

Prevalence of Rifampicin Mono Resistant Mycobacterium Tuberculosis among Suspected Cases Attending at Yirgalem Hospital

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Abstract: *Introduction:* Tuberculosis (TB) is a chronic communicable disease caused by *Mycobacterium tuberculosis* (MTB). *M. tuberculosis* is a slow-growing bacterium, resistant to most conventional antimicrobial agents partly due to its impermeable cell wall. It may persist in a dormant or latent form, unsusceptible to agents targeting growing bacteria. The Gen Xpert MTB/RIF is an automated molecular test which detects DNA sequences specific for MTB and RIF resistance by polymerase chain reaction with fully integrated sample processing in patients suspected of drug sensitive or multidrug resistant pulmonary tuberculosis. *Objective:* to determine Rifampicin Mono-Resistance Mycobacterium tuberculosis among patient attending at Yirgalem Hospital from August-December, 2014. *Method:* A cross sectional study was conducted on Rifampicin Mono-Resistance in Mycobacterium tuberculosis among patient attending at Yirgalem Hospital from August-December, 2014, Yirgalem, Ethiopia. *Result:* A total of 236 participants were included under this study. Among these, males (57.6%) are slightly dominating female. Concerning to treatment history, 177 (75.0%) are new and the rest 59 (25.0%) retreated. Fifty eight (24.6%) of the total subjects were suspected for MDR tuberculosis. Twenty two (9.3%) of the subjects were smear positive. The highest positive finding of rifampicin susceptible Mycobacterium tuberculosis bacilli observed within age group of 16-30. The overall prevalence of pulmonary tuberculosis was 16.5%. From this prevalence, 3.4% was shared by Rifampicin mono-resistant Tuberculosis. *Conclusion:* Based on our study finding, The overall prevalence of pulmonary tuberculosis was 16.5%. From these, 3.4% was account for Rifampicin Mono-Resistance Mycobacterium tuberculosis among study subject. Most of the affected study subjects were productive age group. Therefore, we recommend that there should be enhanced efforts in detection of MDR tuberculosis in study area to control dissemination of the disease among the community.

Keywords: Tuberculosis, Rifampicin, Yirgalem Hospital

1. Introduction

Tuberculosis (TB) is a chronic communicable disease caused by *Mycobacterium tuberculosis* (MTB). *M. tuberculosis* is a slow-growing bacterium, resistant to most conventional antimicrobial agents partly due to its impermeable cell wall. It may persist in a dormant or latent form, unsusceptible to agents targeting growing bacteria [1, 2].

The bacterium infects almost one-third of population globally and during the past decade there has been a resurgence of tuberculosis [3]. The burden of TB epidemic in developing countries is very high. An estimation of 95% of TB cases and 98% of TB deaths occurs in the third world

countries, where peoples are especially susceptible to TB because of poor living conditions and limited access to treatment [4].

Based on the World Health Organization (WHO) Annual Global TB Report (2009), Ethiopia ranked seventh in the world for TB burden, with an estimated annual TB incidence (all forms) of 378 new cases per 100,000 persons and 163 new smear positive cases per 100,000 persons per year [5]. The Ethiopian Federal Ministry of Health (FMOH) hospital statistics data has shown that tuberculosis is the leading cause of morbidity, the third cause of hospital admission (after deliveries and malaria), and the second cause of death in

Ethiopia, after malaria [6]. Based on WHO report in Ethiopia, the incidence of TB of all forms and smear positive TB stand at 341 and 152 per 100,000 population, respectively [7]. The prevalence and mortality of tuberculosis of all forms is estimated to be 546 and 73 per 100,000 population respectively [3].

In the Southern Ethiopia Regional State (SNNPRS), TB is among the leading causes for sickness and death (8). As in many other resource-constrained settings, treatment outcomes for tuberculosis have not been satisfactory, mainly due to poor treatment compliance and low coverage of short course chemotherapy (SCC) (9). Delays in the diagnosis and treatment initiation, the devastating HIV/AIDS epidemic and the potential threat of anti-tuberculosis drug resistance represent serious threats to the TB control effort in the region [10].

Rifampicin resistant heralds higher rates of treatment failure and death for the patient and a poor outcome if the isolate is also resistant to isoniazid. Efficacy of rifampicin chemotherapy can be markedly reduced when infections are caused by M. tuberculosis strains that are rifampin resistant [11].

The GenXpert MTB/RIF is an automated molecular test which detects DNA sequences specific for MTB and RIF resistance by polymerase chain reaction with fully integrated sample processing in patients suspected of drug sensitive or multidrug resistant pulmonary tuberculosis [11].

