

TRANSMISSION OF *MYCOBACTERIUM TUBERCULOSIS* TO HOUSEHOLDS OF TUBERCULOSIS PATIENTS: A COMPREHENSIVE CONTACT TRACING STUDY

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Accepted for publication: 11 October 2009

Background: Tuberculosis (TB) continues to be a major health problem in developing countries. Contact investigation is the most appropriate strategy to interrupt transmission and subsequent development of TB.

Methods: This cross-sectional study was conducted to assess the impact of contact screening on case-finding by using tuberculin skin test chest radiography. Contacts of smear-positive patients with pulmonary TB (index cases) were diagnosed and registered in our center during 2002 – 2004. Contacts, defined as household members living with index cases for >30 days, were screened by sputum examination, tuberculin skin test, and chest radiography.

Results: Sixty-eight patients with smear-positive pulmonary TB were considered as index cases. A total of 224 close contacts with index cases (an average of 3 contacts for each index case) were detected. Age among contacts ranged from 3 months to 74 years. Eighty-three percent of contacts were Iranians and 17% were Afghans. Abnormal radiographs were seen in 49.6% of contacts. Sixteen point five percent of contacts had a positive tuberculin skin test of >10 mm; 7.6% had a positive sputum smear. The mean \pm SD age of Iranian contacts (29.1 ± 16.6 years) was significantly ($P < 0.001$) higher than that of Afghans (18.6 ± 14.1 years). Cavitory formation, nodular pattern, and infiltration were found to have a strong association with a positive sputum smear for acid fast bacilli (100%, 100%, and 87%, respectively).

Conclusion: The rate of TB in contacts was higher than other similar studies. Earlier detection and treatment of adults with TB could interrupt transmission and be a step towards eliminating childhood TB. Contact control and source-case investigations should be emphasized for TB control. Novel strategies are needed to maximize the number of contacts who are not only identified and evaluated, but also completely treated.

Archives of Iranian Medicine, Volume 9, Number 2, 2006; 204– 212.

Keywords: Contact tracing • transmission • tuberculosis

Introduction

Tuberculosis (TB) infection is much more prevalent in developing countries, where resources for control of the disease are lesser than industrialized countries. Despite the public health importance of the disease, TB is rarely investigated, as its diagnosis is difficult among the young age groups and children are usually not infectious. In addition, contact tracing is rarely carried out in developing countries, for lack of resources, and since isoniazid prophylaxis is not systematically provided for contacts, particularly children, who are in contact with individuals suffering from an infectious TB.

Currently, extensive contact investigation among the households is not a routine part of TB control program in most countries. Contact investigation of active TB cases, using tuberculin skin test (TST), is an important epidemiologic tool in identifying the TB infection. In addition, chest radiography is a major screening and diagnostic tool among tuberculin-positive close contacts. In the presence of any chest X-ray abnormalities such as masses, pleural disease, or parenchymal infiltrates, the probability of active TB exceeds 50%, for the time being. TST is the main way of detecting TB infection in those who have not been diagnosed with clinical TB. In addition, in close contacts chest X-ray has the ability to substitute TST. However, the value of chest X-ray, as an initial procedure for studying these patients, has not been well established. The problem with this procedure is its cost and radiation exposure.

Although recommendations and suggested guidelines for contact investigations have been proposed, they are based on expert opinion and not on data obtained from a comprehensive study of outcomes from contact investigations. To the best of our knowledge, this is the first study in Iran on proved cases of TB and their contacts to determine the efficacy of a comprehensive contact tracing protocol to identify new cases of TB. The main purpose of this research was to screen the households of TB close contacts and to detect the impact of active screening on TB case finding.

