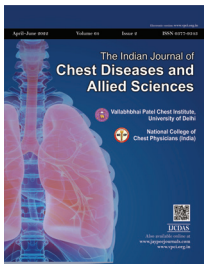
ORIGINAL ARTICLE

Clinical Profile, Adverse Drug Reaction, and Outcome of Category V Patients at a Drug-resistant Tuberculosis Center, Mumbai



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Parikshit Thakare[1], Ketaki Utpat[2], Unnati Desai[3], Jyotsna M Joshi[4]

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Abstract

Background: Drug regimens for the treatment of drug-resistant tuberculosis (DR-TB) are composed of salvage drugs to which a patient has never been exposed to previously.

Methods: A retrospective observational study was conducted in a DR-TB Center attached to a medical college in a metropolitan city using the database of category V patients (n = 100) who were prediagnosed and referred. The clinical records of the patients were reviewed for demographic data, history, sputum examinations, co-morbidities, and adverse drug reactions (ADRs). The therapy outcomes were assessed as per Revised National Tuberculosis Control Programme (RNTCP) guidelines.

Results: Their mean age was 29.1 years; there were 57 males. Mean body weight was 41.8 kg. Pediatric patients (age 12–17) constituted 13%. All the patients had pulmonary TB. Of the 100 cases, 80 were Category IV failure; 5% were defaulters of Category IV; and 15% were treated with second-line drugs adequately in private. Durg-susceptibility test (DST) showed extensively drug-resistant TB (XDR-TB) in 63 and pre-XDR-TB in 37 patients. The outcomes of Category V treatment were cure (7%), died (33%), failed on therapy (4%), transferred out (16%), lost to follow-up (2%), and still on the therapy (35%). Various comorbidities were present in 25% patients. ADRs were seen in 44%, and peripheral neuropathy (18%) was the most commonly observed ADR.

Conclusions: DR-TB patients were younger and males were more affected. Mortality of Category V regimen was high (33%). Most common comorbidities were anemia and hypothyroidism. Adverse reactions were common (44%); ADR peripheral neuropathy being the most common.

Keywords: Adverse drug reaction, Category V, Drug-resistant tuberculosis.

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Abbreviations used in this Article

DR-TB = Drug-resistant tuberculosis; ADR = Adverse drug reactions; RNTCP = Revised National Tuberculosis Control Programme; DST = Durg-susceptibility test; MDR-TB = Multidrug-resistant TB; XDR-TB = Extensively drug-resistant TB; FQ = Fluoroquinolone; AM = Aminoglycosides; ATT = Anti-TB treatment

Introduction

Treatment of drug-resistant tuberculosis poses a challenge to physician. Multidrug-resistant TB (MDR-TB) is caused by *Mycobacterium tuberculosis* resistant to at least isoniazid (H) and rifampicin (R). Preextensively DR-TB (pre-XDR-TB) refers to the disease caused by MDR-TB strains that harbor additional resistance to either any fluoroquinolone (FQ) or any of the injectable second-line aminoglycosides (AM). While XDR-TB refers to MDR-TB with additional resistance to both FQ and AM.[1] Treatment failures of second-line anti-TB treatment (ATT) have serious implications, like a magnification of drug resistance, continued spread of infection, mortality, and morbidity. Drug resistance is a man-made phenomenon. However, it should be stressed that MDR-TB is essentially a man-made phenomenon.[2] Lack of awareness among treating physicians, improper treatment regimes, poor adherence, and drug toxicities are the prime culprits contributing to its occurrence.[3–5] The treatment of MDR-TB is challenging owing to its delayed diagnosis, prolonged duration of therapy, and significant drug toxicities.

[1–4]Department of Pulmonary Medicine, TN Medical College and BYL Nair Hospital, Mumbai, Maharashtra, India

Corresponding Author: Ketaki Utpat, Department of Pulmonary Medicine, TN Medical College and BYL Nair Hospital, Mumbai, Maharashtra, India, e-mail: drketakibarve@gmail.com

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As per the Programmatic Management of Drug Resistant Tuberculosis (PMDT) guidelines of 2012, the patients with MDR-TB are treated with Category IV regimen consisting of second-line drugs. With the widespread use and availability of the second-line drugs, drug resistance to these drugs was also recognized, leading to MDR-TB therapy/Category IV failure.

While there is scarce literature on the clinical profile MDR-TB therapy/Category IV failures, their treatment recommendations also have low-quality evidence. These are treated with a regimen composing of salvage drugs and second-line drugs to which patient has never been exposed to previously, currently known as the category V therapy as per the PMDT guidelines of 2012. This group raises concerns of a future TB epidemic with restricted treatment options and jeopardizes the major gains made in TB control. Hence, we

decided to study the clinical profile of the cases of treatment failures on second line ATT with mention of having a better understanding of this complex problem which will help us in determining causes for the same and avoiding resistance to antituberculous drugs.

