

Short Communication

Cost analysis of GenoType® MTBDRplus and GenoType® MTBDRsl at the State Laboratory of São Paulo, Brazil

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ABSTRACT

Background: We aimed to evaluate the costs of GenoType® MTBDRplus and MTBDRsl incurred during the diagnosis of first- and second-line drug-resistant tuberculosis (TB) in São Paulo, Brazil.

Methods: Mean and activity-based costs of GenoType® were calculated in a referral laboratory for TB in Brazil.

Results: The mean cost value and activity-based cost of GenoType® MTBDRplus were USD 19.78 and USD 35.80 and those of MTBDRsl were USD 54.25 and USD 41.85, respectively.

Conclusions: The cost of GenoType® MTBDRplus was reduced owing to the high number of examinations performed and work optimization.

Keywords: Line Probe Assay. Multidrug-resistant tuberculosis. Molecular diagnosis. Mean Cost. Tuberculosis.

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (MTB) is a major global health concern. Approximately 6.4 million new cases of TB were reported in 2021¹. Although Brazil is not a high-burden country for multidrug-resistant TB (MDR-TB), the underdetection of these cases has reached 67.1% according to World Health Organization (WHO) data¹. The COVID-19 pandemic has negatively affected the search for people with drug-resistant tuberculosis (DR-TB) and the transmission of resistant strains, with a possible increase in primary resistance. In 2022, 1,104 new cases of DR-TB were diagnosed in Brazil².

Most patients with drug-sensitive TB can be treated with shortened first-line regimens with high efficacy. However, in recent years, the increasing number of cases of MDR-TB, which is characterized by resistance to the most effective drugs, such as rifampicin (RIF) and isoniazid (INH), and extensively drug-resistant TB (XDR-TB), which is resistant to drugs such as INH, RIF, and second-line drugs (fluoroquinolone, bedaquiline, and/or -linezolid), has become a threat to public health. MDR-TB and XDR-TB require long, expensive, and less effective treatments; furthermore, these TB forms are associated with a high occurrence of adverse effects and mortality³.

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To improve the fight against TB, the WHO has advocated the use of molecular methods to detect MDR-TB and XDR-TB since 2008⁴. The early and adequate diagnosis of MDR/XDR-TB is key to achieving the "End TB Strategy," which defines goals to be met for the prevention, care, and control of TB from 2016 to 2035^{5,6}.

Cost refers to the value of all the resources invested in performing an activity, including evaluation via diagnostic tests⁶. The mean cost was calculated by dividing the total cost by the quantity produced in the analyzed time interval. Activity-based cost (ABC) analyzes the direct and indirect costs appropriate for complex organizations that consume resources heterogeneously, providing greater accuracy in determining testing costs⁷.

The accuracy and cost of conventional and molecular methods for the diagnosis of MDR-TB have been described in several countries⁸⁻¹⁰, including Brazil¹¹⁻¹³. However, data on the costs incurred with the use of molecular tests in Public Health Laboratories are scarce, and the information obtained can be used to optimize resource management health services in countries with a unified health system, such as Brazil, particularly with the recent incorporation of GenoType® MTBDRplus and GenoType® MTBDRsl¹⁴.

Therefore, the objective of this study was to evaluate the mean cost and ABC of the GenoType® MTBDRplus and GenoType® MTBDRsl tests for the detection of MDR/XDR-TB in clinical isolates at the State Referral Laboratory of Public Health, Brazil.

Cost analysis was performed at the State Laboratory of Public Health of the State of São Paulo, Instituto Adolfo Lutz (IAL). The mean and ABC for the laboratory diagnostic tests GenoType® MTBDRplus and MTBDRsl (Hain Lifescience, Nehren, Germany),

which detect resistance to RIF and INH and second-line drugs (quinolones and injectable drugs, capreomycin, kanamycin, and amikacin), respectively, were calculated according to the data points "infrastructure," "human resources," "inputs," and "equipment."

For such analyses, MTB clinical isolates from the laboratory network in the state of São Paulo, which produce cultures to detect resistance to first- and second-line drugs, were evaluated by the IAL. Initially, the MTB clinical isolates were subjected to the GenoType® MTBDRplus test to detect resistance to INH and/or RIF. Isolates resistant to any of these drugs were subjected to a GenoType® MTBDRsl test using the same DNA. In total, 600 GenoType® MTBDRplus and 45 GenoType® MTBDRsl tests were included in the analysis. Data were collected from May 2020 to May 2021 and the evaluation was performed as described in the Cost Technical Manual⁷. The authors declare no conflict of interest.

The costs are expressed in US dollars (USD) according to the conversion rate of USD 1.00 = R\$ 5.27 as established by the Brazil Central Bank in December 2022. This study was approved by the Research Ethics Committee (CAAE number: 21762719.6.1001.5257) and followed the recommendations of the Ministry of Health¹⁵.

Figure 1. Components of the mean cost and activity-based cost (ABC), where the "Inputs" consisting of the largest component of the mean cost in the GenoType® MTBDRplus and "human resources" in the GenoType® MTBDRsl are observed. The biggest component for ABC was "human resources" in both trials.

