

Original Research Article

Five-year survival rate in successfully treated tuberculosis patients in Mandya district, Karnataka: a cross sectional study

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Received: 14 October 2024

Accepted: 07 December 2024

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ABSTRACT

Background: National Tuberculosis Elimination Programme (NTEP) advises two years of follow up of patients cured from any form of tuberculosis. These patients are known to develop long term sequelae. Several studies have reported lower survival rate among recovered TB patients compared to general population.

Methods: Cross sectional study of 150 cured/treatment completed TB patients who had completed five years period after treatment, were selected across Mandya district by stratified random sampling method from seven taluks/blocks. Survival and regression analysis was done to determine the outcome and its risk factors.

Results: 13.3% of the study participants had succumbed due to various medical reasons. Respiratory and cardiac problems were the most common and 75% of the deaths happened between 3rd and 5th year. Five-year survival rate of the study population was 86.7% and for persons aged more than 60 years it dropped to 62.9%. People with DM, history of smoking, alcoholism was at higher risk of mortality along with age more than 60 years. Mean survival period reduced by 7.5 months, 6.8 months, 8.2 months among diabetic patients, smokers and alcoholics respectively. Eight participants had developed tuberculosis again and two of them were drug resistant cases. Binary logistic regression identified higher probability of death in patients with DM and those consuming alcohol.

Conclusions: Mortality among cured / treatment completed TB patients is 13.3%. Five-year survival rate of this population was 86.7%. DM and alcoholism were important predictors of mortality.

Keywords: Karnataka, Mortality, NTEP, Survival rate, Tuberculosis

INTRODUCTION

Tuberculosis (TB) despite being a preventable disease, affects around 10 million people every year, among which 1.5 million people succumb to it.¹ Persistent respiratory symptoms and lung dysfunction are common in patients with TB. The lung complications include and are not limited to airflow obstruction, fibrosis and bronchiectasis.²

Literature reports an increase in the incidence of non-communicable diseases like diabetes, acute myocardial infarction, and stroke after treatment of tuberculosis.³ In spite of successful anti tubercular treatment (ATT), the survivors are at an increased risk of mortality due to all causes in comparison to the general population with a standardized mortality ratio of 3.8 and a mortality rate of 59/1000 person-years suggesting, reduction in life expectancy.⁴⁻⁷

Studies have identified high risk populations which experience lower survival rate during and post treatment like, smokers, people aged >45 years, resource poor setting, diabetes mellitus (DM) patients, human immunodeficiency virus (HIV) patients and alcoholics.⁸⁻¹²

As reported by the published literature, median survival time after successful completion of tuberculosis treatment was 10.5 years and the survival probability for 11 years after was 70%.¹³ Evaluation of survival after completion of TB treatment and the associated causes of death not only estimate the burden of post-TB mortality in the community, but also identify the vulnerable population and help plan interventions to reduce post-TB sequelae, including death. However, the NTEP in India, follows up patients for two years after treatment completion. This study was conducted to determine the five-year survival rate, timeline of mortality and its determinants among patients successfully treated under Revised National Tuberculosis Elimination Program (RNTCP)/NTEP in Mandya district of Karnataka state.

METHODS

Study design and period

This was cross sectional descriptive study conducted between June 2022 to November 2022. The TB patients who were declared cured/treatment completed between June 2016 to March 2017 were interviewed.

Study population

Consisted of tuberculosis patients enrolled in Mandya district under RNTCP, who had successfully completed treatment and had been declared cured or treatment completed by the national programme.

Inclusion criteria

Pulmonary and extra pulmonary tuberculosis cases declared as cured and treatment completed respectively, residents of Mandya district and gave informed consent were included.

Exclusion criteria

Patients living with HIV and diagnosed to be having TB, patients who expired due to medicolegal causes (homicide, suicide, accidents) in the 5-year follow-up period of this study (2017-2022).

Sample size

Minimum required sample size was calculated to be 125 using formula for estimation of single proportion. Proportion of cured patients surviving at the end of 5 years was taken as 78% with a relative error of 10%.¹⁴ Thus calculated sample size was rounded off to 150.

Sampling method

Stratified random sampling. Mandya district has seven blocks in it. 20 patients from six blocks and 30 patients from one block (which has highest population) were randomly selected by from the registers maintained by Senior Treatment Supervisors (STS).

