

**Case Report**

# GeneXpert's Performance in the Diagnosis of Pulmonary and Extrapulmonary Tuberculosis

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**Abstract:** The diagnosis of tuberculosis is based on the isolation of acid-fast bacilli (AFB) on direct examination or on the culture isolation of mycobacteria tuberculosis complex (MCT). Currently, the introduction of molecular biology, essentially the Xpert / MTB / Rif or GeneXpertR test has increased the sensitivity and speed of diagnosis. The objective of our study is the evaluation of the performance of the Xpert / MTB / Rif molecular technique in the diagnosis of pulmonary and extrapulmonary tuberculosis. This is a descriptive retrospective study over a period of 22 months (June 2016 - April 2018). The study concerned all pulmonary and extrapulmonary specimens sent to the laboratory of bacteriology-virology and molecular biology of the HMA Marrakech for suspicion of tuberculosis. Diagnosis was performed on all specimens by direct examination on Ziehl-Neelsen stained smears, culture on Lowenstein Jensen solid medium (LJ) and GeneXpert molecular technical. Our study included 305 patients, 69% were men and 31% women. The clinical samples included in the study consisted of different specimens with a prevalence of sputum (n = 127). Positivity was higher for GeneXpert MTB / RIF than for Ziehl-Neelsen and culture with respectively 18% (n = 54) for GeneXpert against 13% (n = 40) for culture and 8% (n = 24) for Ziehl-Neelsen. On all positive direct examination specimens, GeneXpert was positive in 100% of cases, on negative direct examination samples, GeneXpert was positive in 5% of cases. The positivity rate of GeneXpert was 10.6% for samples with negative culture and 100% for positive culture samples. The performance of GeneXpert was variable depending on the nature of the samples: sputum (23%), biopsy (15%), pleural fluid (13%). Four cases of resistance to rifampicin have been detected. Our study shows the great contribution of GeneXpert for the diagnosis of pulmonary and extrapulmonary tuberculosis as well as its place in the determination of multidrug resistance.

**Keywords:** Tuberculosis, GeneXpert, Culture, Direct Examination

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## 1. Introduction

Tuberculosis is a real public health problem and is the leading infectious disease in the world with an overall incidence according to WHO of 10.4 million cases in 2016 [1]. It is estimated that nearly 2 billion people, or one third of the world's population, is the reservoir of bacilli [2]. Tuberculosis is responsible for 1.5 million deaths worldwide, 95% of which are in low- and middle-income countries [3]. In Morocco 27,745 new cases were recorded with an incidence of 82 new cases per 100,000 inhabitants and a predominance of

extrapulmonary tuberculosis [4]. The diagnosis of tuberculosis is based on the isolation of acid-fast bacilli (AFB) on direct examination or on isolation of mycobacteria tuberculosis complex (MCT) in culture. However, the detection of Mycobacterium tuberculosis complex in extrapulmonary locations remains difficult because of the presence of mycobacteria in small clinical samples compared to pulmonary infections [5]. Currently, the establishment of molecular biology, essentially the Xpert / MTB / Rif or GeneXpertR test that was approved by the WHO in December 2010, for the first-line diagnosis of pulmonary tuberculosis in

patients living with HIV or suspected of developing multidrug-resistant tuberculosis [6], this tool has increased the sensitivity and speed of diagnosis. However, the limit of PCR is its excessive cost. The objective of our study is the evaluation of the performance of the Xpert / MTB / Rif molecular technique in the diagnosis of pulmonary and extrapulmonary tuberculosis.

## 2. Materials and Methods

This is a retrospective descriptive and analytical study consisting of a collection from the laboratory of bacteriology-virology and molecular biology of the HMA Marrakech, the simultaneous results of Ziehl-Neelsen and GeneXpert MTB / RIF as well as the culture of 305 samples sent to our training for suspicion of tuberculosis. The study was carried out over a 22-month period from June 2016 to

April 2018. The diagnosis was made on all samples by direct examination on Ziehl-Neelsen stained smears, by culture on the solid medium of Lowenstein Jensen (LJ) and the molecular technique of GeneXpert. The study of rifampicin resistance was confirmed by GeneXpert MTB / RIF. The statistical data of our study were entered with the Microsoft Excel 2007 calculation software.

