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Davit Baliashvili

National Center for Disease Control and Public Health

Mathew J. Magee

Georgia State University

Russell R. Kempker

Emory University

Giorgi Kuchukhidze

National Center for Disease Control and Public Health

Ana Aslanikashvili

National Center for Disease Control and Public Health

See next page for additional authors

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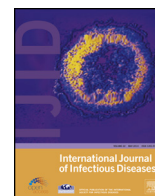
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Authors

Davit Baliashvili, Mathew J. Magee, Russell R. Kempker, Giorgi Kuchukhidze, Ana Aslanikashvili, and Henry M. Blumberg



Short Communication

Contacts of retreatment tuberculosis cases with a prior poor treatment outcome are at increased risk of latent tuberculosis infection



Davit Baliashvili^{a,*}, Matthew J. Magee^b, Russell R. Kempker^c, Giorgi Kuchukhidze^a, Ana Aslanikashvili^a, Henry M. Blumberg^{c,d}

^a National Center for Disease Control and Public Health, 9 Asatiani St., 0177 Tbilisi, Georgia

^b Division of Epidemiology and Biostatistics, School of Public Health, Georgia State University, Atlanta, Georgia, USA

^c Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia, USA

^d Departments of Epidemiology and Global Health, Rollins School of Public Health of Emory University, Atlanta, Georgia, USA

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SUMMARY

Objectives: To estimate the prevalence of and risk factors for latent tuberculosis infection (LTBI) among contacts of index patients with tuberculosis (TB) with a prior history of active TB disease and TB treatment (retreatment cases).

Methods: A cross-sectional population-based study was conducted using data from the national TB contact surveillance program in the country of Georgia. Contacts of retreatment cases were investigated and tuberculin skin testing was offered. Bivariate and multivariable analyses were performed to calculate odds ratios (OR) and 95% confidence intervals for risk of LTBI among contacts.

Results: The prevalence of LTBI was significantly higher among contacts whose index TB patient had had a prior unfavorable treatment outcome compared to those who had had a favorable outcome (OR 3.14). Contacts whose index TB case had previously failed therapy (OR 6.43), was lost to follow-up (OR 5.63), or had completed treatment (OR 3.33) had a significantly higher prevalence of LTBI compared to contacts of previously cured TB cases.

Conclusions: Among contacts of active TB retreatment cases, the risk of LTBI was related to the outcome of the index case's previous TB treatment. Efforts aimed at reducing treatment loss to follow-up should be emphasized to enhance TB control efforts and may also decrease LTBI and active TB among contacts.

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1. Introduction

Tuberculosis (TB) remains a serious global public health problem, including in the country of Georgia. In 2014, the World Health Organization (WHO) reported the incidence rate of TB in Georgia to be 106 cases per 100 000 persons.¹ Georgia has high rates of multidrug-resistant (MDR) TB. Close contacts of persons with active TB disease are at increased risk of latent TB infection (LTBI) and active TB disease.² Contact investigation of close contacts is a recommended control strategy for active TB case finding and for detecting individuals with LTBI who are at increased risk of progressing to active TB disease.^{3–5}

Contact investigations are commonly conducted in high-income, low TB incidence countries, but are generally not part of routine TB control efforts in most low- and middle-income countries (LMIC). Nonetheless, contact investigations are recommended by the WHO in LMIC where the burden of TB disease is greatest.³ In 2012, the National Center for Disease Control and Public Health (NCDC) initiated a nationwide TB contact investigation program in the country of Georgia. Using data from this program, it was aimed to estimate the prevalence of and risk factors for LTBI among contacts of index patients with a prior history of treatment for active TB (retreatment cases).

2. Methods

This cross-sectional study was conducted using surveillance data from the entire country of Georgia. Only the close contacts of

* Corresponding author. Tel.: +995 598 552655.

E-mail addresses: d.baliashvili@ncdc.ge, datobaliashvili@gmail.com (D. Baliashvili).

