

Comparative analysis of GeneXpert MTB/RIF and lipoarabinomannan testing in tuberculosis diagnosis among HIV-positive and HIV-negative patients attending the University Teaching Hospital of Kigali

Authors: Evariste Ntezirizaza^{1,2,*}; Alain Prudence Ishimwe¹; Charles Muhinda⁴; Jeannine Uwimana^{1,2}; Chantal Mukandayishimiye¹; Fidele Mahirane¹; Fidele Habimana¹; Laurence Mizero³; Marie Viviane Akimana³; Innocent Nzabanterura⁵; Celestin Musabyumuremyi¹

Affiliations: ¹Ines-Ruhengeri, Faculty of health Sciences, Department of Biomedical Laboratory Sciences, Rwanda; ²University Teaching Hospital of Kigali, Rwanda; ³University of Rwanda, school of Medicine and Pharmacy, Rwanda; ⁴Rwanda Military Hospital, Rwanda; ⁵University Teaching Hospital of Butare, Rwanda

ABSTRACT

INTRODUCTION: Tuberculosis (TB) is a major health burden in the world, and particularly in individuals living with HIV. This study evaluated the comparative performance of GeneXpert MTB/RIF and Lipoarabinomannan tests against TB culture, in HIV-positive and HIV-negative patients in the University Teaching Hospital of Kigali.

METHODS: A total of 124 participants (37 HIV-positive and 87 HIV-negative) were enrolled. Sputum, urine, and other specimens were tested using GeneXpert MTB/RIF and urinary LF-LAM, with results compared against TB culture on Lowenstein–Jensen media as the diagnostic gold standard.

RESULTS: In HIV-positive patients, LF-LAM had a sensitivity of 75% (95% CI: 47%-91%) and a specificity of 84% (95% CI: 65%-94%), whereas GeneXpert had a sensitivity of 67% (95% CI: 39%-86%) and a higher specificity of 96% (95% CI: 80%-99%). All tests performed better in HIV-positive patients (p-value = 0.0008 for LAM; p-value = 0.0001 for GeneXpert). In the HIV-negative group, GeneXpert's sensitivity was 65% (95% CI: 41%- 83%), significantly outperforming LF-LAM's sensitivity of 35% (95% CI: 17%- 59%). These findings underscore the importance of tailored diagnostic approaches based on patient immune status to optimize TB detection accuracy. The study elucidated the disparities between the LAM test and GeneXpert in diagnosing tuberculosis among patients with or without HIV, paving the way for more targeted and effective diagnostic interventions.

CONCLUSION: The study findings showed a complementary role of both GeneXpert and LF-LAM. LF-LAM is strongly effective as a quick screening test in TB detection and an early intervention tool in HIV-positive patients because it has a much greater diagnostic sensitivity in this population. Integration of the LAM test into TB diagnostic algorithms for immunocompromised populations could improve early detection and treatment initiation, thus reducing TB morbidity and mortality.

Keywords: Tuberculosis, HIV, GeneXpert, LAM, diagnostic accuracy, Rwanda

***Corresponding author:** Evariste NTEZIRIZAZA, Ines-Ruhengeri, Faculty of health Sciences, Department of Biomedical Laboratory Sciences, Rwanda. Email: makoevariste@gmail.com; **Potential Conflicts of Interest (Col):** All authors: no potential conflicts of interest disclosed; **Funding:** All authors: No funding was sought for this study; **Academic Integrity.** All authors confirm that they have made substantial academic contributions to this manuscript as defined by the ICMJE; **Ethics of human subject participation:** The study was approved by the local Institutional Review Board. Informed consent was sought and gained where applicable; **Originality:** All authors: this manuscript is original has not been published elsewhere; **Review:** This manuscript was peer-reviewed by three reviewers in a double-blind review process; **Type-editor:** Shane (USA).

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INTRODUCTION

Tuberculosis (TB) is a contagious disease and one of the leading causes of death globally [1]. In 2023, an estimated 10.8 million people were affected, with 1.25 million deaths, including 161,000 among people living with HIV. Men accounted for 6 million cases, women 3.6 million, and children 1.3 million. TB ranks second among infectious disease causes of death after COVID-19 [2]. WHO estimates that nearly 3 million TB cases remain undiagnosed or unreported annually, and diagnostic delays contribute to ongoing transmission.

