

Status of drug resistant tuberculosis among patients attending a tuberculosis unit of West Bengal: A record based cross-sectional study

Rekha Dutt¹, Ritesh Singh¹, Jitendra Majhi¹, Gandhari Basu²

¹Department of Community Medicine and Family Medicine, All India Institute of Medical Sciences, Kalyani, ²Department of Community Medicine, College of Medicine and JNM Hospital, Kalyani, Kolkata, West Bengal, India

ABSTRACT

Context: Tuberculosis (TB) is one of the main causes of death due to infectious diseases worldwide. Multidrug resistance/rifampicin resistance (MDR/RR) TB remains a public health crisis. India has the highest burden of tuberculosis and multidrug resistant TB (MDR TB) in the world. There is wide geographical variation in the epidemic and its trends that can be updated by regular reporting and sound surveillance systems. The current study tries to fill this gap by analyzing the data of TB patients from a Tuberculosis Unit, studying socio-demographic and clinical profile from December 2017 to November 2019 in Nadia district of West Bengal. **Aims:** The aims of this work were to study socio-demographic and clinical profile of TB patients attending Tuberculosis Unit of West Bengal, and to find out factors associated with drug-resistant TB. **Settings and Design:** Record-based study from Tuberculosis Unit. **Methods:** Records of all patients who undergo CBNAAT in TU are stored as monthly unit. We randomly selected 10 months from a period of December 2017 to November 2019 by using lot method. Data of all patients undergoing CBNAAT at Kalyani – Gayeshpur Tuberculosis Unit during randomly selected 10 months were accessed. **Statistical Analysis Used:** Monthly data was entered in Microsoft Excel and descriptive tests of significance, proportions and Chi-square were applied. **Results:** There was male preponderance for testing of tuberculosis. Seven percent of the TB suspects were HIV positive. The positivity rate of MTB by CBNAAT was 23%. Four percent of the samples were Rifampicin resistance. Tobacco consumption, contact with TB case and Diabetes were common risk factors of TB. Most of the information was missing in the records. **Conclusions:** Most of Rifampicin Resistant cases showed very low Ct value in CBNAAT. Previous history of TB treatment and positive HIV status was significantly associated with RR TB. There is a need to capture complete information on the records of presumptive TB cases.

Keywords: CBNAAT, rifampicin resistance, tuberculosis

Introduction

Tuberculosis (TB) is one of the leading ten causes of death worldwide and the main cause of mortality from a single infectious agent. In 2019 approximately 1.4 million people died, 10 million suffered from TB, and 465000 fell ill with

drug-resistant TB. Multidrug resistance/rifampicin resistance (MDR/RR) TB has become a threat to public health. An estimated 3.3% of new TB cases and 18% of previously treated cases had MDR/RR TB. About half of the global burden of MDR-TB is in three countries viz. India (27%), China (14%), and the Russian Federation (8%).^[1] Rifampicin mono-resistances are rare and are primarily observed in association with Isoniazid resistance. Thus, about 90% of Rifampicin-resistant Pulmonary Tuberculosis (PTB) cases are multi-drug-resistant TB (MDR-TB).^[2]

Address for correspondence: Dr. Rekha Dutt,

Tower 17, 10 G, Genexx Valley, Joka, Kolkata - 700 104,
West Bengal, India.

E-mail: rekha.cmfm@aiimskalyani.edu.in

Received: 26-03-2021

Revised: 09-07-2021

Accepted: 12-07-2021

Published: 31-01-2022

Access this article online

Quick Response Code:



Website:
www.jfmpc.com

DOI:
10.4103/jfmpc.jfmpc_576_21

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Dutt R, Singh R, Majhi J, Basu G. Status of drug resistant tuberculosis among patients attending a tuberculosis unit of West Bengal: A record based cross-sectional study. J Family Med Prim Care 2022;11:84-9.

India has the highest burden of Tuberculosis and multi-drug-resistant TB (MDR-TB) in the world, disproportionately high even for India's population. India ranks first in the global ranking of detecting new cases each year. Nearly one-fourth of all active TB cases detected globally are from India.^[3] In 2020, the total estimated incidence of TB was 193 per lakh population.^[1] It was believed that drug-resistant TB was not easily transmissible, and resistance develops from the failure of people to take anti TB drugs in a proper regimen. So, a high-quality DOTS program was started. Recently it has been reported that drug-resistant bacilli are equally infectious. The risk of transmission is the same regardless of whether the bacilli are drug-resistant or drug-susceptible. As per the latest report of the Government of India in March 2021, the estimated number of MDR/RR-TB cases in India is 124000 (9.1/lakh population).^[4] The level of drug-resistant TB may hamper the progress of India towards the target of TB elimination by 2025.

