Role of Quantiferon Gold Assay in Detection and Follow-up of treatment of Latent Tuberculosis infection in some of acquired immune compromised patients

Thesis

Submitted for Partial Fulfillment of MD Degree
In Chest Diseases and Tuberculosis

By

Azza Hassan Hassan
M.Sc. of Chest Diseases and Tuberculosis
Ain Shams University

Supervised by

Prof. Dr.Emad Eldin Abdel Wahab Korraa
Professor of Chest Diseases and Tuberculosis
Faculty of Medicine - Ain Shams University

Prof. Dr. Ibrahim Aly Dwedar
Professor of Chest Diseases and Tuberculosis
Faculty of Medicine - Ain shams University

Dr. Eman Badawy Abdel Fattah
Assistant Professor of Chest Diseases and Tuberculosis
Faculty of Medicine - Ain shams University

Faculty of Medicine
Ain Shams University
2019


بسم الله الرحمن الرحيم
وَقُل رَّبِّ
زِدْنِي عِلْمًا
صدق الله العظيم
سورة طه آيه ١١٤

Acknowledgement

Chapter 1 The only thanks to ALLAH, who enabled me to carry out this work, and every work.

Chapter 2 Great appreciation to ***Prof. Emad Eldin Abdel Wahab Korraa, Professor of Pulmonology, Ain shams University.*** He continuously followed my work and pushed me forward.

My deep and sincere gratitude to ***Prof. Ibrahim Aly Dwedar, Professor of Pulmonology, Ain Shams University.*** His advices, support and encouragement have been invaluable throughout the work.

I am indebted to ***Dr. Eman Badawy Abdel Fattah, Assistant Professor of Pulmonology, Ain Shams University.*** She has continuously revised and evaluated my work with a combination of scientific advices and encouraging words. She has been hand in hand with me throughout all phases of this work.

Azza Hassan

List of Contents

List of Abbreviations

#P .....P value

ACE .....Angiotensin-converting enzyme

acr .....Alpha-crystallin-like heat shock protein

ADA .....American Diabetes Association

AFB .....Acid Fast Bacilli

AIDS .....Acquired immunodeficiency syndrome

AII .....Airborne infection isolation

ALT.....Alanine Aminotransferase

AP.....Activator protein

AST.....Aspartate Aminotransferase

ATS.....American thoracic society

BAL.....Bronchoalveolar lavage

BALB/c.....Bagg Albino (In bred research mouse strain)

BCG .....Bacillus Calmette–Guérin

BMI.....Body mass index

CBC .....Complete blood count

CDC .....Center of disease control and prevention

CFP-10 .....Culture filtrate Protein-10

CFU .....Colony forming units

cmaA2 .....cyclopropane-mycolic acid synthase 2

COX.....Cyclooxygenase

CR .....Complement receptor

CT.....Computed tomography

CTL.....Cytotoxic T lymphocyte

DM.....Diabetes mellitus

DM-TB .....Diabetic and tuberculosis

List of Abbreviations

DN .....double negative

DOT.....Directly observed therapy

DTH.....Delayed-type hypersensitivity

ELISA .....Enzyme-linked immunosorbent assays

ESAT-6 .....Early secretory antigenic target-6

ESR .....Erthrocyte sedimentation rate

ESX-1.....Early secretory antigenic target secretion system 1

FBG .....Fasting blood glucose

FDA .....Food and drud administration

GREs .....Glucocorticoids responsive elements

gp.....glycoprotein

HbA1c.....Glycosated hemoglobin

HCWs.....Health care workers

HEPA.....High Efficiency Particulate Air

HIV .....Human immunodeficiency virus

HLA Class.....Human Leukocyte Antigen

ICL.....Isocitrate lyase

IDDM ..... insulin dependent diabetes mellitus

IFG .....Impaired fasting glucose

IFN .....Interferon

IgE.....Immunoglobulin E

IgM .....Immunogloubin M

IGRA.....Interferon gamma release assay

IGT .....Impaired glucose tolerance

IL.....Interleukotriens

INH .....Isoniazid

List of Abbreviations

Ipr1 .....Intracellular pathogen resistance 1

LAM.....Lipoarabinomannan

LTBI .....Latent tuberculosis infection

LppX.....LipoproteinX

LRTIs.....Lower respiratory tract infections

MAPK .....mitogen-activated protein kinase

Mce.....Mycobacterial cell entry protein

MCH .....Major histocompatibility complex

MDR .....Multi Drug Resistance

Msr..... methionine sulfoxide reductase

MTB.....Mycobacterial tuberculosis

NF-kB .....nuclear factor-kappa-B

NIDDM.....non- insulin dependent diabetes mellitus

NOS2 .....Inducible nitric oxide synthase

NRP .....non replicating persistent

NTM.....Non-tuberculous mycobacteria

NTP.....National Tuberculosis Program

PBMCs.....Peripheral blood mononuclear cells

pcaA..... cyclopropane synthase gene

PCR .....Polymerase chain reaction.

