

Tuberculosis and HIV coinfection and rifampicin-resistant tuberculosis among patients living with HIV in Northern part of West Bengal, India



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ABSTRACT

Background: India is one of the top most country among the high tuberculosis (TB) burden countries and ranks the third highest human immunodeficiency virus (HIV) burden country in the world contributing to 23% of the total global load. *Mycobacterium tuberculosis* (MTB) and HIV are known to act synergistically and result in higher mortality rates. TB-HIV coinfection and emergence of drug resistant forms of MTB can impact positively on treatment outcomes. **Aims and Objectives:** The aim of this study was to determine of the prevalence of TB-HIV coinfection among MTB and to determine the prevalence of rifampicin (RIF) resistant TB among HIV seropositive patients. **Materials and Methods:** It was a retrospective and observational study carried out in the Department of Microbiology, Malda Medical College, Malda, West Bengal. Records of all patients that tested using CBNAAT during March 2016–December 2019 in the CBNAAT laboratory of Malda Medical College were assessed. Data generated during this period were collected and analyzed. The statistical analysis was done in tabulation form and different charts and tables were used for displaying data. **Results:** A total of 6503 samples were tested in CBNAAT laboratory during March 2016–December 2019. Out of 6503, 3098 samples were positive for CBNAAT (MTB detected). Of 3098 MTB, 8.91% (276/3098) were RIF resistant. Among 3098 MTB, 91.22% (2826/3098) were pulmonary TB (PTB) and 8.78% (272/3098) were extra PTB. Out of 6503 total samples, 664 were reported patients living with HIV. The prevalence of TB-HIV coinfection was 3.91% (121/3098) among MTB positive cases. Of all TB-HIV coinfecting cases, most of the patients (67.77%) were in the age group of 20–39 years and males (77.69%) contributed to more than females. Of 121 TB-HIV coinfecting, 88.43% (107/121) were sensitive to RIF and 11.57% (14/121) were resistant to RIF. **Conclusion:** The present study reported that the prevalence of TB-HIV coinfection was 3.91% and the prevalence of RIF resistant TB in HIV seropositive patients was higher than HIV seronegative patients. Thus, all TB patients should be screened for HIV and all HIV-positive individuals should be screened for TB along with drug resistance for better management.

Key words: Tuberculosis; HIV; Co-infection; Rifampicin

INTRODUCTION

Tuberculosis (TB), one of the most ancient diseases of mankind, is one of the ten major causes of mortality world-wide.¹ TB is caused by a group of closely related

bacterial species termed *Mycobacterium tuberculosis* complex. Today, the principal cause of human TB is MTB. Other members of the MTB complex that can cause TB include *Mycobacterium bovis*, *Mycobacterium microti*, and *Mycobacterium africanum*.²

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As evidenced by several research reports globally, susceptibility to TB increases manifold with concurrent human immunodeficiency virus (HIV) infection. HIV increases the probability of recently acquired TB infection to progress to the status of active disease.³ In the individual patient, HIV infection weakens the immune system and increases the susceptibility to TB. HIV increases the likelihood of reactivation, re-infection and progression of latent TB infection to active disease.⁴ Active TB facilitates the transcription of HIV genes resulting in increased diversity and replication of HIV.⁵

India bears the burden of 2.5 million people infected with HIV. Of these, 40% suffer coinfection with TB. There is a wide variation in HIV seropositivity among TB patients in India, ranging from 9.4% in New Delhi and 30% in Mumbai.³ The emergence of drug resistance and development of multidrug resistant TB (MDR TB) has become a new but significant obstacle for TB control.⁶ (MDR and extensively drug resistant TB are a threat to the TB control programs in developing countries, and the situation is worsened by the HIV pandemic.⁷

The rifampicin (RIF) resistance is a good predictor of MDR TB.⁸ Numerous molecular epidemiological studies have revealed that about 90% of RIF-resistant MTB isolates are also resistant to INH; therefore, RIF resistance can serve as a reliable marker for MDR-TB.⁹ TB/HIV coinfection is one of the main driver of poor outcome for both diseases. Improving case detection of TB/HIV coinfection has the potential to lead to early treatment of both conditions and can impact positively on treatment outcomes.¹⁰

Therefore, the purpose of this study is to determine the prevalence of HIV among TB patients and to determine the frequency of RIF-resistant TB in HIV-positive patients.

