Tuberculosis contact tracing among children and adolescents, Brazil

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Tuberculosis, pulmonar, diagnosis. Tuberculosis, pulmonar, prevention control. Contact tracing. Tuberculin test. BCG vaccine. Mycobacterium tuberculosis. *Cross-sectional studies.*

Abstract

Objective
To detect tuberculosis (TB) disease or infection among contacts of pulmonary TB patients.
Methods
Cross-sectional study in a Primary Healthcare unit in Rio de Janeiro (Brazil) with 184 child and adolescent contacts of pulmonary TB patients between March 1995 and March 1997. Subjects underwent clinical evaluation, chest radiographs, and tuberculin skin tests (TST); sputum smears were performed whenever possible. TB cases found were submitted to treatment and infected patients to chemoprophylaxis. Tuberculin converters, who tested positive for TST eight weeks after an initial negative result, received chemoprophylaxis.
Results
The sample included 98 boys and 86 girls; age ranged from 0 to 15 years; 26.9% were malnourished according to the Gomez criteria. Concerning the source of infection, 170 cases (92.4%) had household contacts, of which 66.5% were the child's parents. BCG vaccination was verified in 98.4% of children, and 14.7% of children had been revaccinated. Strong TST reactions were observed in 110/181 children. Seventy-six children (41.3%) were considered as infected by M. tuberculosis and 25 cases (13.6%) of TB were detected, of which seven (28%) were asymptomatic. There was greater occurrence of disease when the contact lived with more than one source of infection (p=0,02).
Conclusions
The detection of TB disease and infection was high in the studied population. Contact control must be emphasized, for it allows for the diagnosis of TB in children who are still asymptomatic, in addition to identifying infected subjects who may profit from chemoprophylaxis.

INTRODUCTION

Controlling contacts of patients with pulmonary tuberculosis (TB) has played an important role in the identification of cases of TB infection and disease, especially among children. Furthermore, it allows for the detection of new sources of infection, thus making it possible to identify patients in initial stages of the disease, when they are still poorly infective and morbidity still is low.[19]

Contacts of TB patients are at high risk of acquiring either active TB or TB infection, depending on factors such as source infectiousness, type of contact, and environmental characteristics. Host-related factors such as age and immunological status also inter-

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fere with the probability of the patient becoming infected or ill.[3]

Child TB has its highest incidence among the contacts of bacilliferous adults.[3] The present study was motivated by the increase in the number of TB cases in Rio de Janeiro since the 1990's, which was also observed among children.[1] Its aim was to detect TB infection or disease among the contacts of patients with pulmonary TB. As our study was carried out in a basic healthcare unit in the city of Rio de Janeiro, our results may provide a stimulus for public network healthcare professionals to investigate the contacts of TB patients, especially children.

METHODS

This is a descriptive, cross-sectional study, with prospective data collection, carried out at a municipal healthcare center (MHC) in Rio de Janeiro. We investigated 184 consecutive cases of children and adolescents aged 0-15 years, who were contacts of patients with pulmonary TB, and who visited the healthcare facility through their own will between March 1995 and March 1997. Twelve contacts who did not return to the MHC with the exams requested during the first appointment were excluded. TB diagnosis was ascertained through clinical examination, tuberculin skin tests (TST), chest radiographs, and, whenever possible, sputum smears.[18] A clinical form was filled for each child. TSTs were performed and read at the MHC by trained nurses, as recommended by the Brazilian Ministry of Health (MoH). Cutaneous test were considered as positive if = 10mm in individuals not vaccinated with BCG or vaccinated more than two years prior to testing, and if = 15mm in individuals in any stage of vaccination.[5] Children initially non-reactive to tuberculin tests were submitted to further testing after 8-10 weeks in order to verify tuberculin conversion; conversion was defined as an increase greater than 10mm in tuberculin response when the previous test was non-reactive.[14]

Children with BCG scars were considered as vaccinated; the remainder were considered as unvaccinated.

Chest radiographs were taken at a Municipal Secretariat of Health partner clinic, diagnoses being made jointly by a radiologist and by the physician who referred the patient. Sputum was collected from patients able to expectorate at the MHC, and smears were performed at the municipal reference laboratory. Smear results were classified according to MoH recommendations. Based on the results of tuberculin testing, chest radiographs, and sputum smears, children were classified as uninfected, infected, and with disease. Uninfected subjects were referred to expectant conduct, infected subjects were evaluated for receiving isoniazid chemoprophylaxis for a six-month period, and subjects with disease were treated according to MoH recommendations.[6]

Data was analyzed using the Hypothesis test for comparison of two proportions. Epi Info v. 6.0 software was used. P-values below 0.05 were considered as significant.

