MONITORING OF BACTERIOLOGICAL DIAGNOSTIC EFFICIENCY UNDER RNTCP - THE PUNE EXPERIENCE

KAVITA MODI-PAREKH AND ANITA KAR*

Microscopy could be used to detect two-thirds of pulmonary tuberculosis cases. However, in order to screen out the remaining one-third of sputum smear negative cases, a progressively increasing load of symptomatics had to be screened, using indirect tests.

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Diagnosis of smear-negative case of tuberculosis is more expensive than that of a sputum positive case, since diagnosis of the former involves additional costs of antibiotics and radiological examination.

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For every patient of tuberculosis who can be detected using microscopy, nine have to be screened using indirect methods, due to the low sensitivity of microscopy. In addition to the expense, the resulting delay in the initiation of treatment of sputum negative cases has implications in disease control, since there is sufficient evidence of transmission from smear negative patients as well. In the background of the increasing HIV-epidemic, the detection of smear negative cases takes on significance.

I. INTRODUCTION

The cornerstone of the diagnosis of tuberculosis is the direct microscopic examination of appropriately stained sputum specimens for the identification of Acid Fast Bacilli (AFB). The technique is simple, inexpensive, and detects infectious cases who are responsible for continued transmission and maintenance of the epidemic in the community. Currently, sputum smear microscopy is widely used in Tuberculosis Control Programs worldwide for a presumptive diagnosis of tuberculosis. No other diagnostic tool offers the affordability as well as efficiency in diagnosis of tuberculosis in the public health setup, as sputum microscopy does.

Although relatively quick, easy and inexpensive, sputum microscopy has a major limitation (1,2). While the specificity of microscopy is high, ranging between 98-99%, the sensitivity is relatively poor at 50-70% or even lower in the public health setup (3). Between 5,000 and 10,000 tubercle bacilli per millilitre of sputum are required for direct microscopy to be positive. Sputum specimens from patients with cavitary disease are most often sputum smear positive.

The poor sensitivity of microscopy can be improved by examination of more than one smear from a patient. In one study, eight samples of sputa from individuals with abnormal chest X-rays were examined by microscopy (4). The results revealed that the first specimen detected 58% of the culture positive cases, and the first and second specimens together detected nearly 72% of the cases. All cases positive on culture and microscopy were detected by three specimens. Only 6% additional cases were identified by the seventh and eighth specimens together. Currently, three sputum specimens are recommended for the self reporting chest symptomatics under the Revised Tuberculosis Control Programme (RNTCP) for the diagnosis of pulmonary tuberculosis (5,6).

A negative smear result does not exclude the diagnosis of tuberculosis, as about 55% of pulmonary tuberculosis cases worldwide, harbor lower bacillary load, so that the sputum is negative upon microscopic observation. Other variables influencing the results of microscopy include the availability of saliva instead of sputum, as well as the quantity and quality of sputum (7). A large workload may also influence the sensitivity of smear microscopy. World-wide, the ratio of smear positive to smear negative cases varies, from 1:1 in a country like the USA where there is 100% Directly Observed Treatment Short-Course (DOTS) coverage, to 1: 4 in the Russian Federation, where the DOTS coverage is less than 5% (8). In 1999, India had 12,23,127 notified cases of tuberculosis, of which 11,27,553 constituted pulmonary cases. Of these 3,49,770 were sputum smear positive, while 7,77,783 were smear negative cases, giving a ratio of 1:2 (8).

