

# Treatment Initiation among Patients with Multidrug Resistant Tuberculosis in Bhopal District, India

Hemant Deepak Shewade<sup>1\*#</sup>, Arun M. Kokane<sup>2#</sup>, Akash Ranjan Singh<sup>2</sup>, Manoj Verma<sup>3</sup>, Malik Parmar<sup>4</sup>, Sanjay Singh Chahar<sup>2</sup>, Manoj Tiwari<sup>2</sup>, Sheeba Naz Khan<sup>3</sup>, Mukesh Nagar<sup>2</sup>, Sanjai Kumar Singh<sup>2</sup>, Pradeep Kumar Mehra<sup>2</sup>, Ajay M. V. Kumar<sup>1,5</sup>

<sup>1</sup>International Union against Tuberculosis and Lung Disease (The Union), South-East Asia Office, New Delhi, India

<sup>2</sup>Department of Community Medicine and Family Medicine, All India Institute of Medical Sciences (AIIMS), Bhopal, India

<sup>3</sup>State TB cell, Department of Health and Family Welfare, Bhopal, India

<sup>4</sup>World Health Organization, Country Office in India, New Delhi, India

<sup>5</sup>International Union against Tuberculosis and Lung Disease (The Union), Paris, France

Email: \*hemantjipmer@gmail.com

**How to cite this paper:** Shewade, H.D., Kokane, A.M., Singh, A.R., Verma, M., Parmar, M., Chahar, S.S., Tiwari, M., Khan, S.N., Nagar, M., Singh, S.K., Mehra, P.K. and Kumar, A.M.V. (2017) Treatment Initiation among Patients with Multidrug Resistant Tuberculosis in Bhopal District, India. *Journal of Tuberculosis Research*, 5, 237-242. <https://doi.org/10.4236/jtr.2017.54025>

**Received:** August 28, 2017

**Accepted:** November 7, 2017

**Published:** November 10, 2017

Copyright © 2017 by authors and Scientific Research Publishing Inc.

This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

## Abstract

Revised national tuberculosis control programme in India has limited cohort-wise information about what happens to patients diagnosed with multidrug resistant TB (MDR-TB). We determined the pre-treatment loss to follow-up (non-initiation of treatment by programme within 6 months of diagnosis) and time from diagnosis to treatment initiation in Bhopal district, central India (2014). Pre-treatment loss to follow-up was 13% (0.95 CI: 7%, 23%), not significantly different from the national estimates (18%) and median time to initiate treatment was seven days, lower than that reported elsewhere in the country. Bhopal was performing well with reference to time to treatment initiation in programmatic settings.

## Keywords

Multidrug-Resistant Tuberculosis, Operational Research, Pre-Treatment Attrition, Diagnosis and Treatment Pathway, Initial Loss to Follow-Up

## 1. Introduction

India has highest burden of multidrug-resistant/rifampicin-resistant tuberculosis (MDR/RR-TB): an estimated annual incidence of 130,000 cases. Only 33,280

\*HDS and AMK contributed equally and are the joint first authors.

cases were detected (2016) and 27,375 were put on treatment (April 2015-March 2016) giving an approximate estimate of 18% pre-treatment loss to follow-up [1] [2].

Revised national tuberculosis control programme (RNTCP) in India has limited cohort-wise information about what happens to patients with presumptive/confirmed MDR-TB along the care pathway including the delays [1]. Findings related to pre-diagnosis loss to follow-up (between presumptive MDR-TB and confirmed MDR-TB/MDR-TB diagnosis) in programmatic settings in Bhopal district, central India (2014) have been published elsewhere [3]. Here, we report the pre-treatment loss to follow-up (between confirmed MDR-TB and treatment initiation) and time from diagnosis to treatment initiation.

## 2. Methods

Bhopal district is situated in Madhya Pradesh, the second largest state in India. It has a population of 2.53 million and is predominantly urban. Bhopal district contains Bhopal city which is the capital of Madhya Pradesh [4].

