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Urinary LAM grade, culture positivity, and mortality among HIV-infected South African outpatients

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SUMMARY

Setting—Four ambulatory clinics in Durban.

Objective—Test the relationships of patient characteristics, time to mycobacterial culture positivity, and mortality with urinary lipoarabinomannan (LAM) grade category.

Design—Newly diagnosed HIV-infected adults were screened for tuberculosis (TB) by sputum culture, tested for urinary LAM (Determine, Alere), and followed for up to 12 months. We performed multivariable ordinal logistic regression of risk factors for low (1 or 2) or high (3, 4, or 5) LAM grade. We used adjusted Cox regression models to determine the hazard ratios of time to culture positivity and death.

Results—Among 683 HIV-infected adults, median CD4 count was 215 cells/mm³ (interquartile range 86–361 cells/mm³), 17% had culture-confirmed TB, and 11% died during follow-up. Smoking, tachycardia (pulse >100 beats/minute), CD4 count <100 cells/mm³, and TB culture positivity were each associated with higher LAM grade. In multivariate models, a high urine LAM grade was associated with 4-fold increased hazard of culture positivity ($p=0.001$) and 2-fold increased hazard of mortality ($p=0.02$). Among patients treated for TB, these associations were no longer statistically significant.

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Conclusion—In this population, a higher urine LAM grade was associated with both shorter time to culture positivity and mortality, but these associations were not present for those who starting anti-TB therapy.

INTRODUCTION

Tuberculosis (TB) is the leading infectious cause of death globally and the most common cause of death for HIV-infected individuals.¹ Early diagnosis of TB through targeted screening and diagnosis may be critical to end the epidemic.^{2,3} The World Health Organization (WHO) recommends that people living with HIV should be routinely screened for TB-related symptoms (i.e. current cough, fever, night sweats, and weight loss) and evaluated for active TB disease using available diagnostic tests if positive.^{4,5} However, TB symptom screening is non-specific and may be less accurate for people with HIV-infection, which alters TB disease presentation and progression.^{6,7} Diagnostic testing can be challenging due to continued reliance on sputum collection, laboratory requirements for safe sample processing, and prolonged turnaround time.^{3,8}

Lipoarabinomannan (LAM) is a lipopolysaccharide located within the cell wall of *M. tuberculosis* and is excreted in the urine of people with active TB infection.⁹ A low-cost lateral flow urine-based LAM assay can be performed at the clinical point of care in 30 minutes.¹⁰ However, the urine LAM assay has poor sensitivity, suggesting minimal utility as a solitary and common diagnostic test.^{10–16} The urine LAM assay is recommended by the WHO for diagnostic testing only in the restricted population of HIV-infected adults in the most advanced stages of HIV infection;¹⁷ assay sensitivity is highest in individuals with very low CD4 counts.¹⁸

Urine LAM may also have a role in accelerating the diagnosis of TB for those with a high bacillary burden of disease. Several studies have shown that LAM positivity, as predicted by individual traits such as CD4 count, chronic cough, and TB test results, is a heuristic proxy for TB severity or disease status in HIV-infected individuals.^{18–21} LAM positivity is associated with TB mortality^{16,20,22–25} and higher mycobacterial load,^{19–21,26} and urine LAM testing among hospitalized HIV patients can reduce mortality.²⁷ Among HIV-infected adults, the recent STAMP study demonstrated urine LAM testing had a higher diagnostic yield than GeneXpert alone for hospitalized patients, while the XPRES study showed no mortality benefit from GeneXpert alone compared to smear.^{25,28} However, few studies have examined the relationship between LAM grade and clinical outcomes.^{20,22} Furthermore, additional research is needed to determine if urine LAM testing has a benefit among ambulatory HIV-infected populations. We conducted an analysis of urine LAM positivity reflecting the clinician's knowledge at the time of first visit by using LAM-negative as our reference group. We hypothesized that urine LAM positivity and higher grade were associated with faster time to TB culture positivity and mortality in a cohort of outpatient, HIV-infected adults in South Africa.

