Original Research Article

Role of RNTCP in the management of MDR-TB

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Abstract

Background: MDR-TB is defined as resistance to isoniazid and rifampicin with or without resistance to other drugs. India is one of the countries with largest burden of MDR TB in the world. Second line Anti-tuberculous therapy is now available for patients with MDR-TB under the RNTCP Category IV. But there are many challenges for MDR- TB control in India. This study was done to analyses the RNTCP data for MDR-TB maintained at a TU, in the city of Ahmedabad, Gujarat, and to compare it with the data available in literature. This study also aimed to identify challenges faced while treating MDR-TB and to address the same.

Material and methods: We had retrospectively analyzed 353 patients referred to the TU from the respective Direct Microscopy Center (DMC) with suspicion of MDR-TB during a period of January 2014 to December 2014.

Results: Of the 353 suspected MDR-TB patients referred to the TU, 48 patients (13.597%) were diagnosed to have MDR-TB. Of these 48 patients, 46 patients had pulmonary TB (95.833%) and 2 patients had extra-pulmonary MDR-TB (4.166%). Of the 48 patients, 08 (16.67%) patients were transferred to their respective TU and 40 patients (83.33%) were enrolled for Cat IV from our TU. Of the 40 patients enrolled at our TU, 30 patients (75%) were continuing Category IV at the end of 2014 (25 were on intensive phase and 05 were on continuation phase), 03 patients (7.5%) died during treatment, 01 patient (2.5%) defaulted treatment, 05 patients (12.5%) refused treatment and 01 patient had XDR-TB (2.5%). Of the 40 patients, 05 patients (12.5%) had ofloxacin resistance. No patients had intolerance to any oral or injectable ATT. None of the diagnosed MDR-TB patients had HIV co-infection.

Conclusion: Drug resistance in tuberculosis is a "man-made problem". Anti-TB chemotherapy must be given optimally by (i) ensuring adequate absorption of drugs, (ii) timely diagnosis and management of drug toxicities and (iii) treatment adherence. To ensure that all patients get adequate treatment and to have a close follow-up of defaulters and patients who refuse treatment; we need to strengthen our existing management information system and also incorporate private sectors into our system.

Key words

Multidrug Resistance Tuberculosis (MDR-TB), Extensive Drug Resistance Tuberculosis (XDR-TB), Revised National Tuberculosis Program (RNTCP), Directly Observed Therapy Short- course (DOTS), Tuberculosis Unit (TU).

Introduction

MDR-TB is defined as resistance to isoniazid and rifampicin with or without resistance to other drugs [1]. India is one of the countries with largest burden of MDR TB in the world. As per the WHO Global Report on Tuberculosis 2013, India accounts for 62,000 MDR TB cases out of 3,00,000 cases estimated globally [2]. Data from studies have found MDR- TB levels of 2.2% in new TB cases and 16% in re-treatment cases in the SEAR [3]. MDR-TB is a man-made phenomenon- poor treatment, poor drugs and poor adherence to therapy leads to the development of MDR TB [4]. Neivelle, et al. had described the emergence of drug-resistant TB as the third epidemic [5]. The first WHO endorsed DOTS-Plus program began in 2000. At that time Green Light Committee was established to promote access to high quality second line drugs for appropriate use in TB control programs [4]. The Programmatic Management of Drug Resistant TB (PMDT) services under RNTCP category IV for quality diagnosis and treatment of drug resistant TB (DR TB) were initiated in 2007 in Gujarat and Maharashtra. These services were rapidly up scaled and by the end of 2011, MDR TB services were introduced in all states across the country in a phased manner. The plan to extend drug susceptibility testing to all smear positive retreatment cases upon diagnosis, and all new cases that are smear positive early during first line anti TB treatment by 2012 was also achieved [6]. This was further complemented by a nationwide laboratory scale-up plan developed by the program.

Material and methods

This was a retrospective analysis of the RNTCP data maintained at a TU in the city of Ahmedabad, Gujarat. We had included all suspected MDR- TB patients who were referred to the TU between January 2014 and December 2014. These patients were suspected to have MDR –TB on the criteria laid down by RNTCP [7]. The sputum samples of all suspected MDR-TB cases were sent for detection of rifampicin resistance by Cartridge based Nucleic Acid Amplification Testing (CBNAAT) technique at RNTCP certified Culture and DST laboratory. Sputum of diagnosed MDR-TB patients was sent for ofloxacin and kanamycin drug sensitivity testing to exclude XDR-TB [7]. Patients who were diagnosed to have MDR-TB were then started on Category-IV DOTS, which consists of Intensive Phase (Kanamycin, ethionamide, levofloxacin, cycloserine, pyrazinamide and ethambutol) for 6 months and Continuation Phase (levofloxacin, ethionamide, cycloserine and ethambutol) for 18 months as per RNTCP guidelines [8].

