An Outcome-Based Follow-up Study of Cured Category I Pulmonary Tuberculosis Adult Cases from Various Tuberculosis Units under Revised National Tuberculosis Control Program from a Western Indian City

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Abstract

Context: Despite the nationwide implementation of the Revised National Tuberculosis Control Program in India, adverse outcome after treatment is on the rise. Program guidelines propose follow-up of cured patients for 2 years which is rarely done. Objectives: The main objectives of this study is (1) To find the response of treatment in terms of failure and drug resistance (recurrence of symptoms and mortality experience) and (2) Collect client perspective about the program and suggest the same to program managers. Subjects and Methods: Community-based tracking of 365 cured adult Category I pulmonary tuberculosis (TB) cases drawn from three nearby TB units was done with a structured designed questionnaire. It was done to record the adverse events after 1–3 years of completion of treatment and also to record the client perspective about the program. In case of non-survivors, verbal autopsy was conducted by interviewing the next available relative. Results: A total of 365, only 226 (60%) could be covered mainly due to wrong/incomplete address and 35 cases did not survive. Of 191 survivors who were tracked, 94.7% had sputum microscopy at the completion of treatment. Total 54 (23.9%) cases had adverse outcomes, including 31 with symptoms suggestive of TB and 23 died directly/indirectly due to TB. This cohort of cured cases, posttreatment, observed 15 times (annualized) high mortality than their counterparts. Clients or relatives largely rated the program as good/very good. Conclusions: Post-treatment tracking is must to detect an adverse outcome which is high. Most survivors and relatives of expired cases rated the program as good to very good.

Keywords: Category I cases, follow-up of cured tuberculosis cases, pulmonary tuberculosis, Revised National Tuberculosis Control Program evaluation

INTRODUCTION

Globally, tuberculosis (TB) remains a public health problem; India being high-TB burden country contributes 26% of the global burden.[] Despite the nation-wide implementation of the Revised National Tuberculosis Control Program (RNTCP) in India, multidrug resistance (MDR) is on the rise. Intermittent therapy may be effective in the controlled program environment but may not be a wise choice in a strikingly diverse country-like ours.[] Bangladesh implements a daily regimen even during the continuation phase.[15] RNTCP (2014),[] has a provision of follow-up (FU) of cured patients till 2 years at 6, 12, 18, and 24 months after cure which is rarely done, and therefore, we hardly know that what happened to these cases once they are declared as cured and released in the community. Do they suffer excess mortality or fall prey to resistant TB or are cured forever? With this background and to get the answer of this question, the present study was conducted with the objectives include to (1) Explore outcome of cured Category 1 Pulmonary TB (CAT 1 PTB) adult (>18 years) patients regarding failure/drug-resistant TB and excess mortality, if any and (2) Document their socio-demographic profile and get the client perspective about the program and suggest the same to program managers.
subjects and methods

This was a community-based, an outcome-centric tracking of adult cured CAT 1 PTB cases, using a structured, designed questionnaire, containing both close-ended and open-ended questions. Study design and questionnaire were peer-reviewed through a workshop with the member secretary operational research committee of the zonal task force, Western India—and were extensively modified. A detailed checklist for each question was prepared. The study protocol was approved by the Institutional Research Committee. Informed written consent was gathered from the participants before the interview.

study period

Data collection was done between June 2016 and December 2016 with simultaneous data entry and analysis on MS Excel.

sample size

Considering a study from Tamil Nadu with 34% adverse events (15% mortality and 19% sputum positive) taken as $P$, sample size ($n = \left(\frac{1.96}{2}\right)^2 \frac{pq}{L^2}$) at 95% level of statistical significance and 15% allowable error ($L$) came out as 331. Further considering the nonavailability, unwillingness, and migration, etc., 10% was added. Rounding it off, finally, the sample size was 365.

sample technique

As per the protocol, adult cured CAT I PTB patients who completed their treatment till December 31, 2014 (minimum 1.5 years after completing treatment) but not before January 1, 2012 (maximum 5 years after completing treatment) constituted the reference population. Thus, the post treatment duration for the study participants was between 1.5 years and 5 years. Under Ahmadabad Municipal Corporation, there were ten TU units (TUs) until 2014. For feasibility, we took three TUs nearby to the institute, namely, Chandlodiya, Memnagar, and West Zone (old TUs) (established before 2015); treatment cards (TB card) and the patient records were obtained, and all the eligible participants were enlisted. Number of participants from each TU was calculated as per probability proportional to size.

Inclusion criteria

All eligible and willing to participate were included in the study and for the nonsurvivors; available relative was interviewed to ascertain probable cause of death.

Exclusion criteria

Participants not fulfilling any one of the above criteria or unwilling to participate were excluded from the study. Sampled participants in each TU were selected through the simple random sampling with replacement using a random number table. Contact details of all selected patients were obtained from their treatment cards, and efforts were made through visits/visit visits to contact them for the personal interview.