Data collection

These patients were visited at their residence and details were collected using a pre-structured questionnaire. Details were collected from the family members in case the participant was dead. Habits like smoking and alcohol was ascertained as dichotomous data using operational definitions. Patients who consumed alcohol at least once in a week were taken as alcoholics. Those who smoke / smoked either beedi or cigarette for at least five days in a week for more than one year were considered as smoker for this study. Quantification of the substance abuse was not done. TB cards of the patient was also referred with the help of Senior Treatment Supervisors (STS). Hospitalization records were utilized wherever available. Most probable cause of death was noted down from the hospital records.

Statistical analysis

Data was entered in Microsoft excel and analyzed using trial version of IBM-SPSS software. Variables were described using proportion, mean, range and Standard deviation. Bivariate analysis to identify difference in distribution of risk factors of mortality was done using Chi-square test or Fishers' exact test. Relative risk was calculated to estimate the magnitude of risk of mortality associated with various determinants. Kaplan-Meier Survival curves were plotted to analyze survival pattern among determinants which showed significant difference in bivariate analysis. Logistic regression was done to identify predictors and strength of the predictability.

RESULTS

Mean age of participants was 43.83 years (SD 18.34, Q1-30.00 and Q3 75.00 years). Majority of the study participants (44.66%) were between 19-45year age group. Male patients were 115 (76.7%) of the participants and 144 (96.00%) belonged to Hindu religion. Majority (57.30%) of the participants were working in semiskilled jobs when they were diagnosed with tuberculosis, where as 28.00% belonged to homemaker/students/business group and 14.70% were engaged in daily wage jobs. Median years of schooling was 5.5 years (Q1-0 and Q3-10) and 39.90% were non-literate.

Study included both pulmonary and extra-pulmonary patients which accounted for 111 (74.00%) and 39 (26.00%) respectively. Cat-1 cases constituted 135 (89.90%) of the participants and 130 (86.70%) among the total participants had completed treatment in 6 months

before declaring cured or treatment completed. Accredited Social Health Activist (ASHA) was the Directly Observed Treatment Short-course (DOTS) provider for 130 (86.70%) participants. People with DM at the time of diagnosis were 21 (14.00%) and 19 among them were on regular hypoglycemic medication. Smoking and alcohol consumption was practiced by 67 (44.70%) and 56 (37.30%) of the participants respectively. Fifty-three (35%) patients had the habit of both smoking and alcohol consumption. However, quantification of substance use was not done. During the follow up period eight cases developed tuberculosis disease again. Out of eight, five patients (62.50%) had suffered from relapse within first two years. Two cases were drug resistant among them.

A total of 20 deaths were reported among the study participants with a mortality rate of 13.30%. Highest mortality was noticed among patients aged more than 60 years (37.10%). Men had higher mortality rate (16.5%)

compared to females (2.90%). Respiratory failure and cardiac arrest were the most reported cause of death in younger age categories (19-45, 46-60 years). As shown in Figure 1, 75% of the deaths occurred between 3rd to 5th years of follow up.

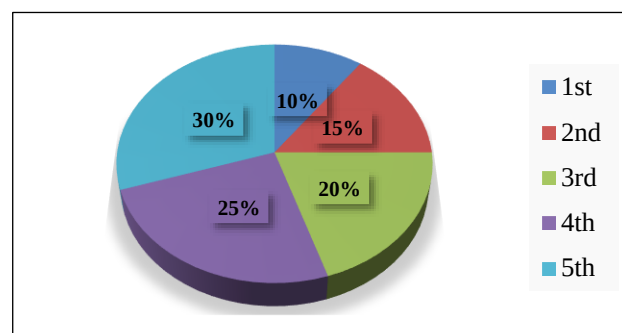


Figure 1: Proportion of deaths in study participants according to year of death.