The National Tuberculosis Elimination Program focuses on diagnosing TB cases as early as possible by molecular testing methods. The Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) is one such method that is capable of detecting the presence or absence of TB in a sputum sample and determine its susceptibility or resistance to Rifampicin in about 2 hours with about 93% sensitivity and specificity.^[5] Rifampicin resistance is a useful surrogate marker for MDR-TB.^[6] Universal drug (Rifampicin) susceptibility testing of all TB patients using CBNAAT has been implemented across the country since January 2018.^[7] There is wide geographical variation in the epidemic and its trends. Severe local epidemics go unreported behind inadequate data and surveillance systems.^[3] TB epidemiology in India is diverse, and one-size policy prescription has poorly served the communities. Hence, region-wise studies should be undertaken to assess the program's quality, effectiveness, efficiency, and accessibility. This study has been planned to fill the lacune by analyzing the data of TB patients from a Tuberculosis Unit in Nadia district of West Bengal, studying their socio-demographic, clinical profile, and the factors associated with RR-TB. The results may cater to the academic need of the health care practitioners who provide comprehensive and continuous care to TB patients and bring their attention to barriers and facilitators to achieve the country's target to eliminate TB by 2025.

Methods

Study design: It is a cross-sectional study based on secondary data analysis of patients' records who underwent CBNAAT from December 2017- November 2019 in a Tuberculosis Unit (TU) of West Bengal. Nadia district, West Bengal, has three CBNNAT sites where samples are tested from suspected cases of drug-resistant TB patients. One of the sites is a teaching hospital situated in the Kalyani Municipality. The CBNAAT laboratory in Kalyani – Gayeshpur TU, located in the teaching hospital, serves a population of approximately 1.8 lakhs. It covers two adjoining municipalities, Kalyani with 1.2 lakhs and Gayeshpur municipality

with 60 thousand population. The sample collectors also bring samples from adjoining areas. On average, 400 samples are tested every month in the CBNAAT laboratory. Reports of all patients are stored month-wise in a folder.

Sample size and study subjects: Records of all patients who undergo CBNAAT in TU are stored in month-wise folders. We have randomly selected ten months from December 2017 to November 2019 by using the lot method. Data of all patients undergoing CBNAAT at Kalyani – Gayeshpur TU during randomly selected 10 months were accessed.

Study Tool: A standardized form of Central Tuberculosis Division, Government of India, titled *RNTCP request card for the examination of biological specimen for TB*, also known as Annexure 15 A, is used as a record of all patients undergoing CBNAAT for diagnosis, drug sensitivity testing and follow-up of TB patients. It contains information on the socio-demographic and clinical profile of patients. Records of patients were studied by accessing form 15 A. Monthly data were entered in Microsoft Excel, and descriptive tests of significance, proportions, and Chi-square were applied.

Ethical Issue: The District Tuberculosis Officer (Nadia) and Medical Officer In-charge of Kalyani – Gayeshpur TU accorded permission to access data for the study. The study proposal was submitted to Institutional Ethics Committee, All India Institute of Medical Sciences, Bhubaneswar, mentor institute of AIIMS Kalyani, and approval was accorded vide reference no. T/IM-NF/Kalyani/19/03 dated 11.01.2020.

Results

Most of the annexure 15 A forms, that are used to record information of presumptive TB patients, were incomplete; hence, the denominator was different in almost all the studied variables. Figure 1 depicts the information of different variables recorded on annexure 15 A forms available at Kalyani- Gayeshpur Tuberculosis Unit, from randomly selected ten months during period of December 2017 to November 2019. Majority (68%) of the presumptive TB patients were males and most of the samples (96%) tested were of sputum. Tobacco use was the commonest risk factor, others being contact with TB patient and Diabetes Mellitus. Twenty three percent of patients had history of TB treatment and 7% were HIV reactive. Results show that 23% of presumptive TB patients were detected MTB positive by CBNAAT and 4% of them were RR.