In Bhopal district, during 2014 the diagnostic facility for MDR-TB was the national reference laboratory (NRL), located in a tertiary public health care facility. It is certified by RNTCP for proficiency in phenotypic (solid/liquid culture and drug susceptibility testing [C-DST]) and molecular diagnostic techniques (line probe assay-LPA and cartridge-based nucleic acid amplification test-CbNAAT). In quarter 1 (January-March) 2014, if specimen was smear positive, then LPA was used upfront. Among smear negative specimens, culture was done followed by LPA, if culture turned out to be positive. Quarter 2 (April-June) 2014 onwards, LPA was used for smear positive and CbNAAT was used for smear negative specimens.

After diagnosis, treatment initiation was ensured at DR-TB center by the district health staff. Treatment was according to RNTCP programmatic management of DR-TB (PMDT) guidelines which were in line with then WHO recommendations [5]. Patients with RR-TB were also treated with the standard MDR-TB regimen. Therefore, MDR-TB included RR-TB as well.

This was a retrospective cohort study involving record review of all patients belonging to Bhopal district and diagnosed with MDR-TB under RNTCP in 2014. Each study participant was tracked from NRL C-DST register to PMDT treatment register at DR-TB center. Variables collected included-age, sex, diagnostic test, type of TB, date of diagnosis, pre-treatment loss to follow up (yes/no) and date of treatment initiation (if applicable).

Data collected in a pre-tested, structured form were double entered, validated and analyzed using EpiData (version 3.1 for entry and version 2.2.2.183 for analysis, EpiData Association, Odense, Denmark). Pre-treatment loss to follow-up was defined as non-initiation of treatment by RNTCP within six months of diagnosis. Key analytic outputs were number (proportion) of patients with pre-treatment loss to follow-up and median (IQR) time in days from diagnosis

to treatment initiation. Association between pre-treatment loss to follow-up/ time to initiate treatment and various demographic and clinical factors was tested using chi square test and one way ANOVA.

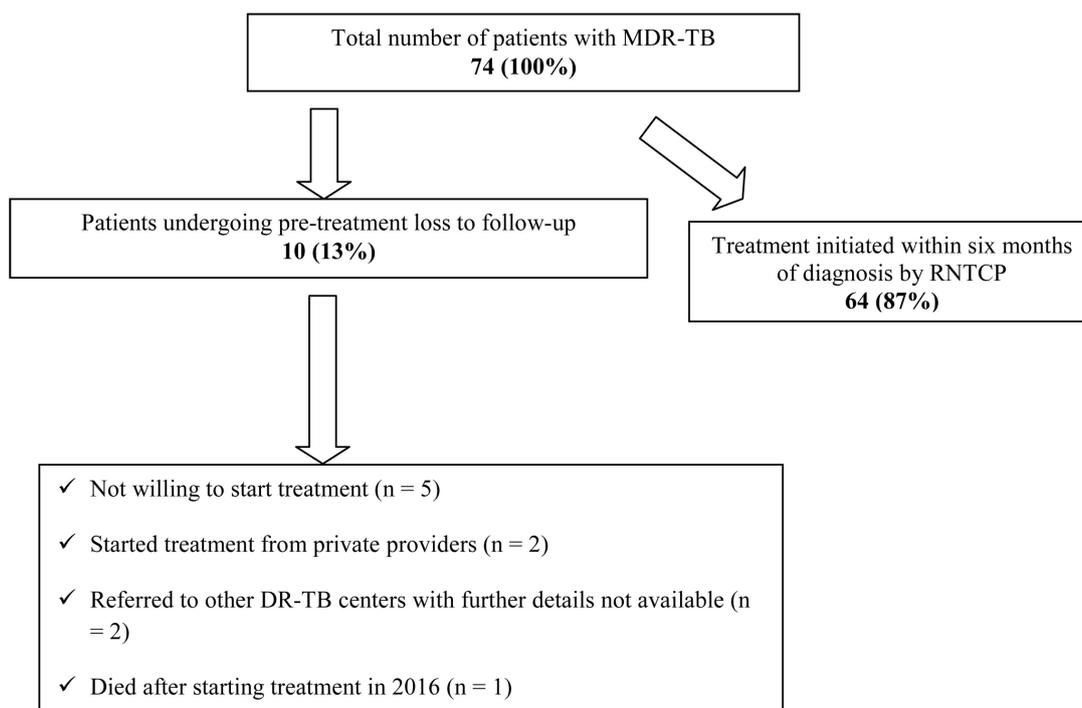
Ethics approval for this study was obtained from the Ethics Advisory Group of The Union, Paris, France and Institute Human Ethics Committee, All India Institute of Medical Sciences (AIIMS) Bhopal, India. Permission and support for the study was sought from the RNTCP programme managers and other relevant authorities. As this study involved record review of already collected data, waiver of informed consent was sought and approved by the ethics committees.

