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GeneXpert MTB/RIF Is Superior to BBD Max MDR-TB for Diagnosis of Tuberculosis (TB) in a Country with Low Incidence of Multidrug-Resistant TB (MDR-TB)

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With 10 million active disease cases, 558,000 cases of rifampin-resistant/multidrug-resistant tuberculosis (MDR-TB), and 1.6 million deaths recorded worldwide in 2017, TB is a leading cause of death from a single infectious agent (1). Early detection of *Mycobacterium tuberculosis* in clinical specimens, its susceptibility to anti-TB drugs (particularly, rifampin), and effective treatment are essential for global TB control efforts (1). Although culture is the gold standard for definitive diagnosis of active TB, molecular methods are now preferred due to their speed and ability to simultaneously detect resistance to rifampin with/without additional resistance to isoniazid for rapid diagnosis of TB and MDR-TB. The GeneXpert MTB/RIF Ultra (Xpert) assay rapidly detects *M. tuberculosis* and its resistance to rifampin (a surrogate marker for MDR-TB) in pulmonary and extrapulmonary specimens (2, 3). BBD Max MDR-TB (BBD Max) is a new test for the detection of *M. tuberculosis* and its resistance to rifampin and isoniazid (MDR-TB). Kuwait is a low-TB-incidence (23 cases/100,000 population) country, and ~1% of *M. tuberculosis* isolates are MDR-TB (4). This study tested the Xpert and BBD Max assays in a head-to-head comparison for the rapid detection of *M. tuberculosis*/MDR-TB using culture and clinical diagnosis of active TB disease as a reference in Kuwait.

Fifty-one pulmonary and 30 extrapulmonary (cavitary fluids, $n = 24$; fine needle aspirate/pus, $n = 6$) specimens collected from 81 consecutive patients presenting with TB-like symptoms were used. Samples were processed for Ziehl-Neelsen staining and culture in the MGIT 960 system (MGIT) (5). The Xpert (Cepheid) and BBD Max (Becton and Dickinson) assays were performed according to the manufacturers' instructions.

M. tuberculosis H37Rv and a well-characterized MDR-TB strain used as a control yielded expected results. Fourteen specimens were culture positive, including nine specimens that were smear positive for acid-fast bacilli. Of 14 culture-positive specimens, 12 were positive for *M. tuberculosis* and one negative for *M. tuberculosis* by both the Xpert and BBD Max assays. One specimen contained nontuberculous mycobacteria. Of 67 smear-negative and culture-negative specimens, eight samples were *M. tuberculosis* positive by the Xpert assay only, one sample was positive by the BBD Max assay only, and 58 samples were *M. tuberculosis* negative by both tests. Six of eight Xpert-positive pulmonary specimens were obtained from patients with a clinical diagnosis of TB who responded to anti-TB treatment.

All *M. tuberculosis*-positive specimens ($n = 13$) were rifampin susceptible by the MGIT and Xpert assays, while 11 specimens were rifampin susceptible by the BBD Max assay, and two specimens yielded indeterminate results. Although two of 13 *M. tuberculosis* isolates were isoniazid resistant by the MGIT assay, the BBD Max assay detected resistance in only one specimen, while 11 specimens were isoniazid susceptible, and one specimen yielded an indeterminate result.

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In conclusion, the Xpert assay performed better than did the BBD Max assay for the rapid diagnosis of active TB/MDR-TB in our setting. Our data also show that indeterminate results are often obtained by the BBD Max assay for rifampin resistance and/or isoniazid resistance detection. Detection of isoniazid resistance in few samples by the BBD Max assay does not offer much advantage over the Xpert assay for low-MDR-TB-incidence settings, such as Kuwait, since the Xpert assay outperformed the BBD Max assay in six pulmonary specimens with low bacterial load from patients who had clinical disease but remained smear negative and MGIT culture negative. Our findings support the use of the Xpert assay over the BBD Max assay for the rapid diagnosis of active TB disease in paucibacillary pulmonary specimens in settings of low prevalence of MDR-TB for effective treatment and for limiting further transmission of infection.

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We declare no conflicts of interest.

REFERENCES

1. World Health Organization. 2018. Global tuberculosis report 2018. WHO/CDS/TB/2018.20. World Health Organization, Geneva, Switzerland.
2. Steingart KR, Schiller I, Horne DJ, Pai M, Boehme CC, Dendukuri N. 2014. Xpert MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults. Cochrane Database Syst Rev 1:CD009593. https://doi.org/10.1002/14651858.CD009593.pub3.
3. Kohli M, Schiller I, Dendukuri N, Dheda K, Denkinger CM, Schumacher SG, Steingart KR. 2018. Xpert MTB/RIF assay for extrapulmonary tuberculosis and rifampicin resistance. Cochrane Database Syst Rev 8:CD012768. https://doi.org/10.1002/14651858.CD012768.pub2.
4. Mokaddas E, Ahmad S, Samir I. 2008. Secular trends in susceptibility patterns of *Mycobacterium tuberculosis* isolates in Kuwait, 1996–2005. Int J Tuberc Lung Dis 12:319–325.
5. Ahmad S, Mokaddas E, Al-Mutairi N, Eldeen HS, Mohammadi S. 2016. Discordance across phenotypic and molecular methods for drug susceptibility testing of drug-resistant *Mycobacterium tuberculosis* isolates in a low TB incidence country. PLoS One 11:e0153563. https://doi.org/10.1371/journal.pone.0153563.