Poor follow-up of paediatric tuberculosis contacts in Tbilisi, Georgia

Nino Gogichadze1, Giorgi Kuchukhidze2, Tsira Merabishvili1, Maya Tsereteli1, Alexandre Tavadze3, Ketevan Chanturishvili4, Martin van den Boom2, Alexandra Kruse5

1National Center for Disease Control and Public Health, Tbilisi, Georgia.
2WHO Regional Office for Europe, Copenhagen, Denmark
3Mrcheveli – European Limbach Diagnostic Group, Tbilisi, Georgia.
4David Tvisiani Medical University, Tbilisi, Georgia.
5Médecins Sans Frontières, Copenhagen, Denmark.

Corresponding author: Nino Gogichadze (email: Ninuka.g@gmail.com)

ABSTRACT

Introduction: Georgia has a high tuberculosis (TB) incidence and is a priority country within the European Region. Children, particularly those under five years of age, are at high risk of developing active TB so it is important to focus on them in contact tracing. The aim of the study was to investigate individuals who were identified as contacts and lost to follow-up after their referral to a TB facility.

Methods: A retrospective cohort study of all paediatric contacts (under 15 years of age) of pulmonary TB patients in Tbilisi, Georgia, conducted in the years 2015–2016.

Results: The study included 594 contacts. In total, 15% (86/594) visited a TB facility for follow-up as planned. The proportion of follow-up visits was similar in both age groups, under five and over five years of age. None of the risk factors analysed (age, index patient’s number of symptoms, drug susceptibility) were associated with loss to follow-up after referral. In the 0–5 years old group (n = 21), 38% (8/21) received treatment for latent TB and none were enrolled in active TB treatment. In the 5–15 years old group (n = 65), 3% (2/65) initiated latent TB treatment, while another 3% (2/65) were in active TB treatment.

Conclusion: Only 15% of paediatric TB contacts were followed up after referral as planned. Among children under five years of age with the highest risk of disease progression, only 38% started treatment as recommended. Implementation of the national recommendations in practice calls for urgent policy action.

Keywords: TUBERCULOSIS CONTACT, PAEDIATRIC, CHILDREN, FOLLOW-UP

INTRODUCTION

Tuberculosis is a global public health priority. Children are particularly vulnerable as they are both more difficult to diagnose and treat (1, 2) and at higher risk of disease progression (1, 3–5). Globally, about 1 million children under 15 years of age annually develop active TB (ATB), which accounts for estimated 10% of all ATB cases (6). About half of the children with ATB are less than five years old (7). This age group is at highest risk of disease progression and considered priority in the World Health Organization (WHO) policy to end TB (2), which is also reflected in Georgia’s TB strategy.

Despite a substantial decrease in recent years, Georgia continues to have a high TB incidence compared to other countries in the WHO European Region (66 ATB cases per 100 000 population in 2017) (1). The proportion of paediatric ATB cases is about 4%, which represents less than half of the global estimate (6, 8) and may indicate that childhood TB is underdiagnosed and underreported. Contact investigation is instrumental in identifying people infected with TB. The national TB guidelines, which are correlated with the WHO recommendations for latent tuberculosis infection (LTBI), recommend that all children under five years of age exposed to a person with ATB initiate treatment for LTBI when ATB is excluded. If the index patient has multidrug-resistant
tuberculosis (MDR-TB), the clinician assesses if LTBI treatment is indicated. Children under five years of age exposed to an individual with ATB would only receive treatment if ATB is confirmed, depending on the symptoms and tests upon presentation (9). For children under five years of age either interferon-gamma release assays or rapid TB tests are used, depending on the available stock in the country.

A study conducted in Georgia among adult contacts found an overall prevalence of 33% LTBI and 3% ATB during a one-year follow-up period (10). Another Georgian study found a significantly higher prevalence of LTBI among contacts whose index TB patient had a prior unfavourable treatment outcome, compared to those with a favourable outcome (11). Despite the improved contact investigation practices in Georgia, gaps may still exist, especially when it comes to children. Children were previously not a target group in the public health approach focusing mainly on contagious patients, in which children are rarely included. In Georgia, TB contact management is administratively divided into contact identification and clinical management. Contacts are identified by an epidemiologist, who advises them to register at the TB facility for a follow-up. Only the contact and not the TB facility is informed. In the TB facility, all contacts are registered when reporting for follow-up after referral, with a note on whether treatment is initiated (electronic and paper-based patient files). Contacts diagnosed with ATB are also entered in the electronic TB registry. The programmes are implemented by different entities and are not directly linked. Thus, the proportions of contact follow-up and diagnoses of LTBI and ATB remain unknown.

