International Journal of Community Medicine and Public Health
Ongwae JM et al. Int J Community Med Public Health. 2025 Sep;12(9):3881-3889
http://www.ijcmph.com
pISSN 2394-6032 | eISSN 2394-6040

DOI: https://dx.doi.org/10.18203/2394-6040.ijcmph20252828

Original Research Article

Combination of urinary lipoarabinomannan assay and GeneXpert MTB/RIF ultra enhances tuberculosis detection among HIV-infected individuals

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Received: 17 June 2025
Revised: 04 August 2025
Accepted: 11 August 2025

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ABSTRACT

Background: Tuberculosis (TB) is a major health concern, responsible for about 10 million morbidities and 1.3 million global deaths, of which 300,000 are HIV co-infected. Timely diagnosis and treatment of TB have saved millions of lives. Lipoarabinomannan (LAM) assays and GeneXpert MTB/RIF Ultra have greatly altered TB diagnosis, but information on their performance in terms of accuracy, efficiency and turnaround time is limited. This analytic cross-sectional study investigated the diagnostic accuracy of urinary LAM and GeneXpert MTB/RIF Ultra in TB detection among adult HIV-positive individuals receiving care at Kisii Teaching and Referral Hospital.
Methods: Participants (n=372) were enrolled from facility Xpert testing log, where all patients with Xpert-positive results were recruited.
Results: There was variation in sensitivity between AlereLAM (10.8%), FujiLAM (53.2%), and EclLAM (66.7%), and generally high specificities: AlereLAM (92.3%), FujiLAM (98.9%), and EclLAM (98.1%). GeneXpert MTB/RIF Ultra had a 90.5% sensitivity and 98.1% specificity, without significant difference in sensitivity or specificity by previous TB history, hospitalization, or HIV status. Xpert and GeneXpert MTB/RIF Ultra results were concordant, with the latter showing a small reduction in specificity (difference 1.9; p=0.01). Considering trace results as positive for all cases increased sensitivity by 2.1% (p=0.01) without reduction in specificity (p=0.08).
Conclusions: FujiLAM and GeneXpert MTB/RIF Ultra have the capacity to improve TB diagnosis, especially in HIV-positive individuals and in high-burden settings, with enhanced sensitivity and specificity. Integrating these assays can boost prompt treatment initiation and better patient outcomes, although further research is needed.

Keywords: Tuberculosis, Lipoarabinomannan, Diagnosis, GeneXpert, Kenya

INTRODUCTION

Tuberculosis (TB) is estimated to be responsible for 10 million morbidities and 1.3 million deaths globally, and among the top ten causes of global deaths, about 300,000 being in TB-HIV co-infected individuals. Timely TB diagnosis and treatment have saved the lives of millions of people.[1] Despite the existing interventions globally, TB remains a major public health concern, especially in the resource-constrained countries, punctuated by the rise of cases of multidrug resistant TB, MDR-TB.[2]

One of the greatest challenges to TB management is delayed diagnosis, which delays treatment initiation, promoting disease progression, and the likelihood of drug resistance, and rampant spread.[3,4] Today, TB diagnosis

has advanced from the traditional microscopy, through culture, and to the more rapid molecular tests.[5,6]

Routinely, microscopy and culture methods are used for diagnosis, the former being the primary and most common method in most peripheral facilities, although its sensitivity is reported to be up to 60%. Whereas TB culture is applied as the gold standard for the diagnosis of TB, it is ineffective in the setups due to the high cost, labour-intensive requirements, and requires about 4-8 weeks to get results compounding the problem of delay in the absence of other confirmatory tests.[7] Lipoarabinomannan assays (LAM) and GeneXpert MTB/RIF Ultra have since been developed to improve TB diagnosis. Information about their performance, in the context of accuracy, efficiency, and turnaround time in the local country setting is limited, and it is known to be context-specific. We evaluated the sensitivity, specificity and the predictive values of TB LAM and GeneXpert using MGIT culture as control (standard), and test the agreement of these results.