Mycobacterium tuberculosis is the primary cause of pulmonary TB, which may be spread to other body organs such as the pleural cavity, abdominal cavity, spinal cord, or other tissues. Early and accurate diagnosis is crucial for minimizing transmission by initiating timely treatment and improving outcomes. It is especially difficult to diagnose in HIV-positive groups, where immunosuppression makes people more vulnerable to TB and distorts the clinical picture, which reduces the usefulness of conventional instruments [3]. The co-infection with TB and HIV is unevenly distributed among the low- and middle-income countries (LMICs), with more than three-quarters of cases worldwide being in sub-Saharan Africa [4]. The disease is further complicated by the presence of paucibacillary disease, atypical symptoms, and comorbidities, which are further reasons to focus on the implementation of efficient diagnostic strategies [5].

WHO-approved TB diagnostic tools include GeneXpert MTB/RIF and the lateral flow liparabinomannan assay (LF-LAM). An amplification test (NAAT) called GeneXpert is used to identify *M. tuberculosis* DNA and rifampicin resistance in less than two hours [6]. LF-LAM identifies mycobacterial antigen in the urine, is cheap, non-invasive, and particularly effective in patients who are severely immunocompromised [6]. In the past, microscopy of sputum smear and culture were employed; however, both have limitations, particularly in HIV positive patients. Smear microscopy is inexpensive but insensitive (50-60) in paucibacillary TB [7], whereas culture is highly sensitive and requires specialized laboratories, competent staff, and a lengthy incubation time [8].

It is used as a first-line test in high-burden settings

because it produces high sensitivity (88-98%) and specificity (>99%), and has a fast turnaround; however, it is resource-intensive and requires stable infrastructure [9,10]. During active disease, LAM, a glycolipid of the *M. tuberculosis* cell wall, can be found in the urine. The Alere Determine TB LAM Ag is popular, and it has been suggested to use among patients who are either infected with HIV extensively or are severely ill [11,12]. Its benefits are low cost, non-invasiveness, low laboratory needs, and it can be used in patients who cannot produce sputum and the sensitivity in HIV-negative patients (30-50%) or patients with greater CD4+ counts [13].

HIV makes the diagnosis of TB complicated by enhancing the extrapulmonary and paucibacillary disease, decreasing the sensitivity of traditional microscopy and GeneXpert, and increasing the probability of LF-LAM to identify antigen in highly immunosuppressed patients [14]. The trials, including STAMP in Malawi and South Africa, showed that the LF-LAM in combination with conventional diagnostics enhanced the identification of TB as well as the death rate among hospitalized HIV-positive patients [14,15].

TB has been recorded as an opportunistic infection in HIV-positive people in Rwanda, and there is a paucity of local comparative data on GeneXpert and LF-LAM performance [16]. This deficiency limits the capacity of national TB programs to optimize diagnostic algorithms for specific patient subgroups. GeneXpert and LF-LAM are not mutually exclusive; rather, they are complementary, and their combination can help increase the quality of diagnosis and patient outcomes. The majority of comparative works are conducted in Southern Africa; however, the epidemiology, health system capacity, and demographics vary, which reduces their relevance in Rwanda [17,18]. The proposed study will address this knowledge gap by assessing the accuracy of diagnosis, feasibility, and possible cost-effectiveness of GeneXpert MTB/RIF and LF-LAM in patients presented to CHUK [19].

METHODS

Study area

This research was conducted in the laboratory of the University Teaching Hospital of Kigali, situated in the Nyarugenge district of Kigali City. Its mission is primary care, quality health services, education,

and research. It attends to patients, primarily those of all district hospitals in Rwanda and the East African area.

Study design and period

The study was a cross-sectional investigation conducted over 3 months, from April 2025 to June 2025. Participants were selected based on the availability of data and specific inclusion criteria. The sampling method employed in the study was non-probability and sampled all eligible TB-suspected patients who were present within the 3-month study duration (n = 124). To verify this, back-calculation with respect to standard sample-size formulas indicates that a finite population of approximately 180-200 people, with a 5% margin of error and a 95% confidence interval, would result in a required sample size of approximately 124 (using the Cochran formula with a finite population correction). Thus, although the sample was based on convenience, it is of the magnitude that should be anticipated given the usual statistical assumptions regarding the study population.

Study population and sample size

The study involved a total of 124 participants, comprising 37 HIV-positive and 87 HIV-negative individuals. The sample collection included a wide range of biological specimen types, with specimens classified as either pulmonary or non-pulmonary. The pulmonary samples, including sputum (54) and bronchoalveolar lavage (7), totaled 61 specimens. The remaining 63 specimens were non-pulmonary samples, which included urine (29), pleural fluid (15), ascitic fluid (8), cerebrospinal fluid (5), stool (3), pus (2), and fine-needle aspirate (1).

