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Diagnostic assessment of Xpert MTB/RIF in a sample of *Mycobacterium tuberculosis* Egyptian patients

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Global *Mycobacterium tuberculosis* (MTB*)* control efforts have been severely hampered by the lack of diagnostic tests that are accurate, simple to use and can be applied at the point of clinical care. This compounded by the widespread inability to test for drug resistance. The newly developed Xpert *MTB*/RIF assay utilizes real-time PCR technology to both diagnose *TB* and detect rifampicin (RIF) resistance concurrently using unprocessed clinical specimens, regardless of their smear status. The study was designed to assess the diagnostic accuracy of Xpert MTB/RIF assay in detecting *MTB* and MDR-*TB* in comparison to the conventional methods in a sample of *MTB* Egyptian patients. Forty (40) sputum specimens were collected from adult patients having pulmonary tuberculosis from Chest hospital, Egypt. Ten (10) external control patients were enrolled. The conventional method, including Ziehl-Neelsen staining showed the presence of *MTB* in 77.5% and bacterial culture in 85%. Whereas, the Xpert *MTB*/RIF test provided detection of 82.5%, in addition it correctly identified five out of six cases of RIF resistant *MTB* with sensitivity and specificity (83 and 100%) respectively, the resistant cases were all previously treated with RIF. Sensitivity, specificity, positive and negative predictive value of Xpert *MTB*/RIF in comparison to conventional culture was 97.14, 100, 100 and 85.7%, respectively. The control group showed no positive results with the Xpert *MTB*/RIF. The sensitivity of Xpert for smear positive, culture positive *TB* was 100% and in smear negative, culture positive *TB* was 66.6% while its specificity in both was 100%. Comparing processed and unprocessed samples, the sensitivity of Xpert *MTB*/RIF was 94 and 97%, respectively while its specificity was 100% in both conditions. Thus, Xpert *MTB* /RIF outperformed smear microscopy, establishing a diagnosis in a proportion of patients with smear negative *MTB*, which detected many highly likely *MTB* by culture, and accurately ruled out rifampicin resistant *TB*.

Key words: Multi Drug Resistance Tuberculosis (MDR-TB), polymerase chain reaction (PCR), *Mycobacteruim tuberculosis* (MTB), extensively drug-resistant TB (XDR-TB).

INTRODUCTION

MDR-TB essentially means that the organism is resistant to both Isoniazid (ISN) and RIF drugs which is considered most effective in treatment of tuberculosis. Patients may be infected by already drug resistant strain or the resistance may develop in erstwhile susceptible strain in the course of treatment. XDR-TB is a form of *TB* caused by organisms that are resistant to ISN and RIF (that is, MDR-TB) as well as any fluoroquinolone and any of the second-line anti-TB injectable drugs (amikacin, kanamycin or capreomycin). About 3.7% of new *TB* patients in the world have MDRTB strains. Levels are much higher in those previously treated - about 20%. The frequency of MDR-TB varies substantially between countries. About 9% of MDR-TB cases also have resistance to two other classes of drugs, and hence fall into the XDR-TB category. By March 2013, eighty four

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countries had reported at least one XDR-TB case (WHO updates, 2013). In a nationwide survey in 2011, MDR-TB was found in 5.2 and 40.8% of patients with new and previously treated TB, respectively. These levels of drug resistance are among the highest ever documented in Africa and the Middle East. This finding presents a serious challenge for *TB* control (Sindani et al., 2013). Worldwide, substantial percentages (˜35%) of patients with drug-susceptible TB remain undiagnosed and a staggering percentage (˜85%) of patients with MDR-TB remains undiagnosed (WHO Global Report, 2011). Of the people diagnosed with *TB*, less than 3% are tested to determine the pattern of drug resistance (Chaisson, 2012). In addition to drug resistance, another major challenge is the accurate detection of smear-negative disease which disproportionately occurs in HIV-positive people with TB (Harries, 2004).

