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Effect of Smoking on Longitudinal Interferon-ϒ Release Assay Results among Close Contacts of People with Pulmonary Tuberculosis

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BACKGROUND

- Diagnosis of *M. tuberculosis* (Mtb) infection in close tuberculosis (TB) contacts is critical for TB control.
- Interferon-gamma release assays (IGRAs) diagnose Mtb infection, but the test is limited by assay variability, including the conversion (negative to positive) and reversion (positive to negative) of IGRA responses that may not always reflect changes in Mtb infection status.
- Several studies have revealed that smoking is a risk factor for Mtb infection and TB disease but its effect on longitudinal IGRA results remains unknown.

METHODS

- We conducted a multi-site prospective study in Brazil, between 2015-2019 among close contacts of adults with culture-confirmed pulmonary TB. IGRA test was performed in two visits: baseline and month 6. If the initial IGRA result was negative, the test was repeated at month 6. Contacts who were within 30 months of enrolling in the study were included and a subsequent IGRA was performed between months ~24-30 after enrollment. Participants with IGRA-indeterminate results were excluded from this study.

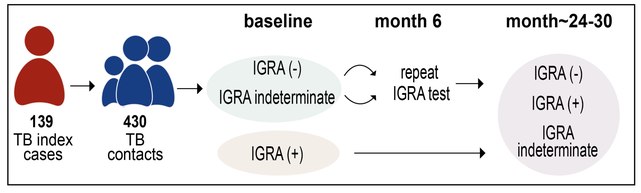


Figure 1. IGRA was performed at baseline on TB contacts enrolled in RePORT-Brazil.

- IGRA results were categorized as IGRA-positive (maintained from baseline to last visit), IGRA-conversion (from negative to positive at any time), IGRA-reversion (from positive to negative at any time), and IGRA-negative (maintained from baseline to last visit).
- Associations between IGRA results and smoking status (current/former vs never) at baseline in contacts were evaluated using propensity score-adjusted logistic regression models to avoid overfitting. Next, this estimated propensity score was used as a covariate in the main outcome model, which regressed the outcome (IGRA-positive, IGRA-conversion, IGRA-reversion) on smoking status.

TB contacts who reported smoking (current/former) had **lower odds of reverting from an IGRA-positive to an IGRA-negative** result.

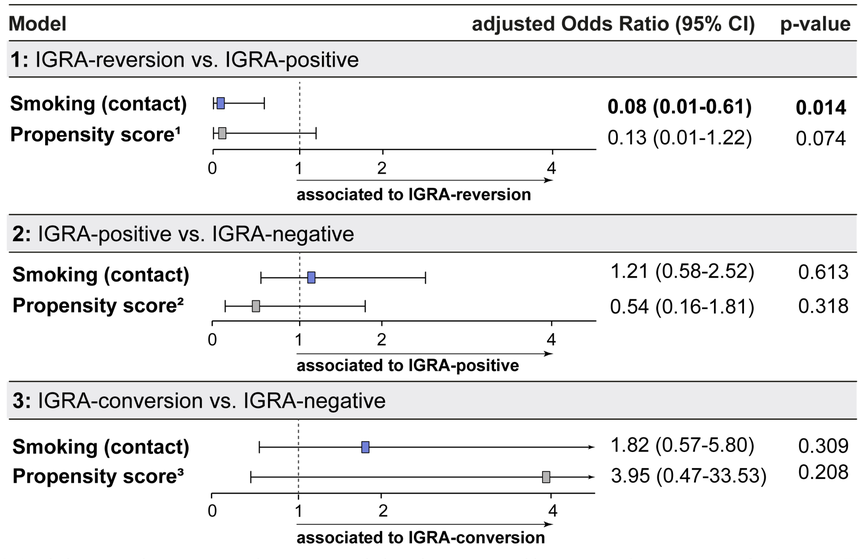


Figure 2. Logistic regressions were used to test associations between smoking among close contacts of pulmonary TB cases and reversion, conversion, and positive IGRA results among TB close contacts. *For "smoking (current/former)" was used as reference "never-smoking". Lasso regression was used for selecting variables that were included in Propensity Score for "smoking". [1]Variables used in the propensity score model: sex, alcohol consumption, illicit drug use, TB preventive treatment, BCG scar, and age (in contacts) + sex, alcohol consumption, sputum smear (+), illicit drug use, cavities on chest X-ray and HbA1c (in TB cases). [2]Variables used in the propensity score model: sex, age, alcohol consumption, illicit drug use, BCG scar and TB preventive treatment (in contacts) + sputum smear (+) and cavities on chest X-ray (in TB cases). [3]Variables used in the propensity score model: sex, alcohol consumption, illicit drug use, TB preventive treatment, BCG scar, and age (in contacts) + sex, alcohol use, smoking, sputum smear (+), illicit drug use, cavities on chest X-ray and HbA1c (in TB cases).
Abbreviations: IGRA: Interferon-ϒ Release Assay, TB: tuberculosis, CI: confidence interval

RESULTS

- There were 430 close contacts of 139 TB cases. Of the contacts, 89 (21%) were IGRA-positive, 30 (7%) were converters, and 30 (7%) were reverters. Additionally, 22 (5.1%) had an indeterminate result.
- The frequency of smoking among contacts in IGRA-positive group was 26 (29.2%), in converters 7 (23.3%) and reverters was 3 (10%).
- Smoking in contacts was associated with lower odds for IGRA-reversion (adjusted odds ratio = 0.08; 95% confidence interval= [0.01; 0.61], p=0.014). We did not detect associations between smoking and IGRA-positive or IGRA-conversion at the 5% level.

CONCLUSIONS

- Contacts who reported smoking (current/former) had lower odds of reverting from an IGRA-positive to an IGRA-negative result, after adjusting for multiple potential confounders in both the close contact and their TB source case.
- Our findings highlight the importance of smoking on longitudinal IGRA results. This has implications for clinical care and clinical trials in which IGRA status is monitored or used as an outcome, such as TB vaccine trials. Due to our findings and the limitations of previous research, additional studies are necessary.

ADDITIONAL KEY INFORMATION

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