The majority of the presumptive TB patients had tested negative in microscopy test. There are slight differences in the number of different categories of results in sputum microscopy in sample A and sample B [Figure 2]. An odd number of 455 (24.6%) out of 1847 sample A tested positive for Mycobacteria under an LED microscope. Similarly, 425 (23.8%) out of 1786 sample B tested positive for Mycobacteria under an LED microscope.

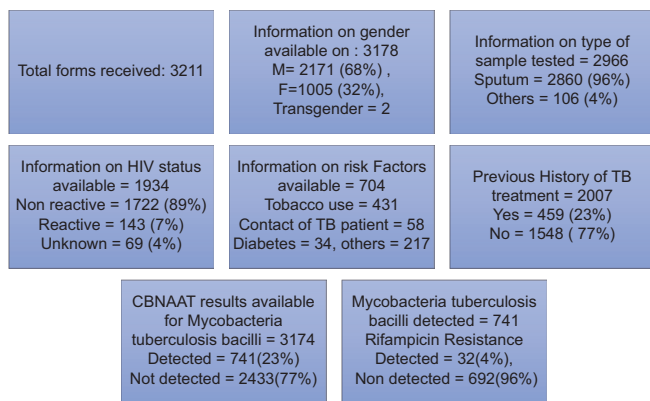


Figure 1: Ten months data of presumptive TB patients accessed from a Tuberculosis Unit during period of December 2017 to November 2019

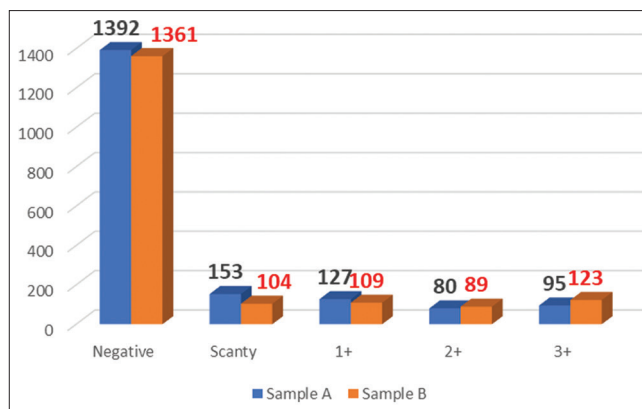


Figure 2: Tuberculosis sputum microscopy result of samples A and B from a ten months data

Table 1: Load of mycobacteria in the samples tested positive in CBNAAT (n=741)*

Ct value	Very low	Low	Medium	High	No data	Total
Frequency	23	37	67	70	544	741

Table 2: Status of Rifampicin Resistance and Ct value*

Rifampicin resistance	Very low	Low	Medium	High	Total
Detected	7	-	2	-	9
Not detected	15	35	63	66	179
Total	22	35	65	66	188

Table 3: Gender and rifampicin resistance (n=724)*

Gender	MTB Positive RR Negative	MTB Positive RR Positive	Chi-square P value
Male	545	27	0.58
Female	147	5	0.45
Total	692	32	

Quantitation of bacillary load by CBNAAT is determined by threshold-cycle [Ct]; High Ct value is <16; Medium Ct value is 16-22; low Ct value is 22-28; very low Ct value is >28.

Low Ct values means high bacilli load and vice versa.^[8]

Table 1 shows that out of 197 samples having data of Ct value, majority ie 70 samples had high Ct value. Table 2 depicts that a very low Ct value, that is, the high bacterial load, is associated with Rifampicin resistance. Similarly, most TB patients who were not resistant to Rifampicin showed high Ct value, that is, low bacterial load.

Table 3 shows that gender was not significantly associated with rifampicin resistance.

HIV status was significantly associated with the presence of Mycobacteria tuberculosis in CBNAAT samples [Table 4].

It can be seen in Table 5 that HIV status was significantly associated with Rifampicin resistance.

Previous history of TB was significantly associated with presence of MTB [Table 6] and Rifampicin resistance [Table 7].

Discussion

Risk factors of TB

It was observed that the majority of the subjects tested for presumptive TB were exposed to risk factors. Approximately 61% of subjects were tobacco users. Various systematic review studies have concluded that there is a causal association between smoking and TB disease. Quitting smoking and avoiding exposure to passive tobacco smoke are essential factors in TB control.^[9,10] Obore *et al.*^[11] observed a two-fold rise in the risk from exposure to second-hand tobacco smoke (RR = 2.15, 95%CI 1.419–3.242), and tobacco smoking doubled the risk of contracting TB (RR = 2.67, 95%CI 2.017–3.527). Zvolnska *et al.*^[12] conducted a review study on barriers and facilitators of smoking cessation in TB patients of low- and middle-income countries suggested that in order to improve the prognosis of treatment, motivational or pharmacological interventions should be repeatedly and routinely undertaken in all TB centers to help TB patients in quitting tobacco use.