The selection of a sample was made according to predefined criteria that ensured an appropriate cohort for evaluating early-stage active TB. Samples enrolled were those gathered among patients with a high level of clinical suspicion of active TB, namely, both HIV-positive and HIV-negative people. On the other hand, excluded samples were from patients receiving anti-tuberculosis treatment (i.e., labeled as TB control), and the unknown or unconfirmed HIV status of the patients. Insufficient quantity and quality of the samples to conduct the necessary laboratory analysis were also excluded.

Both INES-Ruhengeri and the ethics committee of the University Teaching Hospital of Kigali allowed the right to pursue the research. The privacy and

confidentiality of patients' results were taken into consideration, and the data were gathered using an identification code for the samples rather than a patient code or their names. The data collected were utilized in this study only.

Sample reception and handling

Samples that fitted predetermined eligibility criteria (sputum, urine, and other relevant samples) were received and processed systematically in the laboratory. The research did not require direct contact with patients or sampling; instead, the samples were sent to the laboratory via the clinical departments. To ensure the homogeneous quality of the samples and proper requests for examinations, the research protocol, including the types of specimens required and the handling process, was distributed to the departments. These protocols and standard operating procedures were strictly adhered to in order to maintain sample integrity and quality for use in the laboratory. Standard operating procedures were followed to ensure detailed sample handling procedures were carried out. Lateral Flow-LAM assay urine samples were obtained as midstream clean-catch urine samples, and timed specimen collection was used to test and store them at 2 to 8 degrees Celsius when immediate testing could not be performed, as per the departmental laboratory manual. The quality of the samples before culture was determined by a routine decontamination procedure (before culture on L-J) using the N-NALC-NaOH method, as per standard laboratory practice. These steps were always adhered to and recorded in the departmental records to ensure that the samples remained intact and the test results were reliable.

Diagnostic Assays

The samples that were received were tested on three diagnostic platforms:

GeneXpert MTB/RIF Assay: This test is quick and sensitive for detecting *Mycobacterium tuberculosis* complex DNA and for real-time identification of rifampicin resistance using polymerase chain reaction (PCR). The experiments were conducted in accordance with biosafety and manufacturers' standard operating procedures.

Alere Determine TB LAM Ag Assay: The qualitative detection of LAM antigen in a urine sample was performed using an immunochromatographic lateral flow assay (Determine TB LAM Ag by

Abbott). The assays were performed as per the manufacturer's instructions. The test strips were interpreted visually according to the manufacturer's reference scale, and measures to minimize inter-reader variability (such as training or double reading) were implemented, but are not described in detail.

Gold Standard Tuberculosis Diagnosis: To determine a definitive TB diagnosis, the findings of GeneXpert MTB/RIF and Alere Determine TB LAM were compared with culture results on Lowenstein-Jensen (LJ) solid media. LJ culture was used as the reference gold standard in the diagnosis of TB, and the sensitivity, specificity, and predictive values of the rapid diagnostic tests were determined against it. The gold standard for TB diagnosis was performed using culture on Lowenstein-Jensen (LJ) solid media. Two separate LJ slopes were inoculated for each decontaminated sample. The inoculated cultures were incubated at 37°C for a minimum period of eight weeks (56 days) before being declared negative.

Cultures were examined weekly for the presence of characteristic Mycobacterium tuberculosis growth. Any contaminated culture was repeated using a fresh aliquot of the stored sample, provided sufficient material remained. If contamination occurred in the repeat culture, that sample was recorded as contaminated and excluded from further analysis. All cultures demonstrating typical mycobacterial growth were subjected to species confirmation. Confirmation of Mycobacterium tuberculosis complex (MTBC) was performed using the SD BIOLINE TB Ag MPT64 Rapid Test (Standard Diagnostics, Inc.) according to the manufacturer's

instructions. A positive MPT64 test result confirmed the isolate as MTBC. These detailed steps were always adhered to and recorded in the departmental records to ensure that the samples were intact and the test results were reliable.

Statistical Analysis

SPSS Version 29 was used to analyze the data. Each of the diagnostic techniques (GeneXpert MTB/RIF and LF-LAM) was used to compute sensitivity, specificity, PPV, NPV, and odds ratios in relation to culture-confirmed TB status. The precision of the estimates was determined by estimating confidence intervals of sensitivity, specificity, PPV, and NPV. To determine whether there were correlations between test results (GeneXpert and LAM) and culture results in the overall cohort, including stratification by HIV status, Chi-square tests were performed. Comparative analysis using McNemar's test for paired proportions was conducted to evaluate differences in diagnostic performance between HIV-positive and HIV-negative groups, thereby strengthening the validity of subgroup comparisons.

