Original Article

TRENDS IN THE PREVALENCE OF PULMONARY TUBERCULOSIS OVER A PERIOD OF SEVEN AND HALF YEARS IN A RURAL COMMUNITY IN SOUTH INDIA WITH DOTS[@]

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Summary

Setting: Tiruvallur district In Tamil Nadu where DOTS was implemented by the State Government as the tuberculosis control measure in 1999, and monitored by the National Institute for Research in Tuberculosis for over five years.

Objective: To estimate trends in TB prevalence in a rural community with DOTS.

Design: Surveys of pulmonary tuberculosis were undertaken in representative samples of subjects aged $\geq$15 years (N = 83,000 – 92,000), initially and after two and half, five and seven and half years of implementation of DOTS. Sputa were collected from those with abnormal radiograph and/or presence of chest symptoms, and examined by direct smear and culture.

Results: The prevalence of culture-positive tuberculosis was 607, 454, 309 and 388 per 100,000 in the four surveys, and that of smear-positive tuberculosis was 326, 259, 168 and 180. In the first five years; annual decrease was 12.4% (95% CI 10.4 - 14.4%) for culture-positive tuberculosis, and 12.2% (95% CI 8.0–16.2) for smear-positive tuberculosis. This was, however, followed by a significant increase in the next two and half years. The average new smear-positive case-notification rate was 75 per 100,000 during first four years but declined to 49 in subsequent years. There were no methodological differences during this period and information on changes in socio-economic indicators and nutritional standards was unavailable.

Conclusion: Despite the average annual success rate (78%) in this tuberculosis unit being lower than the expected rate of 85%, the implementation of DOTS was followed by a substantial decrease in the prevalence of pulmonary tuberculosis over the seven and half year period. Our findings suggest that sustaining the high effectiveness of DOTS programme needs vigilant supervision. **[*Indian J Tuberc 2013; 60:168-176*]**

Key words: Tuberculosis, DOTS, Prevalence trends

INTRODUCTION

The WHO 2012 Global Tuberculosis Control Report reveals that there were 1.4 million estimated deaths due to tuberculosis in 2011, of which 300,000 were in India.[1] In 1997, the 'Directly Observed Treatment Supervised' (DOTS)-based Revised National Tuberculosis Control Programme (RNTCP) was initiated in India.[2] This programme, as recommended by WHO, was implemented by the Tamil Nadu Government in the peri-urban district of Tiruvallur, south India, in 1999. To investigate the impact of DOTS implementation, periodic disease prevalence surveys were conducted. The findings of the baseline survey and the resurveys at two and half and five years have been reported earlier.[3-5] A further survey was conducted at seven and half years, and its findings are described here.

MATERIAL AND METHODS

Study area and population

Our study was conducted in a TB Unit (covering 500,000 predominantly rural population) in Tiruvallur area. A stratified cluster sampling design was employed [3]. A simple random sample of 50 villages was selected from each of the five blocks, proportionate to the census population, and three towns were selected in a similar manner. In all the

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four surveys (1999-2001, 2001-2003, 2004-2006, 2006-2008), the *same* units were investigated.

All persons aged ≥ 15 years (N = 83,000-92,000) in the four surveys were registered by door-to-door census. The resurvey activity comprises updating the census data through registration of new entrants (new born, settlers and persons missed in the previous survey) in the study population. Specially trained field investigators interviewed all persons in the selected sites at home. A quality check on symptom screening was done by a supervisor on a random sample of 5% of subjects.

All persons were also screened by a chest radiograph (MMR X-ray) for tuberculosis. The radiograph was read independently by two readers and, in case of disagreement, by a third reader. For those with an abnormal chest radiograph and/or chest symptoms or previously diagnosed cases in the earlier surveys, two sputum samples were collected and examined by fluorescent microscopy and culture for *Mycobacterium tuberculosis*. All study subjects were informed of the purpose of the survey, and their written consent was obtained. The Institutional Ethics Committee approved the study.

Treatment in study area

All TB patients diagnosed were treated as per the national policy. National technical guidelines[2] were followed.

Case notification rate

The projected populations were estimated from the 2001 census population and decadal growth rate of 35.3% of Tiruvallur district. Thereafter, the case notification rate (CNR), defined in the RNTCP as the number of newly reported smear-positive TB cases per 100,000 population, was determined.

Treatment success

This was defined as the percentage of new smear-positive PTB cases registered under RNTCP for treatment who were cured or had completed the full course of treatment.

