Sputum Smear and Culture Conversion in Multidrug Resistance Tuberculosis Patients in Seven Districts of Central Gujarat, India: A Longitudinal Study

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Abstract

Objectives: To know the sputum smear and culture conversion among multidrug resistance tuberculosis (MDR-TB) patients.

Materials and Methods: The longitudinal cohort study was conducted for 142 MDR-TB patients registered in 2010 under Revised National Tuberculosis Control Programme of Vadodara region. Three follow-ups were taken for sputum and culture examination, at completion of 6, 12, and 24 months of treatment. Individuals were interviewed to know the reasons for missed dose and default. Results: The sputum smear and culture conversion rate was 43.4%, 47.7%, and 57% at 6 months, 12 months, and 24 months of follow-up, respectively. Treatment default rate was highest (15.2%) within initial 6 months of therapy. The mean time to sputum smear and culture conversion was 120.27 days and 125.02 days, respectively. Conclusions: Most of patients who were culture positive at 6 months remained so even after 12 months. There was not much difference in the time taken for culture and sputum conversion.

Keywords: Culture conversion, default rate, multidrug resistance tuberculosis, smear conversion, time to conversion

INTRODUCTION

Conversion of sputum smear and culture from positive to negative is considered a useful early interim indicator of efficacy of treatment and program effectiveness, as treatment outcomes are only available 18–24 months after treatment starts among multidrug resistance tuberculosis (MDR-TB) patients. From the public health point of view, reducing the time to sputum culture conversion is an important infection control measure.[1,2]

In the present study, the time to sputum smear and culture conversion, along with the possible reasons for “noncompliance,” was studied on initially registered MDR-TB patients’ cohort of the DOTS Plus site - SSGH, Vadodara.

MATERIALS AND METHODS

A longitudinal study was conducted from February 2010 to December 2012 among MDR TB patients of seven districts of central Gujarat, India, registered at DOTS Plus site - SSGH, Vadodara (Gujarat, India) under Revised National Tuberculosis Control Programme (RNTCP) between February 2010 and December 2010. Patients were diagnosed to have MDR-TB if they were found resistant to isoniazid and rifampicin with or without resistance to other first-line drugs on drug-sensitivity testing results.[3] Patients were considered smear or culture converted after having two consecutive negative smear or cultures taken at least 1 month apart. Time to culture conversion was calculated as the interval between the date of MDR-TB treatment initiation and the date of the first of these two negative consecutive cultures. A total of 146 MDR-TB patients registered at DOTS plus site were included in the study.

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after taking written informed consent in the local vernacular language. Seriously ill patients, those unable to give interview, and those patients who did not give consent were excluded. Out of the total 146 registered patients, 4 patients could not be interviewed because of migration, default from treatment, refusal to give consent, or death.

The study was approved by the Institutional Ethics Committee. Data collection was carried out over period of February 2010 to November 2012 by 3 follow-ups for each patient at the end of 6, 12, and 24 months of their DOTS plus therapy. A pretested structured questionnaire was filled up during follow-up visits at the DOTS center of respective districts, and patients were inquired about their follow-up sputum examination, reasons for missed dosage and default, if any. The patient cards at DOTS Plus Site were used for tracking the rest of the required details. The data were entered and analyzed using Epi Info™ version 7.2.0.1 (Center for Disease Control and Prevention Atlanta).

**Results**

Out of 142 patients, half of them (71/142) were in the age group of 30–50 years. Almost three-fourths (102/142) of the patients were males and half (49.29%) were illiterate. About 46.47% of patients had income between 1500 and 3000 rupees/month. Among these MDR-TB patients, 51.03% (74) of them were due to previous treatment failure.

After 6 months of treatment, 35 (24.1%) patients; at 12 months of treatment, 16 (23.9%) patients; and at 24 months of treatment, 10 (11.7%) patients were neither smear and/nor culture converted and were declared as “treatment failure” [Table 1].

Treatment default rate was highest in 22 (15.2%) patients within initial 6 months of therapy. If patients were adherent to treatment for initial 6 months, their default rate was 4.6% and 5.8% at 12 month and 24 month of treatment. The default rate and death rate was 22.07% and 29.66% at different points in time during the course of treatment as shown in Table 1.

Smear and culture reports were not carried out for 9 (6.2%) patients, 8 (7.3%) patients, and 11 (12.8%) patients at 6 months, 12 months, and 24 months follow-up, respectively. Common reasons for this were patients being out of station, not traceable, contamination of sample, or nonavailability of Falcon’s tube. As shown in Figure 1, at the end of 6 months, out of 18 patients who remained smear and culture positive, and who were followed up to 24 months, 10 died, 4 were “treatment failure,” 3 had defaulted, and only 1 was cured.