RESULTS

Study population comprised 98 boys and 86 girls. Age ranged from zero to 15 years, as follows: 12 (6.5%) < 1 year, 59 (32%) 1-4 years, 68 (37%) 5-9 years, and 45 (24.5%) 10-15 years. 47 children (26.9%) were malnourished according to the Gomez classification. The source of infection was internal (household source) in 170 cases (92.4%) – of which 113 (66.5%) were the child's parents and 17 (10%) had contact with more than one relative with TB – and external (non-household) in 14 cases (7.6%). As to sputum smears, 163 index cases (88.6%) were tested positive for direct sputum bacilloscopy, 6 (3.3%) tested negative, and information could not be obtained for 15 cases (8.1%). BCG vaccination was verified in 98.4% of children; 27 schoolchildren (14.7%) had been revaccinated. In all vaccinated children the first dose was given at birth. Among revaccinated schoolchildren, the interval between the second dose of BCG and tuberculin testing varied between 3 and 48 months.

Tuberculin tests were performed on 181 children, of which 110 (59.8%) were strongly reactive and 35.9% (N=66) had tuberculin reactions = 15mm (Table 1).

Table 2 presents the outcomes of tuberculin tests

Table 1 - Correlation between BCG and tuberculin skin tests in 184 child contacts of tuberculosis patients. Rio de Janeiro, 1995-1997.

Vaccination BCG	Tuberculin test Non-reactive	Weakly reactive	Strongly reactive 10-14mm	Strongly reactive ≥15mm	Not tested	Total
Unvaccinated	2	-	-	1	-	3
BCG-1 dose	50	14	32	55	3	154
BCG-2 doses	3	2	12	10	-	27
Total	55	16	44	66	3	184

Table 2 - Tuberculin skin test distribution by age group in 184 contacts of tuberculosis patients. Rio de Janeiro, 1995-1997.

Age group	Non-reactive	Weakly reactive	Tuberculin testing Strongly reactive 10-14mm	≥15mm	Not tested	Total
<1	5	1	3	-	3	12
1-4	20	2	8	29	-	59
5-9	21	6	15	26	-	68
10-15	9	7	18	11	-	45
Total	55	16	44	66	3	184

according to the subject's immunization status. Of the schoolchildren revaccinated with BCG (n=27), 11% (N=3) were non-reactive to tuberculin testing, 7.5% (N=2) were weekly reactive, 44.5% had reactions between 10 and 14mm, and 37% (N=10) had reactions = 15mm. By contrast, it is surprising that 25 out of 55 non-reactors were children under age 4 years, in spite of these children having received BCG vaccination at birth.

As to the source of infection, 60.6% (N=103) of household contacts were strongly reactive to tuberculin testing. As to the number of sources in the household, 75.6% (N=17) of children with more than one source of infection and 59.5% (N=153) of children with a single source of infection were strong reactors (Table 3).

Tuberculin conversion was observed in 15 children. 138 contacts (75%) were asymptomatic, and in the remaining 46 (25%) contacts coughing was the most common symptom. Expectant conduct was adopted for 105 subjects (57%).

Seventy-six children were considered as infected, of which 54 (29.4%) were submitted to isoniazid (INH) chemoprophylaxis with for six months. Chemoprophylaxis indication was more frequent among underfives.

Of the contacts living with more than one relative with TB, 35.3% had developed the disease, whereas among subjects in contact with a single source of infection, even if this source was the subject's father/mother, 11% had developed TB.

Twenty-five cases of TB-disease were detected (13.6%), of which seven (28%) were asymptomatic and six (24%) had coughing as the single symptom. Coughing, alone or associated with fever or weight

Table 3 - Correlation between tuberculin testing and source of infection in 184 child contacts of tuberculosis patients. Rio de Janeiro, 1995-1997.

Source	Tuberculin testing (mm) Age group 0-4	5-9	10-14	≥15	Not tested	Total
Household						
1 source	45	15	38	53	2	153
>1 source	5	-	3	9	-	17
External	5	1	3	4	1	14
Total	55	16	44	66	3	184

Table 4 - Clinical data and conditions related with the source of infection among child and adolescent contacts of tuberculosis patients. Rio de Janeiro, 1995-1997.