RESULTS

The participants in the study were mainly male, with 61.29% of them being males. The age distribution was skewed towards older adults, with the highest number of respondents aged over 55 years (37.10%), and the smallest number being those aged less than 15 years (1.61%) (Table 1). The results showed no statistically significant association between a person's sex or age group

Table 1: The study population demographics

Demographics	Number of participants (N=124)	Percentage (%)
Sex		
Male	76	61.29
Female	48	38.71
Age Group		
<15	2	1.61
16-25	10	8.06
26-35	19	15.32
36-45	20	16.13
46-55	27	21.77
>55	46	37.1

Table 2: The study population positivity rate across gender and age group

Category	Group n=124	GeneXpert Positive Rate (%)	p-value	LAM Positive Rate (%)	p-value
Sex	Male	21.05	0.51	14.47	0.5
	Female	14.58		20.83	
Age Group	<15	50	0.77	0	0.45
	16-25	20		0	
	26-35	21.1		10.5	
	36-45	25		15	
	46-55	14.8		18.5	
	>55	15.2		23.9	

Table 3: Comparison of test positivity across HIV status

HIV Status	Participants	GeneXpert Positive (%)	p value	LAM Positive (%)	p-value
HIV+	37	24.3	0.41	35.1	0.001
HIV-	87	16.1		9.2	
Total	124	18.5		16.9	

and their likelihood of testing positive for either GeneXpert or LAM. This is denoted by the large p-values of sex (0.51 for GeneXpert and 0.50 for LAM) and age group (0.77 for GeneXpert and 0.45 for LAM). The high GeneXpert positivity rate (50%) among the group aged less than 15 should be considered with caution, as the sample size is too small in this age group (Table 2).

The LAM test positivity varied considerably between the HIV-positive patients (35.1%) and the HIV-negative patients (9.2%), with a significant p-value of 0.001. Conversely, positivity between HIV positive (24.3%) and HIV negative (16.1%) samples with GeneXpert was not statistically

significant ($p = 0.41$). To compare the proportion of test performance, McNemar's test was used (Table 3).

The accuracy of the estimates was calculated with the estimation of the sensitivity, specificity, PPV, and NPV confidence intervals. Chi-square tests were performed to identify correlations between test results (GeneXpert and LAM) and culture results in the overall cohort, stratified by HIV status. HIV-positive individuals showed that the LAM test had a higher sensitivity rate (75%) with a lower specificity rate (84%) than that of GeneXpert (67% sensitivity and 96% specificity). On the other hand, GeneXpert had a significantly higher sensitivity (65%) than LAM (35%), and both tests were highly

Table 4: Diagnostic Performance of LAM and GeneXpert across HIV status

HIV Status	TEST	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	P-value (vs. Culture)	OR (vs. Culture)
HIV +	LAM	0.75(0.47–0.91)	0.84(0.65–0.94)	0.69(0.42–0.87)	0.88(0.69–0.96)	0.0008	15.75
HIV +	GENEXPERT	0.67(0.39–0.86)	0.96(0.80–0.99)	0.89(0.57–0.98)	0.86(0.69–0.94)	0.0001	48
HIV-	LAM	0.35(0.17–0.59)	0.97(0.90–0.99)	0.75(0.41–0.93)	0.86(0.77–0.92)	0.0005	18.5455
HIV-	GENEXPERT	0.65(0.41–0.83)	0.96(0.88–0.99)	0.79(0.52–0.92)	0.92(0.83–0.96)	0	40.9444

specific (>96%). GeneXpert had a better specificity, more PPVs, and odds ratios throughout the HIV-positive and HIV-negative groups, which made it a more effective diagnostic and confirmatory test (Table 4).

DISCUSSION

We have shown that the rates of positivity slightly differed among males and females. The p-value of the relationship between sex and GeneXpert positivity was 0.51, and that of LAM was 0.50. This suggests that there will likely be no significant difference in positivity rates between men and women. The findings demonstrate that there is no statistically significant association between a person's sex and their likelihood of testing positive for either GeneXpert or LAM. These results are most compatible with published studies, implying that other clinical and epidemiological factors were more decisive about a positive test result (HIV status and disease severity).

Likewise, the study findings did not report any statistically significant relationship between age group and positivity in GeneXpert ($p = 0.77$) or LAM ($p = 0.45$). Although the data indicated mild differences in positivity rates across age groups, for example, a high positivity rate on GeneXpert in the <15 age group or a generally rising positivity rate on LAM with age, such an observation did not hold significance across the total population. The latter trend can, however, be corroborated with published data that portrays an increased LAM positivity in conjunction with markers of a more advanced disease, including those associated with lower CD4 cell numbers, which are generally indicative of more severe and older individuals [20, 13].

