

## Survival Analysis on Recovery Time of Tuberculosis Patients Undergoing DOTS in Dibrugarh District of Assam

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**Abstract** Tuberculosis (TB) is a highly infectious air borne communicable disease caused by the bacteria bacillus *Mycobacterium tuberculosis*. Tuberculosis has existed for millennia and remains a major global health problem. The incidence and mortality due to TB is alarmingly higher in poor countries in comparison to developed countries. To fight with this menace, in 1997 Revised National Tuberculosis Program (RNTCP) was launched internationally recommended strategy to control TB known as “DOTS” (Directly Observed Treatment Short Course) formulated by WHO. After the implementation of DOTS, present trends showed a significant reduction in the prevalence of TB cases in India. Assam registered one of highest incidence of TB cases in the country. Considering this fact, a study is conducted to assess the recovery time of TB patients who have treated under DOTS in Dibrugarh district of Assam. The study was taken up in a historical cohort and information from the medical charts of patients registered for TB in the

district TB center, Dibrugarh situated in Assam Medical College and Hospital (AMCH). In studying the recovery time different techniques of survival analysis are used. To calculate the average cure time of TB patients undergoing DOTS Kaplan-Meier Product Limit estimator (Kaplan and Meier 1958) is used. The survival curve is also constructed in this regard. To compare the average cure time with respect to different demographic characteristics the log-rank test (Mantel 1966, Peto and Peto 1972) is used. The average recovery time of TB patients undergoing DOTS is found to be 7.2 months (95% C.I. 7.015-7.385). The recovery time of male and female are significantly different. The average recovery time of TB patients is found to be well within the targeted period. Thus implementation of DOTS under RNTCP is found to be quite satisfactory in Dibrugarh district of Assam.

**Keywords** TB, DOTS, RNTCP, WHO, Survival analysis.

### Introduction

Tuberculosis (TB) is an air borne disease caused mainly by the bacteria bacillus *Mycobacterium tuberculosis*. Millions of people developed TB every year around the globe and it is considered as one of the major public health issue. According to World Health Organization (2017) report on TB, 2017, around 10.4 million people developed TB in the year 2016 globally. Mortality due to TB is also very high as it is the ninth leading cause of death worldwide and in the year 2016 alone 1.3 million people die due this disease (World Health Organization 2017). A higher burden

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of TB in a country also increases the socio-economic burden as previous research showed that individuals belonging to the economically active age groups are mostly affected by TB which in turns brings other social and economic issues (Rajeswari et al. 1999, Muniyandi et al. 2006). The incidence and mortality due to TB is alarmingly higher in poor countries in comparison to developed countries. The prime reason behind this may be because of wide spread malnutrition, poverty, deprivation, overcrowding. Past research showed that in poor countries these factors are very much responsible for spreading the infection of the disease (Rieder H. L. 1999, Lienhardt et al. 2001). According to World Health Organization, Indian registered the highest incidence of TB cases in 2016. Five countries viz., India, Indonesia, China, Philippines and Pakistan (according to descending order of incidence of cases) constituted about 56% of the total cases of the world (World Health Organization 2017). In the year 2015, out of estimated global incidence of 10.4 million TB cases, about 2.8 million were estimated to have occurred in India. The dead due to TB is also very high in India where about 4.8 lakh people died due to this disease in 2015 (Ministry of Health and Family Welfare 2017). To fight with this menace the National TB Control Program was initiated in the year 1962 in India. Under this program different measures were taken throughout the country to reduce the prevalence of TB but the results were not encouraging. Then in 1997, the Revised National Tuberculosis program (RNTCP) was launched and expanded across the country in phase manner. Under this program, internationally recommended strategy to control TB known as DOTS (Directly Observed Treatment Short Course) formulated by WHO was launched. After the implementation of DOTS, present trends showed a significant reduction in the prevalence of TB cases in India. The Ministry of Health and Family Welfare, Government of India, in their report claims that there is a 55% reduction in the prevalence of TB cases in 2013 in comparison to 1990. The mortality due to TB is also reduced by 50% in 2013 in comparison to 1990 (Ministry of Health and Family Welfare 2015). The cure of tuberculosis of patients undergoing DOTS is very high in comparison to other forms of treatment which is about 80% (Sivaraj et al. 2014). Under DOTS the duration of treatment is usually 6 to 8 months but

different studies reported different recovery times of TB patients. The study on recovery time to TB is important to a community as it helps in assessing the burden of the disease in that community. Considering this fact, a study is conducted to assess the recovery time of TB patients who have treated under DOTS in Dibrugarh district of Assam. Assam registered one of highest incidence of TB cases in the country.