METHODS

Study setting

Kisii Teaching and Referral Hospital (KTRH) is a level 6 hospital with a 650-bed capacity and the main referral facility in Kisii County, southwestern Kenya. It provides full inpatient services, including renal care, oncology, CT/MRI scanning services, and palliative care.

Research design

A cross-sectional analytic design, involving laboratory testing of urine and sputum specimens from pulmonary tuberculosis patients attending KTRH.

Study population

This study targeted all the 5300 known HIV positive patients who visited KTRH with chest complications, and probable TB cases attending HIV clinic at KTRH between July 2023 and July 2024.

Sample size determination

Participants were drawn from patients at the chest clinic at the KTRH at the time of this study.

The study sample size was calculated using Yamane's (1967) formula:

$$n = \frac{N}{1 + N(e)^2}$$

Where;

N = number of patients who visited KTRH with pulmonary problems in the past year (5300)

n = desired sample size

e = sampling error at 95% confidence level (0.05)

Substituting

n = 371.9 = 372

Sampling

Purposive sampling method was applied to enroll the study participants, where all diagnosed TB patients who were confirmed for TB infection and were eligible based on the inclusion criteria at KTRH during the study period were recruited.

Inclusion criteria

All adults (aged ≥ 18 years referred for sputum-based TB diagnosis. The patients had to be available, willing to voluntarily participate, and of stable health status.

Exclusion criteria

All TB patients with other chronic or acute coinfection, bleeding disorders, endocrine disorders, other organ dysfunctions, and TB patients who had received anti-TB therapy or other antibiotics having anti-TB activity during the previous 12 months were not included.

Sampling procedure and sample collection

The health facility Xpert testing log was reviewed daily, and on each day, every participant with Xpert-positive results was enrolled, plus a random sample (1:1) of Xpert-negative patients. Each participant provided demographic information and medical history, and urine and sputum samples. Each urine sample was subjected to FujiLAM, AlereLAM, and EclLAM assays. Each participant provided 2 sputum samples: the first sample was used for Ultra testing (from all participants) and the other for solid Lowenstein-Jensen (LJ) and liquid BACTEC MGIT 960 mycobacterial cultures (for Xpert-negative samples only). All TB positive cultures were microscopically confirmed using Ziehl-Neelsen (ZN) staining, and CD4 cell count was documented for all HIV-positive participants. To detect any additional microbiological evidence for false-positive results, Alere LAM was used to test urine samples.

Ethical approval

This study obtained ethics clearance from KEMRI Scientific and Ethics Review Unit (SERU) and permission from the Kisii Teaching and Referral Hospital (KTRH). National guidelines for microscopy were applied to ensure quality of the protocol taken.

Data analysis

Sensitivity, specificity and predictive values were determined for TB LAM and GeneXpert using two-by-two tables, with TB culture (MGIT) as gold standard. Sensitivity and specificity of sputum Xpert Ultra was determined using the reference standard definition of TB at 95% CI, and compared by history of TB, HIV status, CD4 cell count, and inpatient status, using Fisher's Exact or Chi-square test, accordingly. Sensitivity analysis was conducted on Ultra trace results, comparing diagnostic accuracy when trace results were considered positive for all individuals or not, using McNemar's paired test of proportions. Kappa statistic was used to test for the agreement between TB LAM, GeneXpert with MGIT culture at 95% CI. The accuracy of the diagnostic assays was evaluated against two standards: microbiological reference standard (MRS), and composite reference standard (CRS). All analyses were performed using STATA version 13.

RESULTS

Participant characteristics

Between July, 2023, and July, 2024, 5300 eligible participants were screened, of whom 372 (121 MTB-positive and 251 MTB-negative) were enrolled into the study (including 187 Xpert-negative controls, of whom 25 were culture-positive). The median age of the participants was 32 (IQR 25–40) years, the males being 214 (58%). Up to 42% of the participants had BMI below 18.5, and 185 (49.7%) were HIV-positive, of whom 41 (22%) had CD4 cell count <100 cells/µl. Most (331, 89%) participants were identified at the outpatient department, and the median Karnofsky score was 80 (IQR 70–90). Up to 14% participants had a TB disease (Table 1).