Table 1. Total values of the mean cost and activity-based cost (ABC) in US dollars and reais (official Brazilian currency). The mean cost was lower than the ABC in the GenoType® MTBDRplus and higher in the GenoType® MTBDRsl.

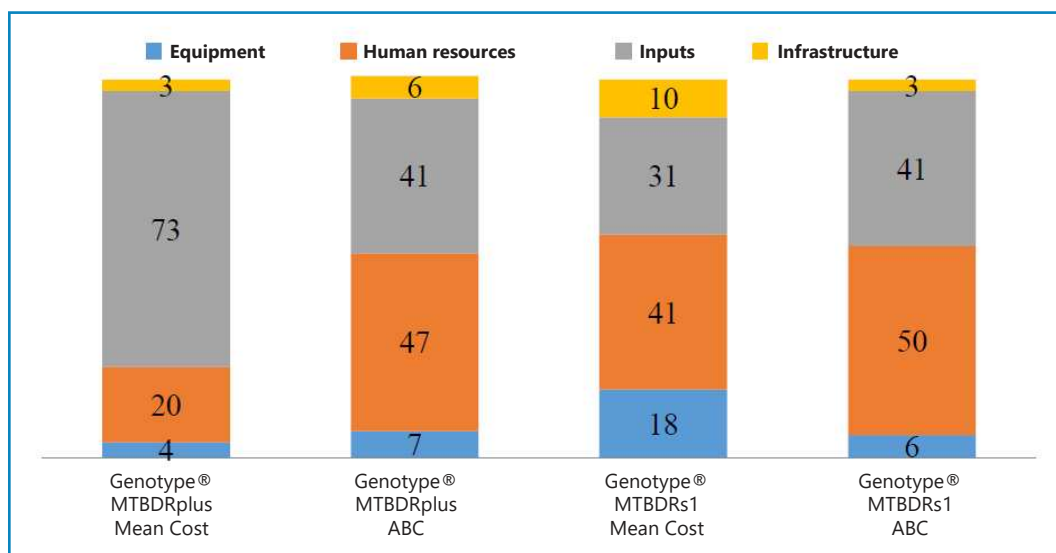


FIGURE 1: Components of mean cost and activity-based cost (ABC) of GenoType® MTBDRplus and MTBDRsl (%).

TABLE 1: Mean cost and activity-based cost.

Method	Samples/Month	Mean Cost (US\$)	Mean Cost (Real)	ABC (US\$)	ABC (Real)
Genotype® MTBDRplus	600	19.78	104,26	35.80	188,64
Genotype® MTBDRsl	45	54.25	285,82	41.85	220,57

USD 1.00 = R\$ 5,27; ABC: activity-based cost.

By calculating the mean cost and ABC, the lower cost of the GenoType® MTBDRplus was observed in relation to MTBDRsl owing to the optimization of the work during both tests in the IAL. The "input" was the component with the greatest impact on the mean cost in the GenoType® MTBDRplus in relation to MTBDRsl. Because the DNA extracted is reused when resistance is detected in the GenoType® MTBDRplus, there are fewer "inputs" in the MTBDRsl.

"Human Resources" was the component with the greatest impact on ABC in both GenoType® MTBDRplus and MTBDRsl, as the process is not fully automated. These results are similar to those of Soares et al. for a study conducted in a tertiary referral hospital in Minas Gerais, Brazil¹¹.

ABC analysis better reflects costs by providing the true value of the examinations, whereas the mean cost depends on the number of tests performed⁷. The mean cost of GenoType® MTBDRsl was higher than that of GenoType® MTBDRplus because a smaller number of second-line tests were performed (45 per month). This shows that an increase in the number of tests performed leads to lower costs, consistent with the workload of the IAL, which has a high demand for these tests. A similar result was observed in Minas Gerais, where the mean cost was higher than the ABC owing to the small number of tests performed¹³.

GenoType® has been incorporated into the Brazilian Unified Health System for the rapid detection of MDR-TB since July 2021; however, few cost studies have been conducted in public health referral laboratories before its incorporation. Although a cost-effectiveness analysis was not performed in this study, another study carried out by the same group showed that the turnaround time (TAT) for the release of MDR isolates is shorter when compared to susceptibility testing with the MGIT 960 system, therefore being dominant in a cost-effectiveness analysis¹¹.

Certain Brazilian studies have also evaluated ABC as a diagnostic method; for the identification test, bacilloscopy had an ABC of US\$ 6.01 and a subsidized Xpert of US\$ 10.86¹². For the cost evaluation of sensitivity methods, the GenoType® MTBDRplus molecular test was US\$ 48.38¹² and, in our study, the ABC of GenoType was US\$ 35.80; the difference are due to the differences in the laboratories where the studies were performed. The phenotypic methods had higher costs, with US\$ 76.56 for the sensitivity test for each drug using BACTEC MGIT 360 and US\$ 136.80 for the proportion method¹¹.

