Original Article

Profile of drug-resistant tuberculosis in Western Maharashtra

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Abstract

Context: Drug-resistant tuberculosis (TB) strains have evolved mainly due to incomplete or improper treatment of TB patients and are one of the hurdles in controlling TB problem. It is better to understand the magnitude and comorbidities associated with drug-resistant TB. **Aim and Objectives:** (1) To study some of the sociodemographic profile and history of TB treatment of drug-resistant TB cases. (2) To study their drug-resistance pattern and their comorbidity profile. **Settings and Design**: It was a record-based study descriptive, cross-sectional study of drug-resistant TB cases that were referred to State TB Training and Demonstration Centre (STDC). **Materials and Methods:** The data were collected by means of use of TB patient treatment register of those tested at STDC during first two quarters of the year 2012 (from January to June 2012). Sputum samples of all the cases were subjected to concentrated microscopy, and all positive samples were tested by GeneXpert and Line Probe Assay for drug susceptibility testing (DST) for isoniazid and rifampicin. **Statistical Analysis:** The findings were analyzed with Epi info7, using the mean, standard deviation, Chi-square test. **Results:** The mean age of the patients was 35.65 ± 13.59 years, majority 71.87% were males. The majority of patients 72.91% had the previous history of TB. A majority 68.75% of the patients had acquired drug resistance, and 73.95% of cases were suffering from multidrug-resistant TB. A total of 28.13% patients had self-reported comorbidity. A majority 62.5% had failure as the treatment outcome for the current episode of TB and mortality was seen in 12.5% cases. **Conclusions:** Majority had failure as a treatment outcome due to advanced disease status or late diagnosis. Rapid diagnosis and DST for first- and second-line drugs will greatly improve the clinical outcome.

Keywords: Acquired drug resistance, initial drug resistance, multidrug-resistant tuberculosis, tuberculosis

Introduction

Drug resistance has emerged as a major problem in the management of pulmonary tuberculosis (TB). If a person has drug-resistant TB, it means that their illness will not respond to at least one of the main TB drugs. Not only has the incidence of drug resistance gone up, but there have also been reports that it is more common in HIV-positive individuals, and vice versa.[1] The two main causes for the development of drug resistance are nonadherence to prescribed therapy and use of inadequate treatment regimens. Important risk factors for drug resistance include previous treatment with antitubercular drugs and contact with a person who has infectious drug-resistant TB.[2]

The emergence and spread of multidrug-resistant TB (MDR-TB) is threatening to destabilize global TB control. The prevalence of MDR-TB is increasing throughout the world both among new TB cases as well as among previously-treated ones. Of the 480,000 cases of MDR-TB estimated to have occurred in 2014, only about a quarter of these 123,000 were detected and

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reported. Globally, an estimated 3.3% of new TB cases and 20% of previously treated cases have MDR-TB, a level that has changed little in recent years. In 2014, an estimated 190,000 people died of MDR-TB. Globally, only 50% of MDR-TB patients were successfully treated.[3] In India, in the year 2015, it was observed that MDR-TB among notified new pulmonary TB patients was 2.2%, and that of among the retreatment cases was 15%.[4] However, even if there is such a small percentage of cases it still translates in India into large absolute numbers. In India, in 2015, a total of 339,478 drug-resistant TB suspects were tested, and 28,876 MDR TB patients were detected. In 2015, in Maharashtra, a total of 45,829 drug-resistant TB suspects were tested, and 5302 MDR TB patients were detected while in Western Maharashtra 521 cases were registered for Cat IV treatment.[5] It has been proved that patients infected with strains resistant to rifampicin (RIF) will experience a higher failure rate with short-course 6-month chemotherapy. Detection of resistance to RIF serves as a reliable proxy for MDR-TB.[6]

MDR-TB patients, who show resistance to both isoniazid (INH) and RIF require treatment for at least 24 months and side effects due to drugs are more.[7] However, despite this long and costly treatment, a considerable number die of their disease and many others have to endure the active and destructive form of TB. Nearly, one in six deaths among people aged 15–49 is due to TB. Furthermore, the public health danger posed by a patient with infectious MDR-TB cannot be underestimated. Identifying the drug resistance is one of the important aspects in the assessment of TB epidemiologic trends and TB control planning.[8] Funded by World Bank through Central TB Division of Government of India, the referral laboratory, State TB Training and Demonstration Centre (STDC) is the second such facility in the State of Maharashtra after Nagpur has been established in 2012.