METHODS

We conducted a prospective cohort study of newly diagnosed, HIV-infected adults in four outpatient sites (two hospitals and two municipal health centers) in KwaZulu-Natal, South Africa, from October 2011 to January 2014. The design of the parent trial (the Sizanani Trial, NCT01188941) has been described previously.^{29,30} Eligible individuals were adults (≥ 18 years), not known to be pregnant, and had not received anti-TB therapy within the prior three months including isoniazid preventive therapy (IPT), which was not widely available at the time. The study was approved by ethics committees at the two local hospitals, McCord Hospital and St. Mary's Hospital, and Partners HealthCare in Boston [#2006-P-001379/40]. All study participants provided written informed consent and were offered ART and anti-TB therapy consistent with local and South African Department of Health guidelines.³¹

All participants provided one urine specimen at the time of enrollment, irrespective of TB symptoms. Study nurses performed two urine LAM tests on each specimen using the Determine™ TB-LAM assay (Alere Inc., Waltham, MA, USA), a low-cost lateral-flow strip that detects lipoarabinomannan in urine. The second reader was blinded to the first result. Partway through the study, nurses began recording the band intensity grade of positive urine LAM results, which ranged from low (1+) to high (5+), according to the manufacturer's reference card with five grades.

All study participants regardless of symptoms were asked to provide one respiratory sputum sample, and individuals unable to provide an expectorated sputum sample received sputum induction with 3% hypertonic saline using a nebulizer (WH-802, Yuehua Medical Instrument Factory Co.; Guangdong, China). A TB-trained microscopist, blinded to the urine LAM results, performed sputum acid-fast bacilli (AFB) smear microscopy on decontaminated samples using Ziehl-Neelson and Auramine stains. Sputum samples were decontaminated with N-acetyl L Cysteine and NaOH to a final concentration of 1.25%, centrifuged at 3,000 revs for 20 minutes, and resuspended in 1 ml of 7H9 broth. 0.5 ml of the suspension was inoculated into Bactec™ 960 mycobacterial growth indicator tubes (MGIT™) (BD; Franklin Lakes, USA), and solid culture Middlebrook 7H11 agar medium. *M. tuberculosis* organism was confirmed via niacin and nitrate testing. GeneXpert testing was not available at the clinic at the time of the study.

Study nurses used standardized questionnaires at baseline to collect demographic and clinical information, and directly measured heart rate and blood pressure. Participants were offered baseline CD4 count testing as part of HIV counseling. Study participants were followed for up to 12 months from study enrollment. Clinical records, phone calls to friends or family members when the participant could not be reached, and the South African National Death Registry, which captures >90% of deaths nationally, were used to determine survival status during the 12-month follow-up period.³⁰

Definitions

Participants were considered AFB smear positive if either Ziehl-Neelson or Auramine stains were positive, and culture-positive if *M. tuberculosis* was identified from liquid or solid

culture media. Participants were determined to have laboratory-confirmed TB if their sputum tested positive on smear and/or culture.

We used only the first urine LAM test result, as our previous studies found no substantial benefit from the second urine LAM test and concordance between the two readers was excellent (weighted kappa = 0.999).¹³ We classified faint positive LAM assay results as negative because these have been found to be false positives.¹³ We categorized the urine LAM grade as low (grade 1 or 2) or high (grade 3, 4, or 5).

Statistical analyses

We excluded participants who were unable to provide a urine sample, were urine LAM-positive but did not have a recorded grade, or were already on anti-TB therapy at the time of enrollment. We summarized categorical variables (e.g. TB symptoms) as proportions, and continuous variables (e.g. age, CD4 count) using mean $\pm$ standard deviation or median and interquartile range (IQR) if considerably skewed.

To assess potential risk factors for a high urine LAM grade, compared to a low grade or LAM-negative test, we performed univariable and multivariable ordinal logistic regression, adjusting for age and sex, and calculated exact 95% confidence intervals (CIs) for two-tailed p-values ($\alpha = 0.05$). We assessed the relationship between urine LAM grade category and time to two key outcomes, liquid MGIT culture positivity and death, respectively, using Kaplan-Meier plots and Cox proportional hazard models. We also used Cox proportional hazard models to estimate the relationship between urine LAM grade category and each of these two outcomes among patients who initiated TB treatment following a positive lab test or empiric diagnosis. We adjusted for age, gender, education, smoking, and CD4 count and approximated exact 95% CIs using the Efron method in the case of ties. All covariates were pre-specified. All eligible participants were included in analyses of LAM band intensity and mortality, while only participants with a recorded MGIT culture result were included in analyses of time to culture positivity. We performed two sensitivity analyses: 1) using only data collected from participants during time period when urine LAM grade was recorded; and 2) including all participants with urine lam testing regardless of LAM intensity band grade.