Our research findings are consistent with other published literature on the epidemiology of tuberculosis, especially the age-based distribution of the condition and the sensitivity of the two GeneXpert MTB/RIF and Alere Determine TB LAM Ag tests. Our findings indicate past-reported trends in the direction of more TB positivity in adults of working age compared to children. As shown by Diriba et al, there is a significant correlation of age with TB positivity and its pediatric yield (<14 years) is lower than that of adolescents and adults (>14 years), which aligns with our results, though the pediatric positivity rate was even smaller, in turn, possibly because of the size of the enrolled cohort

of children in our study [21].

On the same note, Alemu et al. stressed that they had discovered elevated rates of TB in adults aged 15-44 years, and our study identified similar increasing trends in detection [22]. Agustina et al. further supported this finding by explaining that children in the 10- to 18-year age group had a higher probability of being positive by GeneXpert MTB. They also cited that the specificity of GeneXpert was greater compared to its sensitivity when evaluated against culture in pediatric patients [23].

Our stratified population analysis was also found to be consistent with the current data regarding LAM test performance, particularly in older people and people with depressed immunity. According to our results, there appears to be an age gradient pattern in LAM positivity in that none of the participants younger than 25 years were LAM-positive, whereas 23.9 % of the participants aged 55 years and greater were LAM-positive, resulting in a rate of overall LAM positivity of 16.9 % (21/124). This trend aligns with studies suggesting improved LAM sensitivity in the elderly and immunocompromised individuals [24]. LAM test sensitivity was 59% (95% CI: 52-66%) in microbiologically confirmed TB and 67% (95% CI: 59-74%) in HIV-positive patients, as Broger et al. reported [24]. Their meta-analysis approximated the sensitivity of LAM in lung samples to 41% (95% CI: 15-66%) at the level of cases, which further supports the belief that the LAM test may yield decent sensitivity in immunocompromised individuals.

Despite this restriction, the future diagnostic utility of GeneXpert in children appears promising, particularly in high TB-burden countries. However, we cannot draw clear-cut statements regarding its performance with this subgroup based on our data. The diagnostic value of GeneXpert in relation to routine pediatric practice needs to be determined through broader investigations incorporating a large number of pediatric subjects [25, 26]. As long as this is not the case, our and other similar findings should be treated as anecdotal.

The sensitivity of GeneXpert in HIV-positive patients in our study was 67%, and this is close to a lower estimate of the global analysis (60-90%), based on WHO [27]. Our results are also in line with those of Velen et al., who documented the sensitivity of GeneXpert between 26-67% in smear-negative and HIV-positive individual groups that were found to be paucibacillary most of the time [28]. Such

results raise the possibility that the HIV positive TB patients in our cohort had low bacterial loads. However, the 96% specificity of GeneXpert in our study is consistent with the WHO 95-100% global specificity status, which explains why it can be used as a confirming measure [29]. In the meantime, there were comparatively high values of sensitivity (75%) and specificity (84%) when compared with the LAM test on HIV-positive individuals. These rates are higher than the sensitivity rates (30-70%) typically reported in systematic reviews of studies on HIV-positive patients with low CD4 counts [30], but still within the general range of specificity (80-95%) [30, 31].

The increase in sensitivity of LAM compared to GeneXpert in our HIV-positive group could be due to having mainly extrapulmonary samples, where LAM has shown utility, especially during disseminated TB, which is common in late-stage HIV [31]. LAM sensitivity was 75% (95% confidence interval: 0.47 to 0.91), and specificity was 84% (95% confidence interval: 0.65 to 0.94). GeneXpert was a bit less sensitive (67%, 95% CI: 0.39-0.86), but had better specificity (96%, 95% CI: 0.80-0.99). The two tests were statistically significant predictors of culture-confirmed TB (LAM: $p = 0.0008$, OR = 15.75; GeneXpert: $p = 0.0001$, OR = 48.00).

GeneXpert performed better than LAM in sensitivity among the HIV-negative participants. We demonstrated that GeneXpert had a sensitivity of 65% (95% CI: 0.41-0.83) and specificity of 96% (95% CI: 0.88-0.99) and was significantly related to the results of TB culture ($p < 0.0001$; OR = 40.94). This decreased sensitivity is in agreement with other studies, such as those pioneered by Theron et al., who observed that GeneXpert sensitivity may decrease to 55% or less in smear-negative populations or individuals with low bacillary load [32], and Shenai et al., who also postulated sensitivity to be a factor of sample type and bacillary load [33].

Sensitivity and specificity of the LAM test were much lower in HIV-negative persons [35% (95% CI: 0.17 to 0.59) and 97% (95% CI: 0.90 to 0.99), respectively]. The statistical significance of the p -value was found ($p = 0.0005$; OR = 18.54), which proves a prominent (though marginal) diagnostic power of this type of population. This insensitivity is in line with the recommendations of the WHO not to conduct routine LAM testing of people who are negative for HIV because of an insufficient

quantity of urinary antigens [31]. However, its high specificity supports its value as a confirming agent, especially in clinical situations where TB is a possibility [30].

