Original Article

IMPACT OF IMPROVED TREATMENT SUCCESS ON THE PREVALENCE OF TB IN A RURAL COMMUNITY BASED ON ACTIVE SURVEILLANCE

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Summary

***Objective*:** To study the impact of improved treatment outcome of a cohort of patients treated under DOTS strategy on the prevalence of pulmonary tuberculosis (TB) in the community.

***Design*:** The data from TB register of one Tuberculosis Unit (TU) in Tiruvallur district of Tamilnadu, and two TB disease surveys conducted in the same area during 1999-2003 were analysed. The successful treatment outcome was compared to the prevalence of TB in the subsequent cohort.

***Results*:** The proportion of patients who completed treatment successfully was 75.3% in the first cohort period. This higher proportion of treatment success among patients treated under DOTS in the first cohort period (1999-2001) compared to the 51-55% reported during SCC, resulted in a lower prevalence of smear-positive cases, irrespective of culture results observed in the survey conducted during 2001-2003 compared to that in the survey conducted during 1999-2001 (252 vs. 323 per 100,000; annual decline of 9%). Similarly, a decline in culture-positive cases, irrespective of smear results, was also observed (443 vs. 605; annual decline 11%).

***Conclusion*:** The higher proportion of successful completion of treatment after DOTS implementation was associated with a substantial decline in the prevalence of TB. These findings showed that we are in the direction towards achieving the Millennium Development Goals (MDGs). **[*Indian J Tuberc 2008; 55:22-27*]**

Key words: TB, DOTS, Cohort, Treatment outcome, Prevalence

INTRODUCTION

Tuberculosis (TB) is highly prevalent in India in terms of morbidity and mortality[1]. It is estimated that India accounts for one-fifth of world's new TB cases. World Health Organization (WHO) declared tuberculosis a global public health emergency in 1993 because of the high mortality rate among adults, its association with HIV infection and emergence of Multi-Drug Resistance (MDR) TB. After the failure of the National Tuberculosis Programme (NTP) as reviewed in 1992, Government of India revised the tuberculosis control and launched the Directly Observed Treatment Short course (DOTS) under the Revised National Tuberculosis Control Programme (RNTCP) with the aim of achieving 85% cure among new patients diagnosed to have pulmonary tuberculosis and detect at least 70% of the cases in the community[2].

The key components of DOTS strategy are political commitment, sputum diagnosis by smear microscopy, short course chemotherapy under direct supervision, uninterrupted supply of drugs, monitoring, recording and evaluation of the programme. This is an effective and successive programme for the control of the disease. Tuberculosis Research Centre (TRC) in collaboration with Government of Tamil Nadu established a centre in one TU of Tiruvallur district, Tamil Nadu for DOTS implementation, tuberculosis control, training and research.

Government of Tamil Nadu implemented the DOTS strategy in the year 1999 in Tiruvallur district. There are 17 health facilities (HFs) in the study area. Under the DOTS programme, patients are detected by symptom screening at this HFs through the examinations of three sputum smears for acid-fast bacilli. All patients diagnosed based on three sputum

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examinations are put on anti-TB treatment. In this strategy, smear microscopy is the most efficient means of case detection among those persisting with symptoms suggestive of pulmonary tuberculosis (cough of three weeks or more with or without other clinical symptoms). All patients diagnosed with tuberculosis are given directly observed treatment in accordance with RNTCP policies[2]. All the smears are stained and examined by Ziehl – Neelson microscopy for detection of tuberculosis. If the patient is positive on smear microscopy on at least two specimens and not treated previously for TB for more than one month, he is termed as new sputum smear-positive case and put on Category I regimen $2(HRZE)_3$ /$4(HR)_3$ (H-isoniazid; R-rifampicin; Z=pyrazinamide; E=ethambutol; S-streptomycin). Numbers before the letters indicates the duration in months and that in subscript indicates the number of times the drug given in each week). If the patient is sputum smear-positive and treated for more than a month, he is treated under Category II regimen $2(HRZES)_3$ /$1(HRZE)_3$ / $5(HRE)_3$. Such patients will be either a relapse case after declaring cure when treated first or failure case or default case. Other sputum smear-negative cases not seriously ill, extra pulmonary cases are put on Category III regimen $2(HRZ)_3$ /$4(HRE)_3$. In case, the smear is positive only on one specimen out of three specimens examined, the patient is prescribed for one week antibiotic treatment and reviewed after a week with a chest X-ray. If the symptom is still persisting, the patient is put on Category III regimen. Intensive phase treatment of patients in categories I and II is extended for one month if the smear is positive at the end of the intensive phase. Every dose of treatment is to be directly observed in the initial intensive phase of treatment and at least the first of the three doses is to be directly observed during the continuation phase.