All analyses were performed using SAS version 9.4 (Cary, USA). The TB-LAM assay manufacturer (Alere Inc.) did not play a role in the study design, data analyses, or interpretation of results.

RESULTS

The analytical study population included 683 newly diagnosed HIV-infected adults following the exclusion of 31 individuals who were unable to provide a urine specimen, 43 participants who tested urine LAM-positive but had no recorded band intensity grade, and 39 participants who were receiving anti-TB therapy (Table 1). Characteristics of LAM-positive patients with and without recorded intensity band reading were qualitatively similar. The mean age of enrollees was 34.3 years (standard deviation 9.7 years), 361 (53%) were male, 263 (39%) completed high school, and 164 (24%) were current smokers. Mean heart

rate was 94.8 ± 22.7 beats/minute and mean arterial pressure (MAP) was 87.4 ± 15.0 mmHg. Overall, 418 (61%) individuals reported any (1) of the four WHO TB-related symptoms and 107 (17%) had culture-confirmed active TB. Among MGIT culture-positive patients, median time to culture positivity was 11 (IQR 8-13.5) days. No cases of non-TB mycobacterium were identified. Among the 588 (86%) participants who completed CD4 count testing, the median CD4 count was 214 cells/mm³ (IQR 86-361 cells/mm³). Seventy-seven (11%) participants died during the 12-month follow-up period, for whom median time to death was 1.7 months (IQR 0.7-3.9).

Urine LAM Results

Overall, fifty individuals (7%) had a LAM-positive urine test with recorded band intensity of which 14 (25%) were graded 1+, 13 (23%) were 2+, 7 (12%) were 3+, 6 (11%) were 4+, and 10 (18%) were 5+. Of the 23 participants with “high” urine LAM grade, 10 were culture-positive and nine of the 13 smear- and culture-negative participants had a CD4 count <100 cells/mm³. Among the LAM-negative individuals, 471 (79%) participants had no evidence of active TB disease and were not initiated on anti-TB therapy, while 129 (22%) participants either had laboratory evidence of active TB or were initiated on anti-TB therapy. Of the 121 individuals with laboratory-confirmed active TB, 107 (88%) were culture positive and 22 (18%) were LAM-positive.

Urine LAM Grade and Clinical Characteristics

After controlling for age and gender, tachycardia (pulse >100 beats/minute) was associated with a 6-fold increase in the odds of a high urine LAM grade compared to low or negative urine LAM test result in this cohort of HIV-positive adults (95% CI 2.96-12.35, $p < 0.001$) (Table 2). Higher MAP was statistically significantly negatively associated with LAM positivity but had a small effect size (odds ratio [OR] = 0.98, 95% CI 0.95-1.00, $p = 0.04$). TB-related symptoms, smoking, low CD4 count, and culture positivity were all associated with an increase in the odds of a high urine LAM grade ($p = 0.02$ for all).

Urine LAM Grade and Time to Mortality

In our cohort of 683 HIV-infected adults, time to death was shorter among urine LAM-positive patients compared to LAM-negative patients (Figure 1). Time to death was shortest among patients with a high urine LAM grade, followed by low urine LAM grade and urine LAM-negative patients (Figure 2a). Among the 77 participants who died, median time to death was 1.9 months in the urine LAM-negative group (IQR 0.7-4.6) and 1.1 months in the urine LAM-positive group (IQR 0.7-2.2). In univariable and multivariable regression, the hazard for death was highest among participants with a high urine LAM grade (hazard ratio [HR] = 6.00, 95% CI 3.07-11.73; adjusted HR [aHR] = 2.39, 95% CI 1.14-4.98) (Table 3), with CD4 count accounting for much of the difference in the unadjusted and adjusted effect estimates. Among 103 participants treated for TB, urinary LAM grade category was not significantly associated with mortality. Trends were similar in our two sensitivity analyses, which included only data collected from the period when urine LAM grade was recorded and all urine LAM results.

