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SHORT COMMUNICATION

Pretreatment sputum smear grade and smear positivity during follow-up of TB patients in Ahmedabad, India

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In Ahmedabad, India, a retrospective record review was undertaken among 2842 sputum smear-positive tuberculosis patients registered for treatment from April to September 2011 to assess the association of pretreatment sputum smear grade with sputum positivity and the additional yield of a second sputum sample during each follow-up examination. Respectively 39%, 26%, 28% and 7% of patients had pretreatment sputum grade 3+, 2+, 1+ and scanty. The higher the pretreatment sputum grade, the higher the proportion found positive during various follow-up periods. Overall, the additional yield of the second sputum sample was <2%; it did not vary with pretreatment smear grading.

In India, tuberculosis (TB) patients receiving treatment under the Revised National Tuberculosis Control Programme (RNTCP) undergo periodic follow-up sputum smear examinations to monitor response to treatment. The follow-up examinations are conducted at the end of the intensive phase, during the continuation phase and at the end of anti-tuberculosis treatment. Smears of two sputum specimens ('spot' and 'early morning') are examined on each scheduled follow-up visit. A single positive sputum smear is sufficient to label the patient 'smear-positive'. Smear positivity during the follow-up period results in the extension of the intensive phase, a change in treatment category and/or a need for culture and drug susceptibility testing for multidrug-resistant TB.[1]

Although there are many reasons for sputum smear positivity during the follow-up period (irregular/incomplete drug intake, pretreatment smear grading, advanced disease, presence of drug-resistant organisms, dead bacilli in the sputum, comorbid conditions, etc.),[2,3] its association during the entire course of treatment with pretreatment sputum smear grading (an indicator of bacillary load in the sputum) has not been adequately assessed under routine programme conditions in India. Furthermore, previous studies from India have shown that one sputum smear examination at follow-up is as good as two, as the incremental yield of second specimen was very low;[4] however, these studies do not report on the incremental yield of a second sputum smear in relation to pretreatment smear grading.

To understand these crucial operational issues, an operational research study was conducted in Ahmedabad District, India, to study the association between pretreatment sputum smear grades and 1) sputum smear positivity during follow-up, and 2) incremental yield as a result of a second sputum smear examination during follow-up.

METHODS

This was a retrospective cohort study involving review of records routinely maintained under the RNTCP in Ahmedabad District (population: 7.1 million) in Gujarat, West India. There are 71 designated microscopy centres under the external quality assurance of the RNTCP. Trained laboratory technicians maintain laboratory registers in which the sputum smear status of all pulmonary TB patients and follow-up sputum smear examinations of TB patients (at the end of the intensive phase, 2 months into the continuation phase and at the end of treatment) is documented.[1] Sputum smear is graded (negative, scanty, 1+, 2+, 3+) per World Health Organization (WHO) guidelines.[1] Under the RNTCP, all patients are diagnosed, classified and treated in accordance with standard WHO guidelines.[1]

All smear-positive TB patients registered under the RNTCP between April and September 2011 in the district were included in the study. The study variables included pretreatment sputum smear grade, sputum smear status at the end of the intensive phase, extended intensive phase (if applicable), mid-continuation phase and end of treatment.

Data were extracted from laboratory and TB registers into a structured data collection sheet. Double data entry, validation and analysis were performed using EpiData version 3.1 (EpiData Association, Odense, Denmark). Data were summarised as proportions, and χ^2 test for trend was used as test of significance. $P < 0.05$ was considered statistically significant.

Ethics approval was obtained from the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease and the Institutional Ethics Committee of the Byramjee Jeejeebhoy Medical College, Ahmedabad, Gujarat.

RESULTS

Of 2847 smear-positive TB patients, pretreatment smear grade was not recorded for five. Of the remaining 2842 patients, respectively 39%, 26%, 28% and 7% had sputum grade 3+, 2+, 1+ and scanty. The association between pretreatment sputum smear grade and sputum positivity at various follow-up periods is shown in the Table. As the pretreatment sputum smear grade increased from scanty to 3+, the proportion found

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KEY WORDS
pretreatment sputum smear grade; incremental yield; sputum smear positivity

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TABLE Association between pretreatment sputum smear grade with sputum positivity at various follow-up periods among tuberculosis patients registered for treatment, Ahmedabad District, India, April–September 2011