Primary health-care providers play a crucial role in national and global TB control. Primary care physicians are at the forefront of efforts for early recognition of MDR-TB suspects. Therefore, it is important to make them aware of the profile and characteristics of MDR TB cases so that they can suspect early and prevent its further progression and spread in the community by its early referral. It is better to understand the magnitude and comorbidities associated with drug-resistant TB. Hence, this study was planned to know the epidemiological factors associated with drug-resistant TB so that immediate and vigorous preventive and control measures can be planned.

Aim and objectives

- To study some of the socio-demographic profile and history of TB treatment of drug-resistant TB cases
- To study their drug-resistance pattern
- To study their comorbidity profile.

Materials and Methods

It was a descriptive, cross-sectional study of pulmonary drug-resistant TB cases that were referred to STDC. STDC services to Pune, PCMC, Solapur, Satara, Kolhapur, and Sangli and is a reference laboratory (IRL) that performs drug susceptibility testing (DST) for *Mycobacterium tuberculosis*. All the MDR suspected cases from DTOs were referred to STDC. Besides ascertaining MDR cases through a culture sensitivity test, the center aims to provide free treatment. The data were collected by means of use of TB patient treatment register of those tested at STDC during first two quarters of the year 2012 (from January to June 2012). Sputum samples of all the cases were subjected to concentrated microscopy, and all positive samples were tested by GeneXpert and Line Probe Assay for DST for INH and RIF at STDC. All the data regarding to personal characteristics, previous TB treatment details, associated comorbidities were collected from the treatment register and analyzed. As this was a record-based study, informed consent form the patients were not taken. Institutional ethical clearance was taken for this study.

Operational definitions

1. MDR-TB: Resistance to both INH and RIF was defined as MDR[9]
2. Initial resistance: Initial resistance is the resistance in patients who give a history of never having received chemotherapy for TB in the past[9]
3. Acquired resistance: Has often been used with the implication that resistance has developed due to exposure of the strain to anti-TB drugs.[9]

All other definitions for the outcomes for RR-TB/MDR-TB patients treated using second-line treatment.[10]

The data available from the TB register were collected, and the findings were analyzed with EPI INFO™ version 7 (Centers for Disease Control and Prevention, Atlanta, Georgia (USA)), using the mean, standard deviation (SD) Chi-square test for statistical significance assessments. $P < 0.05$ was identified as statistically significant.

Results

A total of 352 suspected patients were tested at STDC during January 2012 to June 2012 (6 months period). Of these, 96 (27.3%) patients diagnosed with drug-resistant TB and were included in the study. All (96) were suffering from pulmonary TB. The mean age of the patients was 35.65 years with SD ± 13.59 (minimum age was 12 years and maximum age was 65 years). A maximum number of cases were seen 31–50 years age group, i.e., 40 (41.66%) followed by <30 years age group [Table 1]. Majority 69 (71.87%) were males. However, it was not statistically significant ($P > 0.05$).

The mean weight of drug-resistant cases at the start of treatment was 43.27 kg with SD ± 10.71, minimum being 14 kg. Totally, 11 (11.45%) cases were having weight <30 kg.

A majority of the patients with drug-resistant TB had acquired drug resistance, i.e., 66 (68.75%) [Table 2]. DST results showed

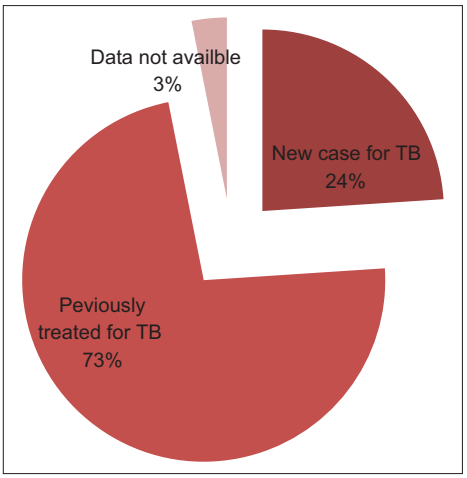

Figure 1: History of tuberculosis

that in a majority of cases, i.e., 71 (73.95%), mycobacteria with RIF resistance also had INH resistance which means that they were suffering from MDR-TB.