Estimation of the number of cases in subjects with no sputum/radiograph

The number of sputum-positive cases among those who did not have sputum collected was estimated from the nature of the radiographic abnormality by utilizing the probability of a positive finding in the appropriate radiographic category in the corresponding survey. To estimate the number of cases among those with no radiograph, the relative risk (RR) of a person with no radiograph having chest symptoms (compared to a person with a radiograph) was taken as a proxy for the RR of this person being a case of tuberculosis. This risk was homogenous in the four surveys (P > 0.3), and the common estimate was 0.6 for males and 0.4 for females, Details of both adjustments have been published earlier.[4,5]

Data analysis and Statistical methods

The population in each selected cluster was stratified by age (15-34, 35-54, ≥ 55 years) and sex, the prevalence estimated, and standardized by the 'Direct' method [6], using the baseline survey population in the same cluster as the 'Standard'. The overall prevalence for each survey was then computed as a weighted average of the cluster prevalences, the weight being the corresponding population size. Next, the variance of the prevalence was estimated allowing for varying size of the clusters[7] and stratification by blocks. Finally, a weighted regression (linear and quadratic) of prevalence on time was undertaken, and the univariate and multivariate correlation (r and R) were determined, using the SPSS version 14.0 (SPSS version 14.0 Chicago, IL, USA). Fuller details of data analytical methods have been described in earlier reports.[3-5,8]

RESULTS

Numbers in study and proportions investigated

Eligible subjects in the four surveys varied from 83,000 to 92,000. Males constituted 49% of the study sample in all the surveys (Table 1). As regards age, there were fewer young adults (15-34 years) in the resurveys at five and seven and half years (48%, 47%) than at the baseline and first resurvey (50%). The proportion investigated for various examinations was consistently high - about 90% for chest radiography and for symptom inquiry, and at least 95% for sputum examination.

Cases of pulmonary tuberculosis detected

The numbers of culture-positive cases detected in the four surveys were 457, 344, 253 and 332, respectively (Table1). Of these, 80% to 83% were males (P=0.7). The age profile also was similar in the four surveys (P=0.6).

The corresponding numbers of smear-positive cases detected in the four surveys were 245, 196, 136 and 155, respectively (Table1). The proportion of males varied between 79% and 85% (P = 0.7). Again, the age profile was similar in the four surveys (P=0.7).

Table 1: Number of eligible persons examined and number of tuberculosis cases detected

	Baseline Survey		2½-year survey		5-year survey		7½-year survey	
	No.	%	No.	%	No.	%	No.	%
Number examined	83425	*100*	85474	*100*	89413	*100*	92255	*100*
Male	40848	*49.0*	41607	*48.7*	43477	*48.6*	44996	*48.8*
Female	42577	*51.0*	43867	*51.3*	45936	*51.4*	47259	*51.2*
15 - 34 years	42118	*50.5*	43138	*50.5*	43044	*48.1*	43702	*47.4*
35 - 54 years	27141	*32.5*	28199	*33.0*	30567	*34.2*	32480	*35.2*
> 55 years	14166	*17.0*	14137	*16.5*	15802	*17.7*	16073	*17.4*
Culture-positive cases	457	*100*	344	*100*	253	*100*	332	*100*
Male	381	*83*	276	*80*	204	*81*	276	*83*
Female	76	*17*	68	*20*	49	*19*	56	*17*
15 - 34 years	73	*16*	63	*18*	35	*14*	46	*14*
35 - 54 years	178	*39*	137	*40*	99	*39*	142	*43*
> 55 years	206	*45*	144	*42*	119	*47*	144	*43*
Smear-positive cases	245	*100*	196	*100*	136	*100*	155	*100*
Male	209	*85*	165	*84*	109	*80*	127	*82*
Female	36	*15*	31	*16*	27	*20*	28	*18*
15 - 34 years	37	*15*	39	*20*	19	*14*	27	*17*
35 - 54 years	101	*41*	78	*40*	60	*44*	70	*45*
> 55 years	107	*44*	79	*40*	57	*42*	58	*37*

Prevalence of pulmonary tuberculosis

The prevalence of culture-positive tuberculosis was 607 per 100,000 at the baseline survey and decreased significantly to 454, 309 and 388 per 100,000 at two and half, five and seven and half years (Table 2). Regression analysis showed that a linear model was inadequate to explain the variation in prevalence with $r^2 = 0.59$, and that a quadratic model improved the fit significantly ($P < 0.001$) and substantially with $R^2 = 0.93$ (Fig. 1). The findings with smear-positive tuberculosis showed the same pattern (Fig. 1), the prevalence being 326, 259, 168 and 180 per 100,000 (Table 2); and the corresponding values of r^2 and R^2 were 0.81 and 0.95, respectively, the quadratic fit being significantly better ($P=0.02$).