### 3. Results

There were 74 patients diagnosed with MDR-TB: mean (SD) age in years was 32 (12) and 46 (62%) were males. History of “previously treated TB” was seen in 54 (73%) cases. The diagnostic test used was LPA for 62 (84%) and CbNAAT for 12 (16%).

Ten out of 74 patients (13%, 0.95 CI (7%, 23%)) underwent pre-treatment loss to follow-up (**Figure 1**). Among 64 patients initiated on treatment and dates being available (n = 59), median time (IQR) from diagnosis to treatment initiation was 7 (4, 11) days and 80% (47/59) were initiated on treatment within 14 days (**Table 1**).

There was no significant association of demographic and clinical factors with pre-treatment loss to follow-up/time to initiate treatment (data not shown).



**Figure 1.** Pre-treatment loss to follow-up among patients with MDR-TB in programmatic settings in Bhopal district, India (2014). MDR-TB: multi drug-resistant tuberculosis; RNTCP: revised national tuberculosis control programme.

**Table 1.** Time to initiate treatment after diagnosis among patients with MDR-TB in programmatic settings in Bhopal district, India (2014)\*. (n = 59).

| Time (in days) | Number | Percentage | (Cumulative percentage) |
|----------------|--------|------------|-------------------------|
| <7             | 28     | 48         | 48                      |
| 7 - 13         | 19     | 32         | 80                      |
| 14 - 20        | 4      | 7          | 86                      |
| 21 - 27        | 3      | 5          | 92                      |
| ≥28            | 5      | 9          | 100                     |

\*MDR-TB: multi drug-resistant tuberculosis; among 74 patients with MDR-TB, 64 were initiated on treatment and dates available for calculation of time among 59.

## 4. Discussion

Pre-treatment loss to follow-up among patients with MDR-TB in programmatic setting was not significantly different from the national estimate of 18% [1]. Median time to initiate treatment was shorter than that reported elsewhere in the country: 19 days in Delhi, 10 days in Puducherry and 20 - 23 days in Chennai [6] [7] [8]. There is further scope for improvement in reduction of pre-treatment loss to follow-up. The programme is concerned about this and understanding why some patients are not willing to start treatment after diagnosis needs further systematic qualitative inquiry.

Previously, we found 60% pre-diagnosis loss to follow-up among patients with presumptive MDR-TB in 2014 in Bhopal, largely contributed by failure to refer patients for DST [3]. Considering the minimal pre-diagnosis loss to follow-up at the level of NRL [3] and the low pre-treatment loss to follow-up identified in this study, we can infer that performance of the diagnostic and treatment pathway was satisfactory once the sample reached the NRL.

Data collected was double entered and validated minimizing data entry errors. Study was conducted in operational settings reflecting the ground realities. The sample size was not being sufficient for risk factor analysis was the major limitation.