Table 1: Patient characteristics (n=372).

Characteristic	N (%)
Age in years, median (IQR)	32 (25–40)
Male	214 (58)
Cough lasting ≥ 30 days	242 (65)
Fever	11 (3)
Hospitalized	41 (11)
Smoking in past 30 days	52 (14)
TB history over previous 1 year	48 (13)
Karnofsky Score median (IQR)	80 (70–90)
BMI <18.5	156 (42)
HIV positive	185 (49.7)
CD4 cell count < 100 cells/µl	41 (22)

IQR interquartile range

Out of 372, 111 (30%) were categorized as having definite TB, 10 (3%) as possible TB, and 251 (67%) as not having TB, according to WHO guidelines. Among the 111 participants having definite TB, 76 (68%) had one or more positive result for fluorescence sputum smear microscopy (SSM). Generally, HIV-TB coinfected participants had shorter mycobacterial growth indicator tube (MGIT) liquid culture detection time, and a greater proportion of the participants had positive SSM and Xpert results, compared to the HIV-negative participants. No patient in the definite TB category showed a positive blood culture result, and only 4 (3.6%) had positive Xpert result on urine, while all (100%) of the latter also had positive sputum Xpert and culture results (Table 2).

Table 2: Demographic and clinical characteristics of the study participants.

Characteristic	All participants (n=372)	HIV- Patients (n=187)	HIV+ Patients (n=185)
Median age in years (IQR)	32 (25–47)	33 (26–48)	31 (24–42)
Sex (n=372)	**N (%)**	**N (%)**	**N (%)**
Female	158 (42)	96 (51)	62 (34)
Male	214 (58)	91 (49)	123 (66)
History of TB	52 (14)	22 (12)	30 (16)
Diagnostic category (n=372)			
Definite TB	111 (30)	32 (17)	79 (43)
Possible TB	10 (3)	1 (1)	9 (5)
Not TB	251 (67)	154 (82)	97 (52)
Reference standard (n=372)			
MRS +ve	111 (30)	32 (17)	79 (43)
CRS +ve	121 (33)	33 (18)	88 (48)
Microbiological reference standard (MRS); n=111		[+ve=32; -ve=79]	
+ve Sputum smear microscopy (any of 3 tests on 3 sputum samples)	76 (68)	15 (47)	61 (77)
+ve Sputum smear microscopy +ve (1 test on first sputum sample)	68 (61)	12 (38)	56 (71)
Blood culture positive	0 (0)	0 (0)	0 (0)
Urine Xpert positive	4 (4)	0 (0)	4 (5)

Continued.

Characteristic	All participants (n=372)	HIV- Patients (n=187)	HIV+ Patients (n=185)
+ve Sputum Xpert (any of 3 tests on 3 sputum samples)	102 (92)	27 (84)	75 (95)
+ve Sputum Xpert (1 test on first sputum sample)	82 (74)	22 (69)	60 (76)
Sputum Xpert result (n=111)**			
Negative	25 (23)	10 (31)	15 (19)
Very low	19 (17)	4 (13)	15 (19)
Low	32 (29)	6 (19)	26 (33)
Medium	28 (25)	7 (22)	21 (27)
High	7 (6)	5 (16)	2 (3)
Mean sputum MGIT time to detection (n=111)			
MGIT –ve (only Xpert +ve)	6 (5)	3 (9)	3 (4)
> 14 days	40 (36)	13 (41)	27 (34)
0–14 days	65 (59)	16 (50)	49 (62)

** after testing on first sputum sample, Xpert was repeated one time using the same sample in case of an indeterminate result

Table 3: Predictive value and likelihood ratio of urine LAM and sputum tests.