Urine LAM Grade and Time to Culture Positivity

Among the 591 adults with MGIT testing and a recorded time to culture positivity, time to culture positivity was shorter among urine LAM-positive patients compared to LAM-negative patients with the largest effect observed among patients with high grade urinary LAM results (Figure 2b). Median time to culture positivity was 12 days for urine LAM-negative patients (IQR 8-14.5) compared to 10 days for urine LAM-positive patients (IQR 8-11). A high urine LAM grade remained strongly associated with shorter time to TB culture positivity after adjustment for confounders (aHR = 3.68, 95% CI 1.68-8.08, $p = 0.001$). A low urine LAM grade had a trend for being associated with a shorter time to TB culture positivity (aHR = 2.49; 95% CI 0.88-7.03, $p = 0.09$) (Table 4). Among 72 culture-positive participants treated for TB, urinary LAM grade category was not statistically significantly associated with time to culture positivity. In the two sensitivity analyses, which included only participants enrolled from the time urine LAM grade was recorded and all participants with urine LAM testing, respectively, these trends were unchanged.

DISCUSSION

In this study of adults newly diagnosed with HIV infection, high urine LAM grade was associated with both shorter time to TB culture positivity and mortality after adjusting for confounders. Among participants who received anti-TB treatment, these statistically significant associations were no longer present. Although the sample size of participants receiving anti-TB treatment was small, potentially precluding our ability to detect a true association, it highlights the potential importance of early treatment for LAM-positive HIV-associated TB. Our results suggest urine LAM positivity and grade may identify patients with higher morbidity, mycobacterial load, and risk of death among ambulatory HIV-infected adults. Including a urine LAM assay in the screening algorithm for TB could enable more rapid diagnosis of those patients most in need of immediate anti-TB treatment initiation, potentially preventing deaths and reducing TB transmission.

While we use culture as the gold standard for TB diagnosis, some immunocompromised patients may have had sputum-negative, LAM-positive TB disease, as was observed in the recent STAMP study.²⁵ In our study, nine of the 11 urine LAM-positive, sputum smear- and culture-negative patients had a CD4 count <100 cells/mm³. Some of these patients likely had unconfirmed extra-pulmonary disease and although we did not test for this, we included all patients who were treated for TB empirically or following culture-confirmation in our TB treatment analyses.

In HIV-positive populations where TB diagnosis is more difficult, urine LAM testing continues to be a promising tool for diagnosing both pulmonary and extra-pulmonary TB.^{6,8} Compared to smear microscopy, GeneXpert improves diagnostic yields but has not been demonstrated to alter mortality due to TB following programmatic implementation.^{28,32} Urine LAM testing among hospitalized HIV patients with advanced immunosuppression reduced all cause 8-week mortality by increasing the proportion of patients initiating therapy and reducing the time to treatment initiation.²⁷ We lack a rapid, sensitive, easy to use, affordable TB diagnostic test for use at the point of care. Recent advances in assay technology could improve sensitivity while preserving specificity, potentially expanding the

utility of a urine LAM assay to less immunocompromised HIV-infected populations and HIV-negative populations.³³

Our findings build up previously published studies of outpatient, HIV-infected, ART-naïve adults in sub-Saharan Africa showing urinary LAM positivity is associated with markers of poor prognosis and higher mycobacterial load.^{16,19–24,26} A recent meta-analysis found the risk of death is 2.5-fold higher among LAM-positive HIV-TB co-infected outpatients receiving treatment compared to LAM-negative patients but effect estimates were variable and the majority of studies were hospital-based.²³ Our study suggests urine LAM positivity is associated with mortality hazard overall, but not among patients who have initiated anti-TB therapy.

Our analyses add evidence that urine LAM grade category may have important prognostic value in identifying the patients most at risk of poor outcomes.^{20,22} These data indicate urine LAM grade category may provide useful information to clinicians by identifying the sickest patients in need of rapid initiation of anti-TB treatment. Future research studies might consider recording urine LAM grade to allow for a better understanding of the relationship between LAM results and prognostic markers of TB severity and mortality.

Strengths of this study include a representative study population from varied geographic locations in South Africa, urine LAM testing on never-frozen samples, ascertainment of sputum for TB by readers blinded to the LAM results, and urine LAM testing and statistical analyses reflective of clinician knowledge at the time of TB screening. This study also had several limitations. Although we controlled for relevant collected confounding variables in our multivariate analysis, there may be residual confounding or confounding variables that were not ascertained as part of the parent study. The number of participants who received TB treatment was small, increasing the likelihood of a type II error. In particular, there is rationale to support the relationship between urine LAM grade and culture positivity remaining the same before and after treatment, but we were unable to detect that association in our data. We included all negative urine LAM results in our analyses but LAM assay band intensity grade was only recorded partway through the study and therefore is missing for the first 43 of 93 (46%) positive urine LAM tests, which were excluded. This likely did not bias our results because excluded participants were qualitatively similar to those included in these analyses and there was no temporal trend in study outcomes. Furthermore, our sensitivity analyses using only data collected from the time urine LAM grade was recorded found the same trends reported here for the larger cohort. Finally, there can be inter-reader variability of the LAM assay. By grouping LAM grades and categorizing the faint readings as negative, we reduced the amount of misclassification in our exposure of interest.

