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**ملاحظات:**





# **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*

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

# قَالَ

سَبَّحَانَكَ لَا إِلَهَ إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ  
الْعَلِيمُ الْعَظِيمُ

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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

**T**uberculosis (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**

**T**he 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

**M**ore 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.