Test	PPV% (95% CI)	NPV% (95% CI)	LR+	LR–	PPV% at 20% prevalence	NPV at 20% prevalence
AlereLAM (n=372)	37.5 (23.7–54.9)	70.7 (66.5–76.2)	1.5	0.98	26.1	80.6
FujiLAM (n=372)	95.2 (86.9–94.1)	83.2 (78.3–86.9)	46.2	0.47	92.2	89.4
EclLAM (n=372)	93.7 (87.0–96.4)	87.4 (82.9–91.4)	34.7	0.36	89.7	91.9
SSM (n=371)	100 (94.7–100.0)	85.8 (81.4–89.3)	0.39	100	90.8	-
Xpert (n=362)	100 (95.5–100.0)	91.1 (87.2–93.9)	0.23	100	95.0	-
FujiLAM + SSM (n=372)	96.3 (89.9–97.9)	88.7 (85.1–90.3)	60.9	0.32	94.1	94.0
FujiLAM + Xpert (n=372)	96.8 (91.3–98.6)	92.8 (88.7–94.6)	70.9	0.19	95.1	96.3

Table 4: Sensitivity and specificity of sputum Xpert Ultra by HIV status and TB history (n=698)[a].

	Previous TB (n=610)		No previous TB[b] (n=88)			
	Sensitivity	**Specificity**	**Sensitivity**	**Specificity**	**Sensitivity**	**Specificity**
Total Cohort	90.6	97.9	90.9	98.7	85.7	95
(n=121 with TB, 251 without TB)	(86.8, 93.4)	(96.1, 99.2)	(87.1, 93.9)	(96.6, 99.6)	(67.3, 96)	(86.1, 99)
HIV-negative	90.8	98.8	91.4	99.5	81.3	94.6
(33 with TB, 154 without TB)	(86.3, 94.1)	(96.5, 99.8)	(87.0, 94.8)	(97.4, 100)	(54.4, 96)	(81.8, 99.3)
HIV-positive	89.8	96.5	89.5	96.7	91.7	95.7
(88 with TB, 97 without TB)	(82.0, 95.0)	(91.2, 99.0)	(81.1, 95.1)	(90.6, 99.3)	(61.5, 99.8)	(78.1, 99.9)
CD4 < 100	96.2	95.0	96.0	93.3	100	100
(26 with TB, 15 without TB)	(80.4, 99.9)	(75.1, 99.9)	(79.6, 99.9)	(68.1, 99.8)	(2.5, 100)	(47.8, 100)
CD4 ≥100	87.5	96.8	86.9	97.3	90.9	94.4
(65 with TB, 79 without TB)	(77.6, 94.1)	(90.9, 99.3)	(75.8, 94.2)	(90.7, 99.7)	(58.7, 99.8)	(72.7, 99.9)

[a]Sensitivity and specificity presented as percentage with 95% CI; [b]>1 year from enrolment date

Diagnostic accuracy of LAM assays (FujiLAM, AlereLAM, EclLAM)

The SSM and Xpert constituted the microbiological reference standard (MRS), so had 100% specificity. Compared with the MRS, the tests showed lower sensitivity: AlereLAM (10.8%), FujiLAM (53.2%), and EclLAM (66.7%). The combined sensitivity of urine FujiLAM and sputum Xpert used together was 83.2%, while the sensitivity of FujiLAM used on urine when

combined with one SSM was 71.2%, higher than that of Xpert alone. The sensitivity of all the assays did not significantly change when CRS was used (AlereLAM = 12.4%, FujiLAM = 48.9%, and EclLAM = 61.8%). Except for AlereLAM, all the tests attained a specificity of ≥98% based on the MRS (AlereLAM = 92.4%, FujiLAM = 98.9%, EclLAM = 98.1%). Comparing the CRS-based with MRS-based analyses, specificity was generally not changed for each of the assays (AlereLAM = 93.2%, FujiLAM = 98.8%, EclLAM = 98.4%).

Table 5: Sensitivity of Ultra performance by trace definition.

