



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

Thesis

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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-κB	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

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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/mm³.

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