Around 8% of subjects had a history of contact with TB patients. A study by Kundu *et al.*^[10] in an adjoining district of West Bengal also observed that 14% of TB patients had a history of TB contacts.

Around 5% of subjects with presumptive TB were suffering from Diabetes Mellitus (DM). Another study of 2020 from West Bengal reveals that 43% of TB patients had Diabetes.^[10] A study undertaken in four high TB burden countries has observed that 12.5% of TB patients were Diabetic.^[13] People with a weak immune system because of chronic diseases such as Diabetes are at a higher risk of developing latent to active TB. DM triples a person’s risk of developing TB. About 15% of TB cases globally may be associated with DM. TB can temporarily cause impaired glucose tolerance, which is a risk factor for developing DM.^[14] Alisjahbana *et al.*^[15] have endorsed the WHO policy of routine bidirectional symptom-based

Table 4: HIV status and presence of MTB in CBNAAT (n=1846)*

HIV status	MTB absent in CBNAAT	MTB present in CBNAAT	Chi-square P value
Reactive	123	17	17.95
Non-reactive	1215	491	0.00
Total	1338	508	

Table 5: HIV status and rifampicin resistance (n=500)*

HIV status	MTB Positive and RR Negative	MTB Positive and RR Positive	Chi-square P value
Reactive	14	3	6.344
Non-reactive	462	21	0.01
Total	476	24	

Table 6: Previous history of TB and presence of MTB in CBNAAT (n=1846)*

Previous history of TB	MTB absent in CBNAAT	MTB present in CBNAAT	Chi-square P value
Yes	365	92	3.29
No	1161	371	0.06
Total	1338	508	

Table 7: Previous history of TB and rifampicin resistance (n=500)*

Previous history of TB	MTB Positive RR Negative	MTB Positive RR Positive	Chi-square P value
Yes	83	8	4.49
No	351	13	0.03
Total	434	21	

*According to ten months data compiled from Form 15 A, accessed from a Tuberculosis Unit during period of December 2017 to November 2019

screening for TB in known DM patients in high TB-burden countries.

It was observed from the available records that 23% of presumptive TB patients were found to be Mycobacteria TB positive by CBNAAT. Similar observations were reported in studies conducted in Karnataka and New Delhi, where 22.3% and 21.8% of subjects, respectively, were positive for MTB.^[16,17] A study conducted in Ethiopia had observed a similar finding of 25% MTB in samples of presumptive subjects.^[2]

There was a male preponderance (68%) among the subjects who had come for the presumptive TB test. The majority of patients (79%) with MTB positive were males. Our findings are consistent with findings of other studies across India conducted during the last few years where Dewan *et al.*,^[18] Jethani *et al.*,^[19] Sumana *et al.*,^[20] Sundaram *et al.*,^[21] and Shankar *et al.*^[22] respectively observed that 76%, 75%, 70.5%, 71% and 72% of the TB patients were males. As per the WHO report of 2021, the highest burden of TB is found in adult males, who accounted for 56% of all TB cases in 2019.^[1]

Bacillary load and rifampicin resistance

CBNAAT offers a quantitative estimation of mycobacterial load in cycle threshold values (Ct) which inversely correlates with the TB bacilli load. Low Ct values imply high bacilli load and vice versa.^[23] In this study, most of the data was missing. Among available information, most of the samples had high/medium Ct values.

It is observed that a very low Ct value, that is, the high bacterial load, is associated with Rifampicin Resistance. Similarly, most TB patients who were not resistant to Rifampicin showed high Ct Value, that is, low bacterial load. The higher bacillary load and Rifampicin resistance showed a statistically significant association. This finding was found consistent with the study by Singh *et al.* conducted in New Delhi.^[8] A study published in the Lancet concur that higher bacillary load is associated with MDR, whereas a very low bacillary load was strongly associated with false rifampicin resistance (OR 63.6, 95% CI 9.9–410.4). The study recommended that the Xpert testing algorithm should include an assessment of retesting in case rifampicin resistance is detected with a high Ct value. The multidrug-resistant tuberculosis treatment should be started after rifampicin resistance has been confirmed on repeat testing. If the rifampicin resistance is not confirmed on repeat testing, the study proposed that patients be given first-line anti-tuberculosis drugs and monitored closely during the treatment.^[24]