Aims and objectives

The objectives of the study are as follows:

1. To determine of the prevalence of TB-HIV coinfection
2. To determine the prevalence of RIF resistant TB among HIV seropositive patients.

MATERIALS AND METHODS

It was a retrospective and observational study. The study was carried out in the Department of Microbiology, Malda Medical College, Malda, West Bengal, from March 2016 to December 2019. Data were collected from CBNAAT laboratory of Malda Medical College, Malda.

Ethical issue

The study was approved by the Institutional Ethics Committee.

In this study, records of all patients that tested using CBNAAT during March 2016–December 2019 in the CBNAAT laboratory of Malda Medical College were assessed. We analyzed the records of patients diagnosed with pulmonary and extrapulmonary TB, total number of samples tested using CBNAAT, HIV status of all patients, and RIF resistance.

The statistical analysis was done in tabulation form and different charts and tables were used for displaying data.

Inclusion criteria

All the patients of suspected pulmonary or extrapulmonary TB referred from Revised National TB Control Program (RNTCP) center and also from private practitioners, from March 2016 to December 2019, subjected to cartridge based nucleic acid amplification testing (CB-NAAT) were included in this study. Patients were included in the study if their records appeared to be complete.

Exclusion criteria

Patients having incomplete history, diagnosis, treatment records, or MTB not detected or detected but RIF resistance is indeterminate were excluded from the study.

Trained laboratory technicians from RNTCP center and CBNAAT laboratory collected sputum from suspected cases of pulmonary TB (PTB) and other extrapulmonary samples from suspected cases of extra-PTB (EPTB) using pretested questionnaires. All the samples were investigated in CBNAAT laboratory for detection of MTB as well as resistance to the first-line anti-TB drug, RIF using the Gene Xpert MTB/RIF assay system. 2 ml of inactivated specimen was transferred to the Xpert test cartridge and tested as per the manufacturer's instructions.

RESULTS

A total of 6503 samples were tested in CBNAAT laboratory during the study period, from March 2016 to December 2019. Both pulmonary (sputum) and extrapulmonary (pleural fluid, cerebrospinal fluid, synovial fluid, lymph node aspirate, and ascitic fluid) samples were received from suspected TB patients. Out of 6503, 3339 samples were negative and 3098 samples were positive for CBNAAT (MTB detected) and 66 were of other results (Other results: MTB detected RIF indeterminate, Errors, Invalid tests, no result).

The data in different years (total number of test performed, total number of MTB detected, MTB detected and RIF sensitive, MTB detected and RIF resistant, total number of EPTB out of total number of MTB detected, HIV-positive and RIF sensitive out of total number of MTB detected

and RIF sensitive, and HIV-positive and RIF resistant out of total number of MTB detected and RIF resistant) are presented in a tabular form below (Tables 1-4).

Out of 6437 (6503–66) cases included in the study, MTB was detected in 3098 (48.19%, n=6437) cases. Out of 3098 MTB, 91.09% (2822/3098) were RIF sensitive and 8.91% (276/3098) were RIF resistant. Among 3098 MTB, 2826 (91.22%) were PTB and 272 (8.78%) were EPTB. Among 2826 PTB cases, RIF sensitivity was found in 90.94% cases and RIF resistance in 9.06% (256/2826%) cases. Out of 272 EPTB cases, 92.65% were RIF sensitive and 7.35% (20/272) were RIF resistant (Table 5).

