

# Advocating the Use of Loop-mediated Isothermal Amplification Assay to Improve the Rates of Diagnosis of Pulmonary Tuberculosis in Resource-constraint Settings

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## ABSTRACT

Tuberculosis (TB) continues to remain one of the top infectious diseases on a global scale. Acknowledging the gains observed, specific targets have been set as a part of the Sustainable Development Goals, and global leaders are hoping for significant improvement by 2030. In order to achieve this goal, an end TB strategy has been proposed, and great emphasis has been given toward enhancing case detection. Realizing the need, the World Health Organization (WHO) has given more attention toward the development and evaluation of new diagnostic tools and drug susceptibility testing. A molecular assay based on loop-mediated isothermal amplification (LAMP) has been developed to promote the detection of the *Mycobacterium tuberculosis* (*M. tb*) TB complex. This test can be easily performed at a peripheral level, requires minimal laboratory infrastructure and limited biosafety standards, is easy to use, and results are available in <1 hour. To conclude, there is an indispensable need to adopt newer methods to strengthen the diagnostic aspect of the disease. This need becomes even more important in resource-poor settings, and hence it is of utmost importance to implement cost-effective diagnostic tools to promote early detection and prompt initiation of treatment.

**Keywords:** Loop-mediated isothermal amplification, Tuberculosis, World Health Organization.

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## INTRODUCTION

Tuberculosis (TB) continues to remain one of the top infectious diseases on the global scale, both in terms of annual incidence (10.6 million) and the number of deaths (1.6 million) in the year 2021.<sup>1</sup> Furthermore, it is quite shocking that >80% of deaths have been reported in developing nations.<sup>1</sup> Further, we must acknowledge that 50% of the households wherein a case of TB has been detected have to spend in excess of 20% of their overall income, which in turn can account for serious financial implications. In addition, an alarming estimate has even been reported for multidrug-resistant TB, and all these facts call for urgent comprehensive actions to contain the disease worldwide.<sup>1</sup> Acknowledging the gains observed, specific targets have been set as a part of the Sustainable Development Goals, and the global leaders are hoping for significant improvement by 2030.<sup>1,2</sup>

## NEED TO STRENGTHEN DIAGNOSTIC SERVICES

In order to achieve the global targets, the end TB strategy has been proposed and a great emphasis has been given toward enhancing case detection and diagnosing patients promptly to interrupt the chain of transmission.<sup>1-3</sup> In fact, shortcomings in the diagnostic arm of disease control have been identified as a crucial gap, as almost 37% of the estimated cases of the disease were not diagnosed in 2014 alone, and it is a major cause of public health concern.<sup>2</sup> Moreover, realizing the need for early detection and prompt initiation of appropriate treatment for drug-resistant TB cases (due to prevention of disease transmission and to minimize patient attrition), WHO has given more attention towards the development and evaluation of new diagnostic tools and drug

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susceptibility testing to ensure rapid and accurate detection of disease and drug resistance.<sup>2</sup> In the mission to improve the rates of rapid detection of cases in developing nations, nucleic acid amplification tests (*viz* GeneXpert) have been employed.<sup>1,2</sup>

## TB-LAMP: A Molecular Assay

Along similar lines, a molecular assay based on TB-LAMP has been developed to promote the detection of the *M. tb* complex.<sup>2</sup> Likewise, sputum microscopy, this test can be easily performed at a peripheral level, requires minimal laboratory infrastructure (no sophisticated equipment), limited biosafety standards, easy to use, and results are available in <1 hour.<sup>2,3</sup> In fact, a number of studies have been conducted to evaluate the sensitivity, specificity, and cost-effectiveness of the TB-LAMP test, and most of these studies have revealed encouraging results.<sup>3-5</sup> Further, it has also been highlighted that this method can be easily employed after brief

training, and at the same time, requires minimum infrastructure support.<sup>6</sup>

