Active detection of tuberculosis and paragonimiasis in the remote areas in North-Eastern India using cough as a simple indicator

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One of the essential steps in targeting tuberculosis (TB) intervention is early diagnosis and treatment of patients by reducing the reservoir of infection in the community. In the North-Eastern (NE) region of India pulmonary TB and paragonimiasis are overlapping public health issues. We performed a cross-sectional study in 63 remote villages from the two states Arunachal Pradesh (AP) and Assam to determine the prevalence of undiagnosed TB and paragonimiasis cases using cough as a simple indicator. In AP, 2961 individuals aged five years and above were examined and 1108 (37.4%) were found to have cough for one week or more. Of the 417 individuals who provided sputum, 11 (2.64%) were smear positive for acid-fast bacilli (AFB). All these cases were yet undiagnosed, thus the prevalence of new smear positive TB in AP was 0.37%. In Assam on the other hand 331 (23.5%) subjects out of 1410 individuals who were examined had a cough for one week or more and of the 112 individuals who provided sputum, 13 (11.6%) were smear positive for AFB. The prevalence of new smear positive TB cases was 0.78% in Assam. Sero-positivity of paragonimiasis in coughers of AP was 7.6% ($n = 1091$), which was significantly higher ($p < 0.01$) as compared to that in Assam (1.2%, $n = 321$). The findings of the present study suggest that TB remains a major public health concern in the NE region of India especially in the remote places and there is need to strengthen early case detection of TB.

Keywords: Undetected tuberculosis, Paragonimiasis, Cough, Assam, Arunachal Pradesh

Introduction

Cough is one of the cardinal symptoms of tuberculosis (TB).¹ According to the Revised National Tuberculosis Control programme (RNTCP) a person having cough for two weeks or more with or without hemoptysis is a TB suspect whose sputum should be examined for acid-fast bacilli (AFB) for diagnosis of TB. However, in many cases TB remains undiagnosed in the community and keeps spreading to other persons. In the North-Eastern (NE) region of India the diagnosis of smear negative TB is sometimes confusing because of the co-existence of pulmonary paragonimiasis, which mimics TB because of overlapping clinical presentations such as cough and hemoptysis.² One of the essential steps in targeting

TB intervention is early diagnosis and treatment of patients by reducing the reservoir of infection in the community. Symptom questionnaires, in particular identifying chronic cough, has been found to be a sensitive and cheap way to identify pulmonary TB suspects³ and pulmonary paragonimiasis cases,⁴ which can then be confirmed using sputum microscopy, serology, and/or radiography. In India, human paragonimiasis is known to occur in Manipur,⁵ Nagaland,⁶ and Arunachal Pradesh (AP)^{7,8} where it is co-endemic with TB. A study was undertaken to determine the extent of undiagnosed pulmonary TB and paragonimiasis cases in the remote rural populations of AP and Assam. This goal was important as few prevalence surveys have been conducted to detect the feasibility of active case finding in remote areas. The ethical committee of Regional Medical Research Centre approved this study.

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Methodology

We performed a cross-sectional study between July 2008 and June 2010 in two states, AP and Assam, located in the NE region of India. In AP, which is predominantly a hilly state, six districts (Changlang, East Kameng, East Siang, Lohit, Tirap, and West Kameng) and in the state of Assam two districts (Sonitpur and Karbi Anglong) were randomly selected. Door to door surveys were carried out to detect prevalence of TB and paragonimiasis among coughers in 63 randomly selected villages of the study area. The sample size was 4371 subjects of both the sexes aged five years and above (Assam = 1410, AP = 2961). In this study, the subjects with one or both sputum samples found smear positive for AFB were defined as pulmonary TB cases. People having cough ($\geq$ one week duration) with or without hemoptysis were provided with two sputum collection containers per individual. One sputum sample was collected immediately and the other was collected in the early morning. The sputum samples were examined for AFB using Ziehl–Neelsen staining. Sputum smears were also screened for ova of lung flukes under a microscope using wet mounts. In addition to sputum, blood samples were also collected to detect antibodies against lung flukes. The serum samples were stored at -80°C . All the serum samples collected were tested for the presence of antibodies against adult Excretory Secretory (ES) antigens of lung flukes using indirect ELISA as described in our previous paper.⁹ Written informed consent was obtained from all the study participants or their guardians in the case of minors.

Results

The results of the study are given in Tables 1 and 2. In AP (Table 1) 2961 individuals aged five years and above were examined and 37.4% were found to have cough for one week or more. Of the 417 individuals who provided sputum in AP, 11 (2.64%) were smear positive for AFB. All these cases were yet undiagnosed thus the prevalence of new smear positive TB in AP was 0.37%. On the other hand sero-positivity

of paragonimiasis in coughers of AP was 7.6% ($n = 1091$).

In Assam (Table 2) on the other hand 23.5% (out of 1410 individuals examined) had cough for one week or more. However, of the 112 individuals who provided sputum 11.6% were smear positive for AFB. Out of these, two cases were already undergoing treatment for TB thus the remaining smear positive cases were undiagnosed. Hence the prevalence of new smear positive TB cases was 0.78% in Assam. On the other hand sero-positivity of paragonimiasis in coughers of Assam was 1.2% ($n = 321$).

Discussion

Thus the present study revealed that the prevalence of cough in AP was significantly high as compared to that in Assam ($p < 0.01$). In AP the sero-positivity of paragonimiasis was significantly ($p < 0.01$) more as compared to that in Assam. However, the prevalence of new smear positive TB cases was significantly higher in Assam as compared to that in AP ($p < 0.001$).