In this present study, MTB was detected in 3098 (48.19%, n=6437) cases and 664 were reported PLHIV (patients living with HIV). Out of 3098 cases, 121 (3.91%, n=3098) were reported positive for HIV. Of 121 coinfecting (HIV+TB) cases, 107 (88.43%) were sensitive to RIF and 14 (11.57%) were resistant to RIF (Table 6).

Sex-wise distribution showed that 94 (77.69%, n=121) were males and 27 (22.31%) were females. The most common age group affected was 30–39 years (41.32%) followed by 20–29 years (26.45%) and all cases were above 20 years (Figure 1 and Table 7).

DISCUSSION

In this present study, a total of 6503 samples, both pulmonary and extrapulmonary from suspected TB patients, were tested in CBNAAT laboratory. Out of these, 3098 (48.19%, n=6437) were positive for CBNAAT (MTB/MTB detected).

In India, the prevalence of MDR TB is about 1–3% in new cases and around 12–17% in previously treated cases.¹¹ In our study, overall RIF resistance was found in 8.91% (276/3098) MTB cases. Similar findings were also observed by Devi et al., (7%) from Manipur and Deshmukh (9%) from Maharashtra.^{12,13} Although in other studies from Bihar (19.68%) and Uttar Pradesh (26.1%), high RIF resistance rate was reported.^{8,14}

In our study, out of 3098 MTB, 91.22% (2826/3098) were PTB and 8.78% (272/3098) were EPTB. We found RIF resistance 9.06% (256/2826) in pulmonary and 7.35% (20/272) in extra-PTB. Almost similar RIF resistance rate was found by other authors, Kashyap et al., (8.5%, 10.3%) and Mathur et al., (6.98%, 9.67%).^{15,16} However, higher RIF resistance rate (27.6%, 21.0%) was observed by Gautam et al., from Uttar Pradesh.⁸

Indicator	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
Total number of test performed using CBNAAT (RNITCP and private sector)	69	53	58	110	136	161	123	59	91	103	963		
Total number of MTB not detected	35	38	41	72	89	82	73	41	30	63	382		
Total number of MTB detected	33	32	33	59	76	72	66	32	60	39	568		
MTB detected and RIF sensitive (MTB+/RIF-)	9	6	8	13	13	10	7	9	7	9	91		
MTB detected and RIF resistant (MTB+/RIF+)	0	0	1	2	6	6	6	4	4	2	31		
Number of EPTB sample processed	0	0	0	2	5	4	2	3	2	1	19		
Total number of EPTB out of total number of MTB detected	0	0	0	2	5	4	2	3	2	1	19		
RIF sensitive EPTB	0	0	0	2	5	4	2	2	2	1	18		
RIF resistant EPTB	0	0	0	0	0	0	0	1	0	0	1		
PLHIV out of total number of test performed	2	0	0	6	7	7	14	1	1	11	49		
HIV positive and RIF sensitive out of total number of MTB detected and RIF sensitive (MTB+/RIF-)	1	0	1	1	2	0	1	0	0	1	8		
HIV positive and RIF resistant out of total number of MTB detected and RIF resistant (MTB+/RIF+)	0	0	0	0	2	0	0	0	0	0	2		
Other results (MTB detected RIF indeterminate, Errors, Invalid tests, no results)	1	2	2	0	1	2	0	2	0	2	2	1	13

RIF: Rifampicin, EPTB: Extrapulmonary tuberculosis, MTB: Mycobacterium tuberculosis, HIV: Human immunodeficiency virus