Confirming the appropriateness of the quadratic model, further analysis showed that the prevalence of culture-positive tuberculosis declined steadily in the first five years by 12.4% per annum

Table 2: Prevalence of culture-positive/smear-positive tuberculosis by sex and age (per 1,00,000 population

Pulmonary tuberculosis	Group		Baseline Survey	2.5 years*	5 years*	7½ years*
Culture-positive						
		Total	607	454	309	388
	Sex	Male	1043	752	513	665
		Female	189	168	114	122
	Age (years)	15 - 34	194	168	95	118
		35 - 54	742	546	360	487
		= 55	1576	1129	849	999
Smear-positive						
		Total	326	259	168	180
	Sex	Male	572	448	278	305
		Female	89	77	62	61
	Age (years)	15 - 34	99	102	51	67
		35 - 54	420	312	220	236
		= 55	817	623	416	410

* The prevalence at 2½, 5 and 7½ years was standardized by sex and age to the baseline survey population.

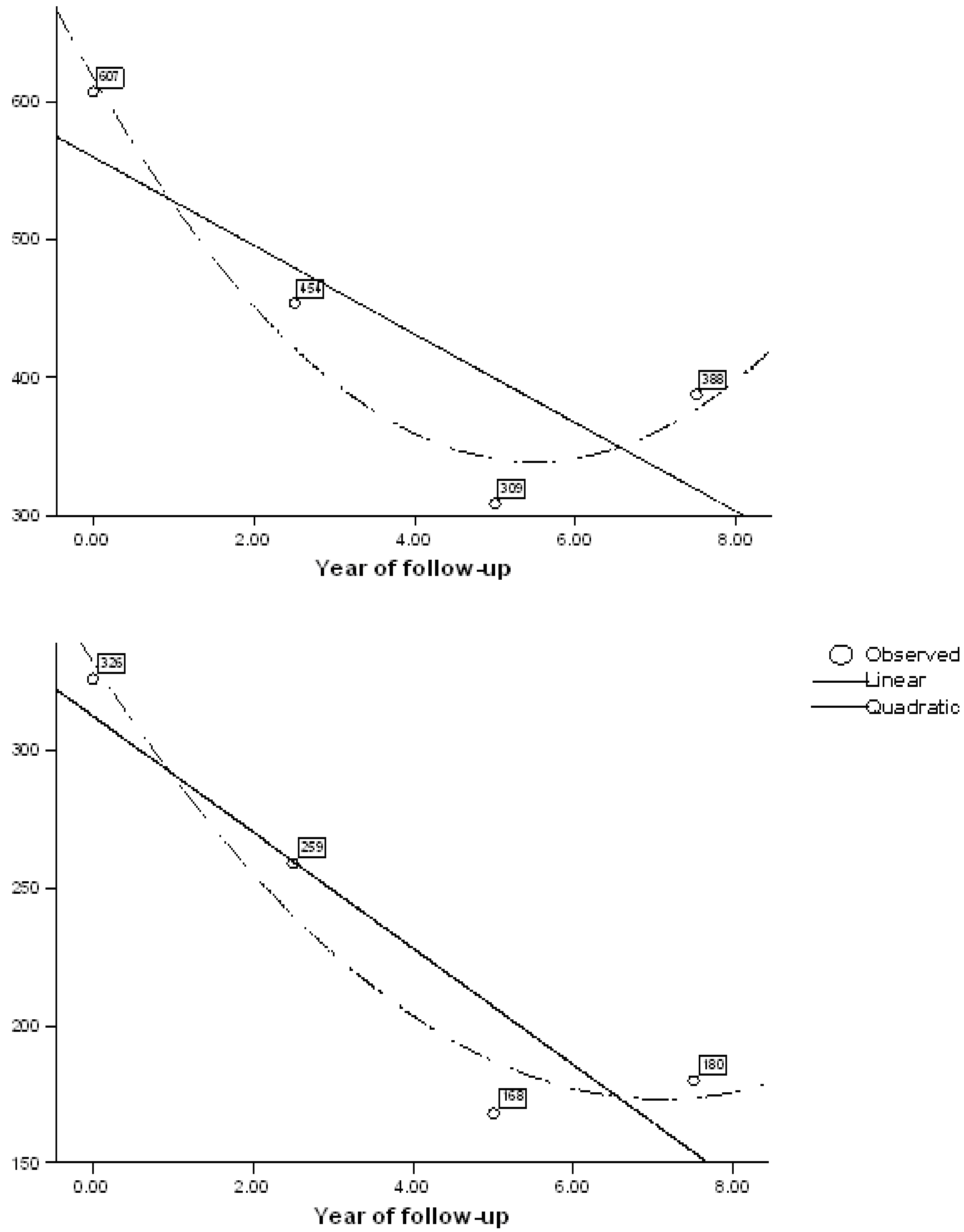

Figure 1: Model-fitting to the prevalence of culture-positive (C+)/smear-positive (S+) PTB per 100,000 population

(95% CI: 10.4 - 14.4%), but increased significantly thereafter to 388 per 100,000 at seven and half years (P < 0.005). This pattern was seen in both sexes and in all three age-groups. Similar findings were observed for the prevalence of smear-positive tuberculosis, namely, a significant decrease from 326 to 168 per 100,000 at five years at the rate of 12.2% (95% CI: 8.0 - 16.2%) per annum,. followed by a slight increase to 180 per 100,000 at seven and half years (P = 0.3). Next, analysis was undertaken by radiographic and chest symptom status (Table 3). In all the groups, the same pattern was seen.