Sputum positivity during follow-up	Total *n* (%)	Pretreatment sputum smear grade				*P* value (χ^2 for trend)
		Scanty *n* (%)	1+ *n* (%)	2+ *n* (%)	3+ *n* (%)	
Total	2842 (100)	200 (100)	801 (100)	738 (100)	1103 (100)	
End of intensive phase						
Positive	516 (18)	13 (7)	96 (12)	138 (19)	269 (25)	<0.001
Negative	1972 (69)	174 (87)	636 (79)	512 (69)	650 (59)	<0.001
Unknown/NA	354 (13)	13 (7)	69 (9)	88 (12)	184 (17)	<0.001
Extended intensive phase*						
Positive	115 (35)	2 (15)	18 (19)	35 (25)	60 (22)	<0.001
Negative	182 (22)	4 (31)	32 (33)	49 (36)	97 (36)	<0.001
Unknown/NA	219 (42)	7 (54)	46 (48)	54 (39)	112 (42)	<0.001
Mid-continuation phase						
Positive	154 (5)	7 (4)	25 (3)	47 (6)	75 (7)	<0.001
Negative	1646 (58)	128 (64)	520 (65)	413 (56)	585 (53)	<0.001
Unknown/NA	1042 (37)	65 (33)	256 (32)	278 (38)	443 (40)	<0.001
End of treatment						
Positive	99 (4)	6 (3)	24 (3)	27 (4)	42 (4)	0.77
Negative	1989 (70)	159 (79)	613 (76)	522 (71)	695 (63)	<0.001
Unknown/NA	754 (26)	35 (18)	164 (21)	189 (25)	366 (33)	<0.001

*Only for those who were sputum smear-positive at the end of the intensive phase ($n = 516$).
NA = not applicable.

sputum smear-positive during follow-up (end of intensive phase, mid-continuation phase) increased by 2–3 times ($P < 0.05$). The proportions of smear-positive results at the end of treatment increased with increase in pretreatment smear grade; however, the trend was not found to be significant ($P = 0.77$). Of the 99 TB patients who were sputum smear-positive at the end of treatment, 32% were also positive at the end of the intensive phase (data not shown).

The additional yield due to the second sputum sample was found to be 9 (0.3%), 1 (0.07%) and 1 (0.09%) at the end of the intensive and mid-continuation phases and at the end of treatment. This additional yield was not associated with any patient characteristics such as age, sex, type of TB, human immunodeficiency virus status or pretreatment sputum grade.

DISCUSSION

This study, conducted in a routine programme setting with a large number of patients, shows that TB patients with higher pretreatment sputum grade are more likely to remain sputum smear-positive during follow-up. The yield of the second sputum sample for follow-up is very low.

The study has the following two major implications for policy and practice. First, patients with higher pretreatment sputum grade were more likely to remain sputum-positive at the various follow-up periods. This indicates that these patients need to be monitored much more rigorously by the programme to ensure the regularity of their drug intake and to investigate for drug resistance and other possible factors for late conversion such as diabetes, smoking, etc. This finding also underlines the need for regular follow-up sputum examinations, continued counselling on cough hygiene and safe disposal of sputum throughout the treatment period.

Second, the low yield of the second sputum sample is similar to reports from other settings in the country,[4] justifying the need to reduce the number of sputum smears examined during the follow-up period from two to one.

Limitations of the study include the fact that the data were extracted from routine programme records, and there were several values missing from the follow-up examinations, assuming that deficiencies in recording and reporting have affected the study results. Furthermore, sputum smear at follow-up may often show bacilli that are dead and do not correlate well with growth of *Mycobacterium tuberculosis* in culture.[5–7] This highlights the need for caution in the interpretation of sputum smear positivity during follow-up.

CONCLUSIONS

Patients with higher pretreatment sputum grades were more likely to be smear-positive during follow-up. There is a need to develop mechanisms to monitor these patients more rigorously. The yield of a second sputum examination during follow-up is very low and the practice should be discontinued.

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On a entrepris à Ahmedabad, en Inde, une révision rétrospective des dossiers de 2842 patients tuberculeux à frottis positif enregistrés pour traitement d'avril à septembre 2011 afin d'évaluer dans quelle mesure le degré de positivité du frottis de crachat avant traitement était en association avec la positivité des crachats et avec un rendement supplémentaire d'un deuxième échantillon de crachats au cours de chaque examen de suivi. On a observé effectivement un niveau 3+ dans près de 39% des crachats avant traitement, un niveau 2+ dans 26%, un niveau 1+ dans 28% et un niveau faiblement positif dans 7%. La proportion s'avérant positive au cours des différentes périodes de suivi est d'autant plus élevée que le degré de positivité du crachat avant traitement est plus élevé. Au total, le rendement supplémentaire d'un deuxième échantillon de crachats est <2% et ne varie pas avec le degré de positivité du frottis avant traitement.

En Ahmedabad, India, se emprendió un examen retrospectivo de las historias clínicas de 2842 pacientes con tuberculosis y baciloscopia positiva del esputo registrados en tratamiento entre abril y septiembre del 2011, con el fin de evaluar si la gradación de la baciloscopia de las muestras de esputo antes del tratamiento se asociaba con su positividad en cada examen de seguimiento y si se mejoraba el rendimiento diagnóstico con una segunda muestra de esputo durante los exámenes de control. La gradación de la baciloscopia de los pacientes antes del tratamiento fue aproximadamente como sigue: 39% de grado 3+, 26% de grado 2+, 28% de grado 1+ y 7% escasos. Se observó que entre más alto era el grado de la baciloscopia inicial de los pacientes, mayor era la proporción que presentaba una baciloscopia positiva durante los períodos de seguimiento. En general, la segunda muestra de esputo permitió una ganancia inferior al 2% en el rendimiento y no se observaron variaciones en función de la gradación de la baciloscopia inicial.

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