From the available records, it was studied that overall, 4% of MTB patients were Rifampicin resistant. Gender-wise, 5% and 3.4% of MTB-positive male and female patients, respectively, were having Rifampicin resistance. The first National Drug Resistance Survey revealed that 28% of TB patients were resistant to any drugs (22% among new and 36.82% among previously treated) and 6.19% had MDR-TB, 2.84% among new and 11.62% among previously treated TB.^[4] Kashyap *et al.*^[17] observed Rifampicin resistance as 9.2%, 8.5% and 10.3% of the total, pulmonary and extra-pulmonary samples respectively in M. tuberculosis-positive samples. Our finding is in concurrence to a cohort study in Karnataka, where Rifampicin resistance among MTB-positive patients was found to be 4%.^[22] A study conducted in Zambia reported Rifampicin mono-resistance respectively among 3.9% of the new TB cases and 10.1% of the previously treated TB cases.^[25] MDR-TB can result from the failure of drug-sensitive TB treatment with the development of resistance or direct transmission of an MDR strain. The acquisition of resistance can arise from medical error, inefficient implementation of TB control programs, or poor patient compliance to treatment. A history of TB treatment remains the most crucial risk factor for MDR-TB.^[25]

TB and HIV

It was observed that 7% of the presumptive TB patients were HIV positive. Among MTB-positive subjects, 3.34% were HIV positive. There was a significant association between HIV and MTB coinfection. HIV prevalence among MTB patients is 2.7%

in India.^[1] A study conducted in a neighboring district observed that 2% of TB patients were coinfecting with HIV.^[10] A study conducted in Odisha, a neighboring state of West Bengal, had found HIV coinfection to be 6.22%.^[26] TB is the most common opportunist infection among persons living with HIV. Immune suppression in HIV cases increases the risk of reactivation of latent TB infection and rapid progression to active TB disease. Diagnosis of TB is more difficult in people living with HIV infection, and initiation of HIV treatment can paradoxically worsen TB by restoring immune function. Overall, an estimated 8% of new TB cases are attributable to HIV coinfection. TB coinfection is the main cause of mortality among HIV-infected patients in the developing world.^[27]

Rifampicin Resistance (RR) and HIV

This study had observed the statistically significant association between HIV status and RR. It was observed that 17.64% of HIV-positive persons were found to be having RR. It was also observed that there was a significant association between the previous history of TB and RR. Global data reveals that 9% of TB patients are HIV positive.^[1] A systematic review By Sultana *et al.*^[28] published in 2021 indicates that HIV infection raises the risk of MDR-TB. The odds of MDR-TB among HIV-positive cases were 1.42 times higher, and this was statistically significant, and the pooled odds of MDR-TB was 1.86 times higher for HIV positives than HIV negative individuals (OR = 1.86, 95% CI = 1.30–2.67) in the South-East Asian countries. The upward risk trend of drug-resistant TB is highest in the South-East Asian region, particularly in HIV-infected 40 years of age and older patients. Meta-analysis of 10000 adult MTB-resistant patient data shows that the odds of death were higher, around 2.5 times greater for HIV positive individuals compared to HIV negative. HIV-positive patients not on ART had four times and, on ART were 1.8 times the odds of dying compared to HIV-negative.^[29] Drug malabsorption in HIV-infected patients, especially rifampin, ethambutol and with adverse side effects leading to non-adherence to treatment can cause drug resistance and treatment failure.^[30]

Detailed documentation and treatment of Rifampicin Resistant cases is critical to effective control of TB, as it can avoid raised toxicity with long-term therapy and psychosocial issues by preventing emergence and transmission of drug-resistant TB. Thus, epidemiological studies are essential in providing local data that could be the potential objective of future studies.

Conclusions

The study's key findings based on 2 years of secondary data analysis of a Tuberculosis Unit observed male preponderance for testing of Tuberculosis. Tobacco use, Diabetes mellitus, and history of TB contacts were the risk factors for TB. Seven percent of the TB suspect were HIV positive, while the positivity rate of MTB by CBNAAT was 23%. Four percent of the samples were rifampicin resistance, with most of them associated with very low Ct value. The previous history of TB

treatment and HIV status was significantly associated with drug-resistant TB.