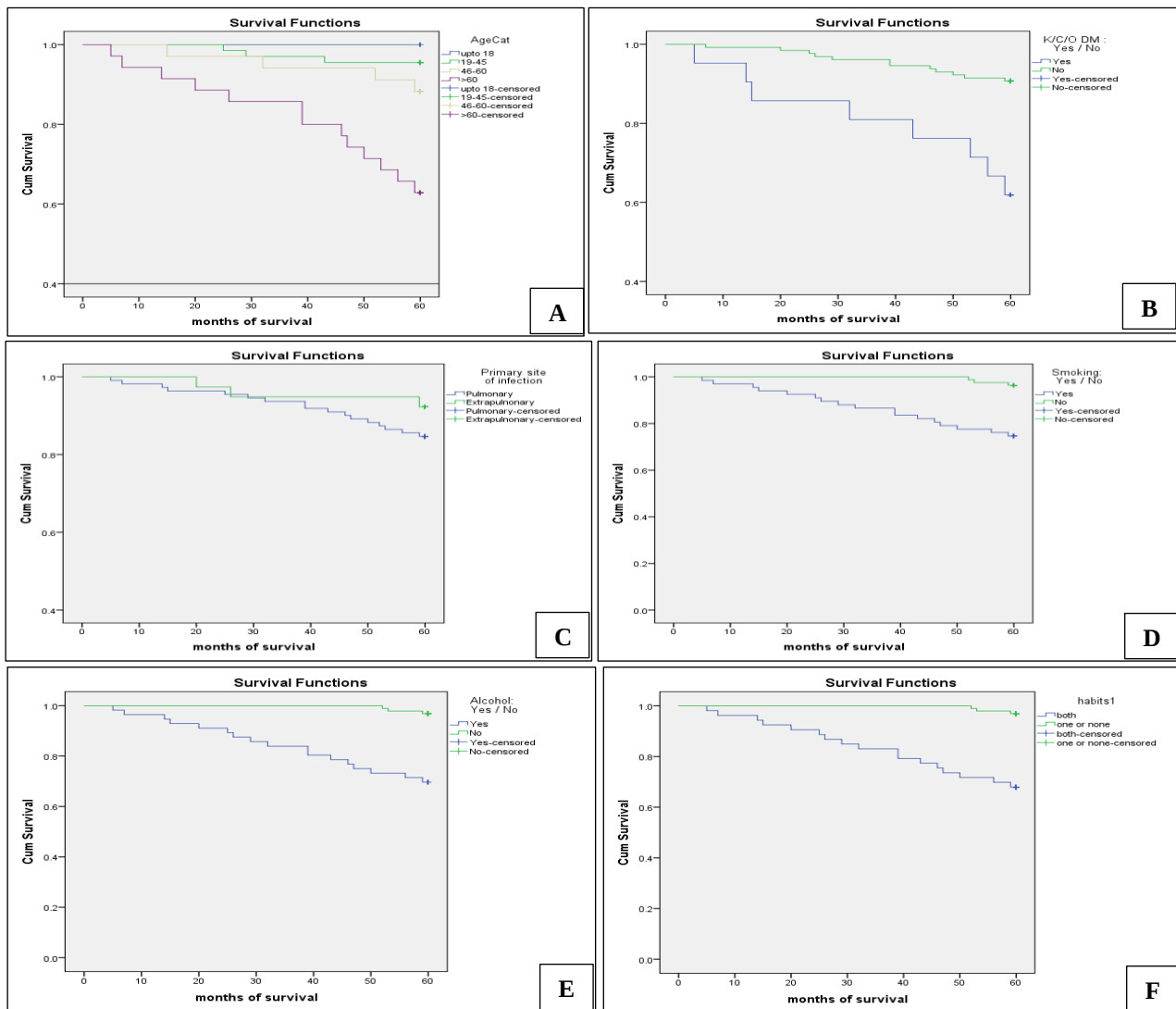
Table 1: Bivariate distribution of outcome in the study participants according to various determinants.