Sputum examination for diagnosis of pulmonary paragonimiasis is a less sensitive method as lung fluke ova are expectorated intermittently. For this reason sero-diagnostic methods are considered more sensitive for diagnosis of paragonimiasis.⁹ In the present study, the ova of lung flukes were detected in the sputum of 21 (24.1%) out of 87 sero-positive cases of paragonimiasis. These ova were identified to be of *Paragonimus heterotremus* based on their characteristic morphology.⁷ In the present study, four out of 24 (16.6%) cases of TB had hemoptysis whereas 35 out of 87 (40.2%) cases of paragonimiasis had hemoptysis. This difference in the prevalence of hemoptysis between TB and paragonimiasis cases was statistically significant ($p = 0.032$). The majority of the cases (95.4%, $n = 87$) of the paragonimiasis were from AP. There was no statistically significant gender specific difference in the prevalence of TB or paragonimiasis ($p \geq 0.05$, for both diseases) in the

Table 1 Showing prevalence of cough (duration one week or more), smear positive TB, and paragonimiasis in the study subjects of Arunachal Pradesh (AP) according to age group and gender

AP				
Categories	No. of subjects examined	Number of cases having cough for one week or more (%)	Number of smears examined for AFB (positive smears in %)	Number of samples studied for ELISA (positive samples in %)
Total	2961	1108 (37.4)	417 (2.64)	1091 (7.6)
Age group (in years)				
Below 15	1537	537 (34.9)	189 (0.53)	525 (9.7)
16–39	972	380 (39.1)	149 (4.03)	377 (7.2)
40 & above	452	191 (42.2)	79 (5.06)	189 (2.6)
Sex				
Male	1374	538 (39.2)	194 (3.1)	530 (7.7)
Female	1587	570 (35.9)	223 (2.24)	561 (7.6)

Table 2 Showing prevalence of cough (duration one week or more), smear positive TB, and paragonimiasis in the study subjects of Assam according to age group and gender

Categories	Assam			
	No. of subjects examined	Number of cases having cough for one week or more (%)	Number of smears examined for AFB (Positive smears in %)	Number of samples studied for ELISA (Positive samples in %)
Total	1410	331 (23.5)	112 (11.6)	321 (1.2)
Age group (in years)				
Below 15	650	167 (25.7)	59 (5.1)	159 (1.9)
16–39	454	102 (22.5)	29 (24.1)	100 (0)
40 & above	306	62 (20.3)	24 (12.5)	62 (1.6)
Sex				
Male	563	142 (25.2)	53 (15.0)	140 (0)
Female	847	189 (22.3)	59 (8.56)	181 (2.2)

study subjects. However, there was statistically significant difference ($p < 0.001$) in the mean age of paragonimiasis cases (17 ± 12.8 years, $n = 87$) as compared to the TB cases (32.7 ± 7 years, $n = 24$). At least 50% of the coughers had cough duration of one month or more. In AP, 47 (1.59%, $n = 2961$) subjects had previous history of TB. All of these cases were found to be smear negative for AFB in the present survey. However, three out of these 47 cases were found to be sero-positive for paragonimiasis and had chronic cough as a clinical presentation and one case also had hemoptysis. On the other hand in Assam significantly more subjects (3.5%, $n = 1410$, $p < 0.01$) had a past history of pulmonary TB. Two out of these 50 cases having past history of TB were found to be sero-positive for paragonimiasis and two cases were found to be smear positive for TB and were under treatment for TB. The rest of the cases from Assam having past history of TB were negative for both paragonimiasis and TB. According to RNTCP guidelines persons having cough for two weeks or more are TB suspects and should be further investigated for diagnosis of TB. In the present study, 12 out of 24 smear positive TB cases (i.e. 50%) had a history of cough duration which was less than two weeks. This may indicate the need to also include such patients as TB suspects where the duration of cough is less than two weeks. The present study suggests that active case finding in symptomatic patients could supplement DOTS (directly observed treatment, short-course) to detect additional AFB positive TB cases in the community. This will prevent spread of TB in the community and facilitate early treatment of TB patients as has been shown by recent studies.^{10–12} In AP, human foci of paragonimiasis were detected earlier⁷ in Changlang district. This study led to the identification of several new foci of paragonimiasis in East Siang, West Kameng, and Lohit districts of AP.

Conclusions

The present study identified human paragonimiasis for the first time in Assam. Detailed travel/migration

history of the newly diagnosed cases of paragonimiasis from Assam confirmed that these patients had acquired infection locally. This was confirmed by examination of locally available crabs which were found to be infected with metacercariae of *Paragonimus westermani*¹³ and *P. heterotremus* (unpublished).

The findings of the present study suggest that TB remains a major public health concern in the NE region of India especially in the remote places where it co-exists with paragonimiasis. Besides, the present study has shown that there is a need to strengthen early case detection of TB, which can be achieved by active case finding and early treatment of patients suffering from TB. Since TB and paragonimiasis are overlapping public health issues in rural communities of the NE region of India, it will be desirable to integrate surveillance and control of pulmonary TB and paragonimiasis under routine RNTCP.

Acknowledgements

This work was supported by grants from Indian Council of Medical Research, New Delhi, India. The authors are thankful to all study subjects for their co-operation without which this study would have not been possible.

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