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Original Research Article

A Retrospective Study on Prevalence and Factors Associated with Rifampicin Resistance Tuberculosis Amongst Tuberculosis Patients of A Tertiary Care Hospital

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Abstract

Background: India accounts for one fourth of the global burden of MDR-TB and about 90% of Rifampicin-resistant tuberculosis (RR-TB) cases are multi drug-resistant. Early detection and prevention of transmission of Drug resistant TB (DR-TB) are the key to successful control of TB. The present study is aimed to estimate the prevalence of rifampicin resistance and to assess the factors associated with rifampicin resistance.

Materials and Methods: A Retrospective record-based study was conducted in department of Pulmonary medicine at a tertiary care hospital. 260 cases registered in RNTCP during the period of May 2018 to April 2021 confirmed by CBNAAT were included in the study. Data pertaining to demographic details, microbiological tests and co-morbidities were analyzed. Prevalence of rifampicin resistance was estimated and the factors associated with rifampicin resistance were assessed using Odds ratio.

Results: Among 327 RNTCP registered cases, only 260 cases had undergone confirmation by CBNAAT and were included in the present study. Prevalence of Rifampicin resistance was 4%. The proportion of Rifampicin resistance was higher in male patients (60%). Majority of the RR-TB cases were found to be in age group 20-40 years. Out of 10 rifampicin resistant cases, 6 (60%) belonged to new cases of TB, 8 (80%) were diagnosed to be having Pulmonary TB. Cases with reactive HIV status and Diabetes mellitus were significantly associated with the development of RR-TB (p=0.005).

Conclusion: Even though the prevalence of rifampicin resistance is low, it is imperative to detect DR-TB at the earliest especially in the patients with co morbidities like Diabetes and HIV to prevent further propagation of DR-TB among community.

Keywords: Rifampicin resistance, CBNAAT, Tuberculosis.

Introduction

Drug-resistant tuberculosis (DR-TB) poses a foremost risk to manage tuberculosis (TB) worldwide. In India, as per the WHO report 2019, the projected proportion of TB cases with multi-drug resistant and rifampicin resistance TB (MDR/RR-TB) were 2.8% in new cases and 14% in previously treated cases. However, the percentage of bacteriologically confirmed Pulmonary TB cases tested for rifampicin resistance were 46% in new cases and 91% in previously treated cases. Of these, MDR/RR-TB cases that tested resistance to second-line drugs (SLDs) were 38,236 [1].

Though recent improvements in notification rates of TB and MDR-TB have seen witnessed, to achieve the global target set under the End TB strategy, there is a need to strengthen case detection of TB and DR-TB. Factors such as treatment failure, poor compliance to treatment, inadequate chemotherapy, pulmonary cavity TB, HIV infection, and diabetes are largely accounted for the development of drug resistance in TB [2, 3, 4]. However, the utmost forecaster for the presence of MDR-TB is a previous history of treatment of TB [3].

Typically, in India, 'presumptive TB symptomatic', are offered microbiological testing for TB, most frequently being smear microscopy: an affordable, feasible, that nonetheless can fail to spot up to half of TB cases [5].

Detection of drug resistance offers added challenges, principally those with a history of TB treatment considering the limited resource feasibility that is presently accessible only to specific risk groups. With these limitations, there has been considerable ambiguity around the predictors of resistance in the TB symptomatic population.

In the present proposed study, we aimed to address the rifampicin resistance among the presumptive TB symptomatic who were offered with highly specific, rapid molecular testing and factors associated with it.

Methodology:

Study Design: This study was a retrospective, observational in nature conducted in Department of Pulmonary Medicine in collaboration with Department of Pharmacology in a tertiary care hospital. After approval from the Institutional Ethics Committee (No: ESICMC/GLB/IEC/38/2022); all the rifampicin resistance patients registered in case records at (Revised National Tuberculosis Control Programme) RNTCP unit during May 2018 to April 2021 were considered in our study and inadequate case records were excluded from the study.

Method of recruitment: After fulfilling the inclusion criteria, the data pertaining to preliminary details, socio-demographic indicators, category of patient, microbiological profile and investigation results namely HIV, Chest X-Ray, FNAC etc were obtained from the records of the patients registered under RNTCP. Rifampicin resistance was detected by the CB-NAAT which is a Cartridge based nucleic acid amplification test; an automated, semi-quantitative real time Polymerase Chain Reaction assay designed for the rapid and simultaneous detection of mycobacterium tuberculosis and rifampicin resistance.