Table 2: Year 2017

Indicator	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
Total number of test performed using CBNAAT (RNTCP and private sector)	81	100	149	57	0	61	122	152	132	89	155	152	1250
Total number of MTB not detected	39	65	88	28	0	27	79	103	78	50	84	75	716
Total number of MTB detected	40	34	55	27	0	31	43	49	54	39	71	77	520
MTB detected and RIF sensitive (MTB+/RIF-)	37	30	48	23	0	28	37	41	45	32	61	67	449
MTB detected and RIF resistant (MTB+/RIF+)	3	4	7	4	0	3	6	8	9	7	10	10	71
Number of EPTB sample processed	7	9	11	2	0	10	12	21	15	8	7	8	110
Total number of EPTB out of total number of MTB detected	7	4	6	1	0	4	4	7	3	3	2	5	46
RIF sensitive EPTB	5	2	6	1	0	4	3	5	3	2	2	5	38
RIF resistant EPTB	2	2	0	0	0	0	1	2	0	1	0	0	8
PLHIV out of total number of test performed	25	37	26	8	0	10	25	27	14	12	14	2	200
HIV positive and RIF sensitive out of total number of MTB detected and RIF sensitive (MTB+/RIF-)	5	5	3	1	0	2	3	0	0	0	1	1	21
HIV positive and RIF resistant out of total number of MTB detected and RIF resistant (MTB+/RIF+)	0	0	1	0	0	0	0	0	1	0	1	0	3
Other results (MTB detected RIF indeterminate, Errors, Invalid tests, no results)	2	1	5	2	0	3	0	0	0	0	1	0	14

RIF: Rifampicin, EPTB: Extra-pulmonary tuberculosis, MTB: *Mycobacterium tuberculosis*, HIV: Human immunodeficiency virus

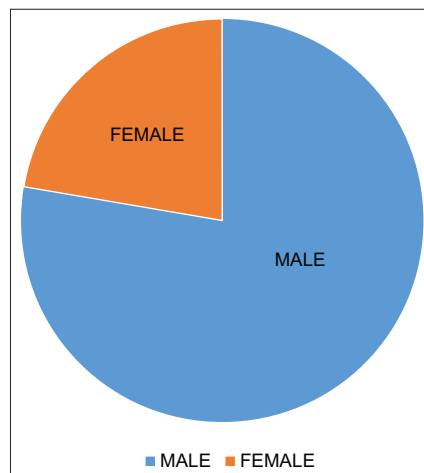


Figure 1: Gender ratio

TB and HIV coinfection

TB is the leading cause of morbidity and mortality among PLHIV. India is the third highest HIV burden country in the world. As per the WHO’s Global TB Report of 2019, among all TB cases, 8.6% were people living with HIV, though only 5% of TB patients are HIV infected in India.¹⁷

The rates of TB-HIV coinfection have been reported to vary in different regions of India. In a study from North India, TB-HIV coinfection was found only 0.4% in 1994–1999 and 9.4% in 2000–2002.¹⁸ In a community-based survey, among TB patients in India during 2005–2006 by Raizada et al., reported HIV seroprevalence among TB patients ranging from 1% to 13.8% in the 15 surveyed districts in India.¹⁹ HIV seroprevalence in TB patients reported 5.54% in a study from Western India in the year 2017–2018.¹⁷ The prevalence of HIV/AIDS among TB patients was observed only 1.2% in a study in 2019 from Kerala, South India.²⁰ In this present study, from 2016–2019, HIV seroprevalence among MTB was 3.91% (121/3098). Comparable result (3.34%) was observed in a study from December 2017–November 2019 from Nadia district nearby Malda district, from West Bengal, Eastern India.²¹

Sex-wise distribution showed that out of 121 TB-HIV coinfection cases, 94 (77.69%) were males and 27 (22.31%) were females. Similar male predominance has been observed in other studies also.^{22,23}

Of all TB-HIV coinfection cases, most of the patients (67.77%) were in the age group of 20–39 years (30–39 years 41.32% and 20–29 years 26.45%) and all cases were above 20 years. It represents the most productive and sexually active age group. Almost similar findings were reported in other studies in India.^{22,24}