Egypt is ranked as a country with middle/ low level of tuberculosis incidence. It is estimated that 11 cases per 100 000 population develop active pulmonary smear positive *TB* annually, while 24 per 100 000 develop all types of *TB* annually. According to WHO TB profile for Egypt (2011), it reported that the new case detection rate of *TB* were as follows: smear positive (52%), smear negative (12%), smear not done (1%), extra pulmonary cases (36%) and as regards the retreatment cases were as follows: relapse (50%) and treatment failure (17%). In addition, WHO (2011) estimated MDR-TB burden in Egypt to be 3.4% for the new cases and 32% for the retreatment cases. Safwat et al. (2011) reported MDR-TB prevalence in Egypt to be around 0.5%, which is much less than that reported by WHO (2011). They posited that this difference underscores the need for better collection and analysis of data, transparency in information gathering, more departments for MDR-TB isolation in other governorates and better notification policy from private sector of health service. Global control of tuberculosis is hampered by slow, insensitive diagnostic methods, particularly for the detection of drug-resistant forms.

Early detection is essential to reduce the death rate and interrupt transmission, but the complexity and infrastructural needs of sensitive methods limit their accessibility and effect (Boehme et al., 2010). Conventional diagnostic methods for *MTB* are slow and/or lack sensitivity. It requires skilled technicians and tools, and lacked either timeliness or sensitivity. Culture methods are highly sensitive, but they take as long as two to six weeks to produce results and demand special materials to support the virulent micro bacteria in the culture. Although, sputum smear test is quicker and produces results in about 30 min, it can only detect 10 to 75% of TB cases and also requires trained persons. In developing countries, the technical expertise and tools needed to perform these tests are limited, and TB is often not diagnosed or treated early, which allows the disease to spread quickly in crowded living quarters and to build resistance to the drugs used in the treatment of the infection.

Current nucleic acid amplification methods to detect *MTB* are complex, labor-intensive and technically challenging. A number of new diagnostic approaches have brought incremental improvements to detection and drug susceptibility testing; however, the technical complexity of these assays and their dependence on sophisticated laboratory infrastructure have limited their adoption, especially in low-resource, high-burden settings (Balasingham et al., 2009; Migliori et al., 2008). The recently introduced Xpert MTB/RIF (manufactured and marketed by Cepheid, Sunnyvale, CA) assay simultaneously detects the presence of *M. tuberculosis* and its susceptibility to the important first-line drug RIF (Helb et al., 2010). It is unique because sample processing and PCR amplification and detection are integrated into a single self-enclosed test unit, the GeneXpert cartridge.

Following sample loading, all steps in the assay are completely automated and self-contained. In addition, the assay's sample reagent, used to liquefy sputum, has potent tuberculocidal (the ability to kill TB bacteria) properties and so largely eliminates biosafety concerns during the test procedure (Banada, 2010). The assay can be performed directly from a clinical sputum sample or from a decontaminated sputum pellet and can generally be completed in less than 2 h (Boehme et al., 2010). These features allow the technology to be taken out of a reference laboratory and used nearer to the patient (Small and Pai, 2011). Thus, investment in the tuberculosis diagnostics pipeline should remain a major priority for funders and researchers in various countries.

That is why the aim of our work was to evaluate the efficiency of Xpert *MTB*/ RIF assay in detecting *MTB* and MDR-*TB* as a point of care test in a sample of mycobacterium tuberculosis Egyptian patients in comparison to the conventional methods of *MTB* detection hopefully that Xpert *MTB*/RIF be used as a simple accurate system in detecting *M. tuberculosis* directly from sputum in less than 2 h thus controlling the spread of *MTB* and consequently the resistant strains in Egypt.

MATERIALS AND METHODS

Forty sputum specimens from adult patients with age from 33 to 58 years old strongly suspected by clinical parameters of having pulmonary tuberculosis as cough, night sweat, weight loss or fever, were studied from Abbassaia Chest Hospital, Cairo, Egypt. Ten external control patients with chest infection confirmed by culture to be bacterial other than *MTB* to exclude the cross reaction of Xpert *MTB* /RIF with other bacterial organisms. They were enrolled in the study in the period from January 2013 to August 2013. Verbal approval was taken from the patients. The following variables were collected through a questionnaire administered during sputum collection: patient sex, age, treatment history (new or previously treated), residence in Egypt. Cases were fallen in three categories: 1) not received anti-tuberculosis therapy, 2) had < 7 days of therapy, or 3) have not received therapy in the last 60 days. Xpert MTB/RIF assay was compared with conventional culture method for detecting *TB* and with conventional phenotypic drug susceptibility

Table 1. Comparative detection of *MTB* in sputum samples using three alternative test methods.