Our analysis reveals that LAM positivity was significantly more frequent in HIV-positive individuals (35.14%) than in HIV-negative individuals (9.20%), a pattern consistent with WHO guidelines and previous studies emphasizing LAM's usefulness in advanced HIV [31, 30]. The high LAM detection rate in HIV-positive patients exemplifies its use in the prompt treatment and care of an HIV-infected person. Its vastly superior sensitivity in highly immunosuppressed demographics has been confirmed by Huang et al. and others [34]. Interestingly, there was no significant difference between HIV-positive (24.32%) and HIV-negative (16.09%) groups concerning GeneXpert positivity ($p=0.4084$). This indicates that GeneXpert's performance is relatively stable across HIV statuses, reinforcing its value as a universal diagnostic tool. In contrast, LAM's rapid turnaround time, non-sputum nature, and elevated performance in HIV-positive individuals, especially those unable to produce sputum, make it a crucial complementary test for this subgroup [35].

The predictive value of GeneXpert was always better than that of LAM in both HIV-positive and HIV-negative populations, and this showed that positive results with GeneXpert were more likely to indicate actual cases of TB. GeneXpert also had better negative predictive value (NPV), especially in HIV-negative persons (92%), which is an indication of its power in eliminating TB. LAM exhibited moderate NPVs (86-88%), though with lower PPVs, particularly among HIV-positive patients, which could put false positives at risk. These results indicate that LAM can be used as an adjunctive screening in the high-risk populations of HIV. This justifies the clinical application of LAM in patients who cannot provide sputum, in which the timely diagnosis of TB is urgently needed.

Our study has a study limitation that the study population is small in terms of demographic groups, which compromises the generalizability and statistical power of our results. The extremely high rate of positivity for GeneXpert (50%) in the sample of children under 15 years old should be regarded with utmost caution, as there are only two individuals in this sample. This raises the issue

of inference for those very small subgroups and the fact that these findings will be anecdotal in nature, potentially not being representative of the broader pediatric population. In addition, there was no a priori calculation of the sample size; instead, we used convenience sampling, including all eligible patients who were available during the three-month study period ($n = 124$). This dependency on patient availability, as opposed to a probability sampling strategy, could have created a selection bias and led to suboptimal statistical power, thereby restricting the extrapolability of the results.

Additionally, the most severe restraint was the lack of comprehensive clinical information, particularly regarding comorbidities and other pre-existing conditions. We did not obtain complete data on diagnostics, and the equipment used to measure CD4 cell counts was not in normal configuration when collecting data. This is a critical issue because published literature suggests that the diagnostic performance of tests like LF-LAM is highly dependent on the patient's immune status. The lack of quality data on CD4 means we cannot discuss the relationship between the level of immunosuppression and the accuracy of the tests, which would have provided insight into our findings. There was a significant relationship between a positive LAM result and HIV status.

CONCLUSION

The present study clearly demonstrates the complementary nature of GeneXpert MTB/RIF and Lateral Flow Urine Lipoarabinomannan (LF-LAM) in the diagnosis of TB disease, particularly in stratification based on HIV status. LF-LAM was found to be much more diagnostic in HIV-positive individuals, and it definitively proves its great effectiveness in terms of early screening and intervention in this immunocompromised group of people. GeneXpert, on the other hand, demonstrated greater total specificity in both groups and retained better sensitivity in HIV-negative patients, which further supports its use as the test of choice as a primary diagnostic and confirmatory test. It is important to consider integrating the strategic application of LF-LAM to early detection in patients with immunocompromised cases, along with GeneXpert as a highly specific tool for confirming the diagnosis in all types of patients, which will lead to better

outcomes in terms of diabetes prompt dress, and based on the achievement of the reduction of TB-related morbidity and death. The research is justified for expanding on these customized diagnostic approaches because future studies with larger and more diverse cohorts, particularly in resource-constrained and rural areas, are needed to provide a stronger evidence base to inform national TB control policies.

