Survival Analysis of Treatment Defaulters among Tuberculosis Patients in Government Medical College and Hospital, Aurangabad

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Abstract

**Context:** Tuberculosis (TB) patients who do not complete treatment pose a potential public health risk through disease reactivation, increased transmission, and development of drug resistance. **Aims:** (1) To determine the duration TB patients stay in the treatment before defaulting. (2) Factors associated with defaulters who had been treated in Government Medical College and Hospital (GMCH), Aurangabad. **Setting and Design:** The study was conducted at TB Unit of GMCH, Aurangabad, and community. This was a retrospective cohort study. **Materials and Methods:** Based on record review of 440 bacteriological-confirmed TB patients enrolled in the TB Unit of GMCH, Aurangabad, in 2015 from January 1, to December 31, we collected information on potential risk factors of all confirmed cases by primary and secondary data. For survival analysis, outcome of interest was treatment defaulter. Kaplan–Meier curves, log-rank test, and Cox-proportional hazard regression analysis were used to model outcome of interest. **Statistical Analysis Used:** Statistical analysis is performed using SPSS version 17. **Results:** Out of total 440 TB patients registered, 13 patients got defaulted in 2015. Overall mean time of default was 279 days, with 276 days for males against 279 days for females. Many patients interrupted treatment during continuation phase. Treatment defaulters had an association with gender, category at the initiation of treatment, HIV status, smoking, and alcohol consumption. **Conclusion:** Targeted intervention with the goal toward adherence in persons abusing smoking and alcohol is recommended. Necessary actions need to be initiated in the program to strengthen the follow-up of patients and to bring behavioral changes by proper counseling.

**Keywords:** Cox proportional hazard, log-rank, survival analysis, treatment defaulters

**INTRODUCTION**

Tuberculosis (TB) is an infectious disease which continues to be the leading cause of death. According to the Global TB Report 2017, released by the WHO, India has topped list of seven countries accounting for 64% of over 10 million new TB cases worldwide in 2016. An estimated 1.7 million people died from TB in 2016.[1]

India accounts for one-fourth of the global TB burden. In 2015, an estimated 28 lakh cases occurred and 4.8 lakh people died due to TB.[2]

TB patients who do not complete treatment pose a potential public health risk. Although DOTS coverage and health workers involvement in TB prevention and control activities is improving, patients still are failing to complete their treatment.[3] Defaulter is defined as a patient whose treatment was interrupted for 2 consecutive months or more.[4]

Many studies have been conducted on TB; however, very few studies that focus specifically on survival analysis of TB patients are present till date. Survival analysis is generally defined as a set of methods for analyzing data where the outcome variable is the time until the occurrence of an event of interest. In survival analysis, subjects are usually followed over a specified time period, and the focus is on the time at which this event occurs. In survival analysis, subjects are usually followed over a specified time period, and the focus is on the time at which this event occurs. In survival analysis, subjects are usually followed over a specified time period, and the focus is on the time at which this event occurs.

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the event of interest occurs. However, the difficulty commonly encountered is only some individuals’ experience the event, and subsequently, survival times will be unknown for subset of the study group. This phenomenon is called censoring. For example, a patient has not experienced the relevant outcome by the time of close of the study or patient lost to follow-up during the study or patient experiences different event.

Duration of treatment is important in deciding survival of patients. Further, improving treatment outcomes and designing effective interventions require understanding of factors that prevent people from adhering and those that help in treatment completion.

Hence, the present study was designed to determine the duration TB patients stay in treatment before defaulting and factors associated with defaulters who had been treated in Government Medical College and Hospital (GMCH), Aurangabad.

### Materials and Methods

The retrospective cohort study was carried out at GMCH, Aurangabad, for all the 440 TB cases registered in TB Unit of the hospital from January 1, 2015, to December 31, 2015. This included smear-positive pulmonary TB (PTB) patients, smear-negative PTB patients, and extra-PTB (EPTB) patients. The study protocol was approved by the ethics committee. Informed consent was taken from the participants before inclusion.

Smear-positive pulmonary case was defined as a patient with one or more initial sputum smear examination (acid-fast bacilli [AFB+]) or one sputum examination AFB+ and radiographic abnormalities consistent with active PTB as determined by a clinician. Smear-negative pulmonary case defined as patient with at least two sputum smear examinations negative for AFB and radiographic abnormalities consistent with active PTB with no response to a course of broad-spectrum antibiotics. EPTB case was defined as a patient with TB of organs other than the lungs.

Secondary data were abstracted from TB treatment registers in GMCH, Aurangabad. These included demographic data (age, sex, residence) and treatment data (treatment observer, category, i.e. Category I and Category II, patient types, i.e. new, relapse, failure, treatment after default, transfer status, HIV status, treatment regimen, sputum smear microscopy results, date of start and end of treatment, and treatment outcome).

To obtain primary data, TB patients were interviewed using a questionnaire by visiting their residence with the help of community health workers who had been trained to collect the relevant information from the patient. The information was collected on alcohol, smoking habits, and other relevant information about the patient.