Before the implementation of DOTS, the Government of India introduced Short Chemotherapy (SCC) on a pilot basis in the District Tuberculosis Programme in 18 districts spread over India. A concurrent cohort analysis of the data collected from these districts during 1985-1991 showed that the overall treatment completion for SCC was 51-55% with a case finding of 41%[3]. Two community surveys were conducted in Tiruvallur district, Tamil Nadu during 1999-2001 and 2001-2003 to estimate the prevalence of pulmonary TB. Patients who were diagnosed based on smear and/or culture were referred and treated under DOTS as per RNTCP guidelines. From the first survey, the prevalence of pulmonary TB was estimated to be 323 per 100, 000 for smear-positive cases and 605 per 100, 000 for culture-positive cases[4]. These estimates served as the baseline information at the end of the SCC and start of the DOTS implementation.

This paper describes the treatment outcome of a cohort of patients registered under DOTS and compares with the prevalence of TB as estimated from the disease surveys conducted after the implementation of the DOTS strategy.

MATERIAL AND METHODS

The study area is a rural population of Tiruvallur district in Tamilnadu where TRC monitored the DOTS programme for a period of about six years since its implementation in 1999. Patients diagnosed at any one of the HFs were treated for TB as per the RNTCP guidelines[2]. TRC has undertaken a series of disease surveys at every two and-a-half years to measure the epidemiological impact of DOTS implemented from 1999 in Tiruvallur district. These disease surveys were undertaken in a random sample of 82,000 adults aged 15 years or more. The sample size estimated for community disease survey was based on an annual incidence of culture-positive TB of 260 per 100,000 population, a precision of 20% at 95% confidence level, with the coverage of examined population 9% and a design effect of two. The methodology of survey is explained elsewhere[4]. In each survey, all persons in the selected villages/units were registered by door-to-door census and all adults aged $\geq$15 years were questioned about chest symptoms and underwent chest radiograph (70 mm photo-fluorogram posteroanterior view) at a nearby centre. For those with an abnormal radiograph suggestive of TB and/or chest symptoms, attempts were made to collect two sputum specimens. Those who were absent for examinations were revisited

the same day or on subsequent days until at least 90% had the required investigations. The sputum specimens were examined by fluorescence microscopy and cultured on Lowenstein-Jensen medium. Those yielding growth were subjected to identification tests for *Mycobacterium tuberculosis* and drug susceptibility tests. A case of tuberculosis was defined as a person with a positive smear (>3 acid-fast bacilli) irrespective of culture results.

The details of all patients started on treatment in a TU are entered in a register called Tuberculosis Register (TB Register) and these patients are monitored in accordance with the RNTCP guidelines. This register is maintained by the Senior Treatment Supervisor (STS). The TB Register is the backbone of the DOTS strategy. Every patient put on treatment is registered under a specific TB number. A TB patient is known by this number and the year in which he/she was registered. The particulars like name, age, sex, category, type, smear result at admission, 2^{nd} /3^{rd} month, 4^{th} /5^{th} month and at the end of treatment are the details entered in the TB Register. The treatment outcome of the patient is an important parameter of the programme available in the TB Register. The international definitions were followed to classify TB patients according to outcome as follows[5]:

1. **Cured**: Initially smear-positive patient who has completed treatment and had negative sputum smears, on at least two occasions, one of which was at completion of treatment.
2. **Treatment Completed**: Sputum smear-positive case who has completed treatment, with negative smears at the end of the initial phase but none at the end of treatment (or) Sputum smear-negative TB patient who has received a full course of treatment and has not become smear-positive during or at the end of treatment (or) extra-pulmonary TB patient who has received a full course of treatment and has not become smear-positive during or at the end of treatment.
3. **Default**: A patient who, at any time after registration, has not taken anti-TB drugs for 2 months or more consecutively
4. **Expired/Died**: Patient who died during treatment, regardless of cause.
5. **Failure**: Smear-positive case who is smear-positive at five months or more after starting treatment. Also, a patient who was initially smear-negative but who became smear-positive during treatment.
6. **Transferred out**: A patient who has been transferred to another TU/District and his/her treatment results are not known.

All new TB patients identified in the two prevalence surveys and treated under DOTS along with other new smear-positive cases detected from other areas not included in the sample and registered in the TU from May 1999 to June 2001 formed the study population.. The data collected from the study was computerized, edited and corrected for any discrepancies. The proportion of patients who successfully completed the treatment was obtained. The potential risk factors for a higher likelihood of default from treatment were identified. The prevalence of the smear-positive and culture-positive cases was estimated from the second survey and compared to that in the first survey. Chi-square test of significance was used to test the difference in proportions. A p value of ≤ 0.05 was considered as statistically significant.

RESULTS

A total of 805 new smear- positive TB patients were registered during the above period; successful treatment completion rate was 75.3% and 15.9% had defaulted. The prevalence of TB (smear-positive cases irrespective of culture results and culture-positive cases irrespective of smear results) estimated from the first survey and second survey is in Table 1[4]. The prevalence of smear-positive cases, irrespective of culture results, was 252 in the second survey as compared to 323 per 100,000 in the first survey. The corresponding figures for culture-positive cases were 443 and 605 per 100,000 respectively. The annual decline in the prevalence of smear-positive cases from the first survey and second survey was estimated to be 9%. The corresponding figure for culture- positive cases

Table 1: Prevalence of pulmonary tuberculosis (per 100000) in two disease surveys conducted during 1999-2001 and 2001-2003 in a TU in Tiruvallur district, Tamil Nadu.