REFERENCES

1. Management Sciences for Health (MSH). Accelerating the End of TB: Field Research from Management Sciences for Health: 2008–2022 Report; 2023.
2. World Health Organization (WHO). Global Tuberculosis Report; WHO: Geneva, Switzerland, 2024.
3. Navasardyan, T.; Petrosyan, M.; Hovhannisyan, A.; Babayan, S. TB and HIV: The Deadly Syndemic. *Lancet Infect. Dis.* 2024, 22, e144–e150.
4. Gupta-Wright, A.; Peters, J.A.; Lawn, S.D.; Wood, R.; Bekker, L.-G. LAM and Xpert Combination Testing. *Lancet Glob. Health* 2018, 6, e46–e56.
5. Heidary, M.; Hashemi, M.; Mohammadi, A.; Rezaei, F. Comparative Evaluation of TB Diagnostic Tools in HIV Settings. *Int. J. Infect. Dis.* 2022, 95, 163–168.
6. World Health Organization (WHO). Global Tuberculosis Report; WHO: Geneva, Switzerland, 2021.
7. Campelo, G.H.; Souza, M.L.; Silva, D.R.; Maciel, E.L.N. Diagnostic Performance of Smear Microscopy in Paucibacillary TB. *BMC Infect. Dis.* 2021, 21, 450.
8. Chopra, K.K.; Sarin, S.K.; Singh, S.; Kumar, A. Culture Methods for TB: Delays and Limitations. *Indian J. Tuberc.* 2020, 67, 230–234. <https://doi.org/10.1016/j.ijtb.2020.02.003>.
9. Gupta-Wright, A. Clinical Utility of GeneXpert in Low-Income Countries. *Lancet Glob. Health* 2019, 7, e1190–e1199.
10. Huang, L.; Zhang, J.; Wang, Y.; Li, X. GeneXpert Sensitivity in HIV-Associated TB. *Am. J. Trop. Med. Hyg.* 2022, 106, 1642–1647.
11. Shah, M.; Hanrahan, C.; Dodd, R.Y.; Lawn, S.D.; Creswell, J. Diagnostic Accuracy of Urine Lipoarabinomannan Testing for TB in HIV-Infected Adults. *Cochrane Database Syst. Rev.* 2016, CD011420.
12. Bjerrum, S.; Kenu, E.; Lartey, M.; Lungu, P;

