Translation from research to clinical practice: Fostering improved patient care through microscopicobservation drug susceptibility for tuberculosis diagnosis in Nigeria

Sir,

Nigeria has the 13th highest tuberculosis (TB) burden in the world with a prevalence of 171 per 100,000 in 2011[1] It is also estimated that 8–16% of cases have multidrug resistant TB (MDR-TB).[2,3] The case detection rate in Nigeria is estimated at 45%.[1] The majority of patients remain undiagnosed for many reasons, but most striking is the lack of diagnostic and laboratory capacity, particularly unavailability of culture testing for these patients. Strikingly, the World Health Organization (WHO) reports that there is one laboratory performing TB culture for every 25 million population in Nigeria, well below the recommended minimum of one culture laboratory per 5 million population.[4] In our setting, which is a teaching hospital serving a large urban deprived area and is also the largest center through which the National Tuberculosis and Leprosy Control Program delivers the directly observed treatment, short-course (DOTS) strategy in Lagos state, diagnosis of TB relies heavily on microscopy, which even in the best of hands is only 50% sensitive.[5] This creates a challenge for diagnosing smear-negative TB, which is partly driven by the HIV/AIDS epidemic in sub-Saharan

Africa and is due to the paucibacillary nature of pulmonary TB in HIV positive patients.[6] To compound this the DOTS strategy's activities in Nigeria are driven by a disease transmission reduction agenda, which has led to a prioritization of smear-positive cases over smear-negative cases and has had the unintended consequence of poorer outcomes for smear-negative cases, with regards to delayed diagnosis, lack of access to medicines, and treatment failures. This has the potential to increase MDR-TB rates.

The case was made to the academic world in South Africa in 2007, in a scientific meeting hosted by Médecins Sans Frontières and entitled "dying for a test" that a lack of adequate diagnostics in resource poor settings was contributing to excessive mortality from TB in these regions of the world. Since then, noncommercial methods for TB diagnosis and drug susceptibility testing have been developed and published in scientific literature.[7,8] However, the challenge of translation of scientific research into clinical practice is ever present. Evidence for the noncommercial culture techniques have been present for several years now and it has been 2 years since the WHO stop TB group published guidance on the use of these culture techniques for resource poor settings.[7,9] Specifically, WHO endorsed the microscopic observation drug susceptibility (MODS) assay for direct testing of sputum samples for *Mycobacterium tuberculosis* and MDR-TB and indirect testing of *M. tuberculosis* isolates for MDR-TB, thereby permitting rapid screening of patients with suspected TB and MDR-TB.

Given limited resources, waiting for scale-up of expensive genotypic or automated liquid culture techniques in our setting is not an option for smear-negative patients in our clinics. The only practical option for these people is diagnosis by one of the noncommercial culture techniques that have been developed and validated in scientific research. In our setting, where the cost of diagnosis is met exclusively by the patient, we hope to make available as routine, an effective and affordable test to make a rapid diagnosis of TB and MDR-TB, which has its basis in the gold standard for diagnosis-culture. A yet to be published study by Ochang in Calabar, Nigeria in 2011 has demonstrated that the translation of MODS technique from the research laboratory to clinical practice can be done in Nigeria and improves patient care. He achieved this at a cost of $7.13 per test.

We are undertaking an implementation study to assess the feasibility of doing routine MODS for early detection of pulmonary TB and MDR-TB in a busy high endemic TB setting in Nigeria and to determine true prevalence of pulmonary TB and proportional prevalence of MDR-TB in our setting. We aim to establish this diagnostic test routinely at Lagos University Teaching Hospital where there is a large and extremely busy TB service. Upon completion of the study, we plan to disseminate the results of our project to other centers in the country by partnering with agencies doing complimentary work and publishing our data in academic journals for use by epidemiologists and clinicians. This work will also add to urgently needed data on smear-negative and MDR-TB prevalence in Nigeria.

Ethics approval for the study was granted by Lagos University Teaching Hospital Health Research and Ethics Committee.

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