For the survival analysis, the outcome of interest was treatment defaulter. For the purpose of our analysis, only the times for patients who were defaulted were taken as event.

Kaplan–Meier curves, log-rank test, and Cox-proportional hazard regression analysis were used to display the probability of treatment defaulter over time for each risk factor. SPSS version 17 was used for statistically significant.

### Results

A total of 440 bacteriological-confirmed TB patients who initiated treatment, 249 (56.59%) were male patients, and 191 (43.41%) were female patients. At the initiation of treatment, 365 (82.95%) were of Category I, 74 (16.82%) of Category II, and 1 (0.23%) patient of Category III. More than half (57.27%) were classified as smear-positive PTB, 12.05% were smear-negative PTB, and 30.68% were EPTB cases. 416 (94.55%) TB patients were from urban area and 24 (5.45%) from rural area. 432 (98.18%) were HIV negative while 8 (1.82%) patients were HIV positive. 135 (30.68%) were smokers and 305 (69.32%) nonsmokers. 147 (33.41%) were consuming alcohol and the rest 293 (66.59%) were nondrinkers [Table 1].

Out of total 440, 13 (2.95%) patients were defaulters. Out of 13 defaulted patients, 12 (92.31%) were males and 1 (7.69%) female. Twelve patients got defaulted during continuation phase. Overall, the mean time of default was 279 days and was 276 days for males against 279 days for females [Table 2 and Figure 1], with significance on log-rank test (P < 0.05) [Table 3]. Hazard ratio (HR): 0.114 showed

### Table 1: Demographic and clinical characteristics of tuberculosis patients initiating tuberculosis treatment at Government Medical College and Hospital, Aurangabad (n=440)

| Variable                        | Frequency (%) |
|---------------------------------|---------------|
| Sex                             |               |
| Male                            | 249 (56.59)   |
| Female                          | 191 (43.41)   |
| Category (patient history)       |               |
| I                               | 365 (82.95)   |
| II                              | 74 (16.82)    |
| III                             | 1 (0.23)      |
| Types of TB                     |               |
| Smear-positive PTB               | 252 (57.27)   |
| Smear-negative PTB               | 53 (12.05)    |
| EPTB                            | 135 (30.68)   |
| Address of patients             |               |
| Urban                           | 416 (94.55)   |
| Rural                           | 24 (5.45)     |
| HIV test/result                  |               |
| Negative                        | 432 (98.18)   |
| Positive                        | 8 (1.82)      |
| Smoking status                  |               |
| Yes                             | 135 (30.68)   |
| No                              | 305 (69.32)   |
| Alcohol consumption             |               |
| Yes                             | 147 (33.41)   |
| No                              | 293 (66.59)   |

TB: Tuberculosis, PTB: Pulmonary TB, EPTB: Extra-PTB
that probability of defaulting was less by 89% in females than males at any given time [Table 4].

Of the total, 5 (38.46%) from Category I and 8 (61.54%) from Category 2 got defaulted and no one defaulted in Category 3. Survival curves showed in [Figure 2]. Log-rank test showed significant difference ($P < 0.001$) [Table 3]. The value of HR: 276.033 for Category I and HR: 2003.025 for Category II indicated that Category II had far more chance of defaulting than Category I with no default in Category III [Table 5].

Out of 13, 1 (7.69%) HIV-positive and 12 (92.31%) HIV-negative patients defaulted with mean duration of defaulter 238 and 280 days, respectively. Log-rank test ($P > 0.05$) was not significant [Table 3]. HR: 0.250 indicated that probability of defaulting was 75% less in HIV-negative defaulter patients as compared to HIV positive [Table 4].

Regarding smoking status, 8 (61.54%) were smokers and 5 (38.46%) nonsmokers with a mean survival time of 254 and 283 days, respectively. Log-rank test was significant ($P < 0.05$) [Table 3]. HR: 0.266 indicates that nonsmokers have 74% less chance of defaulting than smokers with significance at 5% probability level.

In concern with alcohol status, 6 (46.15%) were drinkers and 7 (53.85%) nondrinkers with a mean survival time of 273 and 279 days, respectively [Figure 3]. Log-rank test was not significant ($P > 0.05$) [Table 3]. HR: 0.602 indicated that nondrinkers have 40% less risk of defaulting as compared to drinkers [Table 4].

