Determinants of sputum conversion at two months of treatment under National Tuberculosis Programme, South India

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Abstract

Background: In India, Revised National Tuberculosis (TB) control programme (RNTCP) offers free diagnosis and treatment for TB, based on the Directly Observed Treatment Short (DOTS) course strategy. Under RNTCP, sputum conversion rate (SCR), at the end of 2 months of treatment is an important operational indicator, which is ideally expected to be 90%.

Objective: The objective of the present work was to investigate the factors associated with low SCR at the end of 2 months of treatment in Sira TB unit, Tumkur District, India.

Material and Methods: It is a retrospective cohort study of all new sputum smear-positive patients registered in RNTCP in 2011. Data were retrieved from the TB register maintained at the District TB center. Chi-square and Student's *t*-test were used for analysis of the study variables between patients who were sputum positive and sputum negative at the end of 2 months of treatment. Multivariate logistic regression was applied to determine the risk contributed by the variables towards non-conversion of sputum.

Results: Of the 268 included patients, 66.7% patients were sputum negative. Patients aged ≥ 45 years were twice the risk of being sputum positive (OR = 2.14) (*P* = 0.007). The odds of being sputum positive after 2 months of treatment was observed to be significantly high (OR = 7.12; 95% C.I. = 1.52–33.22; *P* = 0.01) for sputum grade 3+ at the time of diagnosis, respectively.

Conclusion: Elderly patients with a high bacilli load should be advised and counselled well regarding adherence to treatment. Further advice should be given on preventing spread of the disease by practising cough hygiene, as they are more infectious than remaining patients with less sputum-positive grade.

KEY WORDS: Tuberculosis, RNTCP, sputum grade, sputum conversion, pulmonary tuberculosis

Introduction

Tuberculosis (TB) continues to be huge public health challenge globally. The World Health Organization (WHO) Global TB report estimated that 9.6 million people developed TB in 2014 with more than half of patients (58%) in the South-East Asia and Western Pacific Regions. India alone accounts for 23% of the total cases globally[1] and each year 300,000 die of TB.[2]

The Revised National Tuberculosis Program (RNTCP) had been operational in India since 1997 and is based on the WHO recommended Directly Observed Treatment, Short Course (DOTS) strategy of thrice weekly intermittent regimen. The programme is primarily implemented through public sector health facilities. Under the programme, diagnosis is mainly based on sputum microscopy for pulmonary TB cases and treatment is provided free of cost to all TB patients.[3]

As per the RNTCP guidelines, the treatment success of pulmonary TB cases is monitored by follow-up sputum microscopy at every 2 months of treatment. First follow-up sputum

examination is performed at the time of completion of the intensive phase (end of 2 months of treatment), followed by another follow-up at end of fourth month of treatment, and final follow-up at the end of the treatment.[3] Monitoring the sputum conversion rate (SCR) at the end of 2 months of treatment is an important indicator under the programme guidelines, as it indicates the treatment progress at an early stage. Further, pulmonary sputum-positive TB is epidemiologically important as it represents the infectious pool of patients. An untreated patient can actually infect 10–15 patients each year.[4]

Although available evidence suggests that sputum positivity after 2 months of treatment is not predictive of treatment failure, relapse, or pre-treatment Isoniazid resistance, it remains an important operational indicator for the program.[5] The WHO treatment guidelines further suggest that a sputum positive for acid fast bacilli (AFB) at end of 2 months of treatment should trigger an assessment of the patient and further sputum monitoring.[6] Studies conducted across different countries including Morocco, Oman, Spain, Portugal, and Thailand reported age, male gender, high initial sputum AFB grade, and cavitary disease tend to be associated with poor sputum conversion rate at the end of 2 months of treatment.[4,7–10] Studies also indicate the association of diabetes, HIV, and smoking with higher sputum positivity at the end of the 2 months of treatment.[11,12] However, the studies examining factors associated with poor sputum conversion rate has been scant in India.[13–17]

Karnataka province located in South India has been among the few states with poor performance indicators, especially regarding sputum conversion rates.[18] Our research team has been working on strengthening health system in Tumkur District, located in southern part of Karnataka. The district TB officer of Tumkur District observed that sputum conversion rate at the end of 2 months was consistently low (66.8%) in Sira TB unit, among other five TB units. Therefore, an operational research study was conducted in Sira TB unit for determining the factors associated with poor sputum conversion rate at the end of 2 months of RNTCP treatment.

Material and Methods

Setting

The present study was undertaken in Sira TB unit (population 313,758, census 2011) As per RNTCP guidelines, one TB unit is established for every 500,000 population. Under each TB unit, there is one designated microscopic center (DMC) for every 100,000 of the population, which performs free sputum examination. Sira TB unit has five such DMCs.