Results

353 suspected cases of MDR-TB were referred to the TU between January 2014 and December 2014. Of these, 351 were adult patients and 2 were pediatric patients. Of the 353 suspected cases, 48 patients were diagnosed with MDR-TB (13.597%). Of these 48 MDT-TB patients, 46 patients had pulmonary TB (95.833%) and 2 patients had extra-pulmonary MDR-TB (4.166%). Of the 48 patients 37 were male

patients (77.08%) and 11 were female patients (22.92%). All (n=48) patients were adults. We did not have any pediatric MDR-TB patients. (**Table – 1**) The prevalence of primary MDR-TB in our study was 29.17% (n=14) and the prevalence of acquired MDR-TB was 70.83% (n=34). (**Figure – 1**)

Of the 48 patients diagnosed to have MDR-TB, 08 (16.67%) patients were transferred out to their respective TU and 40 (83.33%) patients were enrolled for Cat IV from our TU and started on treatment. Thus of a total of 353 suspected patients tested, 40 MDR-TB cases were put on treatment in 2014 at our unit.

We then analyzed the outcomes of these 40 patients at the end of 2014. We had 30 patients (75%) who were continuing Cat IV at the end of 2014, 25 was on intensive phase and 05 were on continuation phase. Of our 40 patients, 03 patients (7.5%) died during treatment, 01 patient (2.5%) defaulted treatment and 05 patients (12.5%) refused treatment. Of the 40 patients, 01 patient had XDR-TB (2.5%).

Outcome of MDR-TB patients (n=40) enrolled for Cat IV (over a period of year 2014) as on 31 Dec 2014 was as per **Table - 2**.

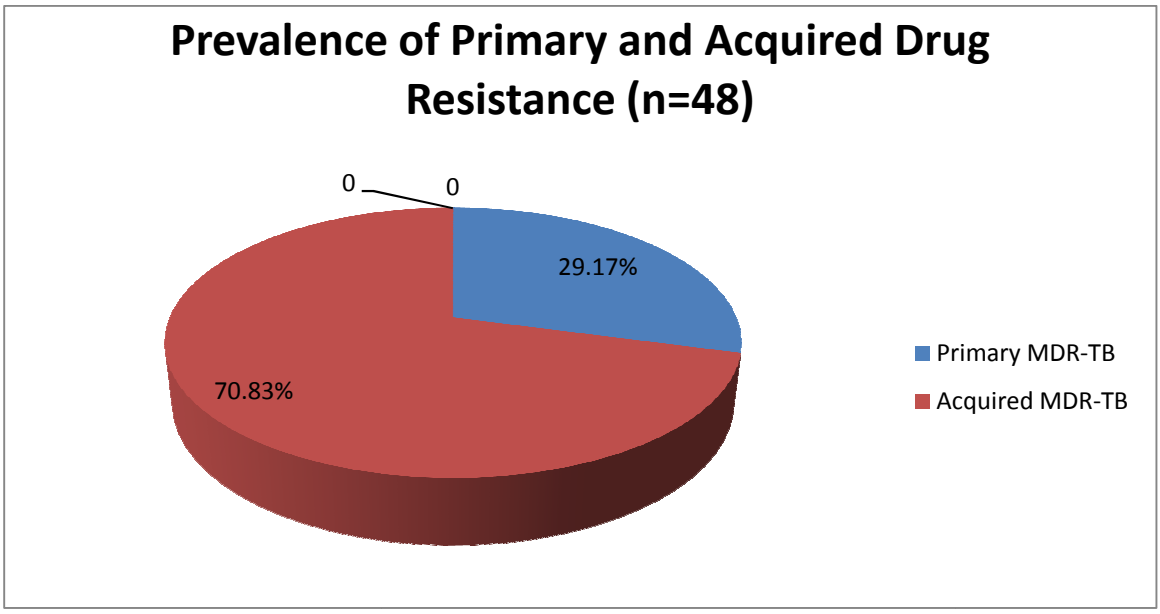
Table – 1: Classification of MDR-TB suspects [3].

