# α GLUTATHIONE S - TRANSFERASE (α GST ) AS A NEW MARKER FOR LIVER DAMAGE IN CHRONIC HEPATITIS C VIRUS (HCV)

Thesis submitted for partial fulfillment of the master degree

in

clinical and chemical pathology

ΒY

#### AMR:FATOUH ABD ELFATAH

M.B., B. CH.

SUPERVISORS

### PROF. DR. MAHMOUD SABRY SALLAM

PROFESSOR OF CLINICAL AND CHEMICAL PATHOLOGY
FACULTY OF MEDICINE - AIN SHAMS UNIVERSITY

### PROF. DR. ABD EL-RAHMAN EL ZAYADI

PROFESSOR OF TROPICAL MEDICINE

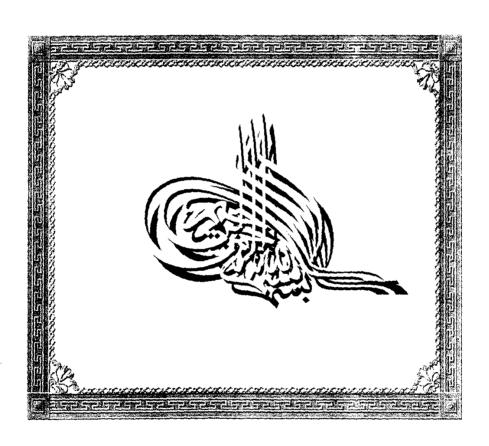
FACULTY OF MEDICINE - AIN SHAMS UNIVERSITY

## PROF. DR. SAWSAN SAID HAFEZ

PROFESSOR OF CLINICAL AND CHEMICAL PATHOLOGY
FACULTY OF MEDICINE - AIN SHAMS UNIVERSITY

FACULTY OF MEDICINE
AIN SHAMS UNIVERSITY
1997







## ACKNOWLEDGEMENT

Before all, I should express my deep thanks to ALLAH without his great blessings, I should never accomplish my work.

I wish to express my sincere gratitude and appreciation to Prof. Dr. MAHMOLID SABRY SALLAM Professor of Clinical and Chemical Pathology, Faculty of Medicine, Ain Shams University, for giving me the privilege of working under his supervision, eminent guidance, continuous encouragement and valuable instructions. No words can express my respect to his thoughtfulness and overwhelming kindness.

I want to thank Prof. Dr. Abdel Rahman El Zayadi Professor of Tropical Medicine, Ain Shams University, for his critical mind that brought out the final points of my research and opened new paths of thought which were formerly closed. His contribution is without doubt, great.

My deepest thanks and most sincere gratitude go to Prof. Dr. SAWSAN S. HAFEZ, Professor of Clinical and Chemical Pathology, Faculty of Medicine, Ain Shams University, for her close supervision, generous guidance, enlightening suggestions and creative ideas. I must admit that I consider myself very fortunate and Lam proud to have worked under her supervision.

I am deeply indebted to Dr. BERIHAN HAMDY, Lecturer of Clinical and Chemical Pathology, Faculty of Medicine, Ain Shams University, for her valuable corrections, worthy criticism and great cooperation throughout the whole work. Without her illuminating remarks, vast experience knowledge and continuous meticulous guidance, this work would not have been possible. I stand in great debt for all what She did. I would like to take this opportunity to thank her for everything she has done for me.

Finally, I would like to deeply thank all my colleagues at the department of Clinical and Chemical Pathology, Faculty of Medicine, Ain Shams University, for their encouragement and support.