Table 3: Year 2018

Indicator	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
Total number of test performed using CBNAAT (RNTCP and private sector)	151	186	192	149	156	210	205	178	212	111	154	150	2054
Total number of MTB not detected	78	114	122	97	83	89	112	92	93	40	64	73	1057
Total number of MTB detected	73	79	69	52	64	117	102	95	116	58	79	60	964
MTB detected and RIF sensitive (MTB+/RIF-)	62	74	66	47	58	112	98	86	113	55	75	56	902
MTB detected and RIF resistant (MTB+/RIF+)	11	5	3	5	6	5	4	9	3	3	4	4	62
Number of EPTB sample processed	15	18	16	16	33	27	30	25	12	8	7	12	219
Total number of EPTB out of total number of MTB detected	9	7	5	8	8	11	9	13	4	4	3	5	86
RIF sensitive EPTB	7	7	5	7	7	11	9	13	4	4	3	5	82
RIF resistant EPTB	2	0	0	1	1	0	0	0	0	0	0	0	4
PLHIV out of total number of test performed	12	13	6	15	12	23	15	30	17	12	16	17	188
HIV positive and RIF sensitive out of total number of MTB detected and RIF sensitive (MTB+/RIF-)	1	2	2	3	0	2	2	8	3	9	3	5	40
HIV positive and RIF resistant out of total number of MTB detected and RIF resistant (MTB+/RIF+)	1	0	0	0	0	1	1	0	0	0	0	2	5
Other results (MTB detected RIF indeterminate, Errors, Invalid tests, no results)	0	3	2	0	9	4	2	1	3	5	2	2	33

RIF: Rifampicin, EPTB: Extra-pulmonary tuberculosis, MTB: *Mycobacterium tuberculosis*, HIV: Human immunodeficiency virus**Table 4: Year 2019**

Indicator	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Total
Total number of test performed using CBNAAT (RNTCP and private sector)	141	180	145	188	219	153	210	175	205	158	226	236	2236
Total number of MTB not detected	73	89	63	95	95	86	126	103	113	83	124	134	1184
Total number of MTB detected	68	89	79	93	124	67	83	72	92	75	102	102	1046
MTB detected and RIF sensitive (MTB+/RIF-)	64	83	75	89	114	63	81	69	89	72	98	97	994
MTB detected and RIF resistant (MTB+/RIF+)	4	6	4	4	10	4	2	3	3	3	4	5	52
Number of EPTB sample processed	24	22	20	20	34	18	36	35	28	16	35	38	326
Total number of EPTB out of total number of MTB detected	7	10	14	7	16	7	14	10	8	6	8	14	121
RIF sensitive EPTB	6	9	14	6	14	6	14	10	8	6	8	13	114
RIF resistant EPTB	1	1	0	1	2	1	0	0	0	0	0	1	7
PLHIV out of total number of test performed	7	23	14	15	34	18	23	16	21	21	19	16	227
HIV positive and RIF sensitive out of total number of MTB detected and RIF sensitive	0	6	5	2	6	1	5	1	3	2	4	3	38
HIV positive and RIF resistant out of total number of MTB detected and RIF resistant	0	1	0	0	1	0	0	0	0	0	2	0	4
Other results (MTB detected RIF indeterminate, Errors, Invalid tests, no results)	0	2	3	0	0	0	1	0	0	0	0	0	6

RIF: Rifampicin, EPTB: Extrapulmonary tuberculosis, MTB: *Mycobacterium tuberculosis*, HIV: Human immunodeficiency virus

RIF resistance and HIV

In this present study, out of 121 coinfecting (HIV+TB) cases, 88.43% (107/121) were RIF sensitive and 11.57% (14/121) were RIF resistant. Almost similar RIF resistance was found by Arora et al.,²⁵ but higher RIF resistance rate (27.3%) was found by Sethi et al.,²⁶ and lower RIF resistance

was found by Vidyaraj et al., (5.6%) and Kashyap et al., (8.3%).^{7,15}

In this present study, RIF resistance was higher in HIV seropositive patients (11.57%, 14/121) as compared to HIV seronegative patients (8.80%, 262/2977). Higher number of

