POTENTIAL USE OF URINE LF-LAM IN DIAGNOSING ACTIVE TB IN THAI HIV-POSITIVE ADULTS

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BACKGROUND

- Thailand is one of the highest TB/HIV burdens globally. The 2020 Thail National HIV treatment guidelines recommend rapid TB urine Lateral flow urine lipoarabinomannan assay (LF-LAM) testing as an additional TB diagnostic test to assist with TB diagnosis among people living with HIV (PLHIV) who present with :
 - signs and symptoms of active TB;
 - critical illness (respiration rate >30 breaths/minute, body
 - temperature >39°C, heart rate >120 beats/minute); or - CD4 cell count <200 cells/mm³ for in-patient and <100 cell/mm³ for out-patient with or without signs and symptoms of active TB.
- The objectives were to determine test performance of urine LF-LAM in diagnosing active TB in adult PLHIV and identify predictive factors for LF-LAM positivity among adult PLHIV with TB disease.



METHODS

- Study design: Cross-sectional descriptive study
- All patients in participating hospitals who met eligibility criteria according to the 2020 Thai National HIV treatment guidelines were offered the LF-LAM testing in addition to routine TB diagnosis testing. Data of LF-LAM testing among PLHIV were entered into the webbased National TB/HIV database.
- Data from PLHIV at least 15 years old who met eligibility criteria for urine LF-LAM testing at 17 hospitals in 8 provinces in Thailand from October 2020 to August 2021 were analyzed,

Including:

- Examined urine LF-LAM test performances⁽¹⁾ Sensitivity (SS), Specificity (SP), Negative Predictive Value (NPV), Positive Predictive Value (PPV), and Test Accuracy in diagnosing definite and probable
- Calculated apparent prevalence as the number of LF-LAM positive persons /total number of PLHIV, while true prevalence was calculated as the number of TB cases/ total number of persons in the sample
- Performed random effects logistic regression modeling to identify factors associated with urine LF-LAM positivity
- Conducted a multiple logistic regression and included variables with p< 0.2 from simple logistic regression in the model 1. Larry Hammell. Assay Validation Methods [Internet]. [cited 2022 Jan 20]. Available from: https://www.fws.gov/aah/PDF/aptp.pdf

All TB cases = Definite TB + Probable TB				
DEFINITE Tuberculosis :	 The presence of positive result tuberculosis in a single specime Liquid or solid TB culture O Xpert-MTB/RIF Either result would be conside 			
PROBABLE Tuberculosis : Does not meet criteria for definite TB AND is given full course of TB treatment (continuity of anti-TB regimens during follow-up)	 Met one of these following crite Clinical symptoms Sputum microscope suggest Radiology suggestion 			

for M. en by

ered positive

stion

LF-LAM is helpful for the rapid rule-in test. TB treatment should immediately start after positive result.

We found that CD4 <200 cells/mm³ particularly CD4 <100 cells/mm³, presented overall better LF-LAM performance. This finding was consistent with WHO guidelines.^(2,3)

CD4<100 cells/mm³ regardless of TB symptoms associated with LF-LAM positivity was consistent with previous studies while significant weight loss has not been reported its association to LF-LAM positivity to our knowledge. We found that weight loss might be a predictor of disease severity.

Our finding supports WHO recommendation to screen LF-LAM among both IPD and OPD cases who present with advanced HIV diseases and low CD4. Because the specificity is high, the LF-LAM screening may be used to assist with same-day antiretroviral treatment initiation among PLHIV with advanced HIV disease who have LF-LAM negative.

. World Health Organization. Lateral flow urine lipoarabinomannan assay (LF-LAM) for the diagnosis of active tuberculosis in people living with HIV, Policy update (2019). END TB streategy [Internet]. 2019 [cited 2022 Jan 7]; Available from: http://apps.who.int/bookorders 3. World Health Organization. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach 2021. [cited 2022 Jan 14; Available from: https://www.who.int/publications/i/item/9789240031593

RESULTS

- and 134 (75%) probable TB. No difference in characteristics between definite TB and probable TB was observed.
- 118 (65%) were in-patients, 131 (73%) were male, and the median age was 37 (Interquartile range, IQR = 29-47 years). Median CD4 was 38 (IQR = 13-108 cells/mm³).
- Of 179 cases, 117 (65%) were pulmonary TB including one-fifth with smear-negative pulmonary TB, 27 (15%) were extrapulmonary TB, and 35 (20%) were disseminated TB.
- Overall LF-LAM test accuracy, sensitivity and specificity were 79%, 60%, and 90%, respectively and higher among CD4 <200 cells/mm³ at 80%, 63%, and 92%, respectively.
- The Positive Predictive Value was 83% among CD4 <200 cells/mm³ and 41% among CD4 >200 cells/mm³.



