



News Release

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ATS Press Room: 504-670-6926 (May 15 to 20)

Poster session time: 1:30-4:00 p.m. May 16

Location: CC-Room 260-262 (Second Level), Morial Convention Center

False Positives in TB Diagnosis Lead to Real Negatives for HIV Patients

ATS 2010, NEW ORLEANS— HIV-infected patients who are falsely diagnosed as having tuberculosis (TB) have higher rates of mortality than those who are correctly diagnosed with the disease, according to a study conducted by researchers at University of California-San Francisco and Makerere University-Kampala.

“Among HIV-infected persons with suspected TB, falsely diagnosing persons with TB by rapid testing was associated with increased mortality when compared with the group of patients who received the correct diagnosis,” said study lead author Robert Blount, M.D., clinical fellow in pulmonary and critical care medicine at UCSF’s School of Medicine. The results of the study will be presented at the ATS 2010 International Conference in New Orleans, with co-authors Laurence Huang, Lucian Davis, Adithya Cattamanchi, Saskia den Boon, William Worodria and Moses Joloba also in attendance

“Tuberculosis remains a common cause of pulmonary disease worldwide,” Dr. Blount said. “HIV-infected patients are particularly susceptible to TB. Diagnosis can be a challenge, because the standard test-- sputum culture—p although sensitive and specific, often takes several weeks to yield results.”

Physicians and researchers have long understood that missing a positive diagnosis of tuberculosis in patients who actually have the disease can result in poor outcomes and an increase in mortality rates. But the link between mortality and false positives – diagnosing someone with tuberculosis who does not have the disease – has been less widely understood.

In this study, Dr. Blount and his colleagues evaluated the outcomes of 600 HIV-infected patients who were treated at Mulago Hospital in Kampala, Uganda, including patients who were incorrectly diagnosed with tuberculosis following rapid testing.

“Studies tend to emphasize the negative impact of missing the diagnosis of TB,” Dr. Blount noted. “Our study shows that falsely diagnosing patients with TB who do not actually have TB is also associated with negative outcomes.”

Dr. Blount said the poorer outcomes are likely due to the fact that patients who are misdiagnosed are treated erroneously for tuberculosis while the actual underlying condition remains untreated. Because physicians believe tuberculosis is the culprit, any search for the real underlying disease is delayed, as is proper treatment, he said.

Dr. Blount said the study’s results serve to caution physicians to continue monitoring patients who have been diagnosed with tuberculosis to ensure the treatment is working, and to reassess the diagnosis if patients are not improving.

“These results remind us as clinicians that diagnostic tests are not 100 percent accurate, and that falsely diagnosing patients with a disease who do not actually have that disease can lead to negative outcomes,” he said. “We must continue to re-evaluate a patient’s clinical progress. If he or she is not responding as predicted to treatment for a diagnosed disease, we must entertain alternative diagnoses.”

Dr. Blount also noted the results indicate a need for further refinement of rapid diagnostic tests for tuberculosis.

“These rapid tests, however, are not always as sensitive or specific for determining if a person has TB,” he said. “Further research should be focused on the development of more sensitive and specific TB diagnostic tests and the clinical impact of these new tests. Ideally, these tests should be affordable enough to be used in low-income countries, where the burden of tuberculosis is high.”

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“The Effect of False Positive and False Negative Microscopy Results on Mortality Among HIV-Infected Ugandans Undergoing Evaluation for TB” (Session A93, Sunday, May 16, 1:30- 4:00 p.m., CC-Room 260-262 (Second Level), Morial Convention Center; Abstract 1654)

**Please note that numbers in this release may differ slightly from those in the abstract.
Many of these investigations are ongoing; the release represents the most up-to-date data
available at press time.*

The Effect of False Positive and False Negative Microscopy Results on Mortality among HIV-infected Ugandans Undergoing Evaluation for TB