Patients and Methods

During a two-year period (1992 – 1994), a cross-sectional study was carried out in the National Research Institute of Tuberculosis and Lung Disease of Iran, a referral center for research and treatment of TB. All new patients with active pulmonary TB were eligible to participate in this study and considered as “index cases.” In general, other inclusion criteria were age >18 years, a chest radiograph suggestive of pulmonary TB, a positive sputum smear for acid fast bacilli (AFB), and/or positive culture for *Mycobacterium tuberculosis*. Since the bacteriologic confirmation of *M.tuberculosis* is obtained one month after obtaining the sample, the main criterion for entering the study was having at least one respiratory specimen—sputum or bronchoalveolar lavage (BAL), or both—that was positive for AFB. Eligible patients who provided informed written consent were enrolled as index cases.

Evaluation of contacts

We defined a “household contact” as someone who lived for >30 days in the same house as the index case. Data from contacts were collected in questionnaires. Symptoms including fever, cough, bloody sputum/hemoptysis, and weight loss, BCG vaccination, a TST, and a chest radiograph were reviewed. For TST, five tuberculin units of purified protein derivative (PPD) RT 23 (Statens Serum Institute, Copenhagen, Denmark) were administered to each case by the Mantoux method. The result was considered “positive” for indurations >10 mm. Standard chest radiography and sputum smear for AFB (3x) were performed on all the contact cases.

Statistical analyses

Student's t-test was used to compare the means of continuous variables. Univariate analyses of the association existing between the clinical, laboratory, and sociodemographic categorical variables with TST-positivity were performed using the χ^2 test. The two-tailed *P* values were calculated at a significance

level of 0%. Data entry and management were performed using Epi-Info 3.5 (CDC, Atlanta, USA). The Stata 11 software was also used for statistical analyses.

Ethical consideration

This study was approved by the Ethical Committee of the National Research Institute of Tuberculosis and Lung Disease of Iran.

Results

Index cases

During the years 2002 – 2004, 68 patients with smear-positive pulmonary TB (index cases) agreed to participate in this study. Fifty-eight (85.3%) cases were Iranians and 10 (14.7%) were Afghans. Thirty-five (51.0%) were males and 33 (48.0%) were females. The mean ± SD age of the index cases was 40.8 ± 23.1 years. Age distribution in the male and female groups was not significantly different in the Iranian and Afghan index cases.

Close contacts

We identified a total of 224 close contacts within the 68 index cases; on average three contacts for each index case. One hundred and eighty-six (83%) contacts were Iranians and 38 (17%) were Afghans. One hundred and six (47.3%) were males and 118 (52.7%) were females ($P = 0.4$). The median age of the contacts was 20 years (range: 7 months to 44 years) and the mean ± SD age was 27.3 ± 16.6 years. The mean ± SD age of Afghan contacts (18.6 ± 14.1 years) was significantly ($P < 0.001$) lower than that of Iranian contacts (29.1 ± 16.6 years). One hundred and forty-eight (66.1%) contacts had a scar from BCG vaccination. Table 1 shows the number of involved relatives in separate groups, besides the distribution of 44 sputum smear specimens in each group.

Relative	n (%)	Negative for AFB n (%)	Positive for AFB n (%)
Father	27 (12.1)	4 (14.8)	0 (0)
Mother	30 (13.4)	10 (33.3)	0 (0)
Spouse	24 (10.7)	11 (45.8)	0 (0)
Son/daughter	33 (14.7)	11 (33.3)	6 (18.2)
Others	110 (49.1)	23 (20.9)	11 (10.0)
Total	224 (100)	69 (30.8)	17 (7.6)

Generalized Fisher's exact test ($P = 0.000$); *sputum smears were available only for 44 cases. Table shows only the available sputum smears in each group.

Tuberculosis disease among contacts

Sputum smear was obtained from 44 of 224 contacts. The rest of contact cases could not expectorate sputum and thus the sputum smear test for AFB could not be done. A positive smear for AFB was diagnosed in 17 (39%) of 44 available specimens. The distribution of sex and nationality was not significantly different in the positive ($P = 0.7$) and negative ($P = 0.13$) sputum smears. The Afghan contacts had active TB twice the Iranian contacts (38.0% vs. 16.9%, respectively, $P = 0.13$). The majority of the smear-positive contacts were sons/daughters of the cases (aged 16 to 30 yr) or those spending part of the day with the index cases (Table 1). It is worth to note that none of fathers, mothers, or spouses was infected ($P < 0.001$).

