ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Trends in tuberculosis – is a different problem emerging?

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Submission: 02-07-2024 Revision: 03-10-2024 Publication: 01-11-2024

ABSTRACT

Background: Tuberculosis (TB), as a communicable disease, is an ongoing global epidemic that accounts for a high burden of global mortality and morbidity. Drug-resistant TB strains are one of the hurdles in controlling TB problem. TB is the most common opportunistic infection in people living with human immunodeficiency viruses (PLHIV). To accelerate progress toward the goal of ending TB by 2035, it is imperative to outline the incidence and mortality trends of TB in India. **Aims and Objectives:** This study aims to provide deep insights into the recent trends of TB incidence and mortality in India from 2018 to 2023. **Materials and Methods:** This is a cross-sectional type of observational study done, over a period of 6 years from 2018 to 2023. It included 21,223 suspected samples tested for TB and rifampicin (rif) resistance with GeneXpert CBNAAT (cepheid) for infection of *Mycobacterium tuberculosis* (MTB). **Results:** Out of total 21,223 samples tested, 17.97% of samples were positive for MTB. From the year 2018 to 2023, 9.5% decline was seen in overall TB cases. However, the diagnosis of rif resistance is in similar range for all the study years. New patients show slight decline, but previous patients show higher rif resistance. There is decreased TB incidence in PLHIV. **Conclusion:** Overall, the incidence of TB has decreased in the past 6 years. The acquired drug resistance was seen in 32.6% cases. The study found an overall decrease in the incidence of TB in PLHIV.

Key words: Drug resistance; GeneXpert CBNAAT; *Mycobacterium tuberculosis*; People living with human immunodeficiency viruses; Tuberculosis incidence

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v15i11.69170

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Tuberculosis (TB) is a chronic infectious disease caused by *Mycobacterium tuberculosis* (MTB) and persistent cause of high morbidity and mortality remains one of the major public health challenges in India.[1] Globally, an estimated 10 million people develop TB infection and over a million deaths occur annually.[2] India continues to have one of the highest rates of TB incidence and mortality in the world. India accounts for about 25% of global TB burden, with an estimated TB incidence of 2.77 million in 2022.[3] India is committed to end TB by 2025.[4] TB has remained major public health challenge, since its discovery, even after India's continuous efforts to eliminate it, through various TB control activities.

United Nation sustainable development goals and WHO's End-TB strategy aim to end the global TB epidemic with targets to reduce TB deaths by 95% and to cut new cases by 90% by 2035 globally.[5] India's National Strategic plan 2017–2025 aims to achieve a TB free India, 5 years ahead of the global elimination plan.[6] India had launched a National TB program in the 60s and has already taken several critical steps to showcase itself as a leader for a TB-free world.[7] India, despite these impressive commitments, due to its high population, less-than-optimal service delivery

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and various challenges, could not make much progress in terms of achieving substantially high cure rates. It carries the by-far highest burden of TB and multidrug-resistant TB (MDR-TB). The prevalence of TB in India might be higher than the already available prevalence rates. This may be due to the stigma associated with TB and resulting in under-reporting of undiagnosed TB. To accelerate progress toward the goal of ending TB by 2030, India needs to strengthen the public as well as private sector response to TB.

The human immunodeficiency virus (HIV) epidemics have a profound and prolonged impact on TB in Asia and the Pacific.[8] HIV robs a person's body of its natural ability to fight infection, causing them to be more likely to be infected with TB. It not only is an important risk factor for progression to active TB but also has made diagnosis of TB difficult leading to increasing TB burden. It is expected that after the introduction of revised national TB control program (RNTCP), TB incidence, prevalence, and mortality rates in India would have reduced by 5% per year if HIV epidemic had not occurred. William et al., suggested that if HIV-infected TB patients receive anti-retroviral therapy (ART) and TB treatment, RNTCP would result in reversing the increase in TB burden due to HIV.[8]

It is essential to understand the burden of TB infection in a population of a country like India, which is endemic for TB infection. The objective of the present analysis is to find out the prevalence of TB infection among the population in India. The factors associated with TB infection were explored.

Aims

To study recent changes in the trend of Tuberculosis infection.

Objectives

1) To determine the change in TB prevalence over time.
2) To determine the rif resistance pattern over a period of time.

MATERIALS AND METHODS

This is a cross-sectional type of observational study done in a tertiary care center in western Maharashtra, India, over a period of 6 years from 2018 to 2023. This study included 21,223 suspected pulmonary and extra-pulmonary TB patients, of whom relevant clinical samples were received for testing in TB laboratory of department of microbiology of the institution. Samples were collected in 50 mL sterile Falcon tube from MDR-TB suspects registered with the directly observed therapy short-course centers of the national TB elimination program in associated chest clinics. A unique laboratory number was provided to each sample. These samples were tested with GeneXpert CBNAAT (Cepheid) for infection of MTB and rifampicin (rif) resistance.