## 3. Results

Our study included 305 patients, 69% were men and 31% were women. The samples received came from different departments [Figure 1]. The clinical samples included in the study consisted mainly of sputum (n = 127), pleural fluid biopsies (n = 51) (n = 39), ascites fluid (n = 21), pus (n = 21), = 18), bronchial aspiration (n = 13) and CSF (n = 10) [Figure 2].

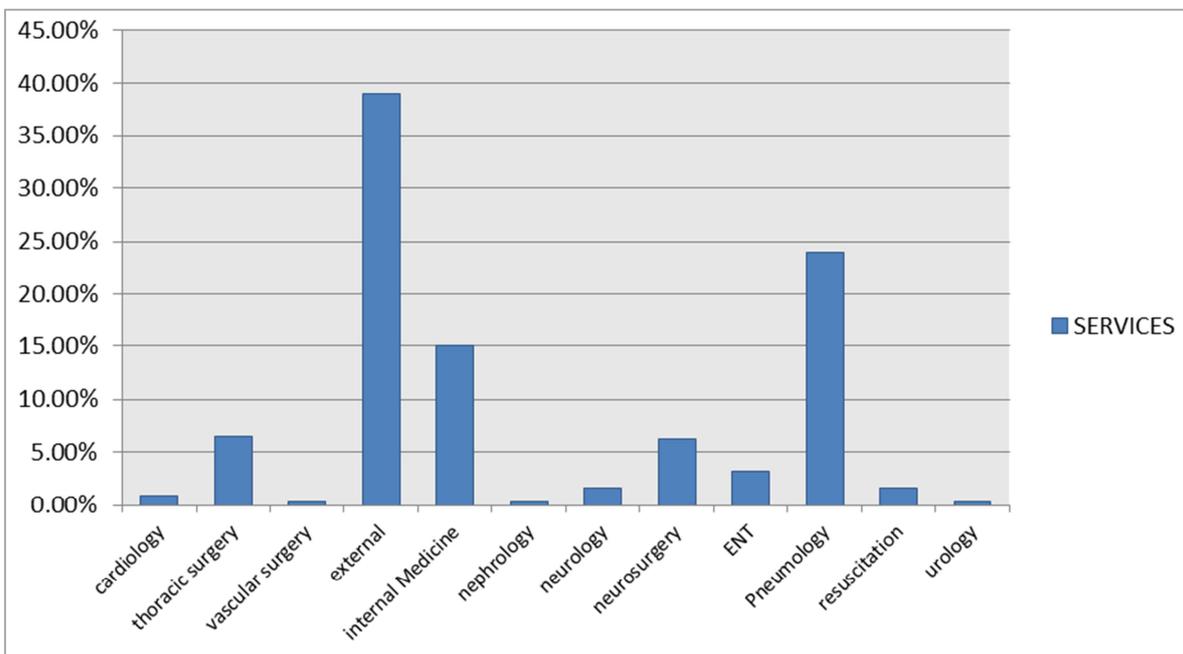


Figure 1. Distribution of samples by services.

