviewed the manuscript. All authors read and approved the final manuscript.

Acknowledgments

We would like to thank Debre Berhan University for giving this opportunity. We also thank laboratory staffs of Debre Berhan referral hospital for their help during data collection process.

References

1. Bhowmik D, Chiranjib A, Chandira RM, Jayakar B, Kumar KPS (2009) Recent trends of drug used treatment of tuberculosis. J Chem Pharm Res 1: 113-133.
2. WHO (2016) Global Tuberculosis Report-2016. Accessed on October 04, 2018.
3. WHO (2013) Global Tuberculosis Report-2013. Accessed on October 04, 2018.
4. Piatek AS, van Cleeff M, Alexander H, Coggin W, Rehr M, et al. (2013) GeneXpert for TB diagnosis: planned and purposeful implementation. Glob Health Sci Pract 1: 18-23.
5. WHO (2013) Definitions and reporting framework for tuberculosis-2013 revision, 2013.
6. WHO (2010) Multidrug and Extensively Drug-Resistant TB (M/XDR-TB): 2010 Global Report of Surveillance and Response. Accessed on October 04, 2018.
7. WHO (2015) Global Tuberculosis Report 2015. Accessed on October 04, 2018.
8. Federal Democratic Republic of Ethiopia Ministry of Health (2013) Guidelines on Programmatic Management of Drug-Resistant Tuberculosis in Ethiopia. 2nd edn. Addis Ababa.
9. Getahun H, Harrington M, O'Brien R, Nunn P (2007) Diagnosis of smear negative pulmonary tuberculosis in people with HIV infection or AIDS in resource-constrained settings: informing urgent policy changes. Lancet 369: 2042-2049.
10. WHO (2009) Pathways to Better Diagnostics for Tuberculosis: A blueprint for the development of TB Diagnostics.
11. Helb D, Jones M, Story E, Boehme C, Wallace E, et al. (2010) Rapid detection of Mycobacterium tuberculosis and rifampin resistance by use of on-demand, near-patient technology. J Clin Microbiol 48: 229-237.
12. Boehme CC, Nabeta P, Hillemann D, Nicol MP, Shenai S, et al. (2010) Rapid molecular detection of tuberculosis and rifampin resistance. N Engl J Med 363: 1005-1015.
13. Van Rie A, Page-Shipp L, Scott L, Sanne I, Stevens WS (2010) GeneXpert MTB/RIF for point of care diagnosis of TB in high-HIV burden, resource limited countries: hype or hope? Expert Rev Mol Diagn 10: 937-946.
14. Mulu W, Abera B, Yimer M, Hailu T, Ayele H, et al. (2017) 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 10: 8.
15. Jaleta KN, Gizachew M, Gelaw B, Tesfa H, Getaneh A, et al. (2017) Rifampicin-resistant Mycobacterium tuberculosis among tuberculosis-presumptive cases at University of Gondar Hospital, northwest Ethiopia. Infect Drug Resist 10: 185-192.
16. Mekonnen F, Tessema B, Moges F, Gelaw A, Eshetie S, et al. (2015) Multidrug resistant tuberculosis: Prevalence and risk factors in districts of metema and west armachiho, Northwest Ethiopia. BMC Infect Dis 15: 461.
17. Wondemagegn M, Daniel M, Mulat Y, Aschalew A, Bayeh A (2015) Risk factors for multidrug resistant tuberculosis patients in Amhara National Regional State. Afr Health Sci 15: 368-377.
18. Nigus DM, Lingerew WM, Beyene BA, Tamiru AA, Lemma MT, et al. (2014) Prevalence of Multi Drug Resistant Tuberculosis among Presumptive Multi Drug Resistant Tuberculosis Cases in Amhara National Regional State, Ethiopia. J Mycobac Dis 4: 152.