One of the most common abnormalities detected on X-ray was fibrocavitary lesions in 37 (38.54%). An equal number 37 (38.54%) of patients had multiple X-ray abnormalities such as a combination of some of the following lesions-infiltration, consolidation, cavitation, pleural effusion, lung abscess, fibrosis, calcification, collapse, lung destruction, collapse, and pneumothorax while 2 (2.1%) no abnormality on X-ray was detected.

A total of 27 (28.13%) patients had a self-reported comorbidity which included 6 (29.62%) patients with diabetes mellitus and 2 (7.40%) patients with diabetes mellitus and hypertension, 3 (14.81%) patients who were HIV positive and 1 (3.70) had HIV with anemia, 1 (3.70%) patient was suffering from hypothyroidism and one patient had hypothyroidism with hypertension and one each had piles, meningitis, ischemic heart disease, and fibroadenoma of breast. Out of 9 (33.33%) patients who reported substance abuse, 5 (55.55%) reported alcohol consumption, 1 (11.11%) tobacco use, and 3 (33.34%) both tobacco and alcohol use.

A total of 23 (23.95%) patients were new cases of TB and 70 (72.91%) had been previously treated for TB [Figure 1].

The data on the previous history of TB were not available for 3 (3.12%) patients.

70 patients with a history of TB contributed to a total of 94 episodes of TB. In 87 (92.5%) episodes, the patients had sought treatment from government agencies while in 7 (7.5%) episodes the treatment had been sought from private sector [Table 3].

Among the 96 patients with MDR-TB, a majority 60 (62. 5%) had failure as the treatment outcome for the current episode of TB. Among the 23 new cases 14 (60.86%) and among the

Table 1: Age and sex wise distribution of drug-resistant tuberculosis cases

Age in years	Male, *n* (%)	Female, *n* (%)	Total, *n* (%)
11-30	25 (36.23)	13 (48.15)	38 (39.58)
31-50	30 (43.47)	10 (37.04)	40 (41.66)
>50	14 (20.30)	4 (14.81)	18 (18.76)
Total	69 (71.87)	27 (28.13)	96 (100.00)

χ^2=1.2, df=2, P>0.05

Table 2: Type of resistance among the drug-resistant tuberculosis cases

Type of resistance	*n* (%)
Initial drug resistance	30 (31.25)
Acquired drug resistance	66 (68.75)
Total	96 (100.00)
Resistance to rifampicin	25 (26.05)
Resistance to isoniazid and rifampicin (MDR-TB)	71 (73.95)
Total	96 (100.00)

MDR-TB: Multidrug-resistant tuberculosis

Table 3: Previous history of tuberculosis among drug-resistant tuberculosis cases

	n (%)
Previous history of TB treatment	
Yes	70 (72.91)
No	23 (23.95)
Data not available	3 (3.12)
Source of treatment for past episodes of TB	
Government health facility	87 (92.5)
Private health facility	7 (7.5)
Treatment outcome of current episodes of TB	
Cured or treatment completed	16 (16.7)
Defaulted	14 (14.6)
Failure	60 (62.5)
Still on second line drugs	3 (3.1)
Unknown	3 (3.1)
Source of treatment for current episode of TB	
Government health facility	91 (92.5)
Private health facility	5 (7.5)

TB: Tuberculosis

70 previously treated cases 44 (62.8%) cases had failure as the treatment outcome. In the present study 12 (12.5%) died, all these patients had failure as their treatment outcome. Out of these, 11 (91.6%) were previously treated with anti-TB drugs, 7 (58.33%) have associated comorbidities and 5 (41.6%) had a history of alcoholism. Majority 91 (92.5%) patients had been receiving treatment from the government sector. Out of the five receiving treatment from the private sector, two were already on second-line regimens.

Discussion

Anti-TB drugs are a two-edged sword while they destroy pathogenic *Mycobacterium tuberculosis*, they also select for drug-resistant bacteria against which those bugs are then ineffective. All 96 (100%) were suffering from pulmonary TB.

In a study from Ahmadabad, Bhatt *et al*.[8] observed that around 98.8% had pulmonary TB. The mean age of the patients was 35.65 years. Maximum number of cases was seen in the young age group. More than two-third (71.87%) of cases were males. Similar findings were found in other study[8] while in the study conducted in Kashmir[11] the mean age of the patients was 39 years. One of the striking findings in this study is the high level of drug resistance among younger patients indicating exposure to drug-resistant cases. The gender difference in TB is well known, and low ratio of female cases should not be a cause for alarm. Accessibility and utilization difficulties of health facilities in the study area also could be the reasons for this. One more reason behind males having higher rates of MDR-TB than females might be due to vulnerability because of their social contacts, exposure to dust, smoking, and consumption of alcohol. Studies in Russia[12,13] showed substance dependence were associated with drug resistance.