Results

Of the 191 survivors who could be contacted, 61.8% were male and 74% were in 18-45 years age group. Among males, 70% were engaged in un/semi-skilled work while most of the females (71%) were housewives. About 76.4% of the study participants were literate; approximately one-fifth males and one-fourth females were illiterate. Total of 191 cases accessed to know about the details of post treatment activities provided by the RNTCP staff, it was found that 181 (94.7%) actually underwent sputum microscopy at the completion of treatment, including three of them who gave the history of being sputum positive at the end of completion of the treatment. Subsequently, they were treated with CAT II in Government facilities. Remaining (10) did not undergo sputum microscopy at the end of treatment. Out of them, five cases completed full treatment and were healthy at the time of visit; rest five did not complete the treatment and of them, three took treatment for 3-4 months from registered TUs and discontinued due to the adverse effect of drugs; two were later put on Category II from other health facilities and one was found terminally ill with TB-HIV co-infection and not taking any treatment. Rest 2 who also discontinued due to side effects of drugs, approached private doctors were declared “NON-TB” by them and stopped any treatment for TB. Incidentally, at the time of the survey, both of them were apparently healthy and devoid of any sign/symptom suggestive of TB.

Of 191, only 56 (29.3%) patients were given advice (s) mainly for sputum microscopy (89%); remaining 70% missed this opportunity for further advice [Table 2]. After tracking 191 cases, it was found that followup for the sputum examination at 6 months and thereafter up to 2 years by care provider was not done, and reasons for no followup was not known by all of them. Based on history and availability of records (if any), 31 (16.2%) were found to have developed symptoms suggestive of TB, of this, 16 (51.6%) developed within 1 year and 15 (48.3%) later. Thereafter, 25 (80%) of 31 cases went to health facility (Government-18, Private-7) where 22 of them underwent sputum microscopy which in 19 cases turned out to be positive for acid-fast bacilli. Of 31 cases, 18 (58%) slipped into CAT 2 and few MDR suspects as per history. However, the exact numbers of MDR cases could not be explored due to nonavailability of treatment records. In three sputum negative cases, two were in need of further
investigations, and one of them underwent magnetic resonance imaging of the thorax and another one was linked to a local medical college for further evaluation [Table 3].

When 191 survivors were asked to rate their experiences with RNTCP on a Likert scale (1–5) ranging from very good (5) to very bad (1). Most (182 or 95.3%) of them rated their experience as good or very good. Very few (4.7%) rated as okay or bad or very bad whereas 1 refused to give any opinion. Similarly, when asked to mention a problem area (if any), which they came across during their interaction with RNTCP, 35 (19.9%) said yes and 151 (79.1%) said no (2 or 4 years and taking an average of 3 years, it works out to be the annualized as 51.3/1000 adult population. The difference regarding this mortality rate between two genders and various age groups was statistically not significant. [Table 4] While gathering the feedback from the relatives of expired 35 cases, except one, none rated it very bad, 30 (85.7%) rated it either as good or very good, whereas four rated it as just okay.

### Discussion

Despite the repeated visits, we could not track more than one-third of cases mainly due to the incomplete or wrong address or migration. This can be minimized by ensuring the recording of correct and complete address, including the mobile number (at the time of registration). It will ensure the better tracking of cases and posttreatment sputum microscopy and counselling. Standards for TB care in India recommendations state that response to therapy PTB cases should be monitored through the sputum microscopy at the time of completion of intensive phase of treatment and also at the end of treatment. Unlike developed countries where TB affects mostly the elderly, more cases (74%) in this study belonged to 18–45 years age group which constitutes the most productive segment of the society. It was higher than reported by Piparva (66.2%) and Ahmed et al. (27.5%) in comparable age groups. A disturbing fact in this study observed, was that ten cases missed the post treatment sputum microscopy. Given the high cost of treatment and potential for disease spread from partially or inadequately treated cases, its crucial for the success of the program to find more about the reasons for such situations.

Out of 191 survivors in this study, 23 (16.2%) developed the symptoms suggestive of TB along with another 31 who died due to the causes directly or indirectly associated with TB taking the proportion of adverse events to 54 (23.9%). It was higher than 12.3% relapse reported from Kolkata during the 18-month period (up to 77% relapse in first 6 months of FU). It is in contrast to another study where up to 90% remained

### Table 1: Details of study participants (n=365)

| Parameters                                      | n (%) |
|-------------------------------------------------|-------|
| Total eligible and enlisted cases               | 365 (100.0) |
| Could be interviewed                            | 226 (61.9) |
| Interviewed directly (survivor)                 | 191   |
| During first visit                              | 155   |
| During second visit                             | 17    |
| During third visit                              | 7     |
| On mobile                                       | 12    |
| Nonsurvivors (verbal autopsy) interview of relatives | 35   |
| Could not be interviewed                        | 139 (38.1) |
| Wrong or incomplete address                     | 90    |
| Migrated out                                    | 40    |
| Others*                                         | 9     |

