Evaluation of Performance of Quantiferon Test in Suspected Pulmonary Tuberculosis Patients in Abassia Chest Hospital

Thesis

Submitted for Partial Fulfillment of the MD Degree in Chest Diseases

By

Eman Abd Al Halem Abd Alah Al Kholy
M.B.B.ch.M.S.C.
Faculty of Medicine, Ain Shams University

Supervised by

Prof. Dr. Laila Ashor Mohammad Helala
Professor of Chest Diseases
Faculty of Medicine Ain ShamsUniversity

Dr. Tamer Mohamed Ali
Assistant Professor of Chest Diseases
Faculty of Medicine Ain ShamsUniversity

Dr. Ashraf Abbas Al Maraghy
Assistant Professor of Chest Diseases
Faculty of Medicine AinShamsUniversity

Dr. Mohammad Samer Abbas
MD Clinical Pathology
Head of Medical Labs in Abbassia Chest Hospital

Faculty of Medicine - Ain Shams University
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Eman Abd Al Halem

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List of Abbreviations

Abb.	Full term
ADA	*Adenosine Deaminase*
AFB	*Acid-Fast-Bacilli*
AG	*Antigen*
AIDS	*Acquired immune deficiency syndrome*
AMTD	*Amplified M. Tuberculosis direct test*
ART	*Antiretroviral Therapy*
AUC	*Area under Curve*
BCG	*Bacille Calmette and Guerin*
CFP10	*Culture Filtrate Protein 10*
DNA	*Deoxyribonucleic acid*
DOTS	*Directly-Observed Treatment Short Course*
DST	*Drug-Susceptibility Testing*
E. coli	*Escherichia coli*
ECDC	*European Centre for Disease Prevention and Control*
ELISA	*Enzyme Linked Immunoassay*
ELISPOT	*Enzyme-Linked Immunospot*
ESAT6	*Early Secretory Antigen Target 6*
FDA	*Food and Drug Administration*
HBC	*High Burden Country*
HCWs	*Health Care Workers*
HIV	*Human Immunodeficiency Virus*
IFN-γ	*Interferon Gamma*
IGRAs	*Interferon-Gamma Release Assays*
IL	*Interleukin*
INH	*Isoniazid*
IU	*International Units*
LMIC	*Low-Middle Income Country*

List of Abbreviations (Cont...)

Abb.	Full term
LTBI	*Latent Tuberculosis Infection*
M. africanum	*Mycobacterium africanum*
M. bovis	*Mycobacterium bovis*
M. leprae	*Mycobacterium leprae*
M. microti	*Mycobacterium microti*
M. tuberculosis	*Mycobacterium tuberculosis*
M. tuberculosis complex	*Mycobacterium tuberculosis complex*
MDG	*Millennium Development Goal*
MDR-TB	*Multidrug-Resistant Tuberculosis*
MGIT	*Mycobacteria Growth Indicator Tube*
MIRU	*Mycobacterial Interspersed Repetitive Units*
Mtb	*Mycobacterium tuberculosis*
NAA	*Nucleic Acid Amplification*
NICE	*National Institute for Health and Clinical Excellence*
NTM	*Nontuberculous mycobacteria*
OD	*Optical Density*
PCR	*Polymerase Chain Reaction*
PHC	*Primary Health Care*
PPD	*Purified Protein Derivative*
PTB	*Pulmonary Tuberculosis*
PUO	*Pyrexia of Unknown Origin*
QFT-G	*QuantiFERON-TB Gold test*
QFT-GIT	*QuantiFERON–TB Gold In-Tube test*
RD1	*Region of Difference 1*
RFLP	*Restriction Fragment Length Polymorphism*
RIF	*Rifampin*

List of Abbreviations (Cont...)