	Alive (%)	Dead (%)	Chi square/Fischer exact test	P value	RR
Age categories (yrs)					
Upto 18	14 (100)	0	19.880*	<0.001	-
19-45	64 (95.52)	3 (4.48)			
46-60	30 (88.23)	4 (11.77)			
>60	22 (62.85)	13 (27.15)			
Gender					
Male	96 (83.47)	19 (16.53)	4.336*	0.045	5.78
Female	34 (97.14)	1 (2.86)			
Primary site of infection					
Pulmonary	94 (84.68)	17 (15.32)	1.451	0.117	0.97
Extrapulmonary	36 (92.30)	3 (7.70)			
Category of treatment					
Cat 1	117 (86.66)	18 (13.34)	0.001*	1	1
Cat 2	13 (86.66)	2 (13.34)			
Occupation when TB was diagnosed					
Unskilled	20 (90.09)	2 (9.91)	7.782*	0.02	-
Semiskilled	69 (80.02)	17 (19.98)			
Homemaker/student/self employed	41 (97.61)	1 (2.39)			
Smoking					
Yes	50 (74.60)	17 (25.40)	15.189*	<0.001	8.33
No	80 (96.40)	3 (3.60)			
Alcohol consumption					
Yes	39 (69.60)	17 (30.40)	22.412	<0.001	10.00
No	91 (96.80)	3 (3.20)			
Both smoking & alcohol consumption					
Yes	36 (67.90)	17 (32.10)	24.914	<0.001	10.66
No	94 (96.9)	3 (3.10)			
Known case of DM					
Yes	13 (61.90)	8 (38.10)	12.957	0.002	4.09
No	117 (90.69)	12 (9.31)			
Hospitalized for complaints of TB affected organ					
Yes	9 (60.00)	6 (40.00)	11.006	0.001	4.09
No	120 (90.29)	13 (9.71)			

*Test statistic for Fischers exact test.

Table 2: Survival time estimation of mortality among study population (n=20).

Estimated mean survival time	Std. Error	95% Confidence Interval		log rank (Mantex Cox)	
		Lower bound	Upper bound	Chi-square	P value
Overall	56.831	0.846	55.173	58.489	-
Known case of DM					
Yes	50.333	3.792	42.900	57.766	14.457
No	57.822	0.717	56.417	59.227	
Smoker					
Yes	53.015	1.771	49.543	56.487	15.944
No	59.807	0.127	59.559	60.056	
Alcohol consumption					
Yes	51.643	2.070	47.585	55.701	24.166
No	59.830	0.112	59.610	60.050	
Both alcoholic and smoker					
Both	51.170	2.170	46.918	55.422	27.141
One or none	59.835	0.109	59.622	60.048	

**Figure 2: Kaplan Meier Survival curves of study participants according to; A) Age categories, B) Diabetic status, C) Site of infection, D) Habit of smoking, E) Alcohol consumption and; F) Both smoker and alcoholic.**

As seen in Table 1, on follow up bivariate analysis of the outcome and various determinants revealed a significantly higher mortality among the participants. Chi square/Fischers exact test found higher risk of mortality among men, geriatric age group, those in semiskilled occupations, Diabetic patients, smokers and alcoholics. As seen in Figure 2, Kaplan Meier survival analysis of the study participants with death as outcome measure, showed significant lower five-year survival rate among geriatric population, diabetic patients, alcoholics, smokers and both substance users. Over-all five-year survival rate was 86.7% and mean survival period among died participants, was found to be 56.77 months. Mean survival period reduced by 7.5 months, 6.8 months, 8.2 months and 8.7 month among diabetic patients, smokers, alcoholics and both substance users respectively as seen in Table 2.

Binary logistic regression with death as outcome variable found out having DM and habits of alcoholism to be significant predictor of mortality in five years, with an Odds ratio of 4.24 (0.867-20.73) in five years despite successful treatment of TB. However, the regression model could explain only 31.4% of the predictability by study variables.

New cases of tuberculosis were diagnosed in the family members of four participants. All were in direct household contacts like husband, father-in law, brother-in law and daughter. In all these families' participant was female patient and all were home-makers.

Ten participants were diagnosed with DM during the follow up period and half of them developed in first two years of completing ATT. Another six were diagnosed with complications related to organ affected by tuberculosis. A total of 15 participants required in-patient care for complaints related to TB affected organ.

DISCUSSION

Out of the 150 participants, 20 had succumbed in five years after successful completion of TB treatment in the present study. This accounts for 13.3% five-year mortality rate. Most (75%) of the deaths were witnessed between 3rd to 5th year of post treatment.