Criteria A	**Number of suspects**	**Number diagnosed MDR-TB**
All failures of new TB cases	04	01
Smear +ve previously treated cases who remain +ve at 4th month onwards	03	00
All pulmonary TB cases who are contacts of MDR-TB	01	00
Criteria B		
All smear +ve previously treated pulmonary TB cases at diagnosis	219	28
Any smear +ve FU result in new or previously treated case	Cat I – 63 Cat II- 30	Cat I- 13 Cat II- 04
Criteria C		
All smear negative previously treated pulmonary TB at diagnosis	26	00
HIV TB co-infected cases at diagnosis	05	00
Other		
Extrapulmonary cases (tissue sent for culture and sensitivity)	02	02

Table – 2: Outcome of MDR-TB.

Outcome	Number of patients	Incidence (%)
On Intensive Phase	25	62.5
On Continuation Phase	05	12.5
Died on treatment	03	7.5
Defaulter	01	2.5
Refused Cat IV	05	12.5
Diagnosed XDR-TB	01	2.5

Figure – 1: Prevalence of primary and acquired drug resistance.



Of the 40 patients, 05 patients (12.5%) had ofloxacin resistance and these patients were put on modified Cat IV which consisted of kanamycin, ethionamide, cycloserine, pyrazinamide, ethambutol, moxifloxacin and PAS granules in the Intensive phase. No patients had intolerance to any oral or injectable ATT. Of the 5 cases with HIV TB co-infection none were diagnosed to have MDR-TB.

Discussion

Drug resistance TB poses a major threat to control of TB world- wide. In a study by James P, et al. [9] in 2011; of the suspected DRTB patients, 58.2% patients had MDR-TB as compared to our study (13.597% of the suspected cases had MDR-TB). We also had a very high prevalence of primary MDR-TB cases in our study group. These patients were suspected to have MDR-TB only if they were sputum smear positive during Cat I or at the end of treatment. Also they were not high risk for MDR-TB, i.e. there was no history of contact with MDR-TB cases, no previous history of tuberculosis of ATT consumption and they were all HIV negative. For early diagnosis of these cases, we need to screen all newly diagnosed patients of pulmonary TB for drug resistence, irrespective of their past tuberculosis history. As per the 2014 WHO Global TB Report, of the total MDR-TB cases registered under RNTCP, 48% were successfully treated, 22% died, 18% defaulted and 6% failed treatment [10]. We had a lesser number deaths and defaulters in our study. This could be due to the one year study period. However a significant number of patients in our study refused Cat IV. These are the patients who need a close follow up as they are infectious cases of drug resistant tuberculosis. They need to be counseled adequately and encouraged to take treatment. In case any of these patients have started treatment from private practitioner, he needs to be closely followed up to ensure that he completes treatment. To ensure that all patients get adequate treatment we need to strengthen our existing management information system and also incorporate private sectors into our system. Nikshay, a case based, web enabled system for recording and reporting of TB cases has been developed by Department of IT, Ministry of Communication and Information Technology, Government of India, in collaboration with RNTCP to enable better surveillance and tracking of all TB cases including those in private sector [11].

On an average, an estimated 9.0% of people with MDR-TB have XDR-TB [2]. In our study 1 patient (2.5%) was diagnosed with XDR-TB [12]. In a study by R Ramachandaran, et al. amongst 216 MDR-TB isolates, 52 (24%) were ofloxacin (OFX) resistant [13]. We noted a lower rate of ofloxacin resistance. These patients were given kanamycin, ethionamide, cycloserine, pyrazinamide, ethambutol, moxifloxacin and PAS granules in the Intensive phase. Various adverse effects of ATT have been documented in literature [14], but none of our patients' complaint of any major adverse events necessitating stoppage of drug.

Conclusion

Drug resistance in tuberculosis is a "man-made problem". Anti-TB chemotherapy must be given optimally by (i) ensuring adequate absorption of drugs, (ii) timely diagnosis and management of drug toxicities and (iii) treatment adherence. New classes of anti-TB drugs are needed; but are unlikely to become available soon. It is vital that the 21st century physicians understand the basic principles of TB chemotherapy to ensure efficient use of available drugs to postpone or even reverse epidemics drug-resistant TB.

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