Therefore, to our knowledge there is no previous study on prevalence of Rifampicin mono resistant Mycobacterium tuberculosis among suspected cases in the study area so that the objective of this study is to determine Rifampicin mono resistant Mycobacterium tuberculosis among patient attending Yirgalem Hospital.

2. Methodology

2.1. Study Setting

Yirgalem Hospital is a tertiary health care hospital serving the population of south nations and nationalities (SNNPR). There are about 15 million populations are getting service by the hospital from South Nation and Nationalities Region (SNNPR) and the neighbor Oromia region. The hospital located 317 km south from capital Addis Ababa and 45 km from Hawassa town. In the hospital a Directly Observed Therapy; Short-Course (DOTS) clinic is operating under the National Tuberculosis and Leprosy Control Program (NTLCP) of Ethiopia, under which the diagnosis of pulmonary TB is followed by examination of three sputum smears (spot morning spot) by Zihel-Nielsen staining method for acid fast bacilli (AFB). Chest radiographs and pathological investigations are also used to support the diagnosis. Patients diagnosed with tuberculosis are referred to the DOTS clinic where they are registered and treated according to the national TLCP guideline (Ministry of Health of Ethiopia (MOH) [11]. In addition hospital also equipped with Gene Xpert that used to

determine Rifampicin mono resistant Mycobacterium tuberculosis.

2.2. Study Design

A cross sectional study was conducted on Rifampicin Mono-Resistance in Mycobacterium tuberculosis from August-December, 2014 at Yirgalem Hospital.

2.3. Data Collection

Data collection was carried out using structured questionnaire to ask different variables and Laboratory examination on sputum specimen collected for direct microscopy to identify Acid fast bacilli (AFB) and determination of the Rifampicin resistant Mycobacterium tuberculosis from study subjects.

2.4. Sputum Collection and Processing of Sputum Samples for Microscopic Examination

Three sputum specimens were collected from every consenting TB suspect using coded and sterile plastic containers by laboratory personnel according to national TLCP guideline (Ministry of Health of Ethiopia (MOH) [6]. Portion of the collected specimen was used for direct smear microscopy immediately and the remaining portion was stored at 4 °C in refrigerator until further molecular analysis done. Purulent portion of sputum sample was taken and smear was made on one end frosted slide. After air dry, the smear was stained using standard procedure and examined under 100X objective of bright field Microscope. The stored portions of three sputum samples of each study subject were pooled in one container for GenXpert analysis.

2.5. Processing of Sputum Samples for Gene Xpert

1 ml of pooled sputum sample was mixed with 2 ml of buffer (Cepheid AB Rontgenven 5 SE-171 54, Solna) to liquefy the sputum and incubated at room temperature for 10 minutes. Thereafter, 2 ml of the diluted sample was transferred to the cartridge (Cepheid AB Rontgenven 5 SE-171 54, Solna) for ultrasonic lysis of mycobacteria to release target DNA. The cartridge was loaded into the Gene Xpert machine (Cepheid) to proceed with the rest protocol. After 2 hours, the comprehensive test result was read on computer screen [11].

2.6. Ethical Clearance

Institutional ethical clearance was obtained from the Institutional Review Committee of Hawassa University Medicine and Health Sciences College. Moreover official permission was obtained from Yirgalem Hospital. In addition, the consent was obtained voluntary study subject. All the information obtained from study subject was kept confidential.

2.7. Statistical Analysis

Data will be cleaned, edited, coded after it was entered into

Epi Info version 3.5.1 and exported to SPSS version 16. Using SPSS version 16, descriptive statistics will be used to determine indices. For categorical data, we used proportions with 95% confidence intervals, Odds ratio and Chi-square test to compare different groups. P values of less than 0.05 were considered statistically significant.

3. Result

A total of 236 participants were included under this study. Among these, males (57.6%) are slightly dominating female. The mean age of the study subjects was 36.9 ± 13.6 with the minimum and maximum ages were 2 and 80 years old respectively. Regarding to HIV status, eleven (4.7%) of the study subjects were HIV positive and the remaining 146 (61.9%) and 79 (33.5%) are negative and unknown status respectively. Concerning to treatment history, 177 (75.0%) are new and the rest 59 (25.0%) retreated. Fifty eight (24.6%) of the total subjects were suspected for MDR tuberculosis. Twenty two (9.3%) of the subjects were smear positive and thirty nine (16.5%) Mtb positive under Xpert MTB/RIF test. Among positive sample, eight (3.4%) were contained Rifampicin resistant.