PMDT in Bhopal was performing well with reference to time to treatment initiation among patients with MDR-TB. There is a need to increase counselling and patient tracking mechanisms if we are to minimize pre-treatment loss to follow-up, time to treatment initiation and ensure survival for all patients diagnosed with MDR-TB.

## Acknowledgements

We acknowledge the contribution of the TB programme staff of district Bhopal, India who assisted in data collection. The authors alone are responsible for the views expressed in this publication and these views do not necessarily represent the decisions or policies of The Union, WHO, AIIMS Bhopal or the Government. We thank the Department for International Development (DFD), UK, for funding the Global Operational Research Fellowship Programme at the Interna-

tional Union against Tuberculosis and Lung Disease (The Union), Paris, France in which HDS works as a Senior Operational Research Fellow. La Fondation Veuve Emile Metz-Tesch supported open access publications costs. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

### Authors' Contribution

HDS was the principal investigator; AMK was the site principal investigator; AMVK was the senior author; HDS, AMK, ARS, MP and AMVK conceived and designed the protocol; HDS and ARS developed the data collection tool and plan of analysis; HDS, AMK, ARS, MV, SSC, MT, SNK, MN, SKS and PKM collected and entered the data; HDS and ARS analysed and interpreted the data; HDS prepared the first draft; all authors were involved in critically reviewing the paper and giving approval for the final version to be published. HDS is the guarantor of the paper.

### Funding

The study was conducted as an operational research under the programme conditions using programme staff. Therefore, no separate budget was required.

### Competing Interests

The authors declare no competing interests.

### Availability of Data and Materials

Additional material containing the list of variables and their details, EpiData REC and CHK file containing the dataset and EpiData program file used for analysis are available on request to the corresponding author.

### References

- [1] Revised National Tuberculosis Control Programme (RNTCP) (2017) TB India 2017. Annual Status Report. New Delhi.
- [2] World Health Organization (WHO) (2017) Global Tuberculosis Report 2016. Geneva.
- [3] Shewade, H.D., Kokane, A.M., Singh, A.R., Verma, M., Parmar, M., Chauhan, A., *et al.* (2017) High Pre-Diagnosis Attrition among Patients with Presumptive MDR-TB: An Operational Research from Bhopal District, India. *BMC Health Services Research*, **17**, 249.
- [4] Government of India. Ministry of Home Affairs. Office of Registrar General and Census Commissioner. (2011) Census of India. [http://www.censusindia.gov.in/2011-common/census\\_2011.html](http://www.censusindia.gov.in/2011-common/census_2011.html)
- [5] Central TB Division. Directorate General of Health Services. Ministry of Health & Family Welfare. Government of India. (2012) Guidelines on Programmatic Management of Drug Resistant TB (PMDT) in India. New Delhi.
- [6] Singla, N., Satyanarayana, S., Sachdeva, K.S., Van den Bergh, R., Reid, T., Tayler-

- Smith, K., *et al.* (2014) Impact of Introducing the Line Probe Assay on time to Treatment Initiation of MDR-TB in Delhi, India. *PLoS One*, **9**, e102989.
- [7] Nair, D., Navneethapandian, P.D., Tripathy, J.P., Harries, A.D., Klinton, J.S., Watson, B., *et al.* (2016) Impact of Rapid Molecular Diagnostic Tests on Time to Treatment Initiation and Outcomes in Patients with Multidrug-Resistant Tuberculosis, Tamil Nadu, India. *Transactions of The Royal Society of Tropical Medicine and Hygiene*, **110**, 534-541. <https://doi.org/10.1093/trstmh/trw060>
- [8] Shewade, H.D., Govindarajan, S., Thekkur, P., Palanivel, C., Muthaiah, M., Kumar, A.M.V., *et al.* (2016) MDR-TB in Puducherry, India: Reduction in Attrition and Turnaround Time in the Diagnosis and Treatment Pathway. *Public Health Action*, **6**, 242-246. <https://doi.org/10.5588/pha.16.0075>