### TB-LAMP: A Diagnostic Tool

The WHO has recommended it as an effective tool for the diagnosis of symptomatic adult pulmonary TB cases and even as a follow-up tool to sputum microscopy in adults for testing negative sputum specimens.<sup>2</sup> The current consensus is to consider it as a replacement tool for sputum microscopy for diagnosis of pulmonary TB in intermediate and high TB-burden nations.<sup>2</sup> The findings of a systemic review and meta-analysis that was carried out to estimate the diagnostic accuracy of TB-LAMP it was concluded that TB-LAMP could be looked upon as an alternative option for sputum smear microscopy.<sup>7</sup> The results from a study done in high-prevalence TB/human immunodeficiency virus (HIV) rural settings of Uganda, it was concluded that TB-LAMP delivered encouraging results in the diagnosis of pulmonary TB when compared with sputum smear microscopy.<sup>6</sup> The findings of a study done with an aim to estimate the sensitivity and specificity of TB-LAMP in establishing the diagnosis of extrapulmonary TB against culture were found to be 85.71 and 88.89%, respectively. On a similar note, when the sensitivity and specificity of TB-LAMP were compared against Xpert, it was found to be 88 and 86.67%, respectively.<sup>8</sup>

### ADDITIONAL CONSIDERATIONS

Even though the TB-LAMP molecular assay has been linked with multiple merits, there have been concerns pertaining to the bot being quite effective in terms of detection of rifampicin-resistant TB or detection of the disease among HIV positive patients.<sup>2-4</sup> In addition, issues pertaining to temperature maintenance or testing of samples other than sputum have to be also dealt with.<sup>2,5</sup> There is also a need to take into account other attributes like financial cost, feasibility, and acceptability among the users.<sup>6</sup> Finally, there is immense scope for conducting research activities to further explore the utility of the method before recommending the method for universal usage.<sup>2</sup>

### CONCLUSION

To conclude, there is an indispensable need to adopt newer methods to strengthen the diagnostic aspect of the disease. This need becomes even more important in resource-poor settings, and hence it is of utmost importance to implement cost-effective diagnostic tools to promote early detection and prompt initiation of treatment.

### REFERENCES

1. World Health Organization. Tuberculosis – Key Facts; 2022. Available from: <https://www.who.int/en/news-room/fact-sheets/detail/tuberculosis> [Last accessed on 2022 Dec 2].
2. The use of loop-mediated isothermal amplification (TB-LAMP) for the diagnosis of pulmonary tuberculosis: policy guidance. Geneva: World Health Organization 2016.
3. Ou X, Wang S, Dong H, et al. Multicenter evaluation of a real-time loop-mediated isothermal amplification (RealAmp) test for rapid diagnosis of *Mycobacterium tuberculosis*. *J Microbiol Methods* 2016;129:39–43. DOI: 10.1016/j.jmimet.2016.07.008
4. Gray CM, Katamba A, Narang P, et al. Feasibility and operational performance of tuberculosis detection by loop-mediated isothermal amplification platform in decentralized settings: results from a multicenter study. *J Clin Microbiol* 2016;54(8):1984–1991. DOI: 10.1128/JCM.03036-15
5. Nliwasa M, MacPherson P, Chisala P, et al. The sensitivity and specificity of loop-mediated isothermal amplification (LAMP) assay for tuberculosis diagnosis in adults with chronic cough in Malawi. *PLoS One* 2016;11(5):e0155101. DOI: 10.1371/journal.pone.0155101
6. Nakiyingi L, Nakanwagi P, Briggs J, et al. Performance of loop-mediated isothermal amplification assay in the diagnosis of pulmonary tuberculosis in a high prevalence TB/HIV rural setting in Uganda. *BMC Infect Dis* 2018;18(1):87. DOI: 10.1186/s12879-018-2992-1
7. Shete PB, Farr K, Strnad L, et al. Diagnostic accuracy of TB-LAMP for pulmonary tuberculosis: a systematic review and meta-analysis. *BMC Infect Dis* 2019;19(1):268. DOI: 10.1186/s12879-019-3881-y
8. Singh P, Kanade S, Nataraj G. Sensitivity and specificity of loop-mediated isothermal amplification assay for diagnosis of extra-pulmonary tuberculosis: a cross-sectional study. *European Resp J* 2019;54:PA554. DOI: 10.1183/13993003.congress-2019.PA554