No. of specimens examined	Observed outcome per test Method					
	Microscopy (ZN staining)		Culture		Xpert *MTB*/RIF	
	No. positive (%)	No. negative (%)	No. positive (%)	No. negative (%)	No. positive (%)	No. negative (%)
40	31 (77.5)	9 (22.5)	34 (85)	6 (15)	33 (82.5)	7 (17.5)

testing for detecting RIF resistance. Eligible patients provided three sputum specimens each. Two specimens were processed with N-acetyl-L-cysteine and sodium hydroxide before microscopy, solid culture, and the *MTB*/RIF test, and one specimen was used for direct testing with the Xpert *MTB*/RIF test. Children were excluded from the study and specimens obtained by gastric aspiration were equally not included.

Processing of specimens

Specimens were processed within 24 h after collection. Modified Petroff's method using double the volume of NaOH (4%) was adopted. The specimens were kept in a shaker for homogenization and then decontaminated for 20 and 10 min respectively. The processing was stopped by the addition of distilled water up to the brim and centrifuging in a shielded centrifuge (3000 g) for 15 min. The supernatant fluid was then discarded and the sediment was used for inoculation by conventional methods. All specimens were subjected to Ziehl-Neelsen staining and smear grading as per the guidelines under the Revised National Tuberculosis Control Program (Rieder et al., 2008). The samples were cultivated on solid Lowenstein Jensen (LJ) medium and were subjected to species identification by a macroscopic analysis of colonies on LJ medium and microscopic analysis. In addition, complementary niacin, nitrate-reduction assay which is based on the ability of *MTB* to reduce nitrate to nitrite, which can easily be detected with specific reagents producing a color change were done. Initially, the test was performed on solid Löwenstein-Jensen medium with the addition of a NO_3 source. Antibiotics were added to the medium as per the classical proportion method. Reading of the results after induction of the color change performed within 7 to 14 days of incubation (Golyshevskia et al., 2006; Kristian et al., 2002). Etest (bioMerieux) is a predefined, stable gradient of 15 antibiotic concentrations on a plastic strip was used for MIC determination for a variety of antibiotic. RIF E test was used and was done based on BioMerieux application guide (2010). Results obtained within 5 to 15 days. This was compared with the Xpert *MTB*/RIF assay. The Xpert MTB/RIF assay and the GeneXpert instrument have been described in detail by Helb et al. (2010). In brief, the assay consists of a single-use multi chambered plastic cartridge preloaded with the liquid buffers and lyophilized reagent beads necessary for sample processing, DNA extraction and hemi nested real-time PCR. Clinical sputum samples or decontaminated sputum pellets that were treated with a NaOH and isopropanol-containing sample reagent (SR).

The SR is added to the sample at a 3:1 ratio for sputum pellets and 2:1 ratio for unprocessed sputum samples) and incubated at room temperature for 15 min. This step is designed to reduce the viability of *MTB* in sputum at least 10^6-fold to reduce risk of infection. The treated sample is transferred into the cartridge, the cartridge is loaded into the Gene Xpert instrument, and an automatic process completes the remaining assay steps. Following sample loading, all steps in the assay are completely automated and self-contained. The test material is combined with the assay sample reagent, mixed by hand or vortex, and incubated at room temperature for 15 min. After the incubation step, 2 ml of the treated sample are transferred to the cartridge and the run initiated (Helb, 2010). The assay cartridge also contains lyophilized *Bacillus globigii* spores which serve as an internal sample processing and PCR control. The spores are automatically resuspended and processed during the sample processing step, and the resulting *B. globigii* DNA is amplified during the PCR step. The standard user interface indicates the presence or absence of *MTB*, the presence or absence of RIF resistance, and a semi quantitative estimate of *MTB* concentration (high, medium, low and very low). Assays that are negative for *MTB* and also negative for the *B. globigii* internal control are reported as invalid.

The PCR assay amplifies a 192-bp segment of the *MTB rpoB* gene in a hemi nested real-time PCR. The internal control heminested *B. globigii* assay is multiplexed with the *MTB* assay. *MTB* is detected using five overlapping molecular beacon probes (probes A to E) that are complementary to the entire 81-bp RIF's resistance-determining "core" region of the wild-type *rpoB* gene (El-Hajj et al., 2001; Helb et al., 2010).

