Oral swab testing by Xpert® MTB/RIF Ultra for mass tuberculosis screening in prisons

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A R T I C L E   I N F O

Keywords:
Tuberculosis
Oral swab
Xpert® MTB/RIF Ultra
Prison
Screening

A B S T R A C T

Diagnosis of pulmonary tuberculosis is usually achieved by testing sputum for presence of Mycobacterium tuberculosis by microscopy, culture or nucleic acid amplification tests. However, many individuals are unable to produce sputum, particularly early in the course of illness. Studies have reported that oral swabs, assayed by nucleic acid amplification tests, may be a suitable substitute or complement to sputum testing. To determine whether this method could be useful for case finding, in which bacillary load is often lower, we evaluated it in the setting of a mass tuberculosis screening study in prison inmates in Brazil. For this sub-study, we enrolled 128 individuals with pulmonary tuberculosis confirmed by sputum Xpert testing, and 128 controls who tested negative by sputum culture and Xpert. We collected two oral swabs by participant, prior to starting treatment. Swabs were collected from the tongue by brushing along the surface for 10 times. The sensitivity of a single oral swab was 43% (N = 55/128; 95% CI: 34–52%). Using two consecutive oral swabs the sensitivity increased to 51% (N = 66/128; 95% CI: 43–60%). The specificity was 100% (128/128). In participants with high mycobacterial load in the sputum, the combined sensitivity was 90% (N = 9/10). In the participants with medium mycobacterial load in the sputum, the combined sensitivity was 79% (N = 23/29). In the participants with low or very low mycobacterial load in the sputum, the combined sensitivity was 38% (N = 34/89). Our data suggest that oral swab sampling, assayed by Xpert, has comparable sensitivity to sputum in participants with high and medium mycobacterial load in the sputum. However, 70% (89/128) of individuals identified through our mass screening study (Carbone et al.) had detection number low or very low in their sputum. In this population, oral swab testing may not have sufficient sensitivity as currently performed. Further studies are needed to identify alternative non-sputum sampling strategies in this population.

Funding: JRA reports grants from the National Institutes of Health (1R01AI130058-01) during the study. JC reports grants from the NIH (1R01AI130058-01) and grants and personal fees from the Brazilian National Research Council (310551/2018-8) and Coordination of Superior Level Staff Improvement during the study.

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https://doi.org/10.1016/j.jctube.2020.100148

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of Institutional Review Board. Between 2017 and 2018, inmates from the three prisons in Brazil were screened for tuberculosis by symptom assessment, chest radiography, sputum testing by Xpert® MTB/RIF 4th generation and culture. This sub-study was performed between April and September of 2018 we enrolled 128 individuals with pulmonary tuberculosis confirmed by sputum Xpert testing, and 128 controls who tested negative by sputum culture and Xpert. Two oral swabs were collected by participants. The first swab was collected prior to starting treatment and the second was collected the next day. Swabs were collected from the tongue by brushing along the surface for 10 times.

Swabs were stored in a − 80°C freezer for up to 12 weeks and then retested. Threshold-cycle (Ct) of multiple probes targeting the rpoB gene was used to estimate mycobacterial load. From that, the Xpert MTB/RIF Ultra quantification of mycobacterial load in the sputum, the combined sensitivity was 38% (N = 34/89) (Table 1).

Studies suggest that oral swabs have comparable sensitivity to sputum testing by Xpert in individuals diagnosed with tuberculosis [5]. Oral swabs enable sampling in individuals who cannot provide sputum and potentially reduce bioaerosol hazards during collection. However, these studies did not report results stratified by mycobacterial load.

Our data suggest that oral swab sampling, assayed by Xpert, as comparable sensitivity to sputum in participants with high and medium mycobacterial load in the sputum. However, 70% (89/128) of individuals identified through our mass screening study [6] had detection number low or very low in their sputum. In this population, oral swab testing may not have sufficient sensitivity as currently performed. Further studies are needed to identify alternative non-sputum sampling strategies in this population.

**Table 1**

| Sputum Xpert MTB/RIF copy number classification | Detected by one oral swab (%) | Detected by two oral swabs (%) | Mean number of symptoms* (± SD) |
|-----------------------------------------------|------------------------------|------------------------------|--------------------------------|
| High                                          | 9/10 (90)                    | 9/10 (90)                    | 4.1 (± 2.7)                    |
| Medium                                        | 22/29 (76)                   | 23/29 (79)                   | 3.0 (± 2.6)                    |
| Low                                           | 16/60 (27)                   | 23/60 (38)                   | 2.4 (± 2.4)                    |
| Very Low                                      | 8/29 (28)                    | 11/29 (38)                   | 2.6 (± 1.9)                    |
| All                                           | 55/128 (43)                  | 66/128 (51)                  | 2.7 (± 2.3)                    |

* Tuberculosis symptoms according to World Health Organization guidelines: cough, expectoration, fever, night sweats, weight loss, recent loss of appetite, chest pain, and dyspnea.

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