Had the declining survey prevalence in the first five years persisted, only 127 smear-positive cases should have been expected at seven and half years, but the actual number observed was 180 (Fig. *2*). The corresponding figures for culture-

Table 3: Prevalence of sputum-positive tuberculosis by chest symptom status and radiographic status

	Abnormal radiograph with chest symptoms					Abnormal radiograph with no chest symptoms					Normal radiograph with chest symptoms				
	Specimens examined	Culture-positive No.	%	Smear-positive No.	%	Specimens examined	Culture-positive No.	%	Smear-positive No.	%	Specimens examined	Culture-positive No.	%	Smear-positive No.	%
Baseline survey	1030	165	16.0	112	10.9	2176	214	9.8	92	4.2	5153	73	1.4	38	0.7
Resurvey at 2½ years	1251	163	13.0	120	9.6	1364	116	8.5	58	4.3	7263	57	0.8	14	0.2
Resurvey at 5 years	1317	120	9.1	68	5.2	1660	92	5.5	38	2.3	7030	34	0.5	25	0.4
Resurvey at 7½ years	1131	144	12.7	87	7.7	1378	116	8.4	39	2.8	6569	58	0.9	21	0.3
Independent survey at 7½ years	457	49	10.7	34	7.4	551	59	10.7	30	5.4	3329	28	0.8	11	0.3

* Excluded from analysis as the numbers are very small.

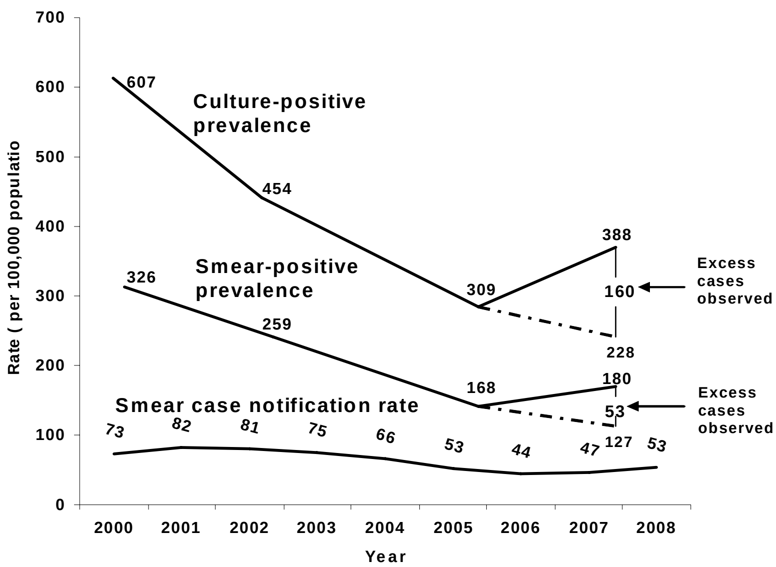

Figure 2: Prevalence of culture-positive/smear-positive tuberculosis and Smear-positive Case Notification Rate (per 1000,000 population) in Tiruvallur district, where the DOTS strategy was initiated in 1999 (the dotted line indicates the extrapolated prevalence at the seven and half year survey, assuming that the decreasing trend observed in the first five years would persist)