A similar study in Brazil (2001 to 2003) reported the possibility of 6-year survival after successful ATT to be 95.9% (95% CI: 94.8–97.0%).¹⁵ Likewise, a study conducted in Tiruvallur district of Tamilnadu noticed high mortality in the initial four years of post-TB treatment among the TB treated cohort.⁷

A Spanish cohort of 762 TB patients from the years 1995 to 1997 with successful treatment, was followed-up till 2005(8 years follow up). Among them, 173 patients (22.7%) died. Also, the cumulative probabilities of dying

at 1, 3, 6 and 9 years of follow-up were 4.5, 11.1, 17.7, and 25.9 percent, respectively.¹² A Mexican cohort revisited 305 patients with pulmonary TB after six years and again after 10 years of their initial diagnosis and treatment. Of the 78 deaths in their study, 38% died during the first-year post-diagnosis, 53% died before the second year, 72% after three years, 86% after four years, and 92.3% after five years. This study also noted poor survival among patients aged over 45 years.¹⁶ However, there was no significant difference between survival curves in terms of sex, which was in contrast to our study, where higher mortality was reported among men. Vietnamese cohort reported significantly higher mortality among patients aged 55 years.¹⁷ Thus, the findings of our study with respect to time of death after the ATT are similar to findings of other studies across the world and re-affirm the importance of longer follow-up of cured patients than just two years, practiced by NTEP.

The causes of death reported in the majority of cases in the present study were respiratory failure and cardiovascular accidents. One Vietnamese cohort, reported causes of death to be lung disease and immunodeficiency.¹⁷ In another study conducted in Denmark, in descending order, non pulmonary cancers, COPD, TB, lung cancer and heart diseases were all significantly more common causes of death among TB cases.¹⁸ A cohort study in Taiwan demonstrated that the overall incidence of ACS was higher in TB patients than in non-TB patients (2.10 vs. 1.51 per 1000 person-years).¹⁹ A systematic review study indicated potential role of TB in Cardiovascular disease.²⁰ Thus, the higher chances of cardiovascular accidents, observed in the present study is consistent with studies across the world. However, the follow up period and the mortality due to cardiac events co-incised with the COVID-19 pandemic. Role of COVID-19 as a confounder for cardiac complications in TB survivors should be dealt in detail, which was not done in our study.

Present study observed higher risk of mortality among patients of increasing age, male gender, smokers, alcohol consumption, extra pulmonary form of TB. Unlike present study, a study from Tiruvallur district of Tamilnadu studied mortality rate/1000 person-years and reported higher mortality among pulmonary cases (67.8) compared to extra pulmonary patients (23.5).⁷ Study from Velliyur, Tamilnadu, reported high mortality risk among patients aged >45 years, defaulters, failures and males exposed to both smoking and alcoholism.⁸ In Brazil, a five year survival study among TB patients showed that the relative risk (RR) of dying from TB increased significantly with age (from 4.7 to 10.5); and with male gender (1.6). It also stated that the reduction in survival time was significant among extrapulmonary and mixed clinical presentation (39.6 and 22.2 months, respectively).²¹

In the present study, mortality risk was significantly more among diabetics. In a Korean cohort of MDR TB, the mean survival time of patients with diabetes mellitus was 12 months less than those without DM.²² Spanish study also had 1.7 times higher risk of mortality among alcoholics which is consistent with the present study.¹² DM is identified as one of the most important drivers of TB in the community and the present study reiterates its role in TB mortality also.

CONCLUSION

After successful treatment, five-year survival rate was 86.7% with mortality rate of 13.3%. Highest mortality was observed between 3rd to 5th years after treatment completion. Leading causes of death were respiratory failure and cardiovascular accidents. Mortality was higher among elderly, men, alcoholics, diabetics and extra pulmonary TB.

ACKNOWLEDGEMENTS

We would like to thank the STS of Mandya district for their support in identifying the study population and their co-operation during data collection. We also thank Dr Sharath B. N., Professor and Head of Department of Community Medicine, ESI Medical College Bengaluru and Chairman of State Tuberculosis Operational Research for Karnataka for his valuable inputs.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Hugara S, Srivatsa S, Venugopalan S, Shetty SS, Harshitha, Anusha H. Five-year survival rate in successfully treated tuberculosis patients in Mandya district, Karnataka: a cross sectional study. *Int J Community Med Public Health* 2025;12:256-62.