Statistical Analysis: Data collected were analyzed using Microsoft Excel software and interpreted by applying descriptive analysis and Odd's ratio was conducted to determine the factors associated with rifampicin resistance. A *P* value less than 0.05 were considered statistically significant.

Results

A total of 327 MTB cases were registered in the RNTCP case records during the study period. Among 327 registered cases, only 260 cases had undergone confirmation by CBNAAT and were included in the present study. The mean age of the patients was 40 ± 17.65. Majority of the patients belonged to age group of 21-40 years attributing to 44 % (n = 114). Male sexes were predominant 171 (65%) and 182 (70%) cases resided in the rural area as shown in Table.1.

Table 1: Demographic details of CBNAAT confirmed cases of MTB (n = 260)

Variable	Number	Percentage
Age in years		
<20	35	13
21-40	114	44
41-60	78	30
61-85	33	13
Gender		
Male	171	65
Female	89	34
Residence		
Rural	182	70
Urban	78	30

Table 2 depicts the clinical characteristics of the patients. Out of 260 CBNAAT confirmed cases, 206 (79%) belonged to new cases of TB, 215 (83%) were diagnosed to be having Pulmonary TB and among the key population; 94 (36%) cases were smokers and 69 (27%) were contact TB cases. Of the 260 cases; only 10 (4%) cases were found to be Rifampicin resistant. Majority of the RR-TB were found to be in age group 20-40 years attributing to 50% (n = 5); affecting mostly rural population [80%; n = 8] as described in Table 3.

Table 2: Clinical characteristics of CBNAAT confirmed cases of MTB (n = 260)

Variables	Number	Percentage
Type of patients		
New	206	79
Recurrent	40	15
Others previously treated.	8	3
Treatment after loss to follow up (TALF)	4	1.5
Treatment after failure (TAF)	2	0.8
Site		
Pulmonary	215	83
Extrapulmonary	45	17
Key population		
Tobacco	94	36
Contact TB	69	27
Others	97	37

Table 3: Frequency distribution of CBNAAT confirmed Rifampicin Resistant cases

Variables	RR-TB (N=10)	Percentage
Age in years		
20-40	5	50
41-60	4	40
>60	1	10
Gender		
Male	6	60
Female	4	40
Residence		
Rural	8	80
Urban	2	20
Key population		
Contact TB	5	50
Smokers	5	50
Type of patients		
New	6	60
Recurrent	4	40
Site		
Pulmonary	8	80
Extra pulmonary	2	20
HIV status		
Reactive	2	20
Non-reactive	8	80
DM status		
Diabetes	3	30
Non diabetes	7	70

RR-TB: Rifampicin resistant tuberculosis; HIV- Human Immuno Virus, DM - Diabetes mellitus

Table 4 represents the various factors assessed to be associated with RR-TB. Cases with reactive HIV status and Diabetes mellitus were significantly associated with the development of RR-TB (p=0.005).

Table 4. Factors associated with Rifampicin resistant TB

Variables	RR-TB (N=10)	RS-TB (n=250)	Odds ratio	p value
Gender				
Male	6	165	0.77 (0.2123-2.8126)	0.7
Female	4	85		
Residence				
Rural	8	174	1.74 (0.3625-8.4212)	0.48
Urban	2	76		
Key population				
Smokers	5	89	0.71 (0.1998-2.5878)	0.61
Contact TB	5	64		
Type of patients				
New	6	200	0.375 (0.1019-1.3795)	0.14
Previously treated	4	50		

Site				
Pulmonary	8	207	0.83 (0.1705-4.0500)	0.81
Extrapulmonary	2	43		
HIV status				
Reactive	2	5	12.25 (2.0562-72.97)	0.005*
Non-reactive	8	245		
DM status				
Diabetes	3	13	7.813 (1.808-33.75)	0.005*
Non diabetes	7	237		

* Denotes statistically significant p value <0.05, RR-TB: Rifampicin Resistant Tuberculosis, RS-TB: Rifampicin Sensitive Tuberculosis, HIV- Human Immuno Virus, DM – Diabetes mellitus

Discussion

According to the WHO, 27% of the global TB cases are from India. Besides, India also accounts for 27% of the worldwide burden of rifampicin-resistant TB [6]. DR- TB is one of the obstacles for effective management of TB. The present study has 4% prevalence of rifampicin resistance which corresponds to the study conducted by Dutt et al and Shankar S et al among the MTB detected patients [7, 8]. Other studies have reported relatively higher prevalence of 28.2% and 33.7% by Malhotra et al from Jaipur and Jain et al from Delhi respectively [9, 10].