Table 4: Programme performance in study area, based on official records and registers

Year	Population of all ages* (a)	Populaion aged > 14 yrs* (b)	S+ prevalence** in age > 14 yrs (per 100,000)	Expected number of S+ cases (c)	Notified New S+ cases (d)	CNR^ 100000 x [(d)/(a)]	Previously known S+ cases (e)	Total known S+ cases		Success^^	
								(d+e)	% of (c)	No.	% of (d)
2000	525950	394463	326	1286	386	73	126	512	40	306	79
2001	538365	403774	292	1179	440	82	133	573	49	320	73
2002	557342	418007	259	1083	449	81	134	583	54	357	80
2003	576989	432742	259	1121	430	75	121	551	49	340	79
2004	597328	447996	168	753	394	66	124	518	69	339	86
2005	524376	393282	168	661	276	53	81	357	54	205	74
2006	542860	407145	174	708	241	44	96	337	48	175	73
2007	561996	421497	180	759	263	47	100	363	48	203	77
2008	581806	436356	180	785	307	53	87	394	50	252	82

* Based on 2001 Census population and projected populations based on a decadal growth rate of 35.25% of Tiruvallur district.
(one block consisting of about 76,000 persons in 2004 was excluded subsequently following some administrative reorganization)
** Estimate based on the findings of our periodic prevalence surveys
^ New smear-positive cases notified per 100,000 population of all ages.
^^ Cured or the course of prescribed treatment completed

positive cases were 228 and 388, respectively. Over the seven and half year period, the observed average annual decrease was 5.8% (from 607 to 388) for culture-positive tuberculosis and 7.6% (from 326 to 180) for smear-positive tuberculosis.

Standards of taking symptom history / reading radiographs / laboratory investigations

The proportion of subjects eligible for sputum examination was very similar in the four surveys (12%, 13%, 13%, and 11%). The average agreement between duplicate readers in identifying a radiographic abnormality (among those with an abnormality by one or other reader) was 70%, 69%, 63% and 65%, respectively. As regards bacteriological standards, the proportion with a smear-positive culture-negative result was stable, namely, 2.5, 2.1, 1.9 and 2.0 per thousand in the four surveys (P = 0.6); furthermore, among those with a positive smear result, the proportions not confirmed by culture were 12.3%, 15.8%, 22.1% and 19.4%, respectively (P > 0.05). Finally, the proportion with contaminated culture was 4% or less in all surveys except the first where it was 6%. These findings indicate that, the clinical, radiographic and bacteriological standards were all stable over the seven and half year period of follow-up.

RNTCP performance

The RNTCP case-finding performance in this area during the period of study is presented in Table 4. The newly notified smear-positive cases which ranged from 386 to 449 per annum until 2004 (average 420) declined between 2005 and 2008 to an average of 272 (P< 0.001), a decrease of 35%. The corresponding Case Notification Rates (CNRs) were 75 and 49 per 100,000 (P< 0.001). The success rate varied from 73% to 86% (average: 78%), but showed no consistent trend; the averages in the two periods were similar, namely, 79% and 76%, respectively (P=0.36).

DISCUSSION

This report summarizes the situation at the start of the DOTS-based RNTCP programme in Tiruvallur district in south India, and makes comparisons between a series of consecutive disease prevalence surveys conducted in the area. The prevalence of tuberculosis nearly halved in the first five years, the annual decline being 12.4% for culture-positive tuberculosis and 12.2% for smear-positive tuberculosis. [5] This was substantially more than 2.3% and 2.5% observed over three decades in the pre-DOTS era in the same area[8]. It has also been reported that the prevalence of tuberculous infection among unvaccinated children aged 1-9 years declined during this period from 19.4% to 11.4%, at the rate of 5.2% per annum (95% CI:3.6-6.8%)[9]. There were no methodological differences during this period and information on changes in socio-economic indicators and nutritional standards was unavailable. It is concluded that the substantial declines observed are largely due to the implementation of the DOTS strategy under RNTCP, coupled with efficient case-finding in the community.