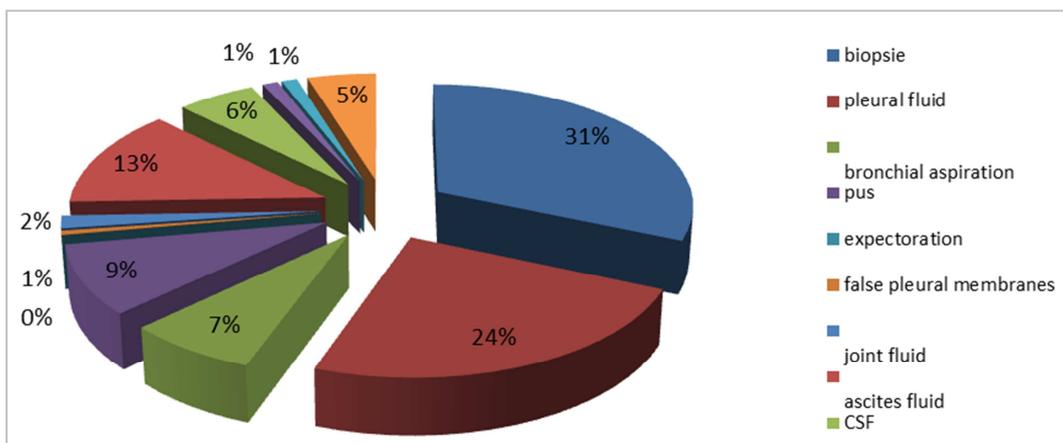


Figure 2. The clinical samples included in the study.

Positivity was higher for GeneXpert MTB / RIF than for Ziehl-Neelsen and culture with respectively 18% (n = 54) for

GeneXpert against 13% (n = 40) for culture and 8% (n = 24) for Ziehl-Neelsen [Figure 3]. The sensitivity and total specificity of GeneXpert was respectively 100% and 89%. On all positive direct examination specimens, GeneXpert was positive in 100% of cases, on negative direct examination samples, GeneXpert was positive in 5% of cases. The positivity rate of GeneXpert was 10.6% for culture-negative

samples and 100% for culture-positive samples. The positivity rate of GeneXpert was variable according to the nature of the samples: in the sputum (23%), in the biopsies (15%), in the pleural fluid (13%), however the sensitivity of GeneXpert for LCR, pleural fluid, Bronchial suction fluid, joint fluid and ascites fluid is 100%.

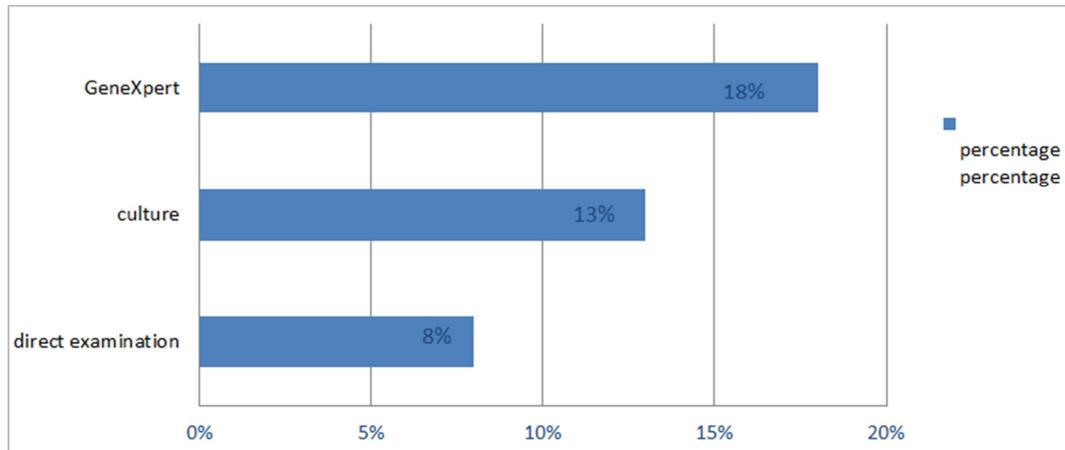


Figure 3. Positivity rate of GeneXpert compared to culture and direct examination.

Our study included 180 respiratory specimens including bronchial aspiration fluid, pleural fluid, protected distal specimens and sputum, of which 8% (n = 14) had a positive culture, 3% (n = 5) had a contaminated, while culture was sterile in 89.4% of cases (n = 161).

However GeneXpert was positive in 20% of the cases (n = 36), distributed as follows:

- 38% of cases (n = 14) had a positive culture.
- 55% of cases (n = 20) had a sterile culture.
- 5% of cases (n = 2) had a contaminated culture.