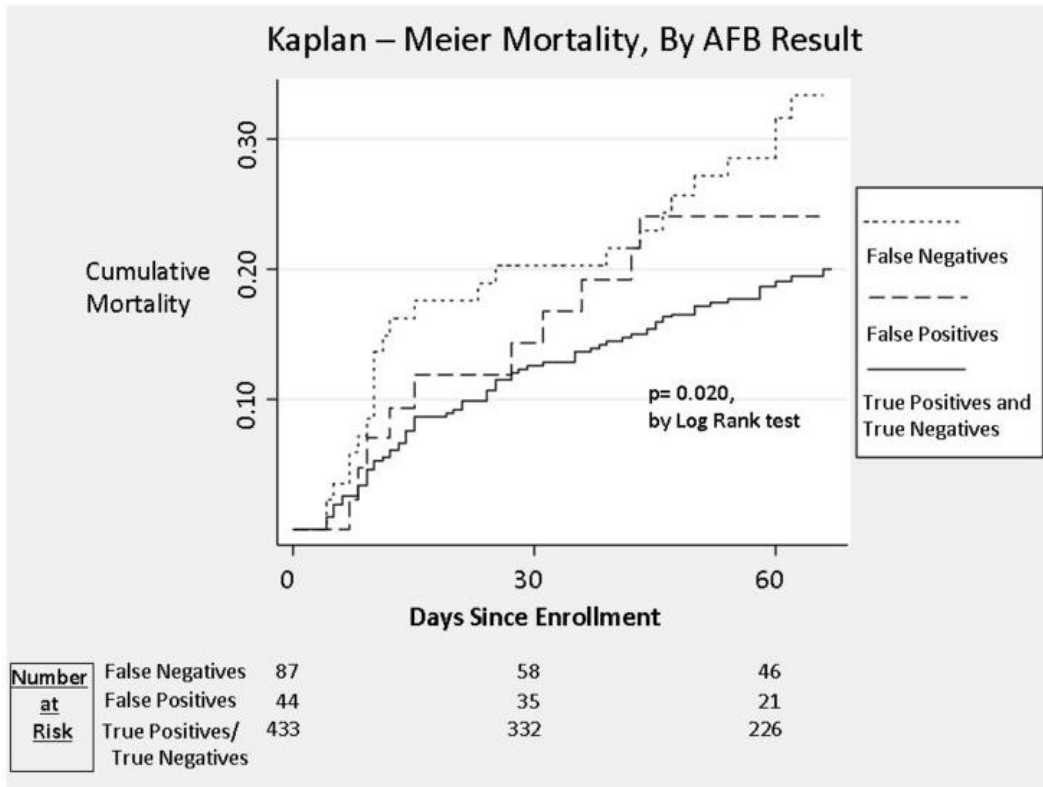
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Rationale: Studies of new tuberculosis (TB) diagnostic strategies frequently emphasize adverse outcomes secondary to false negative results, but less often consider adverse outcomes secondary to false positive results.

Objective: We evaluated the association between correct and incorrect TB diagnoses by AFB-smear microscopy and cumulative two-month mortality in HIV-infected TB suspects.

Methods: Between September 2007 and July 2009, consecutive HIV-infected adults admitted to Mulago Hospital in Kampala, Uganda, with cough ≥ 2 weeks submitted 2 sputum specimens for examination for acid-fast bacilli (AFB). Each sputum specimen was read using both conventional light and fluorescence microscopy; any smear with ≥ 1 AFB per high-powered field was classified as positive. Bronchoalveolar lavage (BAL) was performed on AFB smear-negative patients. Sputum and BAL specimens were cultured on Lowenstein-Jensen medium; any culture growing ≥ 1 colony was read as positive. We categorized smear microscopy readings in reference to TB culture status as follows: correct (true positive or true negative) results, false positive results, or false negative results. After excluding patients who died before complete smear results were available at 72 hours, we performed Kaplan-Meier survival analysis stratified by result category, and compared cumulative 2-month mortality across strata using the log-rank test.

Results: 600 HIV-infected patients were enrolled. Median age was 33 years (interquartile range (IQR) 27-40); 57% were female. Median CD4+ T-lymphocyte count was 48 cells/ μ L (IQR 14-163). 325 (54%) patients had culture-positive TB. Smear microscopy correctly classified 434 (72%) patients as true positives or true negatives. 131 patients were misclassified: 44 (7%) as false positives, and 87 (15%) as false negatives. 35 (6%) patients could not be classified because of unknown TB culture status. The cumulative incidence of death at 60 days was 22%: 19% among correctly classified patients; 24% among false positives; and 31% among false negatives ($p=0.02$). (Figure)



Conclusion: Both false positive and false negative smear microscopy results were associated with increases in 60-day mortality among HIV-infected TB suspects in Uganda. New rapid diagnostic strategies for TB should be evaluated based on the impact of both false positive and false negative results on patient-important outcomes.