The current study is the first report from this region that has observed that the relevant information on most of the forms was missing. Hence, it is concluded that there is a need for micro monitoring to take suitable and timely interventions at the local level to collect the complete information, diagnosis, and treatment considering risk factors and comorbidities in TB patients. Unless a more significant amount of dedication and expertise is applied in microplanning and management at the district level with customized local initiatives, it is difficult to achieve SDG 3 to end the global TB epidemic by 2030.

Limitation of study

The results of this study are based on secondary data analysis and hence are liable for discrepancies due to the incomplete data.

Acknowledgements

The authors are thankful to Dr. Subhasis Chanda, District Tuberculosis Officer, Nadia District, West Bengal, for according permission to access data for the project.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Global TB Report 2020. Available from: <https://apps.who.int/iris/bitstream/handle/10665/336069/9789240013131-eng.pdf>. [Last accessed on 2021 Mar 24].
2. Jaleta KN, Gizachew M, Gelaw B, Tesfa H, Getaneh A, Biadgo B. Rifampicin-resistant Mycobacterium tuberculosis among tuberculosis-presumptive cases at University of Gondar Hospital, northwest Ethiopia. *Infect Drug Resist* 2017;10:185-92.
3. Revised National Tuberculosis Programme. National Strategic Plan for Tuberculosis: 2017-2025, Elimination by 2025. Ministry of Health and Family Welfare. March 2017. Available from: <https://www.tbcindia.gov.in/WriteReadData/National%20Strategic%20Plan%202017-25.pdf>. [Last accessed on 2021 Mar 24].
4. Guidelines for Programmatic Management of Drug Resistance in India. National Tuberculosis Elimination Programme, GOI. March 2021. Available from: <https://tbcindia.gov.in/showfile.php?lid=3590>. [Last accessed on 2021 Mar 24].
5. Scott L, Kerrigan M, Natasha G, Matilda N, Annelies V, Lan V, *et al.* Comparison of xpert MTB/RIF with other nucleic acid technologies for diagnosing pulmonary tuberculosis in a high HIV prevalence setting: A Prospective Study. *PLoS Med* 2011;8:e1001061.
6. Boehme CC, Nabeta P, Hillemann D, Nicol MP, Shonai S, Kropp F, *et al.* Rapid molecular detection of tuberculosis and Rifampicin resistance. *N Eng J Med* 2010;363:1005-15.

