Defining the usefulness of oral swabs in tuberculosis diagnosis

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Rapid microbiological confirmation of *Mycobacterium tuberculosis* (*M tuberculosis*) in sputum with nucleic acid amplification tests (TB-NAAT) is an important step to diagnose tuberculosis and to identify possible drug resistance. These tests significantly increase the diagnostic yield when compared with sputum smear and culture and reduce the time to treatment for people with drug-susceptible or drug-resistant tuberculosis.[1]

Obtaining respiratory specimens remains challenging in children younger than 8 years (because they are unable to expectorate and often swallow sputum) and in people who are not coughing or have non-productive cough. Sputum induction, nasopharyngeal aspirate, and gastric aspirate are not complex procedures, but require training, equipment, and appropriate infection prevention and control measures. Diagnostic biomarkers in blood are not fully developed and urine lipoarabinomannan assay is helpful only in selected patients.[2] These biomarkers do not provide information on the *M tuberculosis* drug-resistance pattern, a key advantage of pathogen-based testing. Sampling the upper airway with swabs is an attractive option in settings where obtaining complex and invasive specimens such as gastric aspirate, induced sputum, and pharyngeal aspirates that require significant assistance is avoided.

The findings of a systematic review of the sensitivity and specificity of swabs of the buccal mucosa and tongue performed by E Chandler Church and colleagues and published in *The Lancet Global Heath* is timely as we consider the potential role of these less invasive sampling approaches in the diagnostic algorithm for tuberculosis in adults and children.[3] The authors included 15 studies in adults and five in children. The sensitivity of oral swabs in adults ranged from 36% to 91%. As expected, due to the paucibacillary nature of disease, sensitivity was lower in children and ranged from 5% to 42%. The overall specificity was high, between 66% and 100% across all studies in children and adults.[3] These findings are similar to the previously published 56·7% (95% CI 44·3–68·2) pooled sensitivity and 91·3% (81·0–96·3) pooled specificity.[4]

The authors highlight knowledge gaps in the preanalytical stages, including the appropriate swab type and site (tongue *vs* buccal mucosa), storage, and laboratory optimisation techniques needed.[3] Ideally, feasibility should be assessed using commercially available automated TB-NAAT. Several studies in this review used in-house tests, possibly contributing to the lower sensitivity and specificity of oral specimens compared with using Xpert MTB/RIF Ultra tests.[3]

Disease severity, increased bacillary load, and ability to expectorate are important determinants of sensitivity of this sampling strategy when compared with sputum.[3] In people with high bacillary load, swabs are likely to perform as well as sputum. Use is less clear when bacillary load is low, such as in people who are unable to expectorate and people presenting for mass screening.[5]

Fewer studies in children were included than studies in adults, and the sensitivity of oral swabs ranged from 5 to 42% in children. The three studies from South Africa enrolled mostly hospitalised children, indicating more severe disease with a higher likelihood of having confirmed tuberculosis than would be seen in children at primary care level.[3] The sensitivity in these studies might reflect the expected yield of this sampling strategy when compared with induced sputum and gastric aspirate in hospitalised children. The largest study of 291 South African children reported sensitivity of oral swabs with Xpert MTB/RIF Ultra as 22% (95% CI 15–32) with confirmed tuberculosis (defined as having a positive Xpert MTB/RIF Ultra or culture on a respiratory specimen other than the oral swab specimens) being the reference. The authors did not report on disease severity according to chest x-ray, but 72 (80·0%) of 90 children with confirmed tuberculosis and 119 (75·8%) of 157 children with unconfirmed tuberculosis were in hospital, suggesting severe disease.[6] The reported sensitivity of oral specimens in the review by Church and colleagues is slightly lower than that reported for stool with Xpert MTB/RIF Ultra with pooled sensitivity of 53% (95% CI 35–70) and pooled specificity of 98% (93–99).[7] However, despite the lower sensitivity, the advantage of oral specimens is clear, as testing is not dependent on bowel movement and the health-care worker can collect the sample on the same day. This advantage is important as it prevents failure to collect the specimens as observed when using stool samples. In a study in hospitalised children from six African counties, 1140 (97·5%) of 1169 children had a nasopharyngeal

aspirate done but only 942 (80·6%) of 1169 had a stool sample collected during hospitalisation.[8]

Oral swabs hold promise but the reported sensitivity is below the WHO cutoff for diagnostic tools.[1,3-4] Hopefully sensitivity can be improved though optimising specimen collection, including self-collection, and testing methods.[3,9] Future studies should include patients with confirmed tuberculosis disease, ranging from non-severe to more severe disease, to measure the sensitivity of oral specimens on the basis of disease severity and therefore place in the diagnostic algorithm. Studies in children should include participants managed in primary care, who are less likely to have severe or confirmed tuberculosis than hospitalised children. Additionally, oral sample yield feasibility and acceptability should be compared with stool samples.

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