Diagnosis of tuberculosis under the RNTCP has been clearly defined (5). Chest symptomatics (especially, those having cough for three weeks or more), are offered sputum examinations. Three samples are collected: a spot specimen on the first day, and early next morning and a spot specimen on the second day. Patients with two or three positive smears are immediately started on treatment. Symptomatics with one positive smear undergo chest X-ray. Those with no positive smears are prescribed a course of antibiotic treatment. Antibiotic non-responders undergo chest X-ray and are re-evaluated. Patients are categorized into appropriate groups and are referred to the DOTS center nearest to the place of residence. The consequence of the low sensitivity of microscopy is that all chest symptomatics, who are not positive by microscopy, have to undergo the indirect screening procedure outlined above, in order to identify the smear negative cases of tuberculosis. The problems inherent in implementing this process is
RNTCP has been in operation in Pune from 1995. PMC has a population of approximately 25 lakhs. There are three Tuberculosis Units (TU), implementing NTP (National Tuberculosis Programme) as well as RNTCP. The three TU’s have, under them, 101 Treatment Observation Centers and 17 Microscopy Centers. A retrospective analysis of tuberculosis data under RNTCP between July 1997 to June 2001, revealed that from 1997, the number of smear examinations increased progressively, showing a 2.3 fold increase over four years. (Fig. la). The number of tuberculosis cases being detected also showed a three fold increase from 736 cases detected in 97-98 to 2273 cases diagnosed in 2000-2001. The majority of the cases being detected were those of pulmonary tuberculosis, ranging from 74% to 83% of all cases diagnosed (Fig lb). However, over the same period, extra-pulmonary (EP) case detection increased nearly five fold, in terms of actual number of cases, from 123 cases diagnosed in 97-98 to 582 in 2000-01. Thus, EP cases, which had constituted 16.7% of all cases in 97-98, increased to 25.6% of all cases being detected under the programme in 00-01.

During the period under review, out of those subjected to smear microscopy, the diagnosis of Pulmonary tuberculosis was made in 14.6%, 20.8%, 28.6% and 18 %, averaging about 20.6(5.9) cases annually (Table 1). In terms of actual numbers, the pulmonary tuberculosis cases being diagnosed increased from 613 cases in 97-98 to 1691 cases of pulmonary tuberculosis in 00-01, showing a 2.7 fold increase over the four years. This increase paralleled the 2.2-fold improvement in the total number of smearings being examined (Fig.la). Table-1, column iv, shows the diagnostic efficiency of microscopy, expressed as the number of sputum smear positive cases diagnosed from amongst total pulmonary tuberculosis cases. This ranged between 58% to 69% annually, averaging around 63.7 (4.57 %). Taking the average for four years, the sputum smear positive cases accounted for 64% of the cases, whilst the smear negatives accounted for 36%, giving a ratio of 2:1. (Fig.Ic).

The ability of microscopy to screen tuberculosis cases from amongst all chest symptomatics visiting or referred to the clinics is presented in Table 1, column v. In tuberculosis surveys, the term screening has been used to identify the population that is eligible for diagnostic tests like sputum examination or chest radiography. (9) The terminology being used here, on the other hand, expresses the ability of microscopy to diagnose tuberculosis cases from among the total number of chest symptomatics being examined annually. Between July 1997 to June 2001, a total of 24,327 symptomatics (i.e. 4173, 5097, 5512 and 9545, by the year shown in Table 2, column i) had approached the clinic and their sputum samples were examined by smear. Of these, 387, 613, 1094 and 1104 were found each year respectively, to be positive by sputum microscopy (Table 2, column ii). This indicated that the efficiency of microscopy to detect smear positive cases improved progressively from 9% to 12%, over the four years. On an average 20.5(6.35) pulmonary tuberculosis cases could be detected from amongst one hundred chest symptomatics under RNTCP, year to year. On the other hand, the sputum smear negative pulmonary tuberculosis (i.e. those cases who were not positive by microscopy), accounted for 5%, 9 %, 9 % and 6 % of the total chest symptomatics. (Table 2 column vi and Fig. Id). In other words, on an average, of the pulmonary tuberculosis cases diagnosed from amongst the chest symptomatics, microscopy could be utilized to identify about 13% (who were smear positive), while 7% of cases had to be identified using indirect methods, like antibiotic treatment/xray chest. Due to the low sensitivity of microscopy, identification of the latter 7% of cases, involved “screening” of the remaining 87% of symptomatics, details of which are shown in Table 2.