Survey (round)	Population	Smear positive*	Culture positive**
First survey (1999-2001)	83390	323	605
Second survey (2001-2003)	85472	252	443
Annual decline (%)	-	9	11

* Irrespective of culture ** irrespective of smear

$$\text{Annual decline (\%)} = \frac{(P_1 - P_2) \times 100}{P_1 \times N}$$

P_1 and P_2 are the prevalence at two time points at an interval of 'N' years.

Table 2: Risk factors for default of patients registered during 1999-2001under a DOTS programme in Tiruvallur district, Tamil Nadu

Factors		Number*	Default (%)	P value
Age	<45	358	44 (12.3)	P<0.001
	≥45	376	84 (22.3)	
Sex	Male	581	114 (19.6)	P<0.01
	Female	153	14 (9.2)	
Education	Illiterate	316	56 (17.7)	P=0.1
	Literate	348	47 (13.5)	
Occupation	Un-employed	173	32 (18.5)	P=0.2
	Employed	493	72 (14.6)	
Patient's Delay	≤ 4 weeks	508	78 (15.4)	P=0.7
	> 4 weeks	136	19 (14.0)	
DOTS convenient	No	97	19 (19.6)	P=0.4
	Yes	447	72 (16.1)	
Smoking	No	350	32 (9.1)	P<0.001
	Yes	314	71 (22.6)	
Alcoholism	No	438	40 (9.1)	P<0.001
	Yes	227	63 (27.8)	
DOTS provider	Private	272	44 (16.2)	P=0.5
	Government	394	57 (14.5)	
DOTS centre	Private	333	60 (18.0)	P<0.05
	Government	333	41 (12.3)	
Supervision-during IP	No	203	27 (13.3)	P=0.4
	Yes	461	74 (16.0)	

*Those successfully completed treatment including default

Note: For variables except for sex and age, the number of patients is less than 734 due to non-availability of all patients at the time of interview.

was 11%. After the implementation of DOTS during this cohort period, case detection was about 80% with a cure rate of 75%. This has resulted in a lower prevalence of smear-positive as well as culture-positive cases in the subsequent survey (323 to 252 and 605 to 443 per 100,000 respectively).

Risk factors for default: The distribution of patients according to those successfully completed the treatment and defaulted is given in the Table 2. A uni-variate analysis showed that a higher default was significantly associated with patient's sex (male), aged < 45 years, smoking, alcoholism and the DOTS centre (private) where patients took treatment. A multivariate analysis showed that age and alcoholism were the independent risk factors associated with a higher likelihood of default.

DISCUSSION

The Tiruvallur area provides a unique opportunity to evaluate the TB situation before and after implementation of DOTS. The epidemiological data generated during the 15 year follow-up of BCG vaccine Trial in this area showed that there was no decline in the prevalence of smear-positive cases over the period 1968-1986 (pre-SCC period) [6]. Using available information indicated in NTP, the efficiencies were about 30% for case finding, 35% for case holding, 80% for chemotherapy and 50% for relative efficiency (ie. the proportion of patients with successful outcome even without completing their prescribed course of treatment relative to the proportion with a favourable response at the end of the prescribed course). From these estimates, the success rate was estimated to be only 16%[7]. The three tuberculin surveys conducted among children aged 1- 9 years in 1969, 1979 and 1984 in this area showed that there was no change in the prevalence of infection namely, 9.0%, 10.2% and 9.1% and the computed ARTI of 1.7%, 1.9% and 1.7% respectively[8].

A repeat survey conducted during 2001-2003 after the baseline survey (1999-2001) in the same population showed that the annual decline was of 9% and 11% for smear-positive and culture-positive cases respectively. The ARTI estimates from the three tuberculin surveys conducted in the same area among children aged <10 years during 1999-2005 were 1.6%, 1.4% and 1.2% respectively[9]. There was a significant decline in the trend of TB infection (annual decline of 6%). An increase in the success rate due to the implementation of the effective DOTS strategy was in association with a substantial reduction in the prevalence of TB and infection as demonstrated from the disease and tuberculin surveys carried out in the area.

The successful treatment outcome obtained in our study was less than the national expected average of 85%. The cure rate was 91% among the category I patients treated under DOTS in one of the chest diseases clinics run by the Municipal Corporation of Delhi[10]. The study concluded that the cure rate could have been more if tracing of defaulter had been intensified. Our study had a higher default rate and we identified old age and alcoholism as the independent risk factors necessitating targeted health education programme through Information, Education and Communication (IEC) for this group of patients. An earlier report from the same area also recommended retrieval action of defaulters in order to increase the successful treatment outcome[11].

We have correlated the activities of the HFs in this area and the programme indicators like conversion and cure[12]. Both were found to be well correlated indicating that success of the DOTS depends on the health function. This emphasizes the need for periodic evaluation of the functioning of each HF for better management of treatment.

CONCLUSION

The study showed that an increase in the successful treatment outcome of the patients treated under DOTS was associated with substantial decline in the prevalence of TB in the community. This would be a milestone towards achieving the MDGs of reverting and reducing the prevalence of TB by 50% in 2015 related to 1990 levels.

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