Sputum smears are prepared by the Ziehl–Neelsen method and are examined for AFB by microscopy. The sputum smears are graded according to the number of AFB observed per high power field (HPF) as follows: > 10 AFB per oil immersion field in 20 fields is 3+ positive, 1–10 AFB per oil immersion field in 50 fields is positive 2+, 10–99 AFB per 100 oil immersion fields in 100 fields is positive 1+, and 1–9 AFB

per 100 oil immersion fields in 100 fields is sputum positive scanty. No AFB in 100 oil immersion fields in 100 fields is declared as sputum negative.[19] These sputum-negative patients undergo repeated sputum examination after a course of antibiotics and if the symptoms persist, chest X-Ray will be ordered to rule out sputum-negative pulmonary TB. Once TB is diagnosed, patients are registered in the RNTCP and they are monitored every 2 months during the course of the treatment. According to the RNTCP norms, sputum smear conversion rate is expected to be not less than 90% and the treatment success rate to be more than 85%.

Study Design

This is a retrospective cohort study of new pulmonary sputum-positive TB patients diagnosed by sputum microscopy at the five DMCs of Sira TB unit, who were started on category I RNTCP treatment in 2011. All patients who completed intensive phase and a continuation phase were included in the cohort. The patients with incomplete records, ones who died and lost to follow-up before completion of 2 months of intensive phase were excluded from the study.

Data Collection and Analysis

The study involved the collection of secondary data from the routine RNTCP registers and reports. Data were retrieved from the TB register maintained at the District TB center for the period of interest (first quarter to fourth quarter of 2011). 'Sputum-positive Cases' were those patients, who did not convert to sputum negative at the first follow-up sputum examination after 2 months of treatment or intensive phase. 'Sputum-negative cases' were those patients, who became sputum negative at the end of intensive phase. All the demographic data were systematically entered into the excel sheet. Patient names were not collected, instead patient TB numbers were used for analysis to avoid any identifiable information of patients.

Statistical analysis was performed using SPSS 16.0 ver. The study findings were presented as percentages and mean with standard deviation (SD). Chi-square and Student's *t*-test were used for analysis of the study variables between sputum-positive and sputum-negative patients at the end of 2 months of follow-up sputum examination. *P*-value less than 0.05 was considered as significant. Further, multivariate logistic regression was applied to determine the risk contributed by the variables.

Results

A total of 280 sputum-positive pulmonary TB patients were initiated on treatment. Among these patients, 12 were excluded from the study (seven had died and five were lost to follow-up, before completing the 2 months of intensive phase). The mean age of patients was observed to be 42.12 ± 15.4 years. Of the total patients, 190 (70.8%) were males and 16 (5.9%) patients were co-infected with HIV.

Table 1: Factors associated with sputum non-conversion at the end of 2 months of treatment

	Sputum negative (*n* = 179)	Sputum positive (*n* = 89)	*P*-value
Mean age ± SD	40.5 ± 15.34	45.2 ± 15.39	0.02
Gender			
Male, *n* (%)	121 (67.6%)	69 (77.5%)	0.09
Female, *n* (%)	58 (32.4%)	20 (22.4%)	
Initial sputum grade			
0, *n* (%)	15 (8.3%)	2 (2.2%)	0.00
1, *n* (%)	65 (36.3%)	16 (17.9%)	
2, *n* (%)	46 (25.7%)	18 (20.2%)	
3, *n* (%)	53 (29.6%)	53 (59.5%)	
Treatment outcome			
Cured, *n* (%)	168 (93.8%)	75 (84.2%)	
Died, *n* (%)	2 (1.12%)	0 (0.0%)	
Default, *n* (%)	4 (2.2%)	5 (5.6%)	
Failure, *n* (%)	5 (2.7%)	9 (10.1%)	
HIV status			
Negative, *n* (%)	166 (92.7%)	86 (96.6%)	0.20
Positive, *n* (%)	13 (7.2%)	3 (3.3%)	

Table 2: Logistic regression to test association of variables with sputum non-conversion at the end of 2 months of treatment

Risk factors	Adjusted odds ratio	95% C.I.	P-value
Age			
0–44	Reference		
45 and above	2.14	1.22–3.74	0.007
Sex			
Female	Reference		
Male	1.48	0.78–2.79	0.23
Initial sputum grade			
Scanty	Reference		
1+	1.62	0.33–7.97	0.55
2+	2.70	0.55–13.26	0.22
3+	7.12	1.52–33.22	0.01

Of the 268 included patients, 179 (66.7%) patients were sputum negative and 89 (33.2%) patients were observed to be sputum positive at the end of 2 months of intensive phase of treatment. The mean age of these patients was found to be 45.2 ± 15.39 years which was significantly higher than mean age of sputum-negative patients (40.5 ± 15.34 years) (*P* = 0.02). Of the sputum-positive patients at the end of 2 months of treatment, 69 (77.5%) were males. Among these patients, 16 (17.9%) had sputum grade 1+, 18 (20.2%) patients had grade 2+, and 53 (59.5%) patients had grade 3+ at the time of initiation of the treatment. Among the sputum-positive patients, 75 (84.2%) were declared cured at the end of the treatment (Table 1).