Table 2, shows the outcome of the differential diagnostic procedures for identification of the smear negative tuberculosis cases. The patients who were found to be negative upon smear microscopy were subsequently given broad spectrum antibiotics (Table 2, column iii). Majority of symptomatics ranging between 71 and 85% (Table 2, column iv) responded to antibiotics, indicating that they possibly did not have tuberculosis.. The efficiency of microscopy and antibiotic treatment, in arriving at a conclusion on diagnosis as a firm smear positive case and as other than a tuberculosis case, under RNTCP diagnostic paradigm, ranged between 91 to 95%, (Table 2 column v). The remaining 226 (5%), 450 (9%) 488 (9%) and 587 (6 %) patients (Table 2 , column vi) were started on Anti-Tuberculous Treatment (ATT) after radiography and confirmation of clinical diagnosis, i.e., more by default, than on positive evidence of active TB.

Table 2, column iii shows that over the four years of observation, the total number of symptomatics who were smear negative and required further diagnostic action, increased from 3786 to 8441 (Table 2, column iii). This was of course due to higher number of chest symptomatics examined, over the years. As a result of this escalation the number of sputum negative cases had also increased 2.6-fold, i.e. from 226 cases in 1997 to 587 cases in 2000. (Table 2, column vi), with a slight increase in the proportion out of the chest symptomatics examined.
Table 1: Screening and diagnostic efficiency of microscopy

<table>
<thead>
<tr>
<th>Year</th>
<th>Total smear Examined A</th>
<th>Pulmonary TB Cases B</th>
<th>Number Detected by microscopy C</th>
<th>Diagnostic Efficiency C/B x 100 (%)</th>
<th>Screening Efficiency C/A x 100 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>4173</td>
<td>613 (14.6)</td>
<td>387</td>
<td>63</td>
<td>9</td>
</tr>
<tr>
<td>II</td>
<td>5097</td>
<td>1063 (21.2)</td>
<td>613</td>
<td>58</td>
<td>12</td>
</tr>
<tr>
<td>III</td>
<td>5512</td>
<td>1582 (28.7)</td>
<td>1094</td>
<td>69</td>
<td>20</td>
</tr>
<tr>
<td>IV</td>
<td>9545</td>
<td>1691 (17.7)</td>
<td>1104</td>
<td>65</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>24327</td>
<td>4949 (20.5%)</td>
<td>3198</td>
<td>64</td>
<td>13</td>
</tr>
</tbody>
</table>

Average for I-IV years

<table>
<thead>
<tr>
<th>Year</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>I 1997-98</td>
<td>I</td>
</tr>
<tr>
<td>II 98-99</td>
<td>II</td>
</tr>
<tr>
<td>III 99-00</td>
<td>III</td>
</tr>
<tr>
<td>IV 00-01</td>
<td>IV</td>
</tr>
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</table>

Table 2: Efficiency of microscopy and antibiotic treatment on differential diagnosis of smear negative cases

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of smear examined</th>
<th>No. Detected by microscopy (a)</th>
<th>No. Undergoing antibiotic treatment (b)</th>
<th>No of cases eliminated i.e. responders to antibiotic treatment (c)</th>
<th>Efficiency (d) (b+d)/a x100 (%)</th>
<th>No. of X-ray Diagnostics E (b)</th>
<th>No. of Positives E/a x 100 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I 1997-98</td>
<td>4173</td>
<td>387(9.27)</td>
<td>3788(90.7)</td>
<td>3560</td>
<td>94.5</td>
<td>226(5.4)</td>
<td></td>
</tr>
<tr>
<td>II 98-99</td>
<td>5097</td>
<td>613(12.0)</td>
<td>4484(87.9)</td>
<td>4034</td>
<td>91.2</td>
<td>(8.8)</td>
<td></td>
</tr>
<tr>
<td>III 99-00</td>
<td>5512</td>
<td>1094(19.8)</td>
<td>4418(80.15)</td>
<td>3930</td>
<td>91.1</td>
<td>488(9.0)</td>
<td></td>
</tr>
<tr>
<td>IV 00-01</td>
<td>9545</td>
<td>1104(11.5)</td>
<td>8441(88.4)</td>
<td>7854</td>
<td>93.8</td>
<td>(6.1)</td>
<td></td>
</tr>
</tbody>
</table>