### Materials and Methods

The study was taken up in a historical cohort and information from the medical charts of patients registered for TB in the district TB center, Dibrugarh situated in Assam Medical College and Hospital (AMCH). This center is one of the oldest established under the Revised National Tuberculosis Program in Assam. The period of study was taken from 1<sup>st</sup> January 2012 to 30<sup>th</sup> June 2014. All the patients registered with TB during 1<sup>st</sup> January 2012 to 31<sup>st</sup> December 2013 were included in the study. The six months period i.e., from 1<sup>st</sup> January 2014 to 30<sup>th</sup> June 2014 is taken for the follow up of the cases specially those who registered late in the inclusion period. From the hospital records information on age, sex, date of starting treatment, outcome of the treatment were collected.

In studying the recovery time different techniques of survival analysis are used. Survival analysis is concerned with analyzing the time to the occurrence of an event. The generic for the time is survival time. It is also called time-to-event data or failure time data. Survival time is a non-negative random variable that measure the follow-up time from a definite starting point to the occurrence of a given event. The word survival is used to signify the time of surviving from occurring of the event. In the present case the starting point is the date of diagnosis of the disease under consideration while the event of interest is the date of cure of the patients; time to cure is calculated from the two dates. Survival data have some special characteristic because of which they are not amenable to standard statistical methods. The most important is the presence of censored observations i.e., exact survival time of all the patients may not known. In the present study patients are considered as censored if

**Table 1.** Profile of the study subjects.

Category		Frequency	Percentage
Sex	Male	1034	56.1
	Female	809	43.9
Disease type	Pulmonary	1175	64.5
	Extra pulmonary	647	35.5
Age categories	0-20	509	27.6
	20-40	903	49.0
	40-60	380	20.6
	Above 60	51	2.8

they are categorized as defaulted (a patient who has not taken anti-TB drugs for 2 months or more consecutively after starting treatment), treatment completed (sputum smear-positive patient who has completed treatment with negative, smear at the end of the intensive phase but none at the end of treatment), transferred out (a patient who has been transferred to another Tuberculosis Unit/District and his/her treatment result (outcome) is not known), failure (any TB patient how is positive at 5 months or more after starting treatment). Failure also includes a patient who was treated with category III regiment but who becomes smear positive during positive during treatments, died (patient who died during the course of treatment regardless of cause).

To calculate the average cure time of TB patients undergoing DOTS Kaplan-Meier Product Limit estimator (Kaplan and Meier 1958) is used. The survival curve is also constructed in this regard. To compare the average survival time with respect to different demographic characteristic the log-rank test (Mantel 1966, Peto and Peto 1972) is used.

## Results and Discussion

During this study period a total of 1843 numbers of

**Table 2.** Comparison of average time to cure with respect to demographic characteristics.

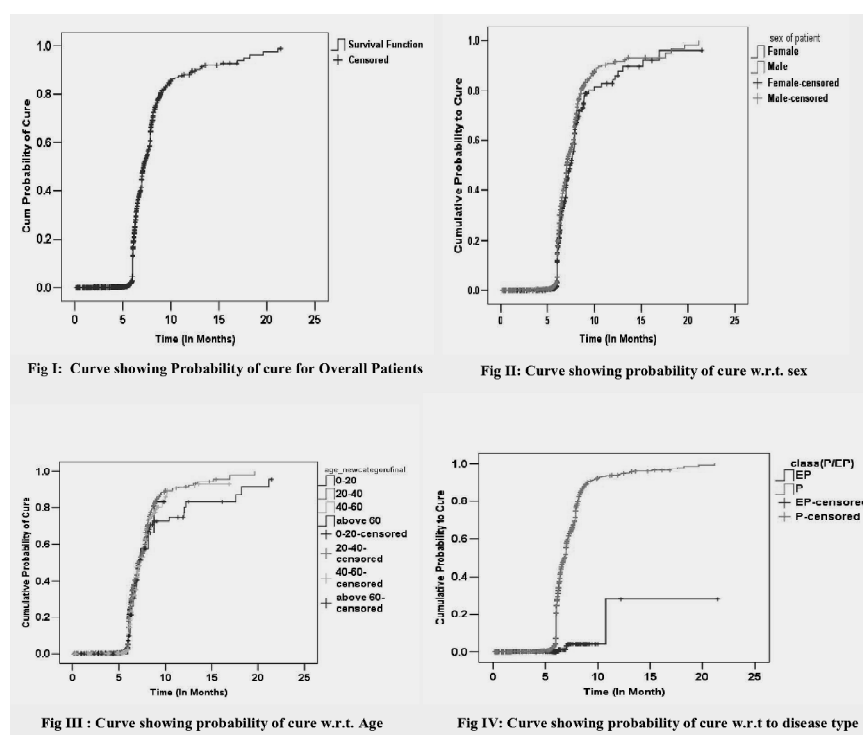
		Average (median) time to cure	95% confidence interval		Log rank statistics	p-value
Sex	Overall	7.200	7.015	7.385	5.946	0.015
	Male	7.067	6.906	7.227		
Age	Female	7.433	7.129	7.738	5.055	0.168
	Below 20	7.200	6.892	7.508		
	21-40	7.133	6.904	7.363		
	41-60	7.333	6.881	7.786		
	61 and above	7.200	6.617	7.783		