A majority, i.e., 66 (68.75%) of the patients had acquired drug resistance, and 71 (73.95%) of cases were suffering from MDR-TB. The 70 (72.91%) patients had a history of TB treatment and majority of the time the patients had sought treatment from government agencies. In a study by Deoskar *et al*.[14] they found the MDR-TB in 65% of the cases and acquired drug resistance in 33.3% of the cases. The relationship between history of receiving anti-TB treatment and drug resistance has been clearly described in several studies.[7,14,15] This may indicate that acquired drug resistance could be a result of previous noncompliance. An alternative reason could be the transmission of TB strains from individuals infected with MDR-TB. Only RIF resistance was seen in 26% cases. The emergence of RIF resistance after introduction of short-term chemotherapy has been noted by other workers also.

A total of 27 (28.13%) patients had a self-reported comorbidity, major comorbidity being diabetes mellitus (29.62%), substance abuse 9 (33.33%), and 3 (14.81%) HIV infection. In a study conducted by Elmi *et al*.[7] found diabetes mellitus in 26.7% of MDR-TB cases and HIV infection in 5.7% of cases while in a study conducted in Kashmir found that 7.6% have diabetes and 1.9% have HIV infection. In a study in Ahmadabad, it was noticed that 57% patients were addicted to tobacco and or alcohol.

One of the most common abnormalities detected on X-ray was fibrocavitary lesions in (38.54%). In a study,[7] they found that cavitary lesions on X-ray were seen in 89.5% of the cases while in other study[16] cavitary lesions were present in 63.4% of cases and the presence of cavities on chest radiography were independent risk factors for the development of MDR-TB.

Drug resistance is associated with a higher risk of treatment failure and relapse. Mortality in patients with MDR-TB is also higher. A majority 62.5% had failure as the treatment outcome for the current episode of TB. Among the 23 new cases 14 (60.86%) and among the 70 previously treated cases 44 (62.8%) cases had failure as the treatment outcome. The treatment success rate was seen in only 16.7% cases which was much lower than the worldwide reported success of 48%.[17] This might be due to late diagnosis of these cases as MDR-TB diagnosis facility was not available in this area before 2012.

In the present study, mortality was in 12 (12.5%), all these patients had failure as their treatment outcome. Out of these, 11 (91.6%) were previously treated with anti-TB drugs, 7 (58.33%) have associated comorbidities and 5 (41.6%) had a history of alcoholism. Many patients had unsuccessful outcomes may be because these patients may also have had resistance to one or more second-line anti-TB drugs. 14.6% of patients defaulted from treatment.

This study was conducted on small sample size of 96 cases, and without a comparison group, so the future studies involving large samples are needed to learn more about resistance pattern and outcome of MDR-TB.

Limitations

1. The study being retrospective in nature and has its inherent limitations of record review studies. Because of the retrospective nature of the study and because all of the source records and reports were not designed for study purposes, some information may be incomplete or contain errors
2. Follow-up time was limited to the completion of treatment. Although this time frame is sufficient for documenting surveillance-based treatment outcomes, it may not be sufficient to assess long-term clinical outcomes
3. Second-line drug susceptibilities were not considered when determining treatment regimens; it is possible that some patients had unsuccessful outcomes because of ineffective treatment owing to resistance to one or more second-line anti-TB drugs.

Conclusions

MDR-TB seen in young age group and among males. The acquired drug resistance was seen in 68.75% cases and MDR resistance was seen in 73.95% cases. A total of 27 (28.13%) patients had self-reported comorbidity; common was diabetes and substance abuse. Most of the MDR cases had a previous history of TB and majority had failure as a treatment outcome due to advanced disease status or late diagnosis. Rapid diagnosis and DST for first- and second-line drugs will greatly improve the clinical outcome. Proper management of MDR-TB relies on early recognition of such patients. Hence, each and every suspect of MDR-TB should be referred immediately and screened to start early second-line treatment so that success of treatment will be increased.

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Conflicts of interest

There are no conflicts of interest.

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