Profile Of Drug-Resistant Tuberculosis In A Tertiary Health-Care Centre In Western India

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Abstract:

Background

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 Tuberculosis (TB) problems. It is better to understand the magnitude and comorbidities associated with drug-resistant TB.

Aim

(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

(3) To study the associated comorbidities

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

Out of 710 suspected cases of tuberculosis who were confirmed and managed by standard Revised National Tuberculosis Control Programme (RNTCP) protocol at our Institute, 107 suspected cases of Drug Resistant Tuberculosis were referred to STDC. The data were collected by means of use of the TB patient treatment register of those tested at STDC from January 2018 to December 2018. 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.

Results:

The mean age of the patients was 35.45 ± 12.52 years, majority 71.96% were males. The majority of patients 74.58% had the previous history of TB. 67.29% of the patients had acquired drug resistance, and 75.71% of cases were suffering from multidrug-resistant(MDR) TB. A total of 29.90% patients had self-reported comorbidity. 61.68% had failure as the treatment outcome for the current episode of TB and mortality was seen in 13.23% cases.

Conclusion:

Majority had failure as a treatment outcome due to advanced disease status or late diagnosis. Rapid diagnosis and Drug Sensitivity Test 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

1) Nonadherence to prescribed therapy and

2) 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 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]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.[5]MDR-TB patients, who show resistance to both isoniazid and rifampicin require treatment for at least 24 months and side effects due to drugs are more.[6] 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.[7]

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.

Materials and methods:

It was a descriptive, cross-sectional study of pulmonary drug-resistant TB cases that attended our Institute.A total of 710 suspected cases of tuberculosis were tested, confirmed and managed by standard RNTCP protocol at our Pulmonary Medicine Department, Sheth V.S General and Sheth C.M Hospital, Smt. N.H.L Municipal Medical College, Ahmedabad, Gujarat, a Tertiary Care Centre in Western India. Out of them 107 suspected cases of Drug Resistant Tuberculosis were referred to STDC (State TB Training And Demonstration Centre), Ahmedabad. STDC at Civil Hospital, B.J Medical College, Ahmedabad is a reference laboratory (IRL) that performs drug susceptibility testing (DST) for *Mycobacterium tuberculosis*.All the MDR suspected cases from DTOs (District TB Officers) 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 the centre. 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 personal characteristics, previous TB treatment details, associated comorbidities were collected from the treatment register and analyzed.

Operational Definitions:

1. **MDR-TB**: Resistance to both INH and RIF was defined as MDR[8]

2. **Initial resistance**: Initial resistance is the resistance in patients who give a history of never having received chemotherapy for TB in the past[8]

3. **Acquired resistance**: Has often been used with the implication that resistance has developed due to exposure of the strain to anti-TB drugs.[8]

All other definitions for the outcomes for RR-TB/MDR-TB patients treated using second-line treatment.[9]

Results:

A total of 710 confirmed cases were managed at our institute . Of these, 107 (15.07%) patients diagnosed with drug-resistant TB were confirmed as MDR cases by STDC and were included in the study. All (107) were suffering from pulmonary TB. The mean age of the patients was 35.45 years with SD ± 12.52 (minimum age was 12 years and maximum age was 70 years). A maximum number of cases were seen in 31–50 years age group, i.e., 43 (40.18%) followed by < 30 years age group [Table 1]. Majority 77 (71.96%) were males.

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

Age in years	Male	Female	Total, %
11-30	26	13	39 (36.44%)
31-50	31	12	43 (40.18%)
>50	20	05	25(23.36%)
Total	77(71.96%)	30(28.04%)	107 (100.00%)

A majority of the patients with drug-resistant TB had acquired drug resistance, i.e., 72 (67.29%) [Table 2]. DST results showed that in a majority of cases, i.e., 81(75.71%), mycobacteria with RIF resistance also had INH resistance which means that they were suffering from MDR-TB.