	Sensitivity, % (95% CI)	% Difference (95% CI)[b]	Specificity% (95%CI)	% Difference (95% CI)[b]
Trace-positive_HIV[a]	90.5 (86.8-93.4)	-	98.1 (96.1-99.2)	-
Trace positive	92.6 (89.2-95.1)	2.1 (0.3 to 3.9)	97.2 (95.0-98.7)	-0.8 (-0.3-2.0)
Trace negative	88.4 (84.5-91.6)	-2.1 (-3.9 to -0.3)	99.2 (97.6-99.8)	1.1 (-0.2-2.6)

[a]Current WHO recommendations; [b]Compared to current recommendation for trace conditional positive

Against the MRS, and with a 30% prevalence, the PPVs were determined: AlereLAM (37.5%), FujiLAM (95.2%), and EclLAM (93.7%). Using a lower pre-test probability (20%), there was a downward shift in the PPV of the assays: AlereLAM (26.1%), FujiLAM (92.2%) and EclLAM (89.7%). On the other hand, the positive likelihood ratios (LR+) were determined for FujiLAM (46.2) and AlereLAM (1.5). Again, assuming a pre-test probability of 20%, the NPVs were determined for AlereLAM (80.6%), FujiLAM (89.4%), and EclLAM (92.2%). The negative likelihood ratios (LR−) were also calculated for FujiLAM (0.47) and AlereLAM (0.98), as presented on Table 3.

Diagnostic accuracy of GeneXpert MTB/RIF Ultra

Sputum Ultra test results showed a sensitivity of 90.6% (95% CI: 85.7% - 92.8%) and a specificity of 97.9% (95% CI: 95.6% - 99.4%), while Xpert and Ultra results showed concordance in 357 (96.0%) of the participants. From the 28 discordant results, 14 (50.0%) were Ultra positive but Xpert negative [7 (25%) were culture positive], while the remaining 14 were Ultra negative, but Xpert positive. Therefore, the sensitivity of Ultra did not significantly differ from the sensitivity of Xpert (90.6% vs 92.6%; p = 0.1). The 7 false-positive Ultra results were however shown to drive a small reduction in specificity, of 1.9% (95% CI: 0.2 - 3.5, p = 0.01) compared to Xpert. Notably, 6 (5%) of the 121 TB patients with positive cultures resulted in negative Xpert and Ultra findings.

Subgroup analysis of Ultra performance

Table 4 shows that Ultra sensitivity and specificity had no significant variation by HIV status (p=0.1). The sensitivity of Ultra was equally not different by CD4 cell count among HIV-positive patients (difference = 8.6, p=0.2). The study also did not report a significant difference based on participant TB history (sensitivity of 85.8% vs. 90.9%, p = 0.38; specificity of 95.1% vs. 98.8%, p=0.06), or based on hospital admission status, categorized as inpatients vs outpatients (sensitivity of 87.3% vs. 90.8%, p=0.47; specificity of 100% vs 97.7%, p=0.34).

False-positive vs trace Ultra results analysis

Out of the 7 participants showing false-positive Ultra results, 4 (57.14%) were HIV-positive (1 having CD4 cell counts under 100 cells/µl). Of the 4, 1 (25%) had prior TB infection, and all (100%) produced trace results. From the remaining 3 HIV-negative participants, 2 reported a previous TB history. Overall, there were 21 trace Ultra results during the study. From the 11 HIV-positive participants reporting trace results, 8 had microbiologically confirmed cases of tuberculosis (2 Xpert-positive with very low semi-quantitative result, 5 were culture-positive, and 1 urine TB LAM-positive). Of the 10 HIV-negative participants with trace results, 8 had microbiological evidence of TB (4 Xpert positive with low [n=1] or very low [n=3] semi-quantitative results, 3 culture-positive, and 1 urine TB LAM-positive). Therefore, 16 (76%) of the 21 participants having trace results had microbiological TB evidence.

Describing the trace results as positive for all the participants achieved Ultra sensitivity of 92.6% and specificity of 97.2%, representing a statistically significant increase in sensitivity (2.1%; p=0.01), but a non-significant reduction of 0.8% in specificity (p=0.08), relative to when trace results were considered positive only in HIV-positive participants. On the other hand, defining trace results as negative for all participants, a sensitivity (88.4%) and a specificity (99.2%) of Ultra reflected a statistically significant reduction in sensitivity (2.1%; p=0.01), and a non-significant increase (1.1%; p=0.05) in specificity (Table 5).