The aim of the study was to identify and characterize paediatric ATB contacts in Tbilisi, Georgia, including follow-up after referral and initiation of treatment for LTBI and ATB. The study also aimed to identify the risk factors for those lost to follow-up (LFU) after referral.

METHODS

STUDY DESIGN
This is a retrospective cohort study of all paediatric household and close contacts of pulmonary ATB patients.

STUDY SETTING
The study was conducted in Tbilisi, the capital of Georgia. In Georgia, tuberculosis management is overseen by the Ministry of Labour, Health and Social Affairs, who provides assistance free of charge through the National Tuberculosis Programme and in accordance with the WHO guidelines. All ATB patients are recorded in the national TB electronic database for disease surveillance and case management at the National Center for Tuberculosis and Lung Disease (NCTLD). TB contact tracing is performed by the National Center for Disease Control and Public Health (NCDC), maintaining a separate electronic database of identified contacts. At the time of the study, contact investigation was conducted for index patients with acid-fast bacilli sputum smear-positive pulmonary TB. According to old recommendations, only sputum smear-positive patients were contagious. However, since 2017 contact tracing has been expanded to include all pulmonary TB patients regardless of smear results.

STUDY POPULATION AND PERIOD
The study covered all children under 15 years of age who were entered in the electronic NCDC TB contact database in Tbilisi from January 2015 to December 2016. Those whose identification number was missing from the registry were excluded from the study.

DATA COLLECTION, SOURCES AND STATISTICAL ANALYSIS
The list of contacts identified in the NCDC TB contact database was compared to the follow-up lists in the NCTLD electronic database of ATB cases and the facility journals of contacts (hard copies), including contacts not diagnosed with ATB. The lists were compared using the unique national identification number.

Data collected included identification number, contact age, symptoms (cough, fever, weight loss, night sweats, chest pain, palpable lymph nodes), index TB drug susceptibility, ATB and LTBI treatment.

Analysis included calculating the proportions of 1) follow-up visits after referral among all contacts, 2) contacts diagnosed with ATB among contacts registered for follow-up after referral, and 3) the coverage of LTBI treatment among follow-up after referral under five years of age. We also analysed risk factors of LFU after referral among all contacts. The risk factors included index patient drug susceptibility, age and symptoms. We calculated crude risk ratios and a 95% confidence interval. Multivariate regression analysis was performed to calculate adjusted relative risks.

ETHICS
A permission to carry out the study was obtained from the NCDC. A local ethics approval was obtained from the NCDC Institutional Review Board. An ethics exemption was also received from the WHO Research Ethics Review Committee.

POOR FOLLOW-UP OF PAEDIATRIC TUBERCULOSIS CONTACTS IN TBILISI, GEORGIA

448
PUBLIC HEALTH PANORAMA
RESULTS

In bivariate analysis we found that, in total, 679 paediatric contacts of ATB cases in Tbilisi were identified. Of those, 85 contacts were excluded due to a missing identification number and 594 children were ultimately included in the final analysis. Of the contacts, 139 (23%) were under five years of age and 455 (77%) were aged 5–14 years. Only 18 contacts (3%) had one or more symptoms at the time of contact investigation. Among the index cases, 20% had MDR-TB, 73% had drug-susceptible TB, and in the remaining 7% cases susceptibility data were missing.

In multivariate analysis we found that only 86 (15%) of all contacts were registered for follow-up in the TB facility for further evaluation by a physician. In the younger age group, that is 0–5 years of age, a similar proportion was registered for follow-up (21 (15%)), 8 (38%) received treatment for LTBI and none were enrolled in ATB treatment. Of the remaining 62%, only 20% could be explained by MDR-TB in the index patient. In the older age group, that is 5–14 years of age, 65 (14%) were registered for follow-up, 2 (3%) received treatment for LTBI and 2 (3%) received ATB treatment (Fig. 1).

None of the risk factors analysed were significantly associated with LFU, whether in bivariate or multivariate analyses.