The overall prevalence of pulmonary tuberculosis was 16.5%. The disease was slightly predominating among male study subjects. From this prevalence, 3.4% was shared by Rifampicin mono-resistant Tuberculosis. Based on finding depicted on Table 1, the overall prevalence of Rifampicin Mono-Resistance Mycobacterium tuberculosis among study subject was 3.4%. Based on Xpert MTB/RIF assay, highest positive finding of rifampicin susceptible Mycobacterium tuberculosis bacilli observed within age group of 16-30. Similarly, rifampicin resistant Mycobacterium tuberculosis detected among productive age group. Based on Fisher's exact test, the positive test result strongly associated with age of the study subjects ($p < 0.001$). Furthermore the microscopic result strongly associated with Xpert MTB/RIF test result ($p < 0.001$). On the other hand the sex of the study subjects has no association with the positive finding ($p > 0.05$).

Table 1. The distribution Rifampicin mono resistant Mycobacterium tuberculosis of the finding among age group of study subjects from August-December, 2014 at Yirgalem Hospital.

Age group	result of MTB/rif			Total	P Value*
	MTB+/Rif-	MTB+/Rif+	MTB-/Rif-		
1-15	4 (44.4%)	1 (11.1%)	4 (44.4%)	9 (100.0%)	0.001
16-30	18 (22.8%)	3 (3.8%)	58 (73.4%)	79 (100.0%)	
31-45	2 (2.2%)	4 (4.3%)	86 (93.5%)	92 (100.0%)	
46-60	7 (14.9%)	0 (0.0%)	40 (85.1%)	47 (100.0%)	
61+	0 (0.0%)	0 (0.0%)	9 (100.0%)	9 (100.0%)	
Total	31 (13.1%)	8 (3.4%)	197 (83.5%)	236 (100.0%)	

*Based on Fisher's exact test

Table 2. The distribution Rifampicin mono resistant Mycobacterium tuberculosis of the finding among HIV status of study subjects from August-December, 2014 at Yirgalem Hospital.

HIV status	result of MTB/rif result			Total
	MTB+/Rif-	MTB+/Rif+	MTB-/Rif-	
Positive	2 (0.8%)	1 (0.4%)	8 (3.4%)	11 (4.7%)
Negative	16 (6.8%)	2 (0.8%)	128 (54.2%)	146 (61.9%)
Unknown	13 (5.5%)	5 (2.1%)	61 (25.8%)	79 (33.5%)
Total	31 (13.1%)	8 (3.4%)	197 (83.5%)	236 (100%)

4. Discussion

Multidrug-resistant (MDR) TB has become a major public health problem and presents new barriers to the control of TB. It is due to human error as the result of poor supply management and quality of anti-TB drugs and inadequate or improper treatment, which is further exacerbated by human immunodeficiency virus (HIV) [12]. Based on WHO recommendation, RMPMR was considered as surrogate marker for MDR TB. Therefore, we have determined the prevalence of Rifampicin mono resistant Mycobacterium tuberculosis among suspected study subject and the finding associated with age and sex.

The overall prevalence of Rifampicin Mono-Resistance Mycobacterium tuberculosis among study subject was 3.4%. The finding of the current study higher than study conducted in northern and Eastern part of Ethiopia with prevalence of 2.5 % and 1.7% [13,14]. This may possibly due to unorganized patient diagnosis, treatment, and follow-up and poor patient adherence that may contribute to the higher prevalence of REF monoresistance strains in the study area. On the other hand our finding is lower than similar study conducted in Nigeria (18.8%) and South Africa 4.9%) than our study [15,16]. This may reflect the variations in sample size, studied population, access to health care facilities, geography and effectiveness of TB control programs.

Based on the study finding, the prevalence of pulmonary Tuberculosis in study area is 16.5%. The study conducted on prevalence of pulmonary tuberculosis in southern Ethiopia showed that higher (19.4%) than current study [17]. On the other study conducted in south western part of Ethiopia shown to be lower than our finding [18]. The probable reason for this variation could be time of study, difference in study population, method of study and difference in study setting. According to our study the disease was slightly predominating among male study subjects. This is comparable with study conducted in northern Ethiopia [19].

Based on current study result pulmonary tuberculosis was more prevalent among productive age group of the study participants (11.4%). This is in agreement with study conducted in Agaro teaching health center in south western Ethiopia [18].

5. Conclusion

Based on our study finding, The overall prevalence of pulmonary tuberculosis was 16.5%. From these, 3.4% was account for Rifampicin Mono-Resistance Mycobacterium tuberculosis among study subject. Most of the affected study subjects were productive age group. Therefore, we recommend that there should be enhanced efforts in detection of MDR tuberculosis in study area to control dissemination of the disease among the community.

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Authors' Contributions

Mesfin Worku conceived and designed the study, performed analysis, Interpretation of data, and drafts the manuscript. Teshome Befikadu performed Laboratory Diagnosis and assisted with the design, performed analysis, interpretation of data and the critical review of the manuscript. Both authors read and approved the final manuscript. Both authors participated in critical appraisal and revision of the manuscript.

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