List of con	<u>tents</u>
List of abbreviations	i
List of tables	iii
List of figures	iv
Introduction & Aim of the work	1
Review of literature	3
Review of interactive	
Structure and genetic diversity of hepatitis C	3
virus • Introduction.	4
• Structure of HCV.	4
• Sequence diversity of HCV.	5
Clinical significance of variability of HCV	6
• Response to interferon in relation to HCV	9
genotype • Quasispecies nature of HCV	10
Transmission of HCV	12
• Introduction	13
• Parenteral transmission:	13
1-Transfusion of blood or blood components.	13
2-Intravenous drug abuse.	14
3-Transmission between hemodialysis patients.	15
4-Patient to patient transmission in hospitals.	15
5-Tattoing and folk remedies.	16
6-Accidental stab injuries.	16
• Non parenteral transmission:	16
1-Sexual transmission.	16
2-Mother to infant transmission.	19
3-Transmission through saliva and tear fluid.	20
4-Intrafamilial transmission.	21
Hepatitis C Virus Infection	22
• Acute hepatitis.	23

List of cont	ents
• Chronic hepatitis.	24
Screening and Diagnosis of HCV Infection	28
I-Detection of circulating HCV antibodies:	29
A-Anti-HCV screening using Enzyme Immunoassays:	30
1-First generation EIA (EIA-1).	30
2-Second generation EIA (EIA-2).	32
3-Third generation EIA (EIA-3).	33
B-Anti-HCV confirmation using immunoblot assay:	34
1-First generation RIBA (RIBA-1).	35
2-Second generation RIBA (RIBA-2).	36
3-Third generation RIBA (RIBA-3).	37
C-IgM anti-HCV significance.	37
II-Detection of HCV viremia:	40
A-Detection of HCV viremia using polymerase chain reaction (PCR).	42
B-Direct detection of circulating HCV RNA without amplification (In situ hybridization).	45
III-Liver biopsy	46
Glutathione S-Transferases (GSTs)	47
• Introduction	48
• GSTs in health	<i>5θ</i>
A-Function of GSTs	5 <i>0</i>
B-Nomenclature and classification of GSTs	51
C-Tissue distribution of GSTs isoenzymes.	53
• GSTs in disease	56
A-GSTs in liver diseases	56
1-Acute liver disease	57
2-Chronic liver disease	60
B-GSTs in malignancy	62
• Methods of Measurements of GST	65

	List of contents
Subjects & Methods	70
Results	77
Discussion	81
Summary	85
Conclusion	88
References	89



#### List of abbreviations

ALT Alanine aminotransferase
AST Aspartate aminotransferase
α-GST alpha glutathione S-transferase

c Core

**CAH** Chronic active hepatitis

cDNA Complementary deoxy ribonucleic acid

CMV Cytomegalovirus

**CPH** Chronic persistent hepatitis

**DEAE** Diethyl amino ethyl

DEIA DNA enzyme immunoassay
DNA Deoxyribonucleic acid

dNTPs Deoxy nucleoside triphosphates
dUTPs Deoxy uridine triphosphates

E Envelope

EBV Ebstein Barr virus
 EIA Enzyme immunoassay
 GSTs Glutathione S-transferases
 GSTa Glutathione S-Transferase α

HAV Hepatitis A virus HCV Hepatitis C virus

HIV Human immunodeficiency virus

HVR Hypervariable region
HBV Hepatitis B virus
IgG Immunoglobulin G
IgM Immunoglobulin M

Kd Kilo dalton

m.w. Molecular weightNANBH Non-A non-B hepatitis

NS Non structural nt Nucleotide

ORF Open reading frame

PBMCs Peripheral blood mononucler cells

PCR Polymerase chain reaction

	c	1.7		
LIST	ot	appr	'evia	tions

RNA Ribonucleic acid RIA Radioimmunoassay

RIBA Recombinant immunoblot assay

**RT-PCR** Reverse transcription-polymerase chain reaction

SH Sulphydryl

SOD Superoxide dismutase

**TR-IFMA** Time resolved-immunofluorometric assay

UTR Untranslated region

L	i	5	t	c	f	ta	b	les

Table 1	Comparison of different classifications of	7
	HCV genotypes	
Table 2	Descriptive statistics for control group	79
Table 3	Descriptive statistics of patients group (60	79
	cases)	
Table 4	Descriptive statistics for group I (49cases)	79
Table 5	Descriptive statistics for group II (11cases)	80