The initial TST was positive (indurations >10 mm) in 16.0% of contacts. Table 2 shows the frequency of TST reaction in different groups and the results of available sputum smears in each group. TST reaction was not significantly different for different sex, nationality, and age groups. In addition, the result of sputum smear test for AFB was not associated with the TST reaction ($P = 0.53$).

Table 2. Distribution of TST induration and the frequency of sputum smear in each group.

TST	n (%)	Negative smear	Positive smear
		n (%)	n (%)
Negative	104 (72.6)	40 (29.6)	8 (16.7)
1-5	3 (1.4)	4 (2.0)	3 (0)
6-10	20 (9.4)	4 (2.0)	3 (42.9)
11-15	19 (9.0)	11 (13.9)	2 (10.4)
>15	16 (7.6)	8 (10.1)	2 (20.0)
Total	212 (100)*	64 (81.0)	15 (19.0)

TST = tuberculin skin test; Generalized Fisher's exact test ($P = 0.03$); *of 224 contacts, 212 individuals returned for follow-up and allowed their purified protein derivative (PPD) to be read by a physician. Therefore, there was 12 patients in the control group who had both the sputum smear and a registered PPD.

Table 3 presents the grading of positive sputum smear in index and contact cases. As could be seen, no statistical association was detected between the grading of positive sputum smear in index and contact cases. Besides, 12.8% of contacts who were smoker and 30.2% of those who did not smoke were smear positive. The frequency of positive smear was not significantly associated with the history of smoking ($P = 0.19$).

Table 3. Grading of sputum smear in index and contact cases.

Index	Contact cases			Total
	n (%)			
	One plus	Two plus	Three plus	
One plus	1 (33.3)	0 (0)	2 (66.7)	3 (17.6)
Two plus	3 (42.9)	1 (14.3)	2 (28.6)	6 (35.2)
Three plus	2 (28.6)	0 (0)	0 (0)	2 (11.2)
Total	6 (30.3)	1 (5.0)	4 (20.0)	11 (100)

Generalized Fisher's exact test ($P = 0.8$). Index: TB sources.

Radiologic findings in contacts

Radiological analyses revealed that 99 (49%) contacts had an abnormal chest radiograph (Table 4). Lymph node calcification and enlargement in hilar and mediastinal zones were the most common manifestations while cavitory lesion, nodular pattern, and infiltration had a strong association with positive sputum smear for AFB (100%, 100%, and 87%, respectively), 17% of patients with calcification and 20% with pleural effusion had a positive sputum smear.

Table 4. Radiologic findings in index and contact cases.

Radiologic finding	Contacts	Index cases
	n (%)	n (%)
Cavity	6 (2.7)	8 (40)
Infiltration	18 (8.3)	13 (60)
Calcification	41 (17.9)	2 (10)
Nodule	4 (2.2)	2 (10)
Lymph node enlargement	34 (15.8)	2 (10)
Pleural effusion	2 (1)	1 (5)
Normal	120 (56.4)	—
Number of contacts and index cases	224	28 *

* 28 out of 28 index cases obtained radiographs.

Discussion

Studies conducted in the 1960s and 1970s showed that household contacts of individuals with TB had a higher risk of acquiring infection than general population.^{1, 2} This was confirmed by several recent studies conducted among children in the New York City,³ Botswana,⁴ and Brazil,⁵ that revealed that contact with a patient with TB is the strongest risk factor for acquiring TB infection.