Out of 63 whose sputum and culture were negative, and who were followed up to 24 months, 40 were cured, 7 had been declared treatment completed, 7 had died, 2 were declared as treatment failure, 4 had defaulted treatment, and 3 were still on treatment.

At the end of 24 months, of 9 who remained smear and culture positive, 8 were declared as treatment failure and 1 had been declared as treatment completed. Out of 11 whose sputum and culture not available, 7 had been declared treatment completed, 1 was declared as failure, 1 was switched to category V (XDR-TB), and 3 were still on treatment. Out of 49 whose sputum and culture were negative, 48 were cured and 1 was still on treatment.

The mean duration required for culture conversion and sputum conversion was 125.02 days (range 82–386 days) with standard deviation of 54.29 days and 120.27 days (range 82–472 days) with standard deviation of 51.64 days while median being 100 days and 99 days, respectively. As apparent from Figure 1, there was not much difference in the time taken for culture and sputum conversion.

![Figure 1: Box and whisker plot for sputum and culture conversion](image)

**Table 1: Comparative treatment response of patients put on multidrug resistance tuberculosis treatment**

| Treatment response                          | At 6 months (n=145), n (%) | At 12 months (n=109), n (%) | At 24 months (n=86), n (%) |
|---------------------------------------------|----------------------------|-----------------------------|----------------------------|
| Smear negative and culture negative         | 63 (43.4)                  | 52 (47.7)                   | 49 (57)                    |
| Smear positive and culture positive         | 18 (12.4)                  | 19 (17.4)                   | 9 (10.5)                   |
| Smear positive and culture negative         | 1 (0.7)                    | 2 (1.9)                     | 0                          |
| Smear negative and culture positive         | 16 (11)                    | 5 (4.6)                     | 1 (1.2)                    |
| Smear positive and culture NA               | 1 (0.7)                    | 0                           | 0                          |
| Smear negative and culture NA               | 1 (0.7)                    | 0                           | 0                          |
| Died                                        | 14 (9.7)                   | 18 (16.5)                   | 11 (12.8)                  |
| Defaulted                                   | 22 (15.2)                  | 5 (4.6)                     | 5 (5.8)                    |
| Smear NA and culture NA                     | 9 (6.2)                    | 8 (7.4)                     | 11 (12.8)                  |

NA: Not available
Thirty-two (21.83%) patients had defaulted from their treatment. Most common reasons for default in treatment were side effect of drugs (34.38%) followed by relief from symptoms (15.63%), complex regimen (6.25%), long-term treatment schedule (6.25%), and long distance from center. Side effect of drugs was most common reason for treatment default among both males and females. Moreover, 89 patients had missed their treatment dose, main reasons being side effects of medicine and patients being out of station. The other reasons for missing treatment were alcohol addiction, social events, relief from symptoms, weakness, pain at injection site, DOT center away from home, false belief in bhuva (Quacks), frequent migration, family problem, and false perception of treatment completion.

**Discussion**

In the present study, at the end of 6 months of treatment, 43.4% were smear negative and culture negative, 12.4% remain smear and culture positive, 9.7% died, and 15.2% were defaulted. Moreover, at the end of 24 months of treatment, 57.6% were smear negative and culture negative, 10.5% remain smear positive and culture positive, 12.8% died, and 5.8% were defaulted. Although the current findings show an increasing trend of sputum smear and culture negativity and decreasing trend of default rates at the end of 6 months, 12 months, and 24 months, the denominator, i.e., the total number of MDR-TB patients continued on treatment is also decreasing (attributed to deaths and defaults and those were lost to follow-up for the present study). Thus, actual number of smear and culture-converted patients reduces. Sputum culture conversion of around 74% at 6 months has been reported from other individual studies.[](#fnref1)

About one-third of the patients remained positive for sputum culture at the end of 6 months. Most common cause of this, as found in the study, was missing the scheduled drug dosages. These patients were considered to be XDR-TB suspects. Main reasons for missing the dosages were alcohol addiction, migration for earning, and refusal to continue further treatment.

Similar findings regarding time to sputum smear and culture conversion was observed in a study done by Datta et al. and Chiang et al.[7,8] In a study carried out at New Delhi, India by Singla et al., 79% achieve sputum conversion within 8 months.[9] A study carried out at Netherland by Mpagama et al. showed that the median time to sputum culture conversion was 2 months.[10]

As per our knowledge, the patient follow-up in literature we found was only up to 6 months, while in our study, it is up to 24 months. This is the strength and uniqueness of this study.

**Conclusion**

Treatment default rate is highest within initial 6 months of therapy, and those patients who were culture negative at the end of 6 months were the ones who showed successful treatment outcome.

Hence, program guidelines on prompt and repeated retrieval actions through home visits for patients missing a dose to prevent defaults should be strictly followed. Default patients should be traced through use of mobile calls or texts, which needs to be explored through further research.

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**Conflicts of interest**

There are no conflicts of interest.

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