In a study conducted in a tertiary hospital in China, the costs were lower in the diagnosis of MDR-TB using GenoType® owing to the reduction of the TAT for result release, but the authors did not include the costs of the multiple components⁹. In another study conducted in Russia¹⁰, the use of GenoType® in routine DR-TB investigations, compared with the use of MGIT 960, was associated with a lower cost and greater success in the treatment of DR-TB.

It is important to emphasize that, in Brazil, variations in the dollar exchange rate and the commercialization of the first- and second-line GenoType® kits by a single company are factors that impact the increase and oscillation of costs.

A limitation of this study is the accuracy of the molecular tests obtained in the IAL, which were not analyzed. In addition, these values cannot be extrapolated to other locations because each laboratory has differences in the components analyzed.

Cost calculations are important and should be used in decision-making by managers and administrators to evaluate the incorporation of diagnostic tests in health institutions. ABC in particular is the best method of evaluating the costs of techniques to provide the real value of testing.

In the present study, we conclude that the costs of GenoType® MTBDRplus were lower than those of GenoType® MTBDRsl owing to the high number of MTBDRplus tests performed in the IAL and work optimization.

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REFERENCES

1. World Health Organization (WHO). Global tuberculosis report. Geneva: WHO; 2022. 5 p.
2. Ministério da Saúde (MS). Secretaria de Vigilância em Saúde e Ambiente. Departamento de HIV/Aids, Tuberculose, Hepatites Virais e Infecções Sexualmente Transmissíveis. Boletim Epidemiológico. Número Especial | Mar. 2023. 28-30p.
3. World Health Organization (WHO). Consolidated guidelines on tuberculosis. Module 4: treatment – drug-susceptible tuberculosis treatment. Geneva: WHO; 2022. VI Ip.
4. World Health Organization (WHO). Update on the use of nucleic acid amplification tests to detect TB and drug-resistant TB: Rapid communication. Geneva: WHO; 2021. 2 p.
5. Al Abri S, Kasaeva T, Migliori GB, Goletti D, Zenner D, Denholm J, et al. Tools to implement the World Health Organization End TB Strategy: Addressing common challenges in high and low endemic countries. Int J Infect Dis. 2020;92S:S60–8.
6. Kritski, A, Andrade KB, Galliez RM, Maciel ELN, Santos MC, Miranda SS, et al. Tuberculosis: Renewed challenge in Brazil. Rev Soc Bras Med Trop. 2018;51(1):2-6.
7. Ministério da Saúde (MS). Secretaria de Ciência, Tecnologia e Insumos Estratégicos. Departamento de Economia da Saúde. Programa Nacional de Gestão de Custos: Manual técnico de custos - conceitos e metodologias. Brasília: MS; 2006. 17 p.
8. World Health Organization (WHO). Consolidated guidelines on tuberculosis. Module 3 : diagnosis - rapid diagnostics for tuberculosis detection, update. Geneva: WHO; 2021. 2 p.
9. Li X, Deng Y, Wang J, Jing H, Shu W, Qin J, et al. Rapid diagnosis of multidrug-resistant tuberculosis impacts expenditures prior to appropriate treatment: A performance and diagnostic cost analysis. Infect Drug Resist. 2019;12:3549–55.
10. Bogdanova EN, Mariandyshev AO, Balantsev GA, Eliseev PI, Nikishova EI, Gaida AI, et al. Cost minimization analysis of line probe assay for detection of multidrug-resistant tuberculosis in Arkhangelsk region of Russian Federation. PLoS One. 2019;14(1):e0211203.
11. Soares VM, Almeida IN, Vater MC, Alves S, Figueredo LJA, Scherer L, et al. Genotype®MTBDRplus and Xpert®MTB/RIF in the diagnosis of tuberculosis and resistant tuberculosis: Cost analysis in a tertiary referral hospital. Rev Soc Bras Med Trop. 2020;53:e20190175.

12. Figueredo LJA, Miranda SS, Santos LB, Manso CGG, Soares VM, Alves S, et al. Cost analysis of smear microscopy and the xpert assay for tuberculosis diagnosis: Mean turnaround time. *Rev Soc Bras Med Trop.* 2020;53:(e20200314).
13. de Almeida IN, Figueredo LJA, Soares VM, Vater MC, Alves S, Carvalho WS, et al. Evaluation of the mean cost and activity based cost in the diagnosis of pulmonary tuberculosis in the laboratory routine of a high-complexity hospital in Brazil. *Front Microbiol.* 2017;8:1-7.
14. Ministério da Saúde (MS). Secretaria de Ciência, Tecnologia, Inovação e Insumos. Estratégias em Saúde. Portaria SCTIE-MS Nº 43, de 6 de julho de 2021.
15. Ministério da Saúde (MS). Secretaria de Vigilância em Saúde. Departamento de Doenças de Condições Crônicas e Infecções Sexualmente Transmissíveis. Manual de Recomendações para o Diagnóstico Laboratorial de Tuberculose e Micobactérias não Tuberculosas de Interesse em Saúde Pública no Brasil. Brasília: MS; 2022. 324 p.