Materials and Methods

This retrospective, observational study was conducted in a tertiary care hospital DR-TB Center. Institutional Ethics Committee approval was taken and 100 patients were included in the study. The study was conducted using a database of MDR-TB therapy/category IV failure patients diagnosed at a tertiary care hospital or prediagnosed patients referred to tertiary care hospital's DR-TB Center. Patients diagnosed on the basis of sputum Gene-Xpert, line probe assay, and conventional drug sensitivity testing and who had started treatment since 2012 and those who completed treatment by December 31, 2017, were enrolled in the study. The clinical records of these Category IV failure patients were reviewed for demographic data, history, sputum examinations, co-morbidities, and ADRs. These patients were treated with Category V therapy under RNTCP. The treatment outcomes of these patients were noted. Patients with incomplete records were excluded.

Statistical Analysis

Qualitative data were presented as percentages. Data were analyzed to assess age, sex wise distribution, weight wise distribution, percentages of retreatment, failure, defaulter, cured, died. The drug sensitivity patterns were studied. Percentages of various comorbidities and ADRs were calculated.

Results

Of the total 1,500 cases enrolled under our DR-TB Center, 100 cases were Category IV failures and were included as the study population and consisted of 4% of total cases. Their mean age was 29.1 years; youngest patient was of age 12 years and the oldest was of age 58 years. Most of the patients (37%) were in the age group 21–30 years and second most common were in the age group of 11–20 years (26%). Thirteen patients were in the pediatric age group of 12–17 years. Majority were male patients, with a male to female ratio of 1.32:1.

Majority of the patients were in the weight band of 31–40 kg (38%); second most common weight band was 41–50 kg (34%). The lowest recorded weight was 22 kg and heaviest was 75 kg. The mean weight was found to be 41.8 kg. All had pulmonary TB. As per the drug-susceptibility pattern, 63 patients had XDR-TB while 37 patients had pre-XDR-TB.

Eighty patients were from failed Category IV treatment under RNTCP, while 20 were referred after they had failed treatment from the private setting. All the study patients were given Category V therapy.

Results of the present study revealed cure (7%), died (33%), and failed on therapy (4%). The transferred out patients were 16%, 2% patients were lost to follow-up, and 35% patients were still on the therapy.

Co-morbidities were seen in 49 patients who failed on Category IV treatment. The most common comorbidity was anemia (51%) patients and second most common comorbidity was gastroesophageal reflux disease (30.6%) patients. Hypothyroidism was noted in four (8.1%) patients while human immunodeficiency virus was seen in three patients and diabetes mellitus in two patients.

Adverse drug reactions were observed in 42 patients during the course of treatment. The most common ADRs noted were peripheral neuropathy in 19 (45.3%) patients followed by drug-induced psychosis in six (14.3%) and drug-induced skin rash in five (11.9%). Other ADRs seen were deafness in four (9.5%), hypothyroidism in three (7.1%), drug-induced hepatitis in two, convulsions, pain at injection site, and abdominal pain in one patient each.

Discussion

The emergence of drug resistance is a worrisome problem which poses a formidable challenge to physicians across the world and hinders effective TB control. Treatment of MDR-TB is complex due to the prolonged regimens, expensive drugs, and high incidence of drug toxicities. This, in turn, contributes to poor treatment adherence and further exponential magnification of drug resistance which can have devastating consequences leading to failure of Category IV treatment. In India, MDR-TB has been persistently identified despite successful implementation of RNTCP. In 2013, the average proportion of MDR-TB cases that were actually XDR-TB was 9%. By 2015, some 105 countries had reported at least one case of XDR-TB. On an average, an estimated 9.7% of people with MDR-TB have XDR-TB.[6]

The latest data reported to World Health Organization (WHO)[7] show a treatment success rate for MDR-TB of only 54% for patients starting treatment in 2014. In 8% of the patients, treatment failed, 16% died, 15% were lost to follow-up, and 7% had no outcome information.

As per our study, 4% patients were Category IV treatment failures. This was lower than the 8% failure rate reported globally. Prevalence of XDR-TB was found to be 5.5% among all TB cases and 12% among MDR-TB cases, as per a prospective study from Mumbai, India.[8]

Our observations of younger age group and male gender being involved more frequently were concordant with most other studies.[9,10] In a study,[11] 34/60 (56.7%) MDR-TB patients who had failed Category IV treatment under the National TB Treatment Guidelines were males. In another study,[12] majority (65.1%) of the patients were males and belonged to the age group 18–50 years, similar to our observations. The peak age group in other study[11] was also a decade older compared to our study. In other studies[13,14] also majority patients were in the economically productive age group of 25–54 years.

Mean weight of the patients was 41.8 kg in our study. Other studies[10,15] reported a higher body weight in DR-TB patients.

In our study, comorbidities were present in 25% patients and the most common comorbidity was anemia and hypothyroidism, similar to another study by Lee et al.[16]

In the present study, patients were treated with a standardized treatment regimen known as Category V (or salvage regimen) with a dismal favorable outcomes of only 5% cure and 2% treatment completion. Similar observations were reported in the WHO report where 10% cure was documented. However, many of our patients were still on treatment while the study is being reported.

Adverse drug reactions were found in 42% patients and peripheral neuropathy being the most common. In other studies, peripheral neuropathy was encountered in 13%,[17] 18.8%,[18] and 25%[19] patients with DR-TB.

Conclusions

Our study highlights the urgent need and importance of identifying, screening, optimally treating, and supervising therapy in patients with DR-TB early, in addition to programmatic advancements in the management of DR-TB.

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