Table 1

Association of index case previous TB treatment outcome and the prevalence of LTBI among their contacts

Outcome of index case, previous TB treatment	Contacts with LTBI (%) n = 46	Contacts without LTBI (%) n = 93	OR (95% CI)	p-Value
Cured	8 (15.1)	45 (48.9)	1.00	<0.01
Completed	16 (37.2)	27 (29.1)	3.33 (1.26–8.82)	0.01
Lost to follow-up	14 (50.0)	14 (15.1)	5.63 (1.96–16.16)	<0.01
Failure	8 (53.3)	7 (7.5)	6.43 (1.81–22.72)	<0.01

TB, tuberculosis; LTBI, latent tuberculosis infection; OR, odds ratio; CI, confidence interval.

retreatment TB cases (index cases) who were sputum AFB smear-positive at the time of diagnosis as a retreatment case, identified between April and December 2012, were included. Epidemiologists affiliated with the NCDC interviewed each index retreatment case to determine close contacts, defined as members of the same household and non-household contacts who had daily contact with the index patient. Contacts were offered tuberculin skin testing; if they accepted, a tuberculin skin test (TST) was carried out using the Mantoux method,⁶ with 0.1 ml tuberculin. An induration of ≥ 10 mm was defined as a positive TST. LTBI was defined as having a positive TST (the first step of investigation) without symptoms of active TB disease. Contacts with a positive TST were referred to a TB physician for further evaluation, but were not followed up as part of this study.

Analyses were performed using SAS version 9.3 software (SAS Institute Inc., Cary, NC, USA). Bivariate analyses and multivariable logistic regression analyses were used to calculate odds ratios (OR) and 95% confidence intervals (95% CI) for the risk of LTBI among contacts. The primary exposure of interest was the index patient's outcome of previous TB episode: cure, completion, loss to follow-up, or failure. Treatment outcomes were defined based on WHO definitions.⁷ Model building and selection was based on the purposeful selection of covariates strategy.⁸ A two-sided *p*-value of <0.05 was considered statistically significant for all analyses. The study was approved by the institutional review boards of Emory University and the Georgian NCDC.

3. Results

Among 583 close contacts of index patients with active TB and a prior history of TB (i.e., retreatment cases), 139 (24%) received a TST and were included in this analysis. The overall prevalence of LTBI among these contacts was 33% (46/139). The prevalence of LTBI was significantly higher among those contacts whose index TB case had had an unfavorable treatment outcome (failed or lost to follow-up) during their prior treatment episode compared to those whose index patient had had a favorable outcome (cured or completed) (OR 3.14, 95% CI 1.48–6.70). Further analysis showed that contacts whose index TB case had failed, was lost to follow-up, or completed treatment had a significantly higher prevalence of LTBI compared to contacts of TB cases who had previously been cured (Table 1).

On multivariable analysis, controlling for sex of the contact and type of contact, independent risk factors for LTBI included being a contact of an index TB case who had completed treatment (adjusted OR (aOR) 3.25, 95% CI 1.20–8.78), was lost to follow-up (aOR 3.67, 95% CI 1.13–11.89), or had failed treatment (aOR 7.75, 95% CI 2.05–29.32), as compared to contacts of TB cases who had had a prior outcome of cure (Table 2).

Table 2

Prevalence of LTBI among contacts of index TB retreatment cases based on the index patient's prior TB treatment outcome

Characteristic	aOR (n = 131)	95% CI
Outcome completed vs. cured	3.25	1.20–8.78
Outcome lost to follow-up vs. cured	3.67	1.13–11.89
Outcome failure vs. cured	7.75	2.05–29.32
Household vs. non-household contact	3.03	0.76–12.08
Male contacts vs. female contacts	1.57	0.69–3.55

LTBI, latent tuberculosis infection; TB, tuberculosis; aOR, adjusted odds ratio (the model included all variables in the table); CI, confidence interval.

4. Discussion

This investigation appears to be the first to report that contacts of index patients with active TB disease who are retreatment cases have a significantly higher risk of having LTBI based on a prior unfavorable treatment outcome in the index TB case. In this study, the risk of LTBI appeared to be dose-dependent, based on the outcome of the index TB case's previous TB treatment. This novel result highlights the importance of completing TB treatment regimens and curing patients, especially in countries like Georgia, where the loss to follow-up rate among MDR-TB patients is high.⁹ Index cases whose initial treatment regimen is not successful are likely to remain infectious for prolonged periods of time, resulting in a greater risk of transmission of *Mycobacterium tuberculosis* among their contacts. Therefore, efforts aimed at reducing treatment loss to follow-up should enhance TB control efforts and may also decrease LTBI and active TB among contacts.

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Conflict of interest: None.

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