Ain shams university
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# Evaluation of GeneXpert, as a new diagnostic tool for detection of pulmonary tuberculosis

Protocol for Thesis
Submitted for partial fulfillment of medical master degree in
Chest Diseases

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# List of abbreviations

AFB : Acid Fast Bacilli

BCG : Bacilli Calmette Guerin

CT : Computed Tomography

DOTS : Directly Observed Treatment Short-Course

DST : Drug susceptibility test

EQA : External Quality Assurance

FIND : Foundation For Innovative New Diagnostics

FN : False Negative

FOB : Freight on Board

FP : False Positive

GLI : Global Laboratory Innovation

Gx : GeneXpert

HIV : Human Immunodeficiency Virus

IFN-γ : Interferon gamma

IGRA : Interferon gamma Release assay

LPAs : Line Probe Assays

LTBI : Latent Tuberculosis Infection

MDR-TB : Multi-Drug Resistance Tuberculosis

MRI : Magnetic resonance imaging

MTB : Mycobacterium Tuberculosis

MTB/RIF : Mycobacterium Tuberculosis/ Rifampicin resistance

MTBC : Mycobacterium Tuberculosis Complex

NAAT : Nucleic Acid Amplification Test

NPV : Negative Predictive Value

NTP : National Tuberculosis Programme

PCR : Polymerase Chain Reaction

PPDs : Purified Protein Derivatives

PPV : Positive Predictive Value

SD : Standard Deviation

TB : Tuberculosis

TN : True Negative

TP : True Positive

TST : Tuberculin Skin Test

TU : Tuberculin Unit

WHO : World Health Organization

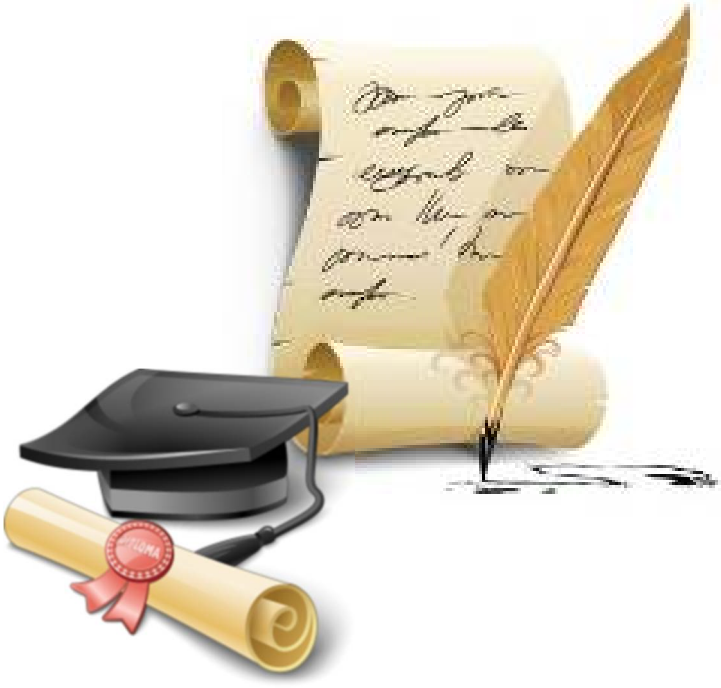
ZN : Ziehl- Neelsen

NK : Natural Killer

MDGs : Millennium Development Goals

SDGs : Sustainable Development Goals

# Introduction



# Introduction

What is now known as infection with *Mycobacterium tuberculosis* has plagued humanity since antiquity. Evidence of infection with tuberculosis has been identified in the bones of Egyptian mummies dating back to 3300 B.C., and was depicted in the artwork and texts from Mesopotamia dating to the seventh century B.C. **(Karamanou, 2012)**

Globally in 2014, there were an estimated 9.6 million incident cases of TB: 5.4 million among men, 3.2 million among women and 1.0 million among children.

Tuberculosis, poses a major problem for developing countries, as;

- 95 percent of all TB cases and 98 percent of TB death occur in developing countries.
- 75% percent of TB cases in developing countries are in the economically productive age group (15-50 years)
- Death from TB comprises 25 percent of all avoidable deaths in developing countries **(WHO, Global tuberculosis report, 2015).**

An adequate strategy for the control of tuberculosis (TB) globally calls for a comprehensive approach to address all the main constraints to control of the disease , including emerging challenges, as well as the main factors influencing the incidence of TB, such as socioeconomic and environmental aspects. Consequently, the scope of activities undertaken by national TB control programmes (NTPs) has increased. **( WHO, Implementing The Stop TB Strategy, 2008 )**

The year 2015 is a watershed moment in the battle against tuberculosis (TB). It marks the deadline for global TB targets set in the

context of the Millennium Development Goals (MDGs), and is a year of transitions: from the MDGs to a new era of Sustainable Development Goals (SDGs), and from the Stop TB Strategy to the End TB Strategy.

