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GeneXpert MTB/RIF: A Useful Tool for Rapid and Accurate Diagnosis of Tuberculosis and Rifampicin Resistance

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1. Abstract

Aim

The primary objective of this study was to show the usefulness and importance of GeneXpert MTB/RIF, a rapid test that simultaneously detects *Mycobacterium tuberculosis* complex (MTBC) and resistance to rifampicin (RIF) in less than 2 hours.

Materials and Methods

We performed a retrospective study including 141 patients with a positive result in GeneXpert, admitted at the Clinical Hospital of Pneumology and Infectious Disease “Dr. Victor Babes” Timisoara, between January 2021 and December 2021. Pulmonary and extrapulmonary samples were examined and the results reported.

Results

Datas from 141 patients were analyzed. We included 99 males (70.2%) and 42 (29.8%) females, with a sex ratio M/F of 2.35. The mean age of the study group was 44.82 (range from 3 to 85 years old). 141 samples were obtained and analyzed from patients, including 129 pulmonary specimens (sputum samples, pleural fluid, bronchial aspirate, bronchoalveolar lavage) and 12 extrapulmonary specimens (gastric lavage, bone marrow aspirate, cerebrospinal fluid, lymph node aspirate, facial fistula secretion). GeneXpert was positive in all 141 cases (100%), including the samples where only traces of *Mycobacterium tuberculosis* were detected. Microscopy was positive in 87 patients (61.7%) and negative for 54 (38.3%) cases. MGIT culture tested positive in 136 cases (96.4%) with only 5 negative samples (3.6%). The cultures performed on Löwenstein-Jensen medium were positive in 138 cases and tested negative for only 3 patients. Rifampicin resistance gene was determined in 11 patients.

Conclusions

GeneXpert offers a rapid and accurate diagnosis of tuberculosis and detection of rifampicin resistance, establishing new horizons for early disease management [1]. The benefits of GeneXpert are evident in the diagnosis of clinical forms of tuberculosis and also in the diagnosis of rifampicin resistance [2].

2. Introduction

MTB still remains one of the main causes of death determined by an infectious agent (above HIV/AIDS) [1]. Every year worldwide, several million people fall ill with tuberculosis [3]. Rapid detection of *Mycobacterium tuberculosis* and rifampicin resistance in infected patients is crucial for early diagnosis and disease management, because of the high rates of transmission from an individual to another and development of multidrug – resistant tuberculosis (MDR - TB) and extensively drug – resistant tuberculosis (XDR - TB). Culture remains the "gold standard" for final diagnosis, but the determination is slow and the results may come up in 2 to 8 weeks. Smear microscopy for AFB (acid – fast bacili) is inexpensive and fast, but the sensitivity is very low. Therefore, rapid diagnosis leads to early treatment initiation, improves the outcome of patients and increases the public health awareness [4]. The GeneXpert MTB/RIF assay is an automated nucleic amplification test,that detects *Mycobacterium tuberculosis* complex and rifampicin resistance associated mutation [5]. The result is obtained in approximately 2 hours giving the clinician a rapid and accurate diagnosis and offering the patient the chance to early initiation of the treatment. The technique is endorsed by the World Health Organization (WHO) as the point – of – care test for diagnosis of pulmonary and extrapulmonary tuberculosis. The sensitivity of the test ranges from 72.5 to 98.2%, both in smear neagative and smear positive samples, and has a specificity of 98.2% [6,7]. It has many advantages, including easy to use, bio – safe, absence of sample contamination. The disadvantages include: shelf life of the cartridge of only 18 months, costs, temperature control, a stable electricity supply and annual recalibration of the analyzer [8].

3. Materials and Methods

We performed a retrospective study, which included 141 patients tested positive for MTB. All patients were admitted at the Clinical Hospital of Pneumology and Infectious Disease "Dr. Victor Babes" Timisoara, between January 2021 and December 2021. Tuberculosis diagnosis was suspected based on epidemiological and clinical findings and confirmed by radiological and laboratory findings. 141 samples were collected and analyzed: 129 pulmonary and 12 extrapulmonary samples. On all specimens collected, the following examinations were performed: microscopic examination, LPA, culture, MGIT culture and GeneXpert MTB/RIF. All the results were interpreted in the Hospital Laboratory and transmitted to clinicians for early diagnosis and treatment of the patients. The origin of the 129 pulmonary samples was as it follows: 114 sputum samples, 5 pleural fluid samples, 8 bronchial aspirate samples and 2 samples obtained by bronchoalveolar lavage. Extrapulmonary specimens were as it follows: 1 lymph node aspirate probe, 1 sample from facial fistula secretion, 7 gastric lavage samples, 2 bone marrow aspirate samples and 1 cerebrospinal fluid sample. The demographics of patients included age, sex and provenance medium (rural or urban). Smear microscopy was performed for all 141 patients. After growth of the culture, in cases in which *Mycobacterium tuberculosis* complex strains were identified, drug susceptibility testing was performed (Streptomycin, Isoniazid, Rifampicin, Ethambutol and Pyrazinamide resistance were also determined in order to identify MDR – TB or XDR - TB). All the procedures for GeneXpert assay were conducted according to the manufacturer's instructions [9]. In samples detected positive by the device, rifampicin resistance was also noted.