In our study, among 224 contacts of 68 index cases, 3.6% had active pulmonary TB, proved by a positive sputum smear. This rate is higher than other studies.¹²⁻¹⁴ We found a mean of three close contacts per index cases, which is less than that in developed countries.¹⁵ Results of TST showed that 16.5% of contact cases had a positive TST (>10 mm, in our region). Caldeira et al found that 41.3% of their contact cases were infected with *M.tuberculosis* and 13.6% had TB.¹¹ Another study done in the United States showed that 4% of contacts were positive for tuberculin test.¹⁶

Our study revealed that the presence of TB was not related to sex and nationality, even though Afghan contacts were affected twice as much as Iranians (38.5% positive sputum smear vs. 16.9%, respectively). This finding could be explained in terms of the poor socioeconomic condition of Afghan refugees and immigrants in Iran. The effect of poor socioeconomic condition and malnutrition on acquiring TB is a well-known entity. In a comprehensive study conducted in Pakistan, Rathi et al¹⁷ showed that poor housing condition is a risk factor for the spread of *M.tuberculosis*. In addition, Afghan contacts were significantly younger than Iranians (mean age of 18.6 vs. 29.1 yr; $P < 0.001$). Both of these findings showed that active TB is more likely to develop in close young contacts.^{13, 14}

Although other studies have shown that the level of infection is directly related to the intensity of exposure to the patient with infectious TB (as assessed through both the geographic proximity to the individual with TB at night time and the extent of activities shared with the individual with TB during day time), as well as the infectivity of the individual with TB,^{11, 18} there was no association between the transmission of TB and the duration of contact in our study ($P = 0.9$).

Our data showed that the grading of the sputum smear of the index cases was not associated with a higher risk of acquiring TB infection among contacts ($P = 0.8$). In contrary, Almeida et al found a strong correlation between the grading of sputum and the PPD induration size.¹¹

In Iran, BCG vaccination is given immediately after the birth and vaccination coverage is reported to be high. On the other hand, the Afghan individuals who were included in this study did not have any history of BCG vaccination for lack of an organized health system in Afghanistan. The value of PPD for screening a person with a history of BCG vaccination is disputed in recent years. Many studies still suggest that PPD is useful to identify patients with TB in endemic areas with a high coverage of BCG vaccination.^{10, 12, 13} Besides, BCG rarely induces a very strong tuberculin sensitivity. However, the majority of vaccinated individuals lose their BCG-induced tuberculin sensitivity gradually after the vaccination.¹⁴ Therefore, the traditional 10-mm cut-off value can be still a valuable tool to find suspected contact cases even in high areas with high coverage of BCG vaccination.

Based on our study, although the number of household contacts in the Iranian individuals is less than most of the developing countries, the percentage of the contact cases with positive PPD test is roughly the same. However, the percentage of contacts with a positive PPD that leads to the TB disease is high (50.4% positive sputum smear vs. 16.5% positive PPD test). The results show that the PPD test, as a single diagnostic method, is unable to detect the disease in the majority of cases. Radiologic findings such as cavity, infiltration, and nodular pattern could be detected in the majority of suspected cases of TB (49.6%). Therefore, radiographic evaluation could be suggested as a way to confirm a PPD test and other criteria for diagnosing and tracing the TB in contacts, particularly when the PPD test and other clinical features are suspicious. Secondly, the problem will be more clarified when we compare this finding with similar studies. The study conducted in the United States, among the homeless individuals, revealed that from 14.6% of TST-positive contacts only 1.6% developed the disease.¹⁰ Moreover, another study done in the United States showed that from 14.5% of contacts with positive TST in the Mississippi State, only 0.9% eventually diagnosed with TB. The Mississippi comprehensive TB program contained an interview

with cases during the first 24 hours of diagnosis, the concentric circle method, and the serial PPD test to identify and evaluate the contacts.¹¹ In Iran, due to the poor systematic investigation of contacts, the high number of contacts with positive TST may lead to active TB.

In conclusion, in our country and among Iranian and Afghan cases, provision of a better quality of life, as well as early diagnosis are the key factors to reduce the number of TB cases and contacts. Beside these factors, the need for an organized and comprehensive TB program to diagnose and investigate contacts as soon as possible is required.

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