*Includes in prison, refused interview, and denied being patient

### Table 2: Details of post treatment activities undertaken by health-care provider (n=191)

| Posttreatment activities                                      | n (%) |
|---------------------------------------------------------------|-------|
| Sputum examination (n=191)                                     |       |
| Yes                                                           | 181 (94.7) |
| Outcome of sputum examination (n=181)                          |       |
| Positive for AFB                                              | 3 (1.7)  |
| Any communication/home visit done (n=191)*                     |       |
| Advice given                                                   | 56 (29.3) |
| If yes, type of advice single response (n=56)                  |       |
| For sputum examination                                         | 50 (89.3) |
| For routine follow-up                                         | 2 (3.6)  |
| Consult a doctor if symptoms develop in future                | 3 (5.4)  |
| Complete treatment                                            | 1 (1.8)  |

AFB: Acid-fast bacilli

about the rude behavior of the staff. As overall rating and experience about RNTCP was good hence when inquired about recommending it to others in need, 181 said yes, whereas rest said no or did not reply. Further, it was found that 13 of these 181 have actually recommended the suspected cases to RNTCP and those who disagreed for the same could not give any specific reason about it.

A total of 226 cases, 35 (death rate 15.4%) died between the completion of treatment and the time of interview. More males (74.3%) and those in the age group of 26–45 years (62.9%) died. This crude death rate was for a period varying between 2 and 4 years and taking an average of 3 years, it works out to be the annualized as 51.3/1000 adult population. The difference regarding this mortality rate between two genders and various age groups was statistically not significant. [Table 4] While gathering the feedback from the relatives of expired 35 cases, except one, none rated it very bad, 30 (85.7%) rated it either as good or very good, whereas four rated it as just okay.
asymptomatic after a 1 year of completion of treatment. In this study, 31 (15.4%) died between the completion of treatment and the time of interview. Another study from Gujarat,[16] followed a cured cohort of 657 cases 2 years after completion and reported 15.3% of them either as dead or relapse and also observed the higher proportion of deaths (7.7%) among those with a history of interrupted treatment than those with uninterrupted treatment (4.2%). All patients in this study declared once as cured, were observed after a variable period between 1.5 years & 5 years. Taking an average of 3 years, it works out as annualized death rate of 51.3/1000; death rates in the comparable population in Gujarat in 2012 were 3.4/1000.[17] Hence, this study cohort experienced 15 times high-death rates. It reveals unusual and alarming high-death rate which in itself can be a case of investigation. In the absence of any other explanation, high rates could be attributed to reappearance/recurrence of TB. In this study, the coexisting illnesses such as HIV, diabetes, and chronic obstructive pulmonary diseases which could contribute to excess mortality were observed in very few cases ranging between 0.5% and 4.7%. However, addictions such as tobacco chewing, smoking, and alcohol were observed in more cases (6.8%-25.1%). A hospital-based audit[18] showed that 48.3% of patients who died of active TB were under 50 years, and older patients who died due to TB had co-existing diseases such as ischemic heart diseases and malignancy. They also opined that delay in diagnosis and failure in management.

### Table 4: Period mortality rates among studied cases regarding age and sex (n=191)

| Variable              | Survivors | Expired cases | Total | Period death rate (%) | Statistical interpretation |
|-----------------------|-----------|---------------|-------|------------------------|---------------------------|
| Age (years)           |           |               |       |                        |                           |
| 18-25                 | 55        | 3             | 58    | 5.2                    | \( \chi^2=7.3 \) df=3 \( P>0.05 \) |
| 26-45                 | 87        | 22            | 109   | 20.2                   |                           |
| 46-60                 | 28        | 7             | 35    | 20.0                   |                           |
| ≥61                   | 21        | 3             | 24    | 12.5                   |                           |
| Sex                   |           |               |       |                        |                           |
| Male                  | 118       | 26            | 144   | 18.1                   | \( \chi^2=1.99 \) df=1 \( P>0.05 \) |
| Female                | 73        | 9             | 82    | 10.9                   |                           |

### Conclusions

Incomplete or wrong address at the time of registration makes the followup and post treatment services such as sputum microscopy and counselling very difficult to provide. Finally, the higher frequency of adverse events and excess mortality in these cured cases within 1–5 years points to one thing that everything is not well with RNTCP. Certain changes have now been done in RNTCP which were earlier not there (introduction of daily regimen and provision of linking with Aadhar card for tracking, cash transfer).[19] Post treatment followup component needs to be strengthened.

### Limitations

1. Findings are based on the data of only three TUs from urban area selected purposively, hence findings cannot be generalised.
2. Although 8% of the extra sample was obtained for nonavailability, unwillingness, migration, etc., However, the proportion of missing cases was much more (38%) and sample became statistically insufficient. Any study in future shall take this fact into the consideration.
3. We do not know the profile and adverse outcome status among expired ones—it can be even worse. Outcome of cured cases was based on the client’s history and available case papers with very limited laboratory-based evidence. Verbal autopsy of expired cases was based on the interview of relatives which has limited validity while attributing the deaths directly or indirectly to TB as only one case had death certificate.
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Conflicts of interest
There are no conflicts of interest.

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