4. Results

141 positive samples were analyzed, all patients being admitted between January and December 2021. The male gender was predominant with 99 cases (70.2 %), for a sex ratio M/F of 2.35. The mean age was 44.82 (range from 3 to 85 years) and the age group of 31 to 60 years was the most represented with 60.2% or 85 cases. Males were predominant in the age group 31-60 and >60 years old, while women were predominant in the interval group <30 years. Divided by the provenience environment, most patients (77 – 54.6%) came from the city. The samples we analyzed comprised of pulmonary samples as sputum (n=114), pleural fluid (n=5), brochial aspirate (n=8), bronchoalveolar lavage (n=2) and extrapulmonary samples as lymph node aspirate (n=1), facial fistula secretion (n=1), gastric lavage (n=7), bone marrow aspirate (n=2) and cerebrospinal fluid (n=1). GeneXpert was positive in all 141 patients, no matter of their provenance (pulmonary or extrapulmonary). MGIT culture was performed in 137 of the 141 cases, 5 cases testing negative, but GeneXpert confirmed a positive result, because it's the only method that can detect MTB in cases with only traces of the infectious agent. Microscopic exam was performed for all 141 cases, testing negative in 54 cases. Culture on Löwenstein – Jensen tested negative for 3 patients. GeneXpert is by far the most accurate and rapid testing tool, providing a reliable result, even in cases in which culture or microscopy appear to be negative, due to small concentration of MTB. From 141 patients, 11 of them also tested positive for rifampicin resistance gene. All 11 patients were male, 7 of them (63.6 %) coming from the city environment. 8 of the patients tested positive for Isoniazide resistance as well, confirming MDR – TB. 3 from the 11 cases with rifampicin resistance, were also resistant to Streptomycin, Isoniazide, Ethambutol and Pyrazinamide.

5. Discussions

In the study, we investigated the performance of the MTB/RIF assay with pulmonary and extrapulmonary specimens obtained during the clinical routine. Tuberculosis is a public health threat, thus early detection is extremely important for reducing transmission and deaths. That's why it is important to have a rapid and accurate diagnosis test. Although smear microscopy is a rapid and inexpensive method to detect AFB, a low number of bacilli presented in the sample can lead to a negative report in smear microscopy. So, smear microscopy can easily miss such cases. Also, smear microscopy fails to differentiate MTB from MTB complex [10,11].

Culture still remains the gold standard for tuberculosis detection, but it demands a longer time for diagnosis extended up to 4 weeks [12,13]. That's why GeneXpert is a very reliable alternative, by improving diagnosis in smear – negative and culture – negative tuberculosis [14]. Being a molecular technique, GeneXpert detects the DNA of MTB (viable or non-viable). In cultures, only viable cells can grow [15,16]. GeneXpert also detects rifampicin resistance. Resistance to anti-tuberculosis drugs is currently one of the major challenges in the management of this disease [17,18]. In our case, we detected 11 cases of resistance to Rifampicin. 8 of them (72.7%) proved to be MDR – TB and 3 of them (27.2%) proved to be XDR – TB. Several studies report similar results [19,20,21].

6. Conclusions

In conclusion, GeneXpert MTB/RIF test depends less on the user's skills, has a short turnaround time and detects simultaneously MTB and RIF resistance and all that in less than 2 hours [22]. GeneXpert can help clinicians to make better and informed decisions in the management of tuberculosis cases. The findings in our study reflect that GeneXpert is a valuable inclusion in the fight against tuberculosis, providing precious advances in tuberculosis control campaigns. The Xpert assay has brought a major change in the speed, simplicity and accuracy, diagnosing not only tuberculosis, but also drug resistance to rifampicin. The utility of GeneXpert in diagnosis of pauci bacillary tuberculosis appears to be the most valuable contribution of this test.

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