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# Diagnostic yield of GeneXpert in bronchoalveolar lavage in smear-negative pulmonary tuberculosis

Thesis

*Submitted for Partial Fulfillment of Master Degree in Chest Diseases and Tuberculosis*

By

**Rana Mahmoud El-Touny**

*M.B.B.Ch*

Under Supervision of

**Prof. Emad El-Din AbdelWahab Koraa**

*Professor of Chest Diseases*

*Faculty of Medicine - Ain Shams University*

**Dr. Eman Badawy AbdelFattah**

*Assistant professor of Chest diseases*

*Faculty of Medicine - Ain Shams University*

*Faculty of Medicine*

*Ain Shams University*

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*Rana Mahmoud*

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# List of Abbreviations

| Abb. | Full term |
|---|---|
| AFB | Acid-fast bacilli |
| AIDS | Acquired immunodeficiency syndrome |
| ALT | Alanine aminotransferase |
| AST | Aspartate transaminase |
| BAL | Bronchoalveolar lavage |
| CECT | Contrast-enhanced CT |
| COPD | Chronic obstructive pulmonary disease |
| CT | Computed tomography |
| CT | Cycle threshold |
| DM | Diabetes mellitus |
| DNA | Deoxyribonucleic acid |
| DST | Drug susceptibility testing |
| ECDC | European Centre for Disease Prevention |
| FIND | Foundation of innovation New diagnostic |
| GERD | Gastroesophageal reflux disease |
| Hb | Hemoglobin |
| HIV | Human immunodeficiency virus |
| HTN | Hypertension |
| IHD | ischemic heart disease |
| INR | International normalized ratio |
| IPF | Idiopathic pulmonary fibrosis |
| IRB | Institutional Review Board |
| LED | Light-emitting diodes |
| LJ | Lowenstein Jenson |
| LPA | Line probe assay |
| MDRTB | Multidrug resistant tuberculosis |

# List of Abbreviations Cont...

| Abb. | Full term |
|---|---|
| MDR-TB | Multidrug-resistant tuberculosis |
| MTB | Mycobacterium tuberculosis complex |
| NAA | Nucleic acid amplification |
| NICE | National Institute for Health and Clinical Excellence |
| NIH | National Institute of Health |
| NTM | Nontuberculous mycobacteria |
| PAHO | Pan American Health Organization |
| PCR | Polymerase chain reaction |
| PLT | Platelet |
| PPD | Purified protein derivative |
| PPV | Positive predictive value |
| PT | Prothrombin Time |
| PTB | Pulmonary tuberculosis |
| RBCs | Red blood cell |
| RR-TB | Rifampicin-resistant TB |
| SR | Sample reagent |
| TB | Tuberculosis |
| TBB | Transbronchial biopsy |
| TLC | Total leucocyte count |
| WHO | World Health Organization |
| ZN | Zeihl Nelson |

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# INTRODUCTION

Tuberculosis (TB) continues to be one of the major endangering public health issues in the underdeveloped world. Microscopy examination of sputum smears for the revelation of acid-fast bacilli (AFB) and specific mycobacterial cultures have been the cornerstone in the diagnosis of pulmonary tuberculosis for many years. Mycobacterial culture (Löwenstein–Jensen) needs 3-6 weeks to grow. Hence, it cannot direct us to start the initial therapy in spite of being the gold standard and the most specific diagnostic test ***(Shin et al., 2012).***

Although sputum examination for acid-fast bacilli (AFB) is simple and economic, only 44% of cases are positive ***(Shin et al., 2012).*** In 2015, European Centre for Disease Prevention (ECDC) reported that, in Italy, in 2014, 68.1% of all TB cases were smear-negative ***(ECDC, 2015).*** Optimal management and better treatment response are not achieved in active smear-negative pulmonary tuberculosis due to delay in diagnosis and poor microbiological reliability ***(WHO, 2014).***

Xpert MTB/RIF is a completely automated real-time hemi-nested PCR system that detects both Mycobacterium tuberculosis complex (MTB) genome and mutations that cause rifampicin resistance. The Scientific and Technical Advisory Board of the World Health Organization has avowed lately this PCR system as the most sensitive quick test for TB diagnosis in

samples obtained from the respiratory system ***(WHO, 2011).*** This assay performs and integrates the steps of bacterial lysis, DNA extraction, amplification, and amplicon detection utilizing a disposable plastic cartridge thus working as a "lab-on-chip" device that runs on the GeneXpert platform and it only demands less than 2 hours for the results to be obtained ***(Lawn et al., 2012).***

# Aim of the Study

The Aim of the study is to assess the diagnostic yield of fiberoptic bronchoscopy guided bronchoalveolar lavage GeneXpert (Xpert MTB/RIF assay) in a smear-negative or sputum scant suspected case of pulmonary tuberculosis.

# Chapter 1

# PULMONARY TUBERCULOSIS

More than two billion people (about one-third of the world population) were estimated to be infected with *Mycobacterium tuberculosis*. In 2018, approximately 10 million individuals became ill with tuberculosis (TB), and 1.5 million died. Prompt diagnosis of active TB facilitates timely therapeutic intervention and minimizes community transmission ***(Bernardo, 2019)***.

The lungs are the major site for ***Mycobacterium tuberculosis*** primary infection and tuberculosis (TB) disease. Clinical manifestations of TB include primary TB, reactivation TB, laryngeal TB, endobronchial TB, lower lung field TB infection, and tuberculoma. Pulmonary complications of TB can include hemoptysis, pneumothorax, bronchiectasis, extensive pulmonary destruction, malignancy, and chronic pulmonary aspergillosis ***(Pozniak, 2019)***.

Pulmonary tuberculosis (PTB) is a contagious disease caused by Mycobacterium tuberculosis. This microorganism not only infects the lung (pulmonary TB) but also other organs such as brain, kidneys and lymph nodes (extra pulmonary TB) ***(Saldaña et al., 2014)***.

## Prevalence:

Tuberculosis (TB) constitutes a global public health problem with a greater impact in less industrialized countries. According to World Health Organization (WHO), there are around 8.7 million new cases every year out of which 0.5 million are children. The Pan American Health Organization (PAHO) notifies 250,000 cases each year with a yearly toll of around 20,000 deaths. It is estimated that in countries of low endemicity, tuberculosis in pediatric age represents less than 5% of all cases of tuberculosis while in high endemic countries; it could be as high as 20% ***(Saldaña et al., 2014)***.

## Risk Factors

Clinical suspicion for tuberculosis may be increased in patients with various risk factors. So, any individual at increased risk is eligible for targeted tuberculosis testing to identify and treat those with latent infection, prevent the development of active disease, and prevent further spread of tuberculosis. Risk factors for tuberculosis can be grouped into two categories:

- Factors that cause increased risk of exposure to tuberculosis,
  a) Individuals at increased risk of exposure include immigrants from endemic regions (Asia, Africa, Russia, Eastern Europe, and Latin America).
  b) Those with a low income and limited access to health care.
  c) Intravenous drug users.