However, in the next two and half years, the prevalence increased to 388 per 100,000 for culture-positive cases and to 180 for smear-positive cases. Confirmation of the higher prevalence came from the finding of an independent random sample survey at seven and half years (on 41773 representative subjects from 39 other villages in the DOTS area), which yielded a culture-positive prevalence of 363 and smear-positive prevalence of 201 per 100,000; the corresponding values standardized to the baseline population were 340 and 184, respectively. It could be argued that the prevalence at five years happened to be unusually low and that at seven and half years was rather high, and that both are consistent with an explanation of a 'steady' decrease over the seven and half-year period. This explanation may, however, be rejected as a model-fitting exercise showed that a linear model was unable to explain the variation in the prevalence.

Detailed analysis was undertaken to check whether the increased prevalence in the last survey could be due to changes in the screening standards adopted, the bacteriological procedures employed, or variations in the sex-age composition of the population studied. These showed that the proportion of subjects eligible for sputum examination was similar in the four surveys, and so was the average agreement between readers in screening for radiographic abnormality. Further, the frequency of smear-positive culture-negative results and the proportion of specimens yielding a contaminated culture were fairly stable throughout. The gender profile was also constant, and although there were some differences in the age composition, with fewer young adults (15-34 years) in the five-year and seven and half-year surveys, these were allowed for by the statistical technique of standardization. Taken together, these findings indicate that the significant increase in prevalence between five and seven and half years was not due to any differences in methodology.

An increase in the incidence could be a possible explanation (the incidence was not measured in this study), but this is unlikely as the potential risk factors for tuberculosis such as tobacco smoking, alcohol use, biomass use, lower socio-economic status, HIV prevalence and MDR TB in the community have not been reported to have changed from the earlier five-year survey period. Other theories for the increase at seven and half years are that a large outbreak of tuberculosis might have occurred during the seven and half-year survey or that the immigration patterns had changed during this period. No evidence was, however, available on either aspect.

Another hypothesis is an increase in the average duration of illness which could have resulted from a number of operational factors involved in the implementation of the control programme. These factors include greater proportion of undetected cases remaining in the community, as suggested by the decreasing CNRs in the later years of the study period. It is likely that such undetected cases persisted in the community and were only discovered at a later survey, resulting in increased survey prevalence at seven and half years (Figure 2). Other possible causes are increased default and greater irregularity in treated cases, but information on these aspects was not available. In this context, it might be relevant to point out that the NIRT supervised the implementation in the first five years, but thereafter the Tamil Nadu Government took over. The STO and STLS from the research organization were withdrawn, and State government personnel were appointed in their place.

Considering experiences elsewhere, DOTS was implemented during 1991-2000 in approximately half of China's population, and the decline in the smear-positive prevalence of pulmonary tuberculosis was 5.7% per annum.[10] In the Philippines where DOTS was initiated in 1997, a national sample survey conducted 10 years later demonstrated a 31% reduction in culture-positive prevalence, and a 27% reduction in smear-positive prevalence;[11] the latter corresponds to an average annual decrease of 3.1% compared with 7.6% in our study area and 5.7% in China. In New

York city, a reduction of 21% in new cases was reported over two years, important contributory factors being implementation of supervised treatment and improved infection-control measures.[12] A nationwide programme in Peru showed that decline in tuberculosis incidence almost doubled between 1991 and 1999 through the implementation of DOTS.[13] Lastly, a community- based DOTS approach in Baltimore resulted in the incidence declining from 36 to 17 per 100,000 in 11 years[14].

One-time baseline prevalence surveys have recently been undertaken in a rural population near Bangalore[15] and in Madhya Pradesh tribals[16]; the estimates were 152 and 207 per 100,000, respectively, for prevalence of culture-positive tuberculosis based on symptom screening alone, and 198 per 100,000 in Bangalore when radiographic screening was also taken into account.[15]

Limitations

Detailed data about performance indicators were not available to verify if the increased prevalence at seven and half years could be attributed to poorer programme implementation. Information on socio-economic change in the community was also not available and so its possible impact could not be assessed. Finally, since HIV infection and MDR TB were not highly prevalent in the study area, our conclusion cannot be generalized to all areas, especially to those with a high prevalence of HIV infection or MDR TB.

CONCLUSION

Despite the average annual success rate (78%) in this tuberculosis unit being lower than the expected rate of 85%, the implementation of DOTS was followed by a substantial decrease in the prevalence of pulmonary tuberculosis over five years in a rural population, but this was partially off-set by an increase in the next two and half years. Although the average annual decline over the seven and half-year period was still significant, our findings suggest that sustaining the high effectiveness of DOTS programme needs vigilant supervision.

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