**Table 3.** Probability of cure at different time points.

Months	Probability of cure S (t)	Standard error
6	0.349	0.015
7	0.545	0.017
8	0.759	0.017
9	0.834	0.017
10	0.867	0.017

patients registered for treatment under DOTS in Dibrugath center. The mean and median age of patients was 30.73 years and 28 years respectively. About 65% of the cases registered are Pulmonary in nature. A male preponderance was observed among the patients (56% male against 44% female). About 50% of the patients are in the age-group 20 to 40 years. The profile of the patients is presented in Table 1.

The median time to cure of TB patients is found to be 7.2 months (95% C.I. 7.015 months to 7.385 months) which may be quite satisfactory considering the fact that under DOTS a patient is treated from 6 to 8 months. The Kaplan-Meier survival curves for overall patients and with respect to sex and age of patients are presented in Figs. 1—4. The median survival time of TB patients with respect to sex, age and disease type are presented in Table 2. The average recovery time of female patients is significantly higher which is 7.433 months (95% C.I. 7.129 months to 7.738 months) in comparison to male counterparts (7.067 months, 95% C.I. 6.906 months to 7.227 months). From the results it can also be observed that the difference in average recovery time with respect to different age groups is no statistically significant. The median survival of time with respect to different demographic characteristics are presented in Table 2.



**Fig. 1.** Curve showing probability of cure for overall patients. **Fig. 2.** Curve showing probability of cure w.r.t. sex. **Fig. 3.** Curve showing probability of cure w.r.t. age. **Fig. 4.** Curve showing probability of cure w.r.t. to disease type.

Table 3 shows the probability of recovery from TB at different time points after the starting of treatment. From this table, it can be observed that probability of recovery at 7 months of treatment under DOTS is 0.545 i.e., about 50% of the patients get cure after 7 months of treatment under DOTS. The probability of recovery after 10 months of treatment is 0.867. Thus, after 10 months of treatment under DOTS about 14 out of every 100 patients do not recover from TB. Past research show that the recovery time of TB patient is 6 to 10 months (Gavrilenko 2001).

### Conclusion

To assess the recovery time from tuberculosis is very important for monitoring and evaluation of the treatment components of tuberculosis control. In this present research work the time to recovery of patients suffering from TB who undergo DOTS is estimated by using the techniques of survival analysis. The average recovery time of TB patients undergoing

DOTS is found to be 7.2 months (95% C.I. 7.015-7.385). Researcher could find very few studies conducted to study the recovery time of patients suffering from TB. A study conducted in Ghana estimated that the average recovery time of TB was 22 weeks (about 6 months) (Jakperik and Ozoje 2012). In the study it was found that the recovery time of male and female are not significantly different. But in the present study it is found that the recovery time of males (7.067 months) is significantly less than female (7.433 months) counterpart. Unlike the study conducted by Jakperik and Ozoje (2012), the present study finds that recovery time of TB patients are not significantly different with respect to age.

From the results it can be concluded that the average recovery time of TB patients is found to be well within the targeted period. Less recovery time helps to reduce the burden of the disease from a community. Thus implementation of DOTS under RNTCR is found to be quite satisfactory in Dibrugarh district

of Assam. The male patients are seem to recover earlier than female counterpart. Age of patient does not seem to influence the recovery time who undergo DOTS.

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