- Obeng-Baah, J.; Lawn, S.D. Urine LAM Testing in TB/HIV Co-Infection. *J. Clin. Tuberc. Other Mycobact. Dis.* 2015, 1, 15–20. <https://doi.org/10.1016/j.jctube.2015.07.002>.
13. Peter, J.G.; Zijlstra, E.E.; Lawn, S.D.; Lessells, R.J.; Kampira, E.; Majanga, E.; Phulusa, J.; Sarvananthan, N.; Nliwasa, M.; N'gongondo, M.; et al. Effect on Mortality of Point-of-Care, Urine-Based Lipoarabinomannan Testing to Guide Tuberculosis Treatment Initiation in HIV-Positive Hospital Inpatients. *Lancet* 2016, 387, 1187–1197. [https://doi.org/10.1016/S0140-6736\(15\)01092-2](https://doi.org/10.1016/S0140-6736(15)01092-2).
14. Bulterys, M.; Kayongo, A.; Nakiyingi, L.; Mwebesa, J.B.; Nsereko, M.; Ssengooba, W.; et al. The STAMP Trial: A Randomized Trial of Lipoarabinomannan Testing for TB Diagnosis. *N. Engl. J. Med.* 2020, 383, 107–116.
15. Lawn, S.D.; Kerkhoff, A.D.; Burton, R.; Ndjeka, N.; Wood, R. Impact of a Point-of-Care, Urine-Based Lipoarabinomannan Assay on TB Diagnosis in Hospitalized HIV-Positive Patients. *BMC Med.* 2012, 10, 89.
16. Rwanda Biomedical Centre (RBC). National Strategic Plan for HIV/AIDS and TB; RBC: Kigali, Rwanda, 2023.
17. Bjerrum, S.; Kenu, E.; Lartey, M.; Lungu, P.; Obeng-Baah, J.; Lawn, S.D. Operational Challenges in LAM and GeneXpert Use. *Clin. Infect. Dis.* 2022, 74, 958–964.
18. Mirandari, A.; Susanto, H.; Lestari, T.; Sari, D. A Systematic Review on Diagnostic Accuracy of GeneXpert and LAM in Different Settings. *J. Infect. Dis.* 2025, 80, 20–25.
19. Reechaipichitkul, T.; Kiertiburanakul, S.; Chaiwatanarungruang, W.; Suksomboon, N. The Feasibility of Implementing GeneXpert and LAM in Low-Resource Settings. *J. Public Health* 2017, 39, 442–448.
20. McNeil Ngongondo, M.C.; Nliwasa, M.; Chilima, B.; Peter, J.G.; Macpherson, L.J.; Kasozi, F.; Nsona, D.; Nsomba, V.; Kumwenda, J.J.; Corbett, E.L.; et al. Urine Lipoarabinomannan Testing in Adults with Advanced Human Immunodeficiency Virus in a Trial of Empiric Tuberculosis Therapy. *Clin. Infect. Dis.* 2021, 73, e870–e875.
21. Diriba, G.; Mitiku, H.; Bekele, H.; Geleta, B. Age-Based Prevalence of TB among Patients in Central Ethiopia. *PLoS ONE* 2022, 17, e0263748.
22. Alemu, A.; Gizaw, Z.; Yewunetu, S.; Adane, A. Predictors of Tuberculosis Positivity among Adults and Children in High Burden Areas. *BMC Infect. Dis.* 2020, 20, 104.
23. Agustina, M.; Supriyadi, T.; Triasih, R.; Setianingsih, T. Diagnostic Yield of GeneXpert MTB/RIF in Pediatric TB: Comparison with Culture. *Paediatr. Indones.* 2019, 59, 303–310.
24. Broger, T.; Guglielmetti, L.; Sossen, B.; Moni, M.A.; Clowes, P.; Mtafya, B.; Mutayoba, B.M.; Marais, B.J.; Geldsetzer, P.; Peter, J.; et al. Diagnostic Accuracy of Three LAM Tests for Tuberculosis Detection in People with HIV. *Lancet Infect. Dis.* 2019, 19, 852–861.
25. Cuevas, L.E.; Browning, R.; Teo, S.S.; Graham, S.M.; McNally, L.M.; Soto, M.A.; et al. Evaluation of Tuberculosis Diagnostics in Children: 1. Proposed Clinical Case Definitions for Classification of Intrathoracic Tuberculosis Disease. *Clin. Infect. Dis.* 2012, 54, S117–S126.
26. Marcy, O.; Huerfano, S.; Loa, C.; Kuodi, P.; Mofana, T.; Ng'ang'a, L.; Ndung'u, J.M. Performance of Xpert MTB/RIF and Alternative Specimens for the Diagnosis of Tuberculosis in HIV-Infected Children. *Clin. Infect. Dis.* 2016, 62, 1161–1168. <https://doi.org/10.1093/cid/ciw036>.
27. World Health Organization (WHO). Global Tuberculosis Report; WHO: Geneva, Switzerland, 2020.
28. Velen, K.; Marais, B.J.; Den Boon, S.; Enarson, D.A.; Nicol, M.P.; Steingart, K.R.; et al. Diagnostic Accuracy of Xpert MTB/RIF in Smear-Negative Tuberculosis: A Systematic Review. *BMC Infect. Dis.* 2021, 21, 1–9.
29. Steingart, K.R.; Metcalfe, J.Z.; Cattamanchi, I.; Huang, L.; Hopewell, P.C.; Ramsay, A.; et al. Xpert MTB/RIF Assay for Pulmonary Tuberculosis and Rifampicin Resistance. *Cochrane Database Syst. Rev.* 2013, CD009593.
30. World Health Organization (WHO). WHO Consolidated Guidelines on Tuberculosis. Module 3: Diagnosis—Rapid Diagnostics for Tuberculosis Detection; WHO: Geneva, Switzerland, 2021.
31. Theron, G.; Peter, J.; Harboe, S.; Mason, P.; Barnaby, D.; Caldwell, J.; et al. High Diagnostic Accuracy of Xpert MTB/RIF in Smear-Negative Patients. *Clin. Infect. Dis.* 2014, 58, 1374–1381.
32. Shenai, S.; Shah, M.; Hanrahan, C.; Johnson, T.; Creswell, J. Diagnostic Accuracy of GeneXpert MTB/RIF in Extrapulmonary Tuberculosis. *J. Clin. Microbiol.* 2017, 55, 1445–1452.
33. Bustamante, M.G.B.F.; de Almeida, C.A.P.R.; de Lima, A.N.P.; de Assis, G.C.A.; Croda, J.; de Lima, G.B. Effectiveness of GeneXpert® in the Diagnosis of Tuberculosis in People Living with HIV/AIDS. *Rev. Saude Publica* 2021, 55, 89.

34. Broger, T.; Guglielmetti, L.; Sossen, B.; Moni, M.A.; Clowes, P.; Mtafya, B.; Mutayoba, B.M.; Marais, B.J.; Geldsetzer, P.; Peter, J.; et al. Novel Lipoarabinomannan Point-of-Care Tuberculosis Test for People with HIV: A Diagnostic Accuracy Study. *Lancet Infect. Dis.* 2019, 19, 852–861.

35. Boehme, C.C.; Nabeta, P.; Hillemann, D.; Nicol, M.P.; Shenai, S.; Krapp, F.; et al. Rapid Molecular Detection of Tuberculosis and Rifampin Resistance. *N. Engl. J. Med.* 2010, 363, 1005–1015. <https://doi.org/10.1056/NEJMoa0907847>.