Table 5: Total number of RIF sensitive and RIF resistant MTB, EPTB, and PTB

Year	Total MTB detected	RIF sensitive MTB	RIF resistant MTB	Total EPTB	RIF sensitive EPTB	RIF resistant EPTB	Total PTB detected	RIF sensitive PTB	RIF resistant PTB	Other results
2016	568	477	91	19	18	1	549 (568–19)	459	90	13
2017	520	449	71	46	38	8	474 (520–46)	411	63	14
2018	964	902	62	86	82	4	878 (964–86)	820	58	33
2019	1046	994	52	121	114	7	925 (1046–121)	880	45	6
Total	3098	2822	276	272 (8.78%, n=3098)	252 (92.65%, n=272)	20 (7.35%, n=272)	2826 (91.22%, n=3098)	2570 (90.94%, n=2826)	256 (9.06%, n=2826)	66

Total PTB= (total MTB-total EPTB), RIF sensitive PTB= (RIF sensitive MTB- RIF sensitive EPTB), RIF resistant PTB= (RIF resistant MTB- RIF resistant EPTB), EPTB: Extrapulmonary tuberculosis, MTB: *Mycobacterium tuberculosis*, RIF: Rifampicin

Table 6: RIF sensitive and RIF resistant MTB-HIV coinfecting cases

Year	Total MTB positive, HIV negative cases	HIV negative, RIF sensitive MTB	HIV negative, RIF resistant MTB	Total MTB and HIV co-infected cases	RIF sensitive MTB-HIV co-infected cases	RIF resistant MTB-HIV co-infected cases
2016	568 (-10)	469 (477–8)	89 (91–2)	10 (1.76%, n=568)	8	2
2017	520 (-24)	428 (449–21)	68 (71–3)	24 (4.62%, n=520)	21	3
2018	964 (-45)	862 (902–40)	57 (62–5)	45 (4.67%, n=964)	40	5
2019	1046 (-42)	956 (994–38)	48 (52–4)	42 (4.02%, n=1046)	38	4
Total	3098 (-121) = 2977	2715, (91.20%, n=2977)	262, (8.80%, n=2977)	121 (3.91%, n=3098)	107 (88.43%, n=121)	14 (11.57%, n=121)

HIV negative, RIF sensitive MTB= [MTB detected and RIF sensitive-RIF sensitive MTB-HIV co-infected], HIV negative, RIF: resistant MTB= [MTB detected and RIF resistant – RIF resistant MTB-HIV co-infected], EPTB: Extrapulmonary tuberculosis, MTB: *Mycobacterium tuberculosis*, RIF: Rifampicin, HIV: Human immunodeficiency virus

Table 7: Sex-wise distribution of TB-HIV coinfecting cases

Age group	Males	Females	Total (%), n=121
20–29	23	9	32 (26.45)
30–39	39	11	50 (41.32)
40–49	24	6	30 (24.79)
50–59	6	1	7 (5.79)
>60	2	0	2 (1.65)
Total	94 (77.69%)	27 (22.31%)	121

TB-HIV: Tuberculosis-human immunodeficiency virus

MDR-TB in the HIV seropositive group as compared to HIV seronegative group was reported by other author also.²⁶

Limitations of the study

In our study, samples were collected both from new and on treatment cases including drug resistant TB. We could not demonstrate the difference in HIV prevalence between new and drug resistant TB.

CONCLUSION

The present study reported that the prevalence of TB-HIV coinfection was 3.91% and the prevalence of RIF resistant TB in HIV seropositive patients was higher than HIV seronegative patients. Surveys in Africa, Asia, and the Pacific have indicated that the HIV prevalence among TB patients is much higher than that observed in the general population. Hence, all TB patients should be screened

for HIV and all the HIV-positive individuals should be screened for TB along with drug resistance. Early detection and early initiation of treatment of both TB and HIV allow a better treatment outcome or chance of survival.

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TM- Concept and design of the study, preparation of manuscript and interpretation of results; **AS-** Reviewed the literature and manuscript preparation, revision of manuscript; **SJC-** Reviewed the literature and revision of manuscript; **JR-** Co-ordination, reviewed the literature and revision of manuscript.

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