Multivariate logistic regression was applied to evaluate the risk contributed by gender, age, and sputum grade on the sputum conversion at the end of the 2 months of treatment. Patients with age 45 years and above were observed to be at two-fold risk (O.R. = 2.14, 95% C.I. = 1.22–3.74) of being sputum positive (*P* = 0.007). Males were found to be at an increased risk but it was not statistically significant. The odds associated with higher sputum grades at the time of diagnosis were 1.62 (95% C.I. = 0.33–7.97), 2.70 (95% C.I. = 0.55–13.26), and 7.12 (95% C.I. = 1.52–33.22) for 1+, 2+, and 3+, respectively. Sputum grade 3+ at the time of diagnosis was found to be significantly associated (*P* = 0.01) with sputum non-conversion at the end of 2 months of follow-up of the treatment (Table 2).

Discussion

The present study, prompted by a low sputum conversion rate at the end of 2 months of treatment under RNTCP setting, found patients of 45 years and above age and initial high sputum grade (3+) were associated with poor sputum conversion at the end of 2 months of follow-up among sputum-positive new pulmonary TB patients.

The present study showed lower sputum conversion rate (66.8%) after 2 months of follow-up sputum examination. While one study from Chennai reported sputum conversion rate to be 60% at the end of 2 months of intensive phase,[13] another study in Mumbai reported conversion rate of 78% after 8 weeks of the follow-up of the treatment.[15]

The mean age of sputum-positive patients was observed to be significantly higher than sputum-negative patients at the

end of the 2 months of follow-up in the present study. The results of the present study corroborates with a study conducted in South India reporting that age more than 45 years is associated with poor sputum conversion rate of 60%.[13] Other studies elsewhere have also reported that higher the age, higher is probability of a poor conversion rate.[4,10,20–22]

In the present study, percentage of males (77%) was higher among sputum-positive patients. although this association was not observed to be statistically significant. Unlike present study, some studies have reported an association of male gender with poor sputum conversion rate.[9,10]

The present study reported significant association of grade 3+ AFB at the initiation of treatment and low sputum conversion at the end of 2 months of follow-up sputum examination. These findings are in congruence with the studies conducted in different cities of India including Delhi, Mumbai, Gauhati, and Chennai for patients treated in the RNTCP by the DOTS regimens.[15–17,23] This finding is of significance as initial sputum smear grading can be used to identify patients with higher probability of not converting to sputum negative after 2 months of treatment.

The major limitation of the present study is that the data were extracted from TB register. Thus, other possible factors affecting sputum conversion like diabetes, smoking, substance abuse, body weight at the initiation of the treatment could not be adjusted for, as this data is not routinely collected in the framework of the program in the TB register. Nonetheless, present study findings help to prioritize patients' age and initial high AFB count for counselling under programmatic conditions. Patients with a high bacilli load should be advised and counselled well regarding adherence to treatment. Further they should be given advice on preventing spread of the disease by practising cough hygiene, as they will be more infectious than remaining patients with less sputum-positive grade.

Conclusion

The problem identified by District TB officer led to the study investigating determinants of low sputum conversion rate. The present study revealed initial high AFB grade and age to be associated with poor sputum conversion rate. Thus, due consideration should be given to these factors for developing guidelines related to treatment and monitoring of the programmes. Programme Managers and field staff should be encouraged to initiate such enquiry in order to strengthen the programme.

Under RNTCP, monitoring the sputum conversion rate (SCR) at the end of 2 months of the treatment is an important indicator. Studies in many countries report age, male gender, high initial sputum Acid Fast Bacilli (AFB) grade, and cavitory disease to be associated with poor sputum conversion rate at the end of 2 months of treatment. However, the studies examining factors associated with poor sputum conversion rate has been scant in India. Karnataka, located in South India, has been among the few states with poor performance indicators, especially regarding sputum conversion rates. The present study reported association of initial high AFB grade and age with poor sputum conversion rate, at the end of the 2 months of treatment, in district of Karnataka province. While monitoring treatment, these associated factors should be considered in the treatment programme.

Acknowledgment

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