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

Type of resistance	n (%)
Initial drug resistance	35 (32.71%)
Acquired drug resistance	72(67.29%)
Total	107(100.00%)
Resistance to rifampicin	26(24.29%)
Resistance to isoniazid and rifampicin (MDR-TB)	81 (75.71%)
Total	107(100 %)

One of the most common abnormalities detected on X-ray was fibro-cavitary lesions in 39 (36.44%). 41 (38.72%) 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 5 (4.67%) no abnormality on X-ray was detected.

A total of 36 (29.90%) cases had a self-reported comorbidity which included 6 (5.88%) cases with diabetes mellitus and 3 (2.80 %) with diabetes mellitus and hypertension, 4 (3.73%) who were HIV positive and 3 (2.80%) had HIV with anemia, 2 (1.87%) cases was suffering from hypothyroidism and 2(1.87%) had hypothyroidism with hypertension and others had piles, meningitis, ischemic heart disease, and fibroadenoma of breast. Out of 40 patients who reported substance abuse, 7 reported alcohol consumption, 25 tobacco use, and 15 both tobacco and alcohol use.

A total of 25 (23.52%) patients were new cases of TB and 80 (74.58%) had been previously treated for TB.The data on the previous history of TB were not available for 2 (1.87%)-patients.

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

	N (%)
Previous history of TB treatment	
Yes	80 (74.58%)
No	25 (23.52%)
Data Not Available	2 (1.87%)
Treatment outcome of current episodes of TB	
Cured/ Completed Treatment	18(16.82%)
Defaulted	15(14.01%)
Failure	66(61.68%)
Still on 2nd line drugs	6(5.6%)
Unknown	2(1.87%)

A total of 25 (23.52%) patients were new cases of TB and 80 (74.58%) had been previously treated for TB.The data on the previous history of TB were not available for 2 (1.87%)-patients.

Among the 107 patients with MDR-TB, a majority 66 (61.68%) had failure as the treatment outcome for the current episode of TB. Among the 25 new cases 15 (14.31%) and among the 80 previously treated cases 66 (61.68 %) cases had failure as the treatment outcome. In the present study 14 (13.23%) died, all these patients had failure as their treatment outcome. All the cases had been receiving treatment from the government sector.

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 107 (100%) were suffering from pulmonary TB. In a study from Ahmedabad, Bhatt *et al.*[7] observed that around 98.8%had pulmonary TB. The mean age of the patients was 35.45years. Maximum number of cases was seen in the young age group. Majority (71.96 %) of cases were males. Similar findings were found in another study[7] while in the study conducted in Kashmir[10] 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 the 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[11,12] showed substance dependence was associated with drug resistance.

A majority, i.e., 72(67.29%) of the patients had acquired drug resistance, and 81 (75.71%) of cases were suffering from MDR-TB. In a study by Deoskar *et al.*[13]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.[6,13,14] 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(24.29%) cases. The emergence of RIF resistance after introduction of short-term chemotherapy has been noted by other workers also.

A total of 36 (29.90%) patients had a self-reported comorbidity, major comorbidity being diabetes mellitus 6 (5.88%), and HIV infection 4(3.73%). In a study conducted by Elmi *et al.*[6] 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 Ahmedabad, it was noticed that 57% of patients were addicted to tobacco and or alcohol.

One of the most common abnormalities detected on X-ray was fibrocavitary lesions in 36.44% cases. In a study,[6] they found that cavitary lesions on X-ray were seen in 89.5% of the cases while in other study[15] 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 66(61.68%) had failure as the treatment outcome for the current episode of TB. Among the 25 new cases 15(14.01%) and among the 80 previously treated cases 66 cases

had failure as the treatment outcome. The treatment success rate was seen in only 16.82% cases which was much lower than the worldwide reported success of 48%.[16] 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 14 (13.23%), all these patients had failure as their treatment outcome. Out of these, 7 were previously treated with anti-TB drugs, 4 have associated comorbidities and 3 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. 14.01 % of patients defaulted from treatment.

This study was conducted on a small sample size of 107 cases, and without a comparison group, so future studies involving large samples are needed to learn more about resistance pattern and outcome of MDR-TB.

Conclusions:

MDR-TB is seen in young age groups and among males. The acquired drug resistance was seen in 72 (67.29%) cases and MDR resistance was seen in 75.71% cases. 29.90% 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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