PDIM .....Phthiocerol dimycocerosates

PGL.....Phenolic glycolipid

PLA2.....phospholipase A2

PPD.....protein purified derivative

PPG .....Post prandial glucose

PZA.....pyrazinamide

List of Abbreviations

QFT-G.....Quantiferon Gold assay test

QFT-2G..... Quantiferon second generation

QFT-GIT .....Quantiferon gold assay test in tube

QFT-TB.....Quantiferon –Tuberculosis

RANTES.....Regulated on Activation, Normal T Cell Expressed and Secreted

RD1 .....Region of difference 1

RIF .....Rifampin

RNIs .....Reactive nitrogen intermediates

ROIs .....Reactive oxygen intermediates

RPT .....Rifapentine

SCID .....Sever combined immunodeficient

SD.....Standard deviation

SLAP1.....src-like adapter protein-1

TAP.....transporter associated with antigen processing

TAT .....Twin arginine transporter

TB.....Tuberculosis

TCH .....Thiophen-2-carboxylic acid hydrazide

TCR .....T Cell Receptor

TDM.....Trehalose dimycolate glycolipid

TGF-beta .....transforming growth factor-beta

THP Cells .....Human Monocytic Cell

TLR .....Toll-like receptors

TNF .....Tumor necrosis factor

TST.....Tuberculin skin test

WHO .....World Health Organization

ZN.....Ziehl-Nielsen

List of Tables

List of Tables (Continued)

List of Tables (Continued)

Table No.	Title	Page

List of Figures

Abstract

Background: In patients latently infected with Mycobacterium tuberculosis, immunosuppression increases the risk of progression to active tuberculosis (TB), which is still considered one of the difficult and frequent opportunistic infections worldwide. Better specificity in the diagnosis of latent tuberculosis infection (LTBI) is shown by Quantiferon-TB Gold In-Tube (QFT-GIT), and has been accepted in many national TB programs in low-endemic countries; QFT-GIT relies on detection of the immune reaction to specific M. tuberculosis antigens, which are not found in Bacillus Calmette–Guérin (BCG) or certain non-TB mycobacteria.

Aim: The aim of this study is to determine the role of the QFT-GIT assay in the detection and follow-up of treatment of latent tuberculosis (LTB) in some acquired immune- compromised patients.

Participants and methods: This prospective study was carried out on 50 immune-compromised patients attending the Abbassia Chest Hospital (either as inpatients or as outpatients). All patients were subjected to an assessment of history and clinical examination, radiological work-up, and laboratory investigations. All patients enrolled in the study were sputum negative for acid-fast Bacilli by Ziehl–Neelsen stain. Both the tuberculin skin test (TST) using the Mantoux technique and the QFT-GIT assay were performed simultaneously and their results were statistically compared, and then QFT-GIT was repeated after preventive treatment.

Results: The sensitivity of QFT-GIT was 20.8% and the sensitivity of TST was 12.5%. The frequency of LTB according to TST was only two (4.5%), that of the QFT-GIT test was only six (12.5%), and that of both QFT-GIT and TST was four (8.3%). Positive QFT-GIT was greater in patients receiving steroids, whereas indeterminate results were found only among HIV patients. Also, positive TST was greater among patients receiving steroids. There was a statistically significant difference between the CD4 count and the results of Quantiferon in HIV patients; indeterminate results were found in patients with CD4 less than 200 cells/mm^3. There was a statistically significant reduction in quantitative QFT-GIT in LTB patients after preventive treatment.

Conclusion: The QFT-GIT assay seems to be more sensitive for the detection of LTBI in immune-compromised patients compared with the TST; however, QFT-GIT gave a considerable proportion of indeterminate results among HIV infected patients. Therefore, the simultaneous use of both TST and QFT-GIT could maximize the screening efficacy for LTBI in immune-compromised patients. The quantitative QFT-GIT assay can be used to monitor the effect of preventive treatment.

Keywords:
Immune-compromised, latent tuberculosis infection, Quantiferon-TB Gold-in-Tube