Conclusions

Overall, among HIV-infected outpatients in a high TB burden setting, a higher urine LAM grade was associated with shorter time to culture positivity and mortality. Participants who were started on anti-TB therapy no longer had a greater risk of mortality, as would be expected. Urine LAM testing may provide useful clinical information for the care of outpatient, HIV-infected adults by rapidly identifying the patients most likely to have poor

outcomes and reducing the number of days and clinic visits to treatment initiation. Further research is needed to determine if urinary LAM testing in this setting may reduce mortality as a result of more rapid diagnoses and earlier TB treatment initiation.

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Figure 1.

Time to death or censorship of LAM-positive (red) and LAM-negative (blue) HIV-infected adults newly diagnosed in an outpatient setting (n=679)

Figure 2a.

Time to death or censorship by urine LAM grade category among HIV-infected adults newly diagnosed in an outpatient setting (n=673)

Figure 2b.

Time to tuberculosis MGIT culture positivity by urine LAM grade category among newly diagnosed HIV-infected adults (n=591)

Table 1

Cohort characteristics of antiretroviral therapy-naïve HIV-infected adults (N=683)

	Mean $\pm$ SD or N (%)
Demographic and Education	
Age (years) (n=679)	34.3 $\pm$ 9.7
Male gender	361 (52.9)
Completed high school (n=678)	263 (38.8)
Clinical	
Currently smoke tobacco	164 (24.0)
Tachycardia (>100 beats/min.) (n=410)	133 (32.4)
Heart rate (beats/min) (n=410)	94.8 $\pm$ 22.7
Mean arterial pressure (mmHg) (n=412)	87.4 $\pm$ 15.0
TB-related Symptoms	
Current cough	235 (34.4)
Having any of 4 TB-related symptoms	418 (61.2)
Having 2 TB-related symptoms	272 (39.8)
CD4 Cell Count	
Median [IQR] cells/mm ³ (n=588)	214 [86, 361]
Clinic-based LAM Testing	
Urine LAM positive	50 (7.3)
Urine LAM grade 1 or 2	27 (4.0)
Urine LAM grade 3, 4, or 5	23 (3.4)
Tuberculosis Test Results	
Sputum smear AFB positive (n=647)	30 (4.6)
Middlebrook 7H11 or MGIT sputum culture positive (n=632)	107 (16.8)
MGIT culture positive (n=630)	100 (15.9)
Empirically started on anti-TB therapy	37 (5.4)
Mortality	
Died during 12-month follow-up	77 (11.3)

SD=standard deviation; IQR=interquartile range; TB=tuberculosis; LAM=lipoarabinomannan; AFB=acid-fast bacilli.

Table 2

Ordinal and multivariate logistic regression of risk factors for urine LAM grade category (reference: negative; Grade 1 or 2; Grade 3, 4 or 5) among ambulatory HIV-infected adults