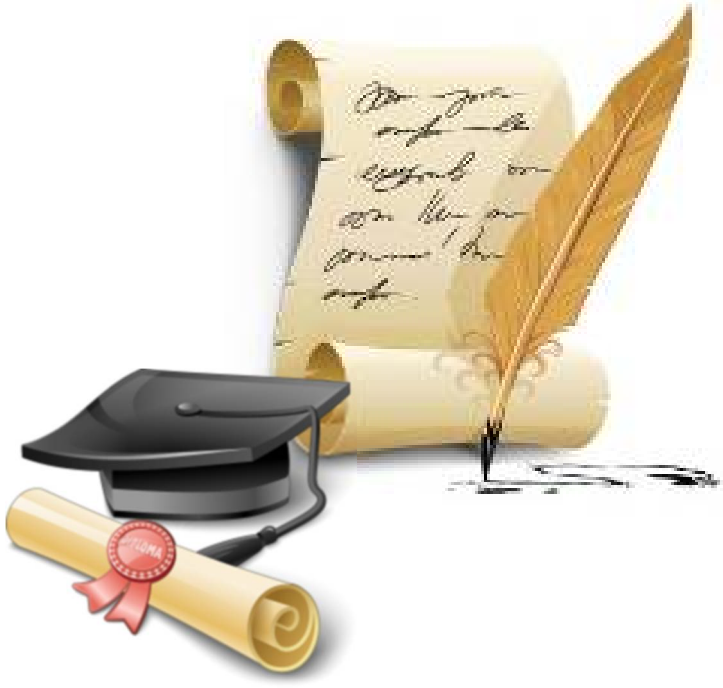
From 2016, the goal is to end the global TB epidemic by implementing the End TB Strategy. Adopted by the World Health Assembly in May 2014 and with targets linked to the newly adopted SDGs, the strategy serves as a blueprint for countries to reduce the number of TB deaths by 90% by 2030 (compared with 2015 levels), cut new cases by 80% and ensure that no family is burdened with catastrophic costs due to TB. **(WHO, Global Tuberculosis Report, 20th edition, 2015)**

While sputum smear microscopy is the first bacteriological diagnostic test of choice where adequate, quality–assured laboratory facilities are available, the evaluation of patients with negative sputum smears should also include culture. Culture adds extra cost and complexity but greatly increases the sensitivity and specificity of diagnosis, resulting in better case detection. **(WHO, Implementing The Stop TB Strategy, 2008)**

The only WHO-recommended rapid diagnostic test for detection of TB and rifampicin resistance currently available is the Xpert MTB/RIF® assay. Of the 48 countries in at least one of the three new lists of high burden countries, 15 had adopted national algorithms positioning Xpert MTB/RIF as the initial diagnostic test for all people with signs and symptoms of pulmonary TB by the end of 2015. These countries accounted for 10% of the estimated global number of incident TB cases in 2015. **(WHO, NTP Egypt, 2017)**

The Xpert MTB/RIF assay is a new test that is revolutionizing tuberculosis (TB) control by contributing to the rapid diagnosis of TB disease and drug resistance. The test simultaneously detects Mycobacterium tuberculosis complex (MTBC) and resistance to rifampin (RIF) in less than 2 hours. In comparison, standard cultures can take 2 to 6 weeks for MTBC to grow and conventional drug resistance tests can add 3 more weeks. The information provided by the Xpert MTB/RIF assay aids in selecting treatment regimens and reaching infection control decisions quickly. **(CDC, A New Tool to Diagnose Tuberculosis, 2013)**

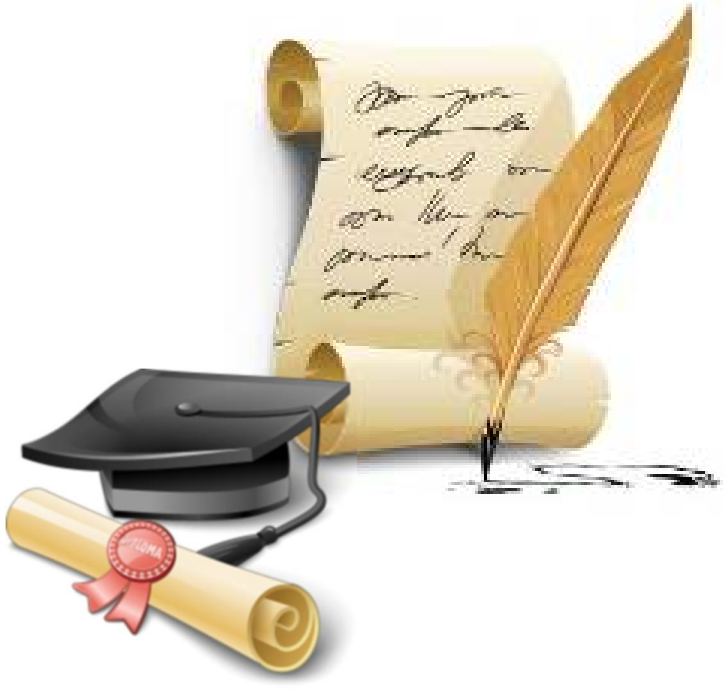
# Aim of the Work



# Aim of the work

**Aim of the Study is** to evaluate the genexpert test in diagnosis of pulmonary tuberculosis in comparison with Z-N smear as a highly sensitive, specific and rapid laboratory tool coincident with LJ culture as a standard test.

# Review of Literature



# Review of Literature

## Background

Consumption, phthisis, scrofula, Pott's disease, and the White Plague are all terms used to refer to tuberculosis throughout history.

Signs of the disease have been found in Egyptian mummies dated between 3000 and 2400 BCE. It appears likely that **Akhenaten** and his wife **Nefertiti** both died from tuberculosis, and evidence indicates that hospitals for tuberculosis existed in Egypt as early as 1500 BCE

In 460 BC, **Hippocrates** identified phthisis (Greek word meaning "consumption") as the most widespread disease of the times and notes that is almost always fatal. In 1882, **Koch** identified the tubercle bacillus and convicts it of causing tuberculosis. **(MOH, NTP Egypt, 2017)**

## Epidemiology

The highest incidence is in sub-Saharan Africa (290 cases per 100,000 populations). High population density countries in Asia (India, China, Pakistan, and Indonesia) account for half the global burden. The countries comprising the former Soviet Union have rapidly increasing rates, because of economic decline, and failing health services, with around 10% multidrug resistance in this area. Globally, around 11% of TB cases are co-infected with HIV, with this number increasing to 38% in sub Saharan Africa, and less than 1% in India and China. **(Chapman et al, 2014)**