DISCUSSION

Introduction

Of the 372 participants, 30% were defined as having definite TB, while 67% were TB-free, and 3% classified as possibly having TB. The 30% case detection is consistent with previous findings from South Africa, Bangladesh, and in Peru and South Africa, but higher than the 20% prevalence earlier reported from a high HIV prevalence setting in Gambella, southwestern Ethiopia.[8-11]

It is important to interpret this with focus to the specific setting, since a gap of 30% has been reported between incident and notified TB cases in a HIV-endemic settings.[9] In this study, about 14% of the participants had a history of TB, an important consideration as Esmail, Tomasicchio earlier reported that about 5% of culture-negative patients had a prior TB history.[12]

The HIV co-infected TB participants had a shorter MGIT time, while a significant section largely had positive Xpert and SSM results compared to HIV-negative TB participants, suggesting a higher mycobacterial load in sputum, or the possible influence of HIV coinfection on TB culture behaviour.[13,14] Furthermore, no participant in the current study categorized as having definite TB produced positive blood culture results, and only 4% of the participants showed positive urine Xpert results, consistent with a report on southern Africa.[15]

Diagnostic accuracy of LAM assays

FujiLAM showed about 99% specificity, and identified about 53% of the positive TB cases, demonstrating a five-fold increased sensitivity in HIV-negative participants compared to AlereLAM. Typically, the FujiLAM test, which recorded a PPV of 95%, was designed to rule-in TB, in order to allow prompt TB treatment initiation.[16] An earlier analysis reported that using a urine-based LAM assay (with 70% and 30% sensitivity in HIV-positive and HIV-negative individuals, respectively) in all individuals showing symptoms of TB could avert up to 30% of mortality due to TB and 18% of TB incidence.[17] While such studies might perhaps overestimate test sensitivity due to the high disease burden in endemic areas, it remains important to also postulate they might also underestimate sensitivity when patients having extrapulmonary TB, or those with difficulty producing, sputum, like young children, are not considered.[18]

Using FujiLAM and Xpert together achieved an 82% sensitivity, with a 99% specificity, a 97% PPV, and an NPV of 93%. The combined use of FujiLAM and SSM, as currently in common use in places where Xpert or other molecular assays are unavailable, showed a high (96%) PPV and NPV (89%). This combination can potentially inform rapid TB treatment initiation in isolated settings.[10] Findings here, like from other studies suggest the potential benefit from integration of LAM-based assays into regular diagnostic procedures in use in the general populations.[5,19,20]

The performance of all LAM assays was generally lower in the HIV-negative than the HIV positive participants, consistent with previous reports from different settings endemic for TB and HIV.[21,22] In addition, FujiLAM PPV in HIV-negative participants in this study was 73%, compared to the 100% in HIV-positive counterparts, possibly due in part to the lower TB prevalence among HIV-negative people.[10,23]

The specificity of FujiLAM among HIV-negative participants in this study was about 99%, higher than that of AlereLAM (92%). A high specificity of any POCT of ≥98% is required to avert unnecessary treatment or chances of overtreatment.[10] Earlier research reported a lower FujiLAM specificity, and the findings of the current study underscore the significance of having a comprehensive reference standard for proper assessments of test specificity of biomarkers using urine.[21] This study further demonstrates the indisputable potential of LAM as an important biomarker for TB diagnosis.