7. India TB Report 2020. Revised National Tuberculosis Control Programme Annual Report. Central TB division. Ministry of health and family welfare. Available from: <https://www.tbcindia.gov.in/showfile.php?lid=3538>. [Last accessed on 2021 Mar 24].
8. Singh UB, Pandey P, Mehta G, Bhatnagar AK, Mohan A, Goyal V, *et al.* Genotypic, phenotypic and clinical validation of genexpert in extra-pulmonary and pulmonary tuberculosis in India. *PLoS One* 2016;11:e0149258.
9. Slama K, Chiang CY, Enarson DA, Hassmiller K, Fanning A, Gupta P, *et al.* Tobacco and tuberculosis: A qualitative systematic review and meta-analysis. *Int J Tuberc Lung Dis* 2007;11:1049-61.
10. Kundu SS, Sikder R, Dey R, Majumdar KK, Joardar G. Study of socio-demographic and treatment profile and other epidemiological correlates of clients attending revised national tuberculosis control programme clinic in a tertiary hospital of West Bengal, India. *Int J Community Med Public Health* 2020;7:742-7.
11. Obore N, Kawuki J, Guan J, Papabathini SS, Wang L. Association between indoor air pollution, tobacco smoke and tuberculosis: An updated systematic review and meta-analysis *Public Health* 2020;187:24-35.
12. Zvolnska K, Pankova A, Nohavova I, Huque R, Elsey H, Boeckmann M, *et al.* A narrative review of facilitators and barriers to smoking cessation and tobacco-dependence treatment in patients with tuberculosis in low- and middle-income countries. *Tob Induc Dis* 2020;18:67.
13. Ugarte-Gil C, Alisjahbana B, Ronacher K, Riza AL, Koesoemadinata RC, Malherbe ST. Diabetes mellitus among pulmonary tuberculosis patients from 4 tuberculosis-endemic countries: The TANDEM Study. *Clin Infect Dis* 2020;70:780-8.
14. Tuberculosis and Diabetes. Available from: https://www.who.int/tb/publications/diabetes_tb.pdf. [Last accessed on 2021 Mar 24].
15. Alisjahbana B, McAllister SM, Ugarte-Gil C, Panduru NM, Ronacher K, Koesoemadinata RC. Screening diabetes mellitus patients for pulmonary tuberculosis: A multisite study in Indonesia, Peru, Romania and South Africa. *Trans R Soc Trop Med Hyg* 2021;115:634-43.
16. Basavaraj VP, Rajani R. CBNAAT: A novel tool for rapid detection of MTB and rifampicin resistance. *Int J Curr Microbiol App Sci* 2016;5:383-8.
17. Kashyap B, Goyal N, Hyanki P, Singh N, Khanna A. Cartridge-based nucleic acid amplification test: A novel rapid diagnostic tool to study the burden of tuberculosis from a tertiary care hospital. *Tropical Doctor* 2019;49:274-81.
18. Dewan R, Anuradha S, Khanna A, Garg S, Singla S, Ish P, *et al.* Role of cartridge-based nucleic acid amplification test (CBNAAT) for early diagnosis of pulmonary tuberculosis in HIV. *J Ind Acad Clin Med* 2015;16:114-7.
19. Jethani S, Kakkar R, Semwal J, Rawat J. Sociodemographic profile of tuberculosis patient: A hospital based study at Dehradun. *Nat J Com Med* 2014;5:6-9.
20. Sumana M, Sreelatha CY, Renuka M, Ishwaraprasad GD. Patient and health system delays in diagnosis and treatment of tuberculosis patients in an urban tuberculosis unit of south India. *Int J Community Med Public Health* 2016;3:796-804.
21. Sunderam S, Kumari S, Haider S, Kashyap V, Singh S. A study on socio demographic profile of patients having cough of two weeks or, more along with their smear microscopy outcome attending a Tertiary Care Hospital of Jharkhand, India. *IJIMS* 2015;2:119-27.
22. Shankar SU, Kumar AMV, Venkateshmurthy NS, Nair D, Kingsbury R, R P, *et al.* Implementation of the new integrated algorithm for diagnosis of drug-resistant tuberculosis in Karnataka State, India: How well are we doing? *PLoS One* 2021;16:e0244785.
23. Najjingo I, Muttamba W, Kirenga BJ, Nalunjogi J, Bakesiima R, Olweny F, *et al.* Comparison of GeneXpert cycle threshold values with smear microscopy and culture as a measure of mycobacterial burden in five regional referral hospitals of Uganda- A cross-sectional study. *PLoS One* 2019;14:e0216901.
24. Ngabonziza JCS, Decroo T, Migambi P, Habimana YM, Deun AV, Meehan CJ. Prevalence and drivers of false-positive rifampicin-resistant Xpert MTB/RIF results: A prospective observational study in Rwanda. *Lancet Microbe* 2020;1:e74-83.
25. Ukwamedua H, Omote V, Etaghene J, Oseji ME, Agwai IC, Agbroko H. Rifampicin resistance among notified pulmonary tuberculosis (PTB) cases in South-Southern Nigeria. *Heliyon* 2019;5:e02096.
26. Dash M, Satyajit S, Swain TR, Behera B, Sahu S, Mahapatra S. Diagnostic yield of cartridge based nucleic acid amplification test in mycobacterium tuberculosis in a tertiary care medical college and hospital of Southern Odisha, India. *Int J Res Med Sci* 2019;7:4460-3.
27. Suchindran S, Brouwer ES, Van Rie A. Is HIV infection a risk factor for multi-drug resistant tuberculosis? A systematic review. *PLoS One* 2009;4:e5561.
28. Sultana ZZ, Hoque FU, Beyene J, Akhlak-Ul-Islam M, Khan MHR, Ahmed S, *et al.* HIV infection and multidrug resistant tuberculosis: A systematic review and meta-analysis. *BMC Infect Dis* 2021;21:51.
29. Bisson GP, Bastos M, Campbell JR, Bang D, Brust JC, Isaakidis P, *et al.* Mortality in adults with multidrug-resistant tuberculosis and HIV by antiretroviral therapy and tuberculosis drug use: An individual patient data meta-analysis. *Lancet* 2020;396:402-11.
30. Patel KB, Belmonte R, Crowe HM. Drug malabsorption and resistant tuberculosis in HIV-infected patients. *N Engl J Med* 1995;332:336-7.