RESULTS

The study was performed on 40 sputum samples from patients presented with symptoms and signs of pulmonary tuberculosis. As shown in Table 1, conventional analyses, including Ziehl-Neelsen staining showed the presence of *MTB* infection in 31 samples (77.5%) and bacterial culture, showed the presence of *MTB* infection in 34 samples (85%). The performance of Xpert *MTB*/RIF for *MTB* and resistance to RIF were assessed with fully integrated sample processing in patients with suspected drug-sensitive or multidrug-resistant pulmonary tuberculosis. The *MTB*/RIF test provided detection of 33 cases of tuberculosis (82.5%) and correctly identified five out of six cases of RIF resistant *MTB* infection with sensitivity and specificity of 83 and 100%, respectively (Table 2). The control group showed no positive cases for *MTB.* Sensitivity, specificity, positive predictive value and negative predictive value of Xpert *MTB*/RIF in comparison to conventional culture technique were found to be 97.14, 100, 100 and 85.7%, respectively (Table 3). Among culture-positive patients, Xpert *MTB*/RIF test detected all 31 cases with smear-positive tuberculosis (100%) and an additional two cases out of nine with smear-negative tuberculosis (22.2%) thus the sensitivity of Xpert for smear positive, culture positive *TB* cases was 100% and its sensitivity in smear negative, culture positive *TB* cases was 66.6% (two out of three cases) and specificity

Table 2. Comparison of *MTB* detection by conventional culture and molecular techniques Xpert *MTB*/RIF.

		Conventional culture technique		Total
		Positive	Negative	
Molecular technique Xpert MTB/RIF	Positive	33	0	33
	Negative	1	6	7
	Total	34	6	40

Table 3. Sensitivity, specificity, positive predictive value and negative predictive value of Xpert *MTB*/RIF in comparison to conventional culture technique.

Sensitivity	TP/TP + FN 34/34 + 1	97.14%
Specificity	TN/FP + TN 7/0 + 7	100%
Positive predictive value (PPV)	TP/TP + FP 34/34 + 0	100%
Negative predictive value (NPV)	TN/TN + FN 6/6 + 1	85.6%

TP: True positive, FP: false positive, TN: true negative, FN: false negative; positive predictive value (PPV), negative predictive value (NPV).

Table 4. Comparison of the sensitivity and specificity of Xpert *MTB*/RIF when dealing with processed and unprocessed samples.

Type of analysis of the specimen	Sensitivity	Specificity
Unprocessed specimens	33/34 (97%)	6/6 (100%)
Processed Specimens	32/34 (94%)	6/6(100%)

is 100% in both cases. Among the 31 smear positive, culture positive cases, the study found that 6 cases were resistant to RIF by the conventional method (19.4%).

On revising the demographic and socioeconomic characteristics of these patients, it was found that they were males; aged 33 to 55 years and they were manual workers, heavy smokers that were previously treated from *TB* (acquired resistance).

Compared with the phenotypic drug susceptibility testing, Xpert *MTB*/RIF testing correctly identified five out of six cases (83.3%) RIF resistant *MTB* with sensitivity and specificity of 83 and 100%, respectively. On comparing the sensitivity and specificity of Xpert *MTB*/RIF when dealing with processed and unprocessed samples, the study showed that the sensitivity of Xpert *MTB*/RIF was 94 and 97% respectively while its specificity was 100% in both the processed and unprocessed samples (Table 4).

DISCUSSION

In this study, comparative detection of *MTB* in sputum samples from patients with pulmonary tuberculosis using three alternative test methods (ZN staining, conventional culture methods and Xpert MTB/RIF) were done and revealed 77.5, 85 and 82.5% of *MTB* respectively. The control group showed no positive cases by Xpert *MTB*/RIF. This is in line with Theron et al. (2011) who reported that Xpert *MTB*/RIF outperformed smear microscopy, established a diagnosis in a significant proportion of patients with smear-negative *TB*, detected many highly likely *TB* cases missed by culture. As well as Lawn et al. (2013) concluded that Xpert *MTB*/RIF assay is a rapid, accurate point-of-care diagnostic test that is affordable and can be readily implemented in urgently needed conditions. Helb et al. (2010) defined Xpert's limit of detection by "the lowest number of colony forming units per sample that can be reproducibly distinguished from negative samples with 95% confidence" (Cepheid, 2009), is 5 genome copies of purified DNA per reaction or 131 colony forming units per ml in *M. tuberculosis* spiked sputum. Toman (2004) previously mentioned that to see *TB* bacilli by microscopic examination, it requires at least 10,000 bacilli per ml of sputum. In addition, Xpert detects