Figure 1: urine LF-LAM test accuracy, sensitivity, and specificity in diagnosing definite and probable TB, 8 provinces Thailand 2020-2021

• Of 488 PLHIV with urine LF-LAM test results, 179 (37%) were TB cases, including 45 (25%) definite TB

- Female
- Median ag Nationalit
- Thai (n= Non-Tha Hospital t
- Tertiary/ Medical
- CD4 (cell/ Less that 101-200 More tha
- **TB** Sympto Night sw
- On ART (n Yes (n=9 No (n=77
- Previous Yes (n=8 No (n=17
- Patient typ IPD (n=′ OPD (n=
- Chest radi Normal
- Probable

TB disease

CONCLUSIONS

- further studied.

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aracteristics	LF-LAM positivity (n= 107)	LF-LAM negativity (n= 72)	Crude OR (95%CI)	P- Value	Adjusted OR (95%CI)	P- Value
9) 131) n=48)	80 (74.77) 27 (25.23)	51 (70.83) 21 (29.17)	0.82 (0.42 - 1.60) REF	0.561		
e (Q1,Q3) (n=170)	37 (31,47)	39 (31,49.5)	0.99 (0.96 - 1.02)	0.531		
r (n=177) 170) i (n=7)	101 (95.28) 5 (4.72)	69 (97.18) 2 (2.82)	1.71 (0.32 - 9.06) REF	0.529		
rpe (n=179) Provincial(n=115) hity (n=33) school (n=31)	71 (66.36) 18 (16.82) 18 (16.82)	44 (61.11) 15 (20.83) 13 (18.06)	1.17 (0.52 – 2.61) 0.87 (0.32 – 2.33) REF	0.710 0.777		
mm ³) (n= 179) in 100 (n=133) (n=26) n 200 (n=20)	89 (83.18) 11 (10.28) 7 (6.54)	44 (61.11) 15 (20.83) 13 (18.06)	3.76 (1.40 – 10.08) 1.36 (0.41 – 4.54) REF	0.009 0.615	<mark>3.59 (1.28 – 10.03)</mark> 1.14 (0.32 – 3.99)	<mark>0.015</mark> 0.841
om (n=179) =110) cough (n=83) oss (n=102) reating (n=54)	68 (63.55) 53 (49.33) 73 (68.22) 33 (30.84)	42 (58.33) 30 (41.67) 29 (40.28) 21 (29.17)	1.25 (0.68 – 2.30) 1.37 (0.75 – 2.51) 3.18 (1.71 – 5.93) 1.08 (0.56 – 2.08)	0.482 0.301 <0.001 0.811	3.31 (1.73 - 6.34)	<0.001
=175) 8) ′) DI (n=179)	58 (54.72) 48 (45.28)	40 (57.97) 29 (42.03)	0.88 (0.47 – 1.62) REF	0.672		
) (1)	4 (3.74) 103 (96.26)	4 (5.56) 68 (94.44)	0.66 (0.16 – 2.73) REF	0.566		
oe at initial visit 16) 63)	73 (68.22) 34 (31.78)	43 (59.72) 29 (40.28)	1.45 (0.78 – 2.70) REF	0.244		
ography (n=171) n=51) al (n=120)	30 (29.41) 72 (70.59)	21 (30.43) 48 (69.57)	0.95 (0.49 – 1.85) REF	0.886		
ll site of disease d TB (n=150) nated TB (n=29)	19 (17.76) 88 (82.24)	10 (13.89) 62 (86.11)	1.34 (0.58 – 3.08) REF	0.492		
diagnosis (n=179) TB (n=45) TB (n=134)	27 (25.23) 80 (74.77)	18 (25.00) 54 (75.00)	1.01 (0.51 – 2.02) REF	0.972		

Table 1: Factors associated with LF-LAM positivity among PLHIV with

• The LF-LAM urine testing can assist in diagnosing active TB with high specificity in PLHIV with CD4 <200 cells/mm³ in Thailand.

 Advanced HIV disease CD4 <100 cells/mm³ or those presenting with unexplained weight loss were significantly associated with LF-LAM positivity in this study.

 LF-LAM should be combined with other TB diagnostics for the most accurate diagnosis.

• The benefits of using LF-LAM in improving patient outcomes should be