Variables	Child contacts Disease Yes	No	Total	P-value
Age group				
≤4 years	11	29	40	0,1107
>4 years	14	76	90	
Sex				
Male	15	56	71	0,5473
Female	10	49	59	
Source of infection				
Household	23	95	118	0,5841
External	2	10	12	
Degree of relatedness with source				
Father	9	31	40	0,4639
Mother	5	27	32	
Numbers of sources in household				
More than one	6	5	11	0,0200
One (father or mother)	14	58	72	

loss, was the symptom most frequently reported among subjects with disease. Mediastinal adenomegaly was the most frequent radiological finding (48%). Table 4 describes clinical and source-related findings. No statistically significant difference was observed between children under and above age four years, nor between sexes (Table 4). A greater frequency of illness was observed among children in contact with more than one household source (p=0.02).

TB diagnosis was made based on epidemiological, clinical, and radiological data in 14 (56%) of the 25 children with disease. The other 11 cases (44%) were also confirmed by sputum culture. All children with disease had been vaccinated with BCG at birth. No disseminated forms of the disease were observed. Subjects with disease were treated according to MoH recommendations.

DISCUSSION

The present study – in which 75% of contacts were asymptomatic – identified 25 cases of TB (13.6%) through contact investigation, a high rate when compared to other studies conducted in Brazil. In a study conducted in São Paulo, Morrone and Solha[15] reported a 3.8% TB incidence among contacts aged 0-15 years. However, higher rates were observed in other countries. In Canada (0-15-year-old contacts) and South Africa (underfive contacts), 38% and 34% TB occurrence were reported, respectively.[9]

Malnutrition is a risk factor for TB, since malnourished children tend to have weaker immunological response and general defense mechanisms.[9] In the present study, 26.9% of children were malnourished, a prevalence similar to that encountered by Beyers et al.[9] in South Africa.

Most of the children included in the present study came from low-income families; 92.4% were household contacts and 88.6% of cases were bacilliferous, which indicates a high risk of transmission between contacts. This happened in spite of BCG vaccination having been verified in 98.4% of cases. Several studies have recognized the importance of contact proximity in case of contacts with positive sputum smears.[17] In a study conducted in Texas, Chapman and Dyerly[10] highlight that, in poorer households, crowding and poor living standards favor TB transmission.

In the present sample, father and mother were equally frequent as sources of infection. The importance of household transmission has been described previously in the literature, relating disease severity with the child's age and with the proximity of contact, especially when the source is the mother.[9,12,13,16]

No disseminated forms of TB were observed in the present study; all 25 children with disease had received a dose of BCG vaccine at birth. Despite this high coverage, it must be considered that individuals exposed to bacilliferous patients, even though immunized, are considered as being at high risk of infection, and that recently infected individuals have a greater probability of developing the disease.[23] Beyers et al.[9] reported that 34% of underfive contacts had the disease and 14% were infected, despite 98.7% of them having received BCG vaccination.

In the present sample, tuberculin skin tests were performed on 181 contacts, of which 60.8% were strong reactors and 36.5% of these had reactions = 15mm. Tuberculin reactions may be due to infection by *M. tuberculosis*, BCG vaccination, and infection by other mycobacteria. It is believed, however, that the possibility of a cross reaction decreases when the diameter of the induration exceeds 10mm.[24] The American Thoracic Society[4] and the American Academy of Pediatrics[2] consider as positive tuberculin reactions those = 5mm in children at high risk of infection, such as those exposed to bacilliferous patients; reactions = 15mm are considered as positive in any individual. Sant'Anna et al[18] consider tuberculin reactions larger than 10mm in individuals unvaccinated with BCG or who received the vaccine more than two years prior to testing as suggestive of TB infection, as are those larger than 15mm, regardless of having received a first dose of BCG. A positive tuberculin test must be interpreted as a marker of infection, even in previously vaccinated individuals. In our sample, 60.8% (N=110) of vaccinated children (181) were strongly reactive to tuberculin. In order to detect TB infection, in addition to the size of the reaction, child age and time since vaccination were also considered.[18] Of the revaccinated children, 44.5% had reactions = 10mm and 37% had reactions = 15mm. Although reactions larger than 15mm are more probably correlated with infection by *M. tuberculosis*,[21] tuberculin reactivity may be influenced by prior vaccination.[11]