	Unadjusted Odds Ratio (95% CI) (n=683)	p-value	Adjusted Odds* Ratio (95% CI) (n=679)	p-value
Demographic and Education				
Age (years) (n=679)	1.02 (0.99-1.05)	0.20	1.02 (0.99-1.05)	0.22
Male gender	1.18 (0.66-2.12)	0.57	1.13 (0.63-2.03)	0.68
Completed high school (n=678)	0.64 (0.34-1.21)	0.17	0.69 (0.36-1.33)	0.27
Clinical				
Currently smoke tobacco	0.50 (0.22-1.13)	0.09	0.39 (0.16-0.94)	0.04
Tachycardia (>100 beats/min.) (n=410)	5.99 (2.92-12.15)	<0.001	6.04 (2.96-12.35)	<0.001
Heart rate (beats/min.) (n=410)	1.04 (1.03-1.06)	<0.001	1.04 (1.03-1.06)	<0.001
Mean arterial pressure (n=412)	0.98 (0.95-1.00)	0.07	0.98 (0.95-1.00)	0.04
TB-related Symptoms				
Current cough	2.21 (1.24-3.94)	0.007	2.19 (1.22-3.93)	0.008
Having any of 4 TB-related symptoms	2.39 (1.20-4.76)	0.01	2.31 (1.15-4.61)	0.02
Having 2 TB-related symptoms	2.44 (1.36-4.39)	0.003	2.39 (1.32-4.34)	0.004
CD4 Count				
Low CD4 (<100 cells/mm ³) (n=588)	4.68 (2.48-8.83)	<0.0001	4.73 (2.48-9.03)	<0.001
Sputum TB Test Results				
Smear AFB positive (n=647)	2.17 (0.73-6.48)	0.17	2.09 (0.70-6.26)	0.19
Middlebrook 7H11 or MGIT culture positive (n=632)	4.15 (2.19-7.83)	<0.0001	4.20 (2.21-7.97)	<0.001
MGIT culture positive (n=630)	2.59 (1.60-4.19)	0.0001	2.50 (1.54-4.06)	<0.001

CI=confidence interval; TB=tuberculosis; LAM=lipoarabinomannan; AFB=acid-fast bacilli; MGIT = mycobacterial growth indicator tubes (MGITTM).

* Adjusted for age and sex.

Table 3
Hazard ratio of time to mortality by urine LAM grade among HIV-infected South African adults

		Unadjusted Models		Adjusted Models*	
	Incidence rate (per 1,000 person-years)	Hazard Ratio (95% CI)	p-value	Hazard Ratio (95% CI)	p-value
All participants		n=679		n=586	
Urine LAM-negative	8.56	<i>Ref.</i>	---	<i>Ref.</i>	---
Urine LAM-positive	39.26	4.21 (2.46-7.21)	<0.001	2.32 (1.28-4.20)	0.006
Urine LAM Grade 1 or 2	26.84	2.95 (1.35-6.46)	0.007	2.23 (0.94-5.26)	0.07
Urine LAM Grade 3, 4, or 5	58.07	6.00 (3.07-11.73)	<0.001	2.39 (1.14-4.98)	0.02
Treated for TB		n=103		n=100	
Urine LAM-negative	9.51	<i>Ref.</i>	---	<i>Ref.</i>	---
Urine LAM-positive	15.66	1.60 (0.43-5.91)	0.48	1.53 (0.39-6.02)	0.54
Urine LAM Grade 1 or 2	13.18	1.35 (0.17-10.63)	0.78	2.40 (0.29-20.12)	0.42
Urine LAM Grade 3, 4, or 5	17.29	1.77 (0.38-8.18)	0.47	1.29 (0.26-6.35)	0.76

CI=confidence interval; LAM=lipoarabinomannan; AFB=acid-fast bacilli.

* Adjusted by age, gender, education, smoking status, and CD4 count.

Table 4

Hazard ratio of time to culture positivity by urine LAM grade among HIV-infected South African adults

	Unadjusted Models		Adjusted Models*	
	Hazard Ratio (95% CI)	p-value	Hazard Ratio (95% CI)	p-value
All participants	n=591		n=505	
Urine LAM-negative	<i>Ref.</i>	---	<i>Ref.</i>	---
Urine LAM-positive	4.90 (2.65-9.04)	<0.001	3.17 (1.63-6.16)	<0.001
Urine LAM Grade 1 or 2	2.81 (1.01-7.80)	0.05	2.49 (0.88-7.03)	0.09
Urine LAM Grade 3, 4, or 5	7.32 (3.58-14.94)	<0.001	3.68 (1.68-8.08)	0.001
Treated for TB	n=72		n=71	
Urine LAM-negative	<i>Ref.</i>	---	<i>Ref.</i>	---
Urine LAM-positive	1.51 (0.62-3.70)	0.37	1.56 (0.62-3.93)	0.35
Urine LAM Grade 1 or 2	1.16 (0.16-8.57)	0.89	1.10 (0.15-8.30)	0.92
Urine LAM Grade 3, 4, or 5	1.61 (0.1-4.22)	0.34	1.71 (0.62-4.69)	0.30

CI=confidence interval; LAM=lipoarabinomannan; AFB=acid-fast bacilli.

* Adjusted by age, gender, education, smoking status, and CD4 count.