both live and dead bacteria (Miotto, 2012). In addition, Lawn and Zumla (2011) laid stress that over 90% of *TB* cases develop among people living in low- and middle-income countries where diagnosis still relies heavily on the use of sputum smear microscopy and chest radiology. Despite microscopy being the diagnostic test most widely used worldwide, only 45% of *TB* cases that were notified in 2009 were sputum smear-positive, and these represented just 28% of the estimated total burden of incident disease globally.

WHO Global tuberculosis control 2010 focused attention on the lack of rapid and accurate diagnostics of *T.B*, which is undermining progress towards the 2015 millennium development goals for *TB* control. Such low rates of case ascertainment reflect the critical deficiency in diagnostic laboratory capacity. The study recorded that among the 31 smear positive, culture positive cases of *TB*, there were 6 cases rifampicin resistant (19.4%) by the conventional methods and E test. The studying of these cases showed that they were all previously rifampicin treated. Although, according to the WHO tuberculosis profile for Egypt 2011, the incidence of new cases of MDR-*TB* was 3.4%, while that of previously treated *TB* cases which was discovered to be MDR-*TB* was 32%. The difference in the values between this study and the WHO profile may be attributed to the small studied volume population, the methodology used and the type of samples collected weather they are pulmonary or extra pulmonary, more departments for MDR-TB isolation were needed. The present study is in line with a previous study done by Ali et al. (2011) in Egypt who reported that 19.5% of the 72 tested *mycobacterium* strains were resistant to each of ISN and RIF (MDR-TB), whereas 26.4% of these strains were susceptible. This indicated that these MDR-TB strains are initially resistant strains.

This recent study identified six cases as being RIF resistant MTB by the conventional method as well as by the Etest. On comparing this with Xpert MTB/RIF, it revealed five out of the six cases to be RIF resistant MTB with sensitivity 83% and specificity with 100%. This is in accordance with Blakemore et al. (2010) who spotlight that the *Xpert MTB*/RIF assay detects *MTB* and RIF's resistance by PCR amplification of the rifampin resistance-determining region (RRDR) of the *MTB rpoB* gene and subsequent probing of this region for mutations that are associated with RIF resistance. Approximately, 95% of RIF-resistant tuberculosis cases contain mutations in this 81-bp region (Van Der Zanden et al., 2003). Steingart et al. (2013) emphasized that Xpert can be used as an initial diagnostic test for TB detection and rifampicin resistance in patients suspected of having *TB*, MDR-*TB* or HIV-associated *TB*.

Xpert may also be valuable as an add-on test following microscopy for patients who have previously been found to be smear-negative as well as they stated that Xpert *MTB*/RIF when used replacing the conventional drug susceptibility, it can detect 94% of RIF resistant *T.B* with high specificity of 98%. The difference in this study and Steingart study could be attributed to volume of studied population, sputum processed method. Regarding the only case which is reported as rifampicin resistant by conventional method and rifampicin sensitive by Xpert *MTB/* RIF was revised and E test was repeated and recorded as borderline. This may clarify the difference in the results between the conventional and the Xpert *MTB*/ RIF method. In addition, this result can also be clarified by Lawn and Nickol (2011) who reported that to enable detection of rifampicin resistance by the Xpert, there must be present between 65 and 100% of the DNA from the rifampicin-resistant isolate depending on the mutation. They suggested that in patients with mixed infections, the Xpert *MTB*/RIF assay might only detect the resistant strain if it is the predominant one present. However, selection of resistant strains during the course of standard *TB* treatment might lead to an apparent switch from a susceptible to a resistant phenotype when comparing baseline testing with repeat testing during treatment. This may be the difference between the conventional phenoltypic drug susceptibility E test method and the Xpert assay. Thus, WHO recommended that if Xpert detects rifampicin resistance in patients considered at risk of MDR-TB, an appropriate MDR-TB regimen should be started while additional sputum specimens are obtained for culture and drug susceptibility testing.