During the period of this study, we received 125 extra-respiratory specimens. The culture was positive in 3.2% of cases (n = 4), sterile in 88% (n = 111) and contaminated in 3.2% (n = 4). GeneXpert was positive in 14.4% of cases (n = 18), 10 of which had a negative culture.

Four cases of resistance to rifampicin were detected at a frequency of 7%.

## 4. Discussion

Tuberculosis is a contagious disease that comes under two nosological entities: latent tuberculosis infection and tuberculosis disease. The evolution towards tuberculosis disease is due to a certain number of factors, such as the risky medical acts (intubation, extubation, bronchial drainage by physiotherapy, necropsy), also the age less than 2 years, the immunosuppressive, the hematological malignancies, carcinoma of the head suddenly, type 2 diabetes, silicosis, weight loss, alcoholism is renal failure [7]. The diagnosis of tuberculosis is based on clinical and radiological arguments, but confirmation is necessarily bacteriological and / or histological. The culture remains the gold standard. Technological progress, especially in the field of molecular

biology, is providing the clinician with new means of diagnosing tuberculosis. The Xpert® MTB / RIF test has proved its usefulness in the diagnosis of tuberculosis [8], it is an automated real-time PCR that detects the presence of Mt along with the most frequent mutations (resistance rifampicin) in less than 2 hours [2]. The performance of GeneXpert in the diagnosis of pulmonary and extra-pulmonary tuberculosis is variable according to the studies [9]. In our study GeneXpert has a much higher sensitivity and specificity than Ziehl-Neelsen and culture. Our results are consistent with other studies that have confirmed the efficacy of GeneXpert in the diagnosis of pulmonary and extra-pulmonary tuberculosis [10].

On all positive direct examination specimens, GeneXpert was positive in 100% of cases, in direct negative specimens GeneXpert was positive in 5% of cases. This can be explained by the fact that the extraction of nucleic acids is done automatically in the cartridge, there is neither loss nor contamination by DNA [11]. The positivity rate of GeneXpert was 10.6% for culture-negative samples and 100% for culture-positive samples. These values are comparable to those obtained by other studies [12].

The performance of GeneXpert and culture over microscopy can be explained by the fact that the detection limits of culture and GeneXpert would be 10-100 CFU / ml and 131 CFU / ml respectively, whereas microscopy would be between 5,000 and 10,000 CFU / ml. [13]

GeneXpert's evaluation of the results and in comparison with the results of the culture, GeneXpert revealed a higher rate of positivity.

This makes GeneXpert a powerful tool for fast detection (about 2 hours) for MTB. An additional benefit of the GeneXpert MTB / RIF test is the modality of sample

processing when treated samples can be analyzed directly. [14]

In our study, the sensitivity of GeneXpert for CSF, pleural fluid, bronchial aspiration fluid, joint fluid and ascites fluid is 100%. Indeed, numerous studies have been able to show high sensitivity levels of GeneXpert in extra-pulmonary samples [12, 5]. These results confirm the good performance of GX in the diagnosis of TBEP despite the pauci bacillary nature of extrapulmonary clinical specimens.

The use of GeneXpert MTB / RIF detected a 7% resistance rate to Rifampicin, a marker for the prediction of multi-resistance for tuberculosis, this frequency remains lower than that found in other studies as well as to the WHO estimate of 10% [15].

A study conducted in Iran of the contribution of GeneXpert in the detection of rifampicin resistance has shown that GeneXpert can be a rapid and useful method for the diagnosis of rifampicin resistance. In addition, GeneXpert can provide results in a short time, as it is not necessary to wait for smear results as in the conventional method. As a result, the treatment can be started more quickly [16].

## 5. Conclusion

Our study shows the great contribution of GeneXpert for the diagnosis of tuberculosis and its place in the determination of multidrug resistance, allowing both a rapid diagnosis of tuberculosis and a good sensitivity and specificity. Thus the GeneXpert MTB / RIF test can be used as a confirmatory test for the detection of tuberculosis.

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