**Discussion**

Very few studies on survival analysis of defaulter patients among TB have been carried out till recently. In our study, we found that 13 (2.95%) patients got defaulted while the rate of default was 13.5% in Ethiopian study.\(^3\)

In our study, 92.31% of defaulters were documented during continuation phase. This may be due to less vigilant follow-up of patients during continuation phase as compared to intensive phase. This is similar the findings of Ajagbe et al.,\(^4\) which had

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**Table 2: Survival analysis of defaulters according to gender**

|                | Estimate | SE   | 95% CI       |
|----------------|----------|------|--------------|
|                |          |      | Upper bound  | Lower bound |
| Male           | 275.704  | 3.021| 269.784      | 281.625     |
| Female         | 278.663  | 1.333| 276.050      | 281.276     |
| Overall        | 279.225  | 2.010| 275.285      | 283.165     |

*Estimation is limited to the largest survival time if it is censored. CI: Confidence interval, SE: Standard error

**Table 3: Descriptive statistics of survival data of defaulters (SPSS output of Kaplan-Meier estimator)**

| Covariates     | Log rank | df | Significant |
|----------------|----------|----|-------------|
| Sex            |          |    |             |
| Male           | 6.350    | 1  | 0.012       |
| Female         |          |    |             |
| Category       |          |    |             |
| I              | 15.685   | 2  | 0.000       |
| II             |          |    |             |
| III            |          |    |             |
| HIV status     |          |    |             |
| HIV positive   | 2.053    | 1  | 0.152       |
| HIV negative   |          |    |             |
| Smoking        |          |    |             |
| Yes            | 6.220    | 1  | 0.013       |
| No             |          |    |             |
| Alcohol        |          |    |             |
| Yes            | 0.851    | 1  | 0.356       |
| No             |          |    |             |

**Table 4: SPSS output for covariates with survival time (Cox regression analysis) for gender, HIV status, smoking, and alcohol**

|                | $B$    | SE   | Wald | df | Significant | Exp (B) | 95.0% CI for Exp (B) | Lower | Upper |
|----------------|--------|------|------|----|-------------|---------|----------------------|-------|-------|
| Gender         | −2.174 | 1.042| 4.356| 1  | 0.037       | 0.114   | 0.015                | 0.876 |       |
| HIV status     | −1.385 | 1.045| 1.756| 1  | 0.185       | 0.250   | 0.032                | 1.942 |       |
| Smoking        | −1.323 | 0.570| 5.387| 1  | 0.020       | 0.266   | 0.087                | 0.814 |       |
| Alcohol        | −0.508 | 0.557| 0.833| 1  | 0.361       | 0.602   | 0.202                | 1.791 |       |

SE: Standard error, CI: Confidence interval
shown 70% patients interrupted treatment during continuation phase.

In the present study, we found significant difference in survival curves of male and female in contrast to the findings of Ajagbe et al.,[4] in which no significant difference was found.

In this study, there was more chance of defaulting in Category II than Category I with no default in Category III which is similar to the findings of the study in South India which stated that survival probabilities of Category II patients are less than Category I and III.[5]

In our study, although HIV negative defaulted late as compared to HIV positive, difference was not significant on log-rank test ($P > 0.05$). On the other hand, being HIV-positive appeared to be associated with defaulter in univariate but not in the multivariate analysis in the study of Ethiopia.[3]

In Ajagbe et al.,[4] smokers and alcohol drinkers had hazard of 1.8 and were associated with shorter survival time of defaulters which is similar to the present findings of the study with HR of 0.266 and 0.602 for smoking and alcohol, respectively, indicating that the nonsmokers have 74% less chance of defaulting and nondrinkers have 40% less risk of defaulting.

### Conclusion

The present study showed treatment defaulters had an association with gender, category at initiation of treatment, HIV status, smokers, and alcohol consumption. Hence, enhanced patient pretreatment counseling and constant motivation specifically to males, Category II, HIV positive, smokers, and alcoholic TB patients during follow-ups to complete treatment without interruption are needed. Education on behavior change of patients is essential. Targeted intervention aimed at assuring adherence in persons abusing smoking and alcohol is also recommended. Necessary actions need to be initiated in the TB control program to strengthen the follow-up of patients with TB from start to completion of treatment based on the factors associated with defaulters.

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### Conflicts of interest
There are no conflicts of interest.

### References

1. World Health Organization. Global TB Report 2017. Geneva: WHO; 2017.
2. TB India 2017, RNTCP Annual Status Report, Central TB Division, Nirman Bhavan, New Delhi: Directorate General Services of Health Services, Ministry of Health and Family Welfare; 2017.
3. Akessa GM, Tadesse M, Abebe G. Survival analysis of loss to follow-up treatment among tuberculosis patients at Jimma University Specialized Hospital, Jimma, Southwest Ethiopia. Int J Stat Mech 2015;7:923025. [doi: 10.1155/2015/923025].
4. Ajagbe OB, Kabair Z, O’Connor T. Survival analysis of adult tuberculosis disease. PLoS One 2014;9:e112838.
5. Vasantha M, Gopi PG, Subramani R. Survival of tuberculosis patients treated under dots in a rural tuberculosis unit (TU), South India. Indian J Tuberc 2008;55:64-9.
6. Muture BN, Keraka MN, Kimau PK, Kabiru EW, Ombeka VO, Oguya F, et al. Factors associated with default from treatment among tuberculosis patients in Nairobi Province, Kenya: A case control study. BMC Public Health 2011;11:696.
7. Senbeta A, Woldesergi G, Romha G. Survival analysis and associated risk factors of tuberculosis in-hospital patients’ death in Hawassa city and at Yirgalem town health centers. World J Med Sci 2014;11:382-8.