One of the limitations of the present study was the impossibility of carrying out a more in-depth analysis of the relationship between child age, tuberculin reactivity, and time since BCG vaccination. Arantes and co-workers[8], in population-based studies with São Paulo schoolchildren, showed that the first dose of BCG, when administered during the first year of life, could interfere with the tuberculin profile in school age, which, from the epidemiological perspective, would hamper the determination of the risk of TB infection. However, in a later study, the same author

demonstrated, based on a mathematical model, that BCG vaccination at that stage of life did not affect infection risk calculations, thus qualifying the TST for that purpose.[7] On the other hand, since the present study involved only contacts of TB patients, and considering that *M. tuberculosis* elicits a more potent and long-lasting immunogenic response than BCG vaccination,[7] one can assume that more intense tuberculin reactions are a sign of TB infection, and that the role of BCG has been minimized. Likewise, revaccination with BCG, ongoing in Rio de Janeiro since 1994, is not likely to have interfered with TST results in the present study. Revaccination, which would promptly restore tuberculin allergy in children vaccinated with BCG at birth, but would not interfere in the cutaneous reactivity of TB-infected children,[8,11] had been given only to a small share of children at the time of data collection. We chose, in the present study, not to consider children revaccinated with BCG who were reactive to the test as infected for purposes of chemoprophylaxis eligibility.

For 56% of the TB cases in our study, diagnosis was made without bacteriological confirmation, since, according to Starke,[22] positive TSTs, abnormal radiographs, and history of contact with adults with TB form the 'triad' responsible for most child TB diagnoses worldwide, due to the low efficacy of, and technical difficulties involved in child TB diagnostics.

Mediastinal adenomegaly was the most important radiological finding among contacts in the present study. Of the 25 children with altered chest radiographs, seven (28%) were completely asymptomatic and six (24%) had coughing as their only symptom. These cases would probably not have been detected were it not for contact tracking. The rareness and unspecificity of TB symptoms hinder the diagnosis of pulmonary TB in children.[20] Similarly, López et al.,[12] in Madrid, report that 38.2% of 149 cases of child TB studied had been diagnosed through history of contact with adults with TB and radiological alterations, despite being asymptomatic.

Of the 76 children considered as infected in the present study, 54 underwent chemoprophylaxis according to the official recommendations valid at the time. The remaining children – all of which were above age five years and vaccinated with BCG – once the possibility of disease was discarded, were referred to expectant conduct, that is, were advised to return to the healthcare facility for evaluation in case of respiratory symptoms, fever, or weight loss. The indication of preventive therapy for vaccinated children or for children older than five years was due to these children – some of which were also malnourished – being in intimate contact with bacilliferous adults, and to tuberculin conversion. [7,18] The MoH currently recommends preventive therapy for children under age 15 years who are contacts of bacilliferous TB patients, have no sign of active TB, and have not received BCG vaccination but are TST reactive at = 10mm, or who have received BCG but are reactive at = 15mm.[14]

Of the 25 cases of TB in the present study, 23 were household contacts, which highlights the importance of contact proximity to the risk of infection. The child's parents were the most frequent source of infection. However, a greater percentage of disease was observed in cases of more than one source of infection in the household in comparison with cases with a single source, even if the latter was one of the child's parents. Among children who were household contacts of more than one person with TB, 35.3% developed the disease. When the source of infection was the child's mother or father, 12.4% of children developed the disease. It has been shown that the probability of infection is proportional to the concentration of bacilli in the environment.[17]

There are numerous difficulties in controlling TB contacts in the Brazilian scenario. Although official norms recommend that all contacts of TB patients be screened, [6] the lack of resources for healthcare, typical of developing countries, in which TB incidence is high, causes a shift in attention to the treatment of the existing cases of the disease. Children fail to be evaluated due to cultural and socioeconomic factors and to failures in healthcare management. Limitations inherent to the healthcare system prevent the early diagnosis of a large number of TB cases, thereby increasing disease transmission. In São Paulo, Arantes et al,[6] report that diagnoses of TB cases among contacts in healthcare facilities represented only a small share (2-3%) of the total cases diagnosed, which suggests that the control among this risk group is almost entirely absent.

Contact tracking, despite the feeble resources destined to healthcare in our environment, must be considered as an important preventive measure to be established for TB control purposes. It allows for a diagnosis of the disease in its early stages, or even for TB prevention by hindering the installation of the disease, and may therefore promote the reduction of child TB-related morbidity and mortality.

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