Subsequent testing will confirm the presence of rifampicin resistance and enable testing for drug resistance to isoniazid and other first-line drugs and second-line drugs. Thus ideally, Xpert should be used at the district or sub district health facility level (WHO Policy Xpert, 2011). In the present study, sensitivity, specificity, positive predictive value and negative predictive value of Xpert *MTB*/RIF to detect *MTB* in comparison to conventional culture technique was found to be 97.14, 100, 100 and 85.7%, respectively. Thus, the *MTB/*RIF assay has a sensitivity that approximately approaches that of culture. This is with agreement with Bodmer et al. (2012) who stated that the Xpert *MTB*/RIF assay's overall clinical sensitivity of detecting MTB in sputum of patients with suspected pulmonary TB was 97.6% when compared to culture as the reference. There were also the findings of a prospective multi-center study that involved five study sites (Lima, Peru; Baku, Azerbaijan; Cape Town and Durban, South Africa; Mumbai, India) and a total of 1462 patients. Steingart et al. (2013) found that Xpert sensitivity for smear positive, culture positive *TB* was very high and consistent (98%), while Xpert sensitivity for smear negative, culture positive *TB* was lower and more variable (68%); this was in line to this study who reported the sensitivity of Xpert for smear positive, culture positive *TB* cases was very high (100%) and Xpert *MT*B/RIF sensitivity in smear negative, culture positive *TB* cases was lower (66.6%), two out of three cases and specificity for both is 100%. This present result can also be sup-

ported by study of pulmonary *TB* done by Vadwai et al. (2011) who reported that sensitivity was higher for smear-positive specimens (96%) compared with smear-negative specimens (64%). Thus, Boehme et al. (2011) drew atten-tion that patients with smear-negative *TB*, can make use of these Xpert assay results to reduce the time to start of treatment from 56 days [interquartile range (IQR) 39 to 81) to 5 days (IQR, 2 to 8). Rates of untreated smear-negative culture-positive TB decreased from 39.3% without Xpert to 14.7% using the assay to direct treatment initiation.

In this study, comparison in the sensitivity and specificity of Xpert *MTB*/RIF when dealing with processed and unprocessed samples was done and reported that the sensitivity of Xpert *MTB*/RIF was 94 and 97%, respectively. And as regards the specificity was 100% in both the processed and unprocessed samples. This is nearly in concordance with the study done by Steingart et al. (2013) who reported that the sensitivity of the Xpert between the processed and unprocessed samples was 85 and 91%, respectively and the specificity was 98 and 99%. The difference can be attributed to the difference in size of the studied population between the two studies, as well as to the sputum processing methods like time, rpm centrifugation as well as the condition of the sputum weather they are fresh or frozen. In addition, Boehme et al. (2010) reported that Xpert *MTB*/RIF test provided sensitive detection of tuberculosis and rifampin resis-tance directly from untreated sputum in less than 2 h. Helb et al. (2010) reported that Xpert *MTB*/RIF assay detect *MTB* complex DNA in sputum or concentrated sputum sediments. Thus, finally this present study under-lined the ability of the Xpert *MTB*/RIF assay to rapidly and reliably detect *TB* cases with sensitivity 97.14% and specificity 100% including nearly 66.6% of smear-nega-tive cases. Moreover, Xpert *MTB*/RIF achieved sensitivity of 88% and specificity 100% to RIF resistant *MTB.* In spite that it was limited by the small number of the studied cases and smear negative / culture positive *TB* cases.

Conclusively, the high sensitivity in smear positive and modest sensitivity in smear negative *TB*, along with high specificity of Xpert *MTB*/RIF mean that it may be used as the initial diagnostic test for *TB* detection in individuals suspected of having *TB* and MDR-*TB*. Xpert *MTB*/RIF may also be valuable as add on test following a negative smear microscopy result in patients suspected of having *TB*. In addition, the high sensitivity and specificity of Xpert *MTB*/RIF for RIF resistance detection mean that it may be used as an initial diagnostic test for RIF resistance. These results can be considered as an initial step to use Xpert *MTB*/RIF to control the spread of *TB* and MDR-*TB* in Egypt. Taking in consideration the obstacles faced by this study which is the small studied volume as it is not funded work as well the lack of previous studies done in Egypt by the same method to be comparable by our results in the same country. Lastly, the study suggests that future governmental funded researches should be done in Egypt to assess the diagnostic accuracy of Xpert *MTB*/RIF in peripheral laboratories and clinical settings, especially settings where the test is performed at the point of care on a large studied population.

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