Inclusion criteria

Patients suffering from pulmonary or extra-pulmonary TB were included in the study.

Exclusion criteria

Patients not giving consent for the test were excluded from the study.

RESULTS

Systematic analysis of the data obtained over a period of 6 years was done. Out of total 21,223 samples tested, 3814, that is, 17.97% samples turned out to be positive for MTB.

There was gradual decrease in positive percentage of MTB among the tested samples in this institute (Figure 1). However, number of samples tested was similar every year. In 2018, out of 3543 samples 772, that is, 21.8% of samples were positive, which has declined to 437, that is12.3% out of 3546 in 2023 (Figure 1).

MTB positivity has decreased over the years; however, diagnosis of rif resistance is in similar range for all the study years. Out of total samples, over 6 years, 8.5% resistance rate has been detected (Table 1).

In new suspected patients, the positive rate of MTB has been increased over 6 years of period. In 2018, it was 21.6% which has risen to 34.5% in 2023. Rate of positivity was decreased in the years 2020–2021. Rate of diagnosis of rif resistance in new MTB patients has decreased by the years from 15%, that is, 43 out of 289 positive patients to 11%, that is, 18 out of 187 (Table 2).

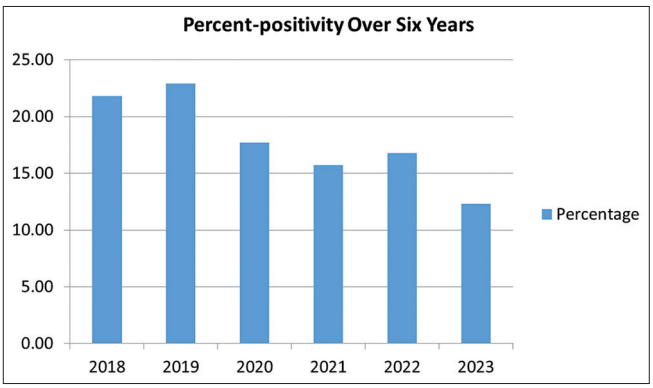

Figure 1: Visual representation of distribution of total samples tested by CBNAAT (GeneXpert) in years from 2018 to 2023

These were the patients having a relapse of MTB after complete treatment or the patients lost during the treatment of MTB. They were detected positive for MTB after repeat testing. The positivity rate and rif resistance rate of such cases have shown up and down course over 6 years, minimum in 2019, 2020–2021, and a maximum in 2022 (Table 3).

A significant decrease was observed in MTB positivity in people living with human immunodeficiency viruses (PLHIV). In 2018, 40 were MTB positive out of 123 HIV-positive patients, that is, 32.5%. However, the MTB positivity rate among PLHIV has been significantly decreased in 2022 to 6.7%, that is, 11 out of 165 (Table 4).

DISCUSSION

India has been grappling with TB for decades. Despite various control efforts, it continues to be a major public health concern. The first national TB control program was launched in India in 1962.

In the present study, as we can see, there is a gradual decrease in the incidence of MTB. In 2018, it was 21.8% which declined to 12.3% in 2023. There is a 9.5% reduction in the period of 6 years (Figure 1). According to the WHO TB data analysis, there has been 16% reduction in TB cases from the year 2015 to 2022.[9] A study published in 2021 also deduced the decrease in TB cases in three decades (1990–2019).[10] Another study published in 2023 also showed decrease in TB cases by 11.2% between the years 2020 and 2021.[11] India is a large country, with large population, which gives rise to challenges, such as lack of awareness, poor infrastructure, drug resistance, poor notification, and overall negligence. Despite these challenges, there has been reduction in rate of TB in the country. It can be attributed to prompt diagnosis, treatment, and prevention of infection which signifies the effective TB control programs in the nation. Strengthening TB control programs, wider access to rapid diagnosis, and provision of effective treatment will lead to successful control of TB globally.

MDR-TB/rif-resistant TB (RR-TB) has emerged due to human intervention and emerging due to poor management of TB and is a threat to TB control. Despite significant efforts, there is a substantial increase in the number of cases, which is estimated to comprise 27% of the world's cases.[12] In the present study, the rate of DR-TB is seen to be up and down every year, however, rif resistance in overall increasing, as it was 9.4% in 2018 while 15.6% in the year 2022 (Table 1). DR-TB has been a constant threat to successful control of TB. In a study published in 2021, rate of rif resistance by GeneXpert was found out to be 21.6%.[13] A similar study carried out in Mumbai in tertiary care hospital in 2016, showed 30.4% rif resistance.[14] Rif resistance in newly diagnosed patient was 15% in 2018 and 10% in 2023 (Table 2), it may be the result of early and appropriate diagnostic strategies and policies for prevention of infection. In a study published in 2020, rate of rif resistance among new patients was 3.1%.[15] Rif resistance in previously diagnosed and treated patients is the matter