The above disparity observed in the prevalence could be due to different patient groups, socioeconomic class, sampling methods, the period of sampling and regional variations in tuberculosis prevalence.

However, a study carried out in South India showed gradual decline in MDR-TB from 5.06% in 2015 to 1.34% in 2018, pointing to the effectiveness of the RNTCP in the state [11].

The proportion of rifampicin resistance was higher in males (60%) which is found to be consistent with findings of studies conducted by Dutt et al and Shankar S et al which also reported 79% and 72% respectively [7, 8]. The reason for male preponderance could be attributed to more frequent travels and more social contacts among men compared to women, difference in health seeking behaviour and greater exposure of male to smoking and alcoholism. And also, as per WHO report 2021, adult males contributed to the highest burden of TB which accounted for 56% of all TB cases in 2019 [12].

Majority of the patients in this study were in age group of 20-40 years with the mean age of 40 ± 17.65 which is comparable to study done by Gautam PB et al and Sharma et al [13, 14]. The high number of DR-TB among this particular age group shows the greater chances of contracting varying diseases and propagating resistant TB among the community as they are more active in life and constantly travelling compared to older age with sedentary lifestyle. Further, rifampicin resistance was found to be more common among the patients with pulmonary TB than extra pulmonary TB which corraborated with results from the study by Gautam PB et al [13]. This might be due to inadequate capacity of people involved in the collection of extra-pulmonary specimens, the methods and volume/size of the sample required, non-availability of mechanisms for early transportation of these samples and non-availability of concentration methods or testing capacity for such samples at all the Xpert laboratories [8], which in fact is supported by one of the previous study where MDR-TB patients with extra pulmonary TB had 50% higher risk of not getting tested

when compared to patient with pulmonary TB [8, 15]. In the present study the number of rifampicin resistant cases were more in new patients compared to previously treated category, which is in contrary to the findings reported by Gautam PB et al, Adhikary et al Ahmed et al [13, 16, 17]; where the prevalence of rifampicin resistance TB were high in previously treated patients when compared to new cases. The resistance in new cases may be indicative of the transmission of resistant strains of the bacilli, while resistance in previously treated cases may be an indicator of poor compliance, lack of treatment supervision, and ineffective TB Control Programme [18]. It was observed in the present study that the people residing in rural area had high risk of developing rifampicin resistance than those in urban area which could be explained by the fact that poor healthcare facility in the rural areas, delay in the diagnosis and treatment could have increased the chances of community transmission of drug resistant TB.

In the present study the number of contact TB patients with rifampicin resistance is about 50% which is slightly high but not significantly associated with rifampicin resistance. A meta-analysis published by Shah NS et al [19] showed that 47% of the DR-TB patients' were household contacts [19]. Therefore, implementing the Tuberculosis preventive therapy would be essential to reduce the DR- TB among contact TB cases [20].

In the present study, out of total 10 cases of rifampicin resistance, 2 patients were coinfected with HIV infection and 3 patients were diabetic and these factors were significantly associated with rifampicin resistance which corresponds to the study conducted by Gaude et al and Shah AM et al respectively [21, 22].

In patients with HIV, there is increased chance to acquire TB because of reduced treatment adherence due to high pill burden received due to co-administration of Antiretroviral therapy with Antitubercular agents. Also, the drug-drug interactions and adverse effects increases the chances of failing treatment and hence developing DR-TB.

One of the limitations of the present study is smaller sample size and hence findings cannot be generalized to the community as a whole. Low reporting of the cases due to restrictions during COVID-19 pandemic might be the reason for smaller sample size. Other factors associated with RR-TB like socioeconomic status of the patients, nutritional status and alcohol consumption could not be verified due to nature of study design. However, the strength of the present study is that we were able to highlight some of the some of the important risk factors for development of RR-TB in this region.

Conclusions

The low prevalence of RR-TB doesn't rule out the risk of propagating DR-TB among the community. Efforts should be made to detect DR-TB at the earliest, which needs strengthening of the diagnostic capacity across the country and increase availability of Drug sensitivity testing especially among HIV co-infected individuals and those residing in rural areas. The other factors also should be looked upon like compliance of the patients and creating awareness among the community regarding the threats of RR-TB.

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