Abb.	Full term
ROC	*Receiver Operator Curve*
rpf	*Resuscitating Promoting Factors*
SD	*Standard Deviation*
SDGs	*Sustainable Development Goals*
TB	*Tuberculosis*
Th	*T helper*
TNF	*Tumor necrosis factor*
TPE	*Tuberculous Pleural Effusions*
TST	*Tuberculin Skin Test*
US	*United States*
WHO	*World Health Organization*
Wt	*Weight*
XDR TB	*Extensively Drug-Resistant Tuberculosis*
ZN	*Ziehl-Neelsen*

INTRODUCTION

TB is a contagious and often severe airborne disease caused by infection with Mycobacterium tuberculosis (Mtb), TB typically affects the lungs, but it also can affect any other organ of the body. It is usually treated with a regimen of drugs taken for 6 months to 2 years depending on the type of infection ***(National Center for Biotechnology Information, 2014),*** overall, a relatively small proportion of people infected with *M. tuberculosis* will develop TB disease. However, the probability of developing TB is much higher among people infected with HIV ***(WHO, 2014),*** the majority of TB cases occurred in large urban centers, amongst young adults, those from countries with high TB burdens, and those with social risk factors for TB ***(Annual report on tuberculosis surveillance in the UK, 2009).***

TB ranks as the second leading cause of death from an infectious disease worldwide, after the human immunodeficiency virus (HIV), there were 9.0 million new TB cases in 2013 and 1.5 million TB deaths (1.1 million among HIV-negative people and 0.4 million among HIV-positive people) ***(WHO, 2014),*** the eastern mediterranian Region is responsible for about 6–7% of the global burden of TB, with an estimated 670 000 TB cases in 2013 and an incidence rate of 109 per 100 000 population ***(WHO, 2015).***

- **Role of quantiferon test in TB diagnosis:**

According to Centers for Disease Control and Prevention, 2014:

TB blood tests: TB blood tests (also called interferon-gamma release assays or IGRAs) measure how the immune system reacts to the bacteria that cause TB. An IGRA measures how strong a person's immune system reacts to TB bacteria by testing the person's blood in a laboratory.

Two IGRAs are approved by the U.S. Food and Drug Administration (FDA) and are available in the United States:

1. QuantiFERON–TB Gold In-Tube test (QFT-GIT)
2. T-SPOT.TB test (T-Spot)

   - **Positive IGRA:** This means that the person has been infected with TB bacteria. Additional tests are needed to determine if the person has latent TB infection or TB disease. A health care worker will then provide treatment as needed.
   - **Negative IGRA:** This means that the person's blood did not react to the test and that latent TB infection or TB disease is not likely.

Table (1): Cut off values of quantiferon test

Nil (IU/ml)	TB Antigen minus Nil (IU/ml)	Mitogen minus Nil (IU/ml)*	QFT result	Report/Interpretation
≤ 8.0	< 0.35	≥ 0.5	Negative	M. tuberculosis infection NOT Likely
	≥ 0.35 and <25% of nil value	≥ 0.5	Negative	M. tuberculosis infection NOT Likely
	≥ 0.35 and ≥25% of nil value	Any	Positive↑	M. tuberculosis infection likely
	< 0.35	< 0.5	Indeterminate↕	Results are indeterminate for TB-Antigen responsiveness
	≥ 0.35 and <25% of nil value	< 0.5	Indeterminate↕	Results are indeterminate for TB-Antigen responsiveness
> 8.0§	Any	Any	Indeterminate↕	Results are indeterminate for TB-Antigen responsiveness

* Responses to the Mitogen positive control (and occasionally TB Antigen) can be commonly outside the range of the microplate reader. This has no impact on test results.

↑Where M. tuberculosis infection is not suspected, initially positive results can be confirmed by retesting the original plasma samples in duplicate in the QFT ELISA. If repeat testing of one or both replicates is positive, the individual should be considered test positive.

↕Refer to the troubleshooting section for possible causes.

§In clinical studies, less than 0.25% of subjects had IFN-γ levels of > 8.0 IU/ml for the Nil value.