* The figures in this column are estimates since many patients referred to the TUs undergo antibiotic treatment in the private sector.
The pertinent observations that arise from this analysis are as follows. The results show that (i) in the RNTCP of PMC, microscopy could be used to detect two-thirds of pulmonary tuberculosis cases. (Table 1 column iv) (ii) However, in order to screen out the remaining one-third of sputum smear negative cases, a progressively increasing load of symptomatics had to be screened, using indirect tests, (iii) In the PMC area the number of symptomatics being screened by sputum smear over the last four years has more than doubled (Table 1, column i). (iv) The increase in the number of sputum smear positive cases and smear negative cases has been similar (2.8 and 2.5 fold respectively), indicating that smear negative cases constitute a significant portion of the tuberculous case load (Table 2, column ii & vi). (v) Diagnosis of smear-negative case of tuberculosis is more expensive than that of a sputum positive case, since diagnosis of the former involves additional costs of antibiotics and radiological examination. These observations raise the possibility that as attendance of symptomatics to the centres for diagnosis improves, a comparatively greater proportion of resources are likely to be diverted to screening chest symptomatics in order to identify sputum negative cases of pulmonary tuberculosis.

A glimpse of how extensive this problem might be on a national level is illustrated from the data on number of sputa examined in 1998-1999 (10). The data reports that 38,93,213 sputa were examined. Taking into consideration that three sputa samples were examined from each patient, the number of patients approaching the National Program with chest symptoms were possibly 12,97,738. Of these, 24.8% (3,21,920) were found to be sputum positive. Using this data, if a theoretical consideration is made that all chest symptomatics are examined using the diagnostic algorithm of RNTCP, a total of 9,75,818 symptomatics should be subjected to antibiotic treatment, followed by radiography of the non-responders, in order to diagnose the sputum smear negative cases of tuberculosis.

In a seminal study, Baily, et. al. shows that for every 100 patients visiting a general peripheral health institution, and suffering from any type of complaint, nearly 2 will have chest symptoms and require a sputum examination (11). For 10 such sputa examined, one will be sputum smear positive, and nine will require further investigations. This means that for every patient of tuberculosis who can be detected using microscopy, nine have to be screened using indirect methods, due to the low sensitivity of microscopy.

In addition to the expense, the resulting delay in the initiation of treatment of sputum negative cases has implications in disease control, since there is sufficient evidence of transmission from smear negative patients as well. For example, in a study to determine the infective potential of patients who are smear-negative, culture positive, it was found that smear-negative patients were at least 22% as likely as smear positive patients to transmit tuberculosis (12). In the background of the increasing HIV-epidemic, the detection of smear negative cases takes on significance since majority of HIV positive tuberculosis cases are smear negative.

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LEGEND OF FIGURE

Fig.1. Trends in tuberculosis case detection under RNTCP, Pune from July 1997 to June 2000. (a) shows the progressive increase in the total smears examined and the number of pulmonary and extra-pulmonary cases detected. The increasing trend of extra-pulmonary case detection is shown in (b). (c) represents the proportional distribution of sputum smear positive and smear negative cases of pulmonary tuberculosis, while the proportion of these cases to the total chest symptomatics is shown in (d).
Fig. 1(c) Proportional distribution of sputum smear positive and smear negative cases

Year

IV

35% 65%

III

31% 69%

II

42% 58%

I

37% 63%

Fig. 1(d) % sputum smear positive and smear negative tuberculosis cases amongst chest symptomatics

Year

IV

6% 12%

III

9% 20%

II

9% 12%

I

5% 9%

TB

Negatives

Sputum positive

% cases

% cases