Table 1: Rate of rifampicin resistance among total positive samples for MTB

Year	Positive	Rif-resistant (%)
2018	772	82 (9.4)
2019	877	69 (10.6)
2020	650	42 (8.2)
2021	510	33 (5.8)
2022	568	68 (15.6)
2023	437	30 (6.9)
Total	3814	324 (8.5)

MTB: *Mycobacterium tuberculosis*

Table 2: Positivity and rif resistance in newly tested patients

Year	Tested (new patients)	Positive (%)	Rif-resistant (%)
2018	1338	289 (21.6)	43 (14.9)
2019	711	158 (22.2)	19 (12.02)
2020	1143	150 (13.1)	16 (10.7)
2021	742	101 (13.6)	9 (8.9)
2022	947	232 (24.5)	24 (10.3)
2023	484	167 (34.5)	18 (10.8)
Total	5365	1097 (20.4)	129 (11.8)

Rif: Rifampicin

Table 3: Repeat positivity and rifampicin resistance in previously diagnosed patients

Year	Tested (Prev. patients)	Positive (%)	Rif-resistant (%)
2018	174	57 (32.8)	11 (19.3)
2019	0	0 (0)	0 (0)
2020	13	1 (7.7)	0 (0)
2021	49	6 (12.2)	0 (0)
2022	42	24 (57)	13 (54.2)
2023	23	10 (43.5)	2 (20)
Total	301	98 (32.6)	26 (26.5)

Rif: Rifampicin

Table 4: MTB positivity and rifampicin resistance in people living with HIV

Year	Tested (PLHIV)	Positive (%)	Rif-resistant (%)
2018	123	40 (32.5)	3 (7.5)
2019	26	4 (15.4)	0 (0)
2020	1680	6 (0.36)	0 (0)
2021	192	22 (11.5)	1 (4.5)
2022	198	24 (12.12)	3 (12.5)
2023	165	11 (6.7)	1 (9)
Total	2384	107 (4.5)	8 (7.5)

Rif: Rifampicin, PLHIV: People living with human immunodeficiency viruses, MTB: *Mycobacterium tuberculosis*

of concern. They may be defaulters, or relapse cases; they show resistance in 54% of cases in 2022 (Table 3). In a study published in 2020, rif resistance in previously diagnosed patients was 37%.[15] The prevalence of RR-TB among new and previously treated was 7.6% and 27.4% in a study done in 2019.[16] Prevalence of rif resistance among various studies is variable, which may be attributed to geographical variations. To prevent such cases of TB, early diagnosis and appropriate, timely and complete treatment of DR-TB is crucial.[17] 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).[18]

TB is a serious threat, especially for PLHIV. PLHIV are more likely to become sick with TB than others. Worldwide, TB is one of the leading causes of death among PLHIV. Rate of TB in PLHIV has reduced from 32.5% in 2018 to 6.7% in 2023 in the present study which shows reduction by 25.8% (Table 4). In a study done in year 2020, there was 12.4% decrease in rate of TB in PLHIV over a period of 4 years.[19] Similarly, in a study of year 2023, the prevalence of TB among PLHIV was 6%.[20] This decrease in TB patients among PLHIV must be attributed to the well-functioning NACO and ART treatment programs. Raised CD4 count in PLHIV helps in preventing TB infection among them. Rif resistance among PLHIV can also be raised, that is, 12.5% in 2022 (Table 4). Similar rif resistance was seen in PLHIV in studies done in year 2014 and 2019, that is, 11.4% and 12.5%, respectively.[21,22]

Limitations of the study

Geographical limitation- the study is done in a specific region, the results may vary if the region is changed.

CONCLUSION

Government of India is making a lot of efforts to bring down the problems associated with TB through revised plans and their implementation across the country. This study shows that the overall incidence of TB has decreased in the past 6 years in the study setting. The acquired drug resistance was seen in 32.6% cases. The study found an overall decrease in the incidence of TB in PLHIV.

ACKNOWLEDGMENT

We are thankful to our technicians Mrs. Swati Dixit, Mr. Pankaj Ade, and Mr. Pramod Bhalchim for carrying out the tests and keep in maintaining the proper turnaround time for TB testing. We would also like to thank department of pediatrics, department of chest medicine, and department of medicine for sending samples for TB testing.

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Authors' Contributions:
TO- Design, definition of intellectual content, data analysis, data acquisition, manuscript preparation; **PS**- Definition of intellectual content, data analysis, manuscript editing; **SP**- Concept, manuscript editing; **VG**- Manuscript review; **SD**- Manuscript review; **RK**- Manuscript review, guarantor.

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Source of Support: Nil, **Conflicts of Interest:** None declared.