FIG. 1. FLOWCHART OF PAEDIATRIC CONTACTS IN THE YEARS 2015–2016, TBILISI, GEORGIA
TABLE 1. RISK FACTORS ASSOCIATED WITH LOSS TO FOLLOW-UP AFTER REFERRAL, TBILISI, 2015–2016 (n = 594)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total n (%)</th>
<th>No FU n (%)</th>
<th>FU n (%)</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug susceptibility</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug-susceptible</td>
<td>435 (73%)</td>
<td>376 (74%)</td>
<td>59 (69%)</td>
<td>1.39</td>
<td>[0.81, 2.41]</td>
<td>0.232</td>
</tr>
<tr>
<td>MDR</td>
<td>117 (20%)</td>
<td>96 (19%)</td>
<td>21 (25%)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>42 (7%)</td>
<td>36 (7%)</td>
<td>6 (7%)</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Under 5</td>
<td>139 (24%)</td>
<td>118 (23%)</td>
<td>21 (25%)</td>
<td>0.94</td>
<td>[0.55, 1.6]</td>
<td>0.809</td>
</tr>
<tr>
<td>5–14</td>
<td>455 (77%)</td>
<td>390 (77%)</td>
<td>65 (76%)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>More than one symptom</td>
<td>576 (97%)</td>
<td>491 (97%)</td>
<td>85 (99%)</td>
<td>0.34</td>
<td>[0.01, 2.23]</td>
<td>0.494</td>
</tr>
<tr>
<td>Less than one symptom</td>
<td>18 (3%)</td>
<td>17 (3%)</td>
<td>1 (1%)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (mean +/- SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.32 (+/- 4.46)</td>
<td>8.42 (+/- 4.51)</td>
<td>7.72 (+/- 4.13)</td>
<td>0.7 (+/- 0.49)</td>
<td>[0.27, 1.66]</td>
<td>0.156 (0.136)</td>
<td></td>
</tr>
</tbody>
</table>

Legend:
FU – follow-up
MDR – multidrug-resistant
Symptoms = cough, fever, weight loss, night sweats, chest pain, lymphadenopathy
Total n – total number of contacts identified
No FU n – contacts who did not visit a TB facility after referral
FU – contacts who visited a TB facility after referral
CI – confidence interval
SD – standard deviation

DISCUSSION

Among 594 paediatric TB contacts identified, we found that only 15% reported for follow-up after referral, among both age groups, over five years of age and under five years of age. We found no significant risk factors of LFU. In the younger age group, only 38% initiated treatment, all for LTBI. In the older age group, 6% of the children followed up the initiated treatment, 3% for ATB and another 3% for LTBI.

Our study reveals that follow-up after referral was poor. Similarly, in a study in Uganda, the proportion of follow-up after referral among high-risk contacts including children under five years of age or HIV-positive was low (20%) (12). A likely explanation is the lack of monitoring and coordination between the different entities in charge. It is the contact's responsibility to actively register in the TB facility to ensure follow-up after referral. Furthermore, the general information provided for this purpose may not explicitly highlight the increased disease risk for children. Although only 3% reported symptoms at the time of contact investigation, ATB among children may present with atypical symptoms (1). Since the paediatric burden of TB in Georgia is less than half of the WHO estimate, it may indicate that TB in children is underdiagnosed. It calls for urgent policy action to ensure improved follow-up after referral of this vulnerable group of contacts.

Due to increased risk of disease progression, WHO and national guidelines recommend treatment of all contacts under five years of age, either for ATB or LTBI, depending on symptoms and signs. The only exemption is if the index patient has MDR-TB, in which case indication for LTBI treatment is subject to the physician's individual assessment. However, in our cohort only 38% started LTBI treatment. Only 20% of the remaining 62% could be explained by MDR-TB in the index patient. Only 3% had reported symptoms at the time of investigation, and only one third of those reported for follow-up after referral. The main strengths of our study are the large paediatric cohort and adherence to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines (13). The major limitation of the study is the retrospective data collection of programmatic data and missing identification numbers.

This study points out programmatic limitations in existing management of paediatric TB contacts, which can lead directly to improving current policy.

CONCLUSIONS

Georgia does not appear to be following the national guidelines recommending follow-up and treatment for all paediatric TB contacts under five years of age. In this study of 594 children...
under 15 years of age, only 15% were followed up after referral in both the younger and older age group. No risks were identified. Among children under five years of age, 38% received treatment, all for a latent TB infection. This inadequate follow-up after referral and treatment initiation among children, who are at particular risk of disease progression, calls for urgent policy action.

Acknowledgements: The authors thank the national tuberculosis counterparts NCDC and NCTLD for defining research questions and providing data for this study, and the Secretariat of the European Tuberculosis Research Initiative (ERI-TB) at the WHO Regional Office for Europe for organizing the Structured Operational Research Training (SORT-TB) for six eastern European countries supported by the USAID-WHO regional partnership project to end TB in eastern Europe. The SORT-TB curriculum was an adaptation to the eastern European context of the Structured Operational Research and Training Initiative (SORT IT) course led by the Special Programme for Research and Training in Tropical Diseases (TDR).

Sources of funding: This study was funded by the United States Agency for International Development. The funder played no role in the study design, data collection and analysis, decision to publish or preparation of the manuscript.

Conflicts of interest: none declared.

Disclaimer: The authors alone are responsible for the views expressed in this publication and they do not necessarily represent the decisions or policies of the World Health Organization.

REFERENCES


1 All references were accessed 11 December 2019.