In this study, EclLAM assay attained about 67% sensitivity and 98% specificity. Previous research has shown that lower detection limits often lead to higher diagnostic sensitivity.[12] In practice, EclLAM is still mainly used in research, using laboratory equipment, and has not been customized for point of care use.[10] Collectively, the findings of this study illustrate that urine of most HIV-negative individuals contain LAM, and improved assays for its detection can enhance its diagnostic accuracy.[24]

Diagnostic accuracy of GeneXpert MTB/RIF

GeneXpert MTB/RIF Xpert Ultra showed high sensitivity (91%) and specificity (98%) for pulmonary TB, overall, as well as across key sub-groups, including prior TB history, HIV status, and hospitalization. The accuracy of GeneXpert MTB/RIF Ultra for the diagnosis of pulmonary TB did not differ from previous studies. For example, an earlier meta-analysis of reports from 10 studies in different settings with high TB prevalence reported that Ultra could detect pulmonary TB with an 86% sensitivity and a 97% specificity.[25] In HIV-positive people, this study also reported an Ultra sensitivity similar to that from previous studies in other HIV-endemic settings, where a sensitivity ranging 87–90%, without notable difference between HIV-positive and HIV-negative individuals.[26] However, a previous TB history has been associated with reduced Ultra specificity, which could have occasioned differences in observation in this study, since participants who had had TB in the preceding one year were excluded.[27] The contribution of hospitalization on the effectiveness of the TB diagnostic tests is not well documented, and this study did not find any significant difference in the performance of the various TB diagnosis approaches when comparing inpatients and outpatients.

This study did not detect any significant difference between the sensitivity of Xpert compared to that of GeneXpert MTB/RIF Ultra, which largely agreed with some previous findings, but contrasted a meta-analysis that reported GeneXpert MTB/RIF Ultra was about 5% more sensitive in general, and had 13% higher sensitivity in HIV-positive TB individuals.[25,28,29] It is plausible the lower yield in the current study was because of the low (7%) proportion of culture-positive participants who were not detected by Xpert, compared to the 17% that Dorman,

Schumacher reported from adults with pulmonary TB symptoms visiting healthcare facilities in Kenya, Uganda, South Africa, Belarus, Georgia, Brazil, India, and China).[30] It is highly probable that including Xpert in the reference standard in this study could have potentially enhanced the observed differences.[31,32] In addition, that about 5% of culture-confirmed cases were negative for both Ultra and Xpert emphasizes the necessity for continued search for more novel diagnostics, which can enhance case detection in individuals having paucibacillary TB.

This study found no increase in specificity after defining trace results as negative, although expanding the operational definition of a positive test to encompass trace results in HIV-negative patients caused an increase in sensitivity, without lowering the corresponding specificity, likely since most HIV-negative participants with trace results had microbiologically confirmed TB. Defining trace results as either negative or positive needs a balance between higher case detection and the cost of potential overtreatment.[29,33,34] A prior study reported that although Ultra trace results expanded overtreatment by more than 50%, it prevented deaths by a similar proportion, implying GeneXpert MTB/RIF Ultra and trace results portend the biggest benefit in places with high HIV and TB burden.[30]

This study was limited by the fact that only adult were included, making it difficult to extrapolate to younger populations, where getting sputum samples may be difficult. In addition, the possible effect of the various antimycobacterial regimens used by the participants was not investigated.

CONCLUSION

There is potential of FujiLAM to significantly boost the rapid diagnosis of tuberculosis among HIV-positive individuals at point-of-care settings. Combination of FujiLAM with other diagnostic methods, like Xpert or SSM, further enhances its diagnostic accuracy. Integration of FujiLAM into diagnostic algorithms could facilitate immediate treatment initiation for FujiLAM-positive patients, potentially improving patient outcomes in high-burden TB settings.

Recommendation

The Ministry of Health should consider scaling up FujiLAM use in near-patient settings to improve TB diagnosis and rapid treatment initiation. We recommend the integration of LAM assays with other diagnostic algorithms to enhance overall diagnostic accuracy at the health facility level. Ultra should be widely adopted in regions with high TB and HIV prevalence to enhance early and accurate TB detection. Healthcare workers in facilities with limited access to culture or other confirmatory tests should be adequately trained to interpret Ultra results.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Ongwae JM, Onguru D, Ogolla S. Combination of urinary lipoarabinomannan assay and GeneXpert MTB/RIF ultra enhances tuberculosis detection among HIV-infected individuals. Int J Community Med Public Health 2025;12:3881-9.