Hepatitis B Surface Antigen Detection, Qualitative Versus Quantitative: A comparative study

Thesis

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وأنزل الله عليك
الكتاب والحكمة
وعَلَّمَكَ مَا لَمْ تَكُن
تَعْلَمُ وكَانَ فَضْلُ اللَّهِ
عَلَيْكَ عَظِيماً
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Dedication

I would like to dedicate this thesis to allmembers inMy **Family,** *specially,* **Mother and Father for** *supporting me and pushing me forward all the time.*

Special dedication to my **Husband** *for dealing tactfully and patiently during this work.*

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List of Abbreviations

Abbrev.	Full term
ADV	Adefovir
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
Anti-HBc	Antibody to hepatitis B core antigen
Anti-HBs	Antibody to hepatitis B surface antigen
anti-HBx	Anti hepatitis B x
APC	Antigen presenting cell
AST	Asprtate Transaminase
BCR	B cell receptor
BDL	Below detection limit
BL	Borderline
BSA	Bovin serum albumin
cccDNA	Covalently closed circular DNA
CD	Cluster of Differentiation
CDC	Centers of disease control and prevention
CEDIA	Cloned enzyme donor immunoassay
CHB	Chronic hepatitis b
CMIA	Chemilumescent microparticle immunoassay
CTL	Cytotoxic T lymphocyte
DC	Dendritic cell
DNA	Deoxyribonucleic acid
DR	Direct repeats
ECLIA	Electrochemiluminescence
EIA	Enzyme immunoassay
ELISA	Enzyme linked immunosorbent assay
EMIT	Enzyme multiplied immunoassay technique
ER	Endoplasmic reticulum
ETV	Entecavir

List of Abbreviations *(Cont...)*

FasL	Fas Ligand
FIA	Florescent immunoassay
FPIA	Fluorescence polarization immunoassay
GGT	Gamma-glutamyltransferase
GM-CSF	Granulocyte-macrophage colony-stimulating factor
HAS	The French National Authority for Health
HBcAg	Hepatitis B core antigen
HBeAg	Hepatitis B envelope antigen
HBIG	Hepatitis B immunoglobulin
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HBx	Hepatitis B virus x protein
HCC	Hepatocellular carcinoma
HCG	Human chorionic gonadotropin
HCV	Hepatitis C virus
HDV	Hepatitis delta virus
HIG	Human immunoglobulin G
HIV	Human immune deficiency virus
HRP	Horseradish peroxidase
HS	Highly significant
HSPGs	Heparan sulphate proteoglycanes
I125	125 Iodine
IC	Immune clearance
ICU	Intensive care unit
IFN	Interferon
IFN-α/β	Interferon alpha/beta
IFN-γ	Interferon gamma
Ig	Immunoglobulin
IgG antibodies	Immunoglobulin G antibody
IgM Anti-HBc	Immunoglobin M Antibody to hepatitis B core
IgMHBcAb	Immunoglobulin M hepatitis B core antibody

List of Abbreviations *(Cont...)*

IHL	Intra-hepatic lymphocytes
IL	Interleukin
INF	Interferon
IQR	Interquartile range
IRF	Interferon regulatory factor
IRMA	Immunoradiometric assay
IT	Immune-tolerant carrier
LAM	Lamivudine
LC	Low replicative phase
Ldt	Telbivudine
LHB	Large hepatitis B proteins
LN	Lymph node
MDA5	Melanoma differentiation associated gene 5
mDC	Myeloid dendritic cell
MEIA	Microparticle Enzyme Immunoassay
MHB	Middle hepatitis B proteins
MHC	Major histocompatibility complex
MIA	Magnetic immunoassay
MIP	Macrophages inflammatory protein
mRNA	messenger Ribonuclic acid
NAT	Nucleic acid testing
NC	Negative control value
NF- κβ	Nuclear factor- κβ
NK	Natural killer cell
NKT	Natural killer T cell
NR	Nonreactive
NS	Non significant
OD	Optical densieties
ORF	Open reading frame
PCR	Polymerase chain reaction

List of Abbreviations *(Cont...)*

PD-1	Programmed death-1
PDL1	Programmed death ligand-1
PEI	Paul Ehrlish Institute
PEG-IFN	Pegylated interferon
PRR	Pattern recognition receptor
qHBsAg	Quantitative hepatitis B surface antigen
RIG-I	Retinoic acid-inducible gene I
QT	Quantitative technique
RFLP	Restriction fragment length polymorphism
RIA	Radioimmunoassay
RLU	Relative light unit
RNaseH	Ribonuclease
RT	Reverse transcriptase
S	Significant
SD	Standard deviation
SHB	Small hepatitis B proteins
SPSS	Statistical package for social science
SVR	Sustained virologic response
T4	Thyroxin
TCR	T cell receptor
TH	T helper
TLRs	Toll-like receptors
TNF	Tumer necrosis factor
Total Anti-HBc	Total hepatitis B core antibody
TP	Terminal protein
TRAIL	TNF-related apoptosis-inducing ligand
WHO	World health organization

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Introduction

Hepatitis B virus (HBV) infection is a major global health problem. It is one of the leading causes of both liver cirrhosis and hepatocellular carcinoma, and is responsible for more than 500,000 deaths per year ***(Sorrell et al., 2009)***.

Chronic HBV carriers are the main source of HBV infection in the population. Thus, the detection of HBV infection in pregnant women and blood donors is required to prevent spread of the infection ***(Lee et al., 1998)***.

Hepatitis B surface antigen (HBsAg) is a major envelope protein of HBV, and can serve as an epitope and provide the host with immunity***(Hsu et al., 1997).***

HBsAg is one of the first serum markers to appear during the course of HBV infection and can be detected 2 to 8 weeks beforebiochemical evidence of liver dysfunction and the onset of jaundice.HBsAg is cleared within a few months in self-limiting illness.If HBsAg persists for more than 6 months, spontaneous clearanceis very improbable and the infected individual is considered achronic HBVcarrier***(Weber et al., 1993).***

Among the many commercially licensed HBsAg assays available, enzyme-linked immunosorbent assays(ELISA) are currently the most frequentlyused. These assays use either monoclonal or polyclonal anti-HBsbound to a solid phase and a second labelled anti-HBs to detectthe captured antigen. Despite

the high-level performance of screeningassays, transfusion-associated HBV infection is still reported. To reduce the residual risk of transfusion-associated hepatitis B, the sensitivity of HBsAg screening assays is continuously improved ***(Hoofnagle, 1990).***

Antiviral agents such as lamivudine and interferon-α (IFN- α) have been used as standard therapies for the treatment of chronic hepatitis B, and new drugs have been or are being developed to treat refractory mutant viral infections***(Cuestas et al., 2010).*** Quantitative measures of HBsAg level in serum are important for monitoring response to anti-viral treatment during the management of patients with a chronic HBV infection***(Jung et al., 2010).***