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Abstract 9922

Unmasking Higher-than-Expected Prevalence of *Mycobacterium tuberculosis* DNA in Respiratory Samples from US-born Patients in a Safety Net Hospital in Boston.

Edward Jones-Lopez*[1;2], Nancy Miller[3;4], Berverley Orr[3], Laura F. White[5], Solange Alves Vinhas[6], Moses Mpeirwe[7], Patrick Orikiriza[8], Juliet Mwanga[7], Moisés Palaci[6], Reynaldo Dietze[6], Yap Boum[7;8], Guillermo Madico[2]

[1]University of Southern California, Keck School of Medicine of USC, Los Angeles, United States, *[2]Boston University School of Medicine, Department of Medicine, Boston, United States*, *[3]Boston Medical Center, Clinical Microbiology Laboratory, Boston, United States*, *[4]Boston University School of Medicine, Department of Pathology and Laboratory Medicine, Boston, United States*, *[5]Boston University, Boston University School of Public Health, Boston, United States*, *[6]Universidade Federal do Espírito Santo - UFES, Núcleo de Doenças Infecciosas, Vitória, Brazil*, *[7]Epicentre, Médecins sans Frontières, Mbarara, Uganda*, *[8]Mbarara University Of Science And Technology, Epicentre, Médecins sans Frontières, Mbarara, Uganda*

Background: The recent description of sequential inflammatory stages characterizing early tuberculosis (TB) disease and reports of disease caused by differentially culturable *M. tuberculosis* have significantly complicated the diagnostic landscape. These detection gaps threaten global TB elimination goals.

Materials/methods: During early development of a new ultrasensitive molecular TB assay, we tested consecutive anonymized respiratory samples submitted to the microbiology laboratory for routine non-TB testing from patients admitted to a safety net hospital in Boston, and consecutive anonymized control samples from a community hospital. We subsequently performed a longitudinal study to determine clinical associations and outcomes.

Results: 18/146 (12.6%) anonymized specimens tested positive for *M. tuberculosis* DNA (TB-DNA), compared to 1/50 (2%) controls (p=0.03). The prospective study included 101 patients (median age 59, 63% male, 70% US-born); 16/101 (15.8%) tested TB-DNA positive, with a clear bimodal age distribution. Whereas older TB-DNA positive subjects (n=12, mean age 62) had various infectious and non-infectious clinical syndromes commonly encountered in hospitalized patients, 3/4 young TB-DNA positive patients (mean age 22) presented with acute chest syndrome (3/16 vs. 0/85; p=0.003). TB-DNA positive individuals were more likely to have been tested for *M. tuberculosis* infection prior to study inclusion (p=0.03), to be TST or IGRA-negative (p<0.001), and to have anemia (p=0.002) a known laboratory marker of TB disease. During a median 1,819 days [interquartile range 1,658–1,842] of follow up, 6/16 (38%) TB-DNA positive patients died a median 390 days [5–694] after hospital discharge, compared to 21/85 (25%) of those TB-DNA negative that died after a median 26 days [14–102] after discharge (p=0.30). Most TB-DNA positive patients died from septicemia (67% vs 14%, p=0.02).

Conclusions: We unexpectedly detected *M. tuberculosis* DNA in a presumably low TB risk population. In addition to unmasking novel clinical associations, our findings suggest a paucibacillary and inflammatory form of TB disease that is currently clinically unsuspected and undetectable with existing tools. These results require further investigation given the potential implications for patient outcomes and public health.

Presenter email address: joneslop@usc.edu