

Salwa Ak1



بسم الله الرحمن الرحيم

مركز الشبكات وتكنولوجيا المعلومات

قسم التوثيق الإلكتروني



Salwa Ak1



جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها

على هذه الأقراص المدمجة قد أعدت دون أية تغييرات



Salwa Akl



بعض الوثائق الأصلية تالفة
وبالرسالة صفحات لم ترد بالأصل



B18480

**EVALUATION OF α - GLUTATHIONE S
TRANSFERASE AS A MARKER OF
HEPATOCELLULAR DAMAGE IN PATIENTS
WITH CHRONIC HEPATITIS C**

Thesis

**SUBMITTED FOR PARTIAL FULFILLMENT OF MASTER
DEGREE IN CLINICAL AND CHEMICAL PATHOLOGY**

BY

**BASEM BASIONY AZAB
M.B.B.CH**

SUPERVISORS

**Professor Dr.
SAMIA HASSAN KANDEEL
Professor of Clinical Pathology
Faculty of medicine
Menoufia University**

**Professor Dr.
AHMED ABBAS RAOUF
Dean of the liver institute
Chairman of Biochemistry Dept.
Faculty of medicine
Menoufia University**

**Professor Dr. EMAD FAHIM ABD ELHALIM
Assistant Professor of clinical pathology
Faculty of medicine
Menoufia University**

**Faculty of medicine
Menoufia University**

1999⁶

CONTENTS

	page
• Acknowledgment	I
• List of Abbreviations	II
• List of Figures	IV
• List of Tables	V
• Introduction	1
• Aim of the Work	3
• Review of Literature	4
#Viral Hepatitis	4
Hepatitis A	6
Hepatitis B	7
Hepatitis D	7
Hepatitis E	8
Hepatitis G	8
# Hepatitis C	10
#Clinical Types of Hepatitis	15
#Laboratory Diagnosis of Hepatitis	22
#Glutathione S Transferases	34
• Subjects and Methods	55
• Results	79
• Discussion	95
• Conclusion and Recommendation	99
• References	100
• Arabic Summary	111

LIST OF ABBREVIATIONS

ALT	Alanine aminotransferase
ALB	Albumin
AST	Aspartate aminotransferase
ALP	Alkaline phosphatase
CAH	Chronic active hepatitis
bdNA	Branched deoxy ribonucleic acid
cdNA	Complementary deoxy ribonucleic acid
CMV	Cytomegalovirus
CPH	Chronic persistent hepatitis
Dbil	Direct bilirubin
DCNB	3,4-dichloro-nitrobenzene
DEAE	Diethyl amino ethyl
dL	Deciliter
DNA	Deoxy ribonucleic acid
EBV	Eberstein Barr virus
EIA	Enzyme immunoassay
FIB	Fibrosis
g	Gram
GGT	γ Glutamyltransferase
GST	Glutathione S transferase
HAV	Hepatitis A virus
HBV	Hepatitis B virus
HBsAg	Hepatitis B surface antigen
Hb _c Ag	Hepatitis B core antigen
HCV	Hepatitis C virus
HGV	Hepatitis G virus

HIIV	Human immunodeficiency virus
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IU	International unit
Kd	Kilo dalton
LN	Lobular necrosis
^{mg} Mg	Milligram
m.w.	Molecular weight
NANBH	Non-A Non-B hepatitis
ORF	Open reading frame
PCR	Polymerase chain reaction
PN	Piecemeal necrosis
PI	Portal inflammation
RNA	Ribonucleic acid
RIA	Radioimmunoassay
RIBA	Recombinant immunoblot assay
RT-PCR	Reverse transcription polymerase chain reaction
SH	Sulfhydryl
SOD	Superoxide dismutase
T-F	Total score without fibrosis
TS	Total score
TP	Total protein
Tbil	Total bilirubin

List Of Figures

	page
Fig 1 Structure of Hepatitis B virus	13
Fig 2 Structure of Hepatitis D virus	13
Fig 3 Structure of Hepatitis C virus	14
Fig A Mean for patients, controls and t-test for GST, ALT, and AST.	83
Fig B Mean for patients, controls and t-test for GGT, ALP, and ALB.	84
Fig C Mean for patients, controls and t-test for TP, T Bil, and D Bil.	85
Fig D ROC curve for GST	89
Fig E ROC curve for ALT	90
Fig F ROC curve for AST	91
Fig G ROC curve for GST, ALT, AST	92

List Of Tables

- Table A Sequence homology between GST to define gene families.
- Table B Physical and Catalytic properties of GST subunits.
- Table 1 Statistical comparison of different studied parameters for HCV patients and control group.
- Table 2 Correlation (ρ Spearman) between biochemical data and components of Knodel score.
- Table 3 Correlation (ρ Spearman) between GST and other liver parameters.
- Table 4 ANOVA for GST, ALT, AST between patients groups and healthy controls.
- Table 5 Study of sensitivity, specificity and diagnostic efficacy of GST at different cut off levels
- Table 6 Raw Data of All tested parameters for patients group
- Table 7 Raw Data of All tested parameters for control group

ACKNOWLEDGEMENT

I would like to express my gratitude, deep appreciation, and gratefulness to the supervisors of this work.

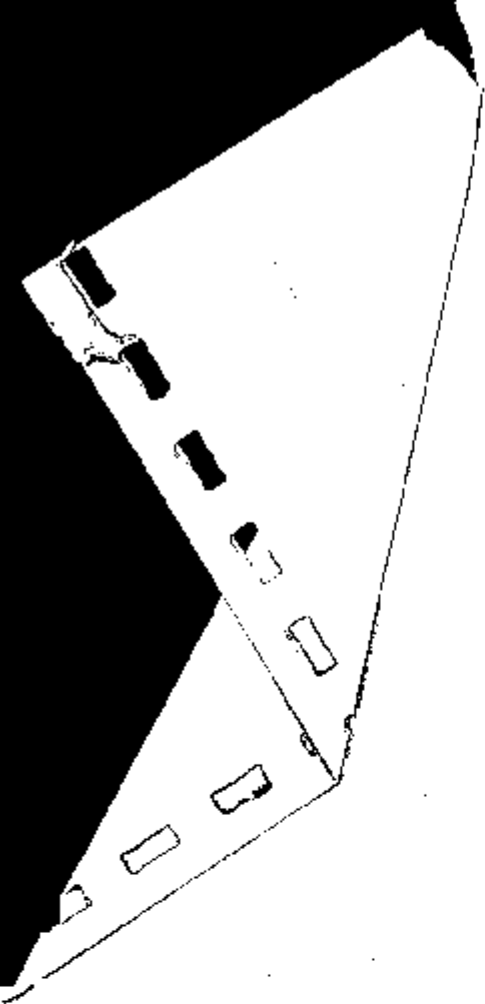
Prof. Dr. Samia Hassan Kandil, Professor of clinical pathology, faculty of medicine, menoufiya university for her Advice, encouragement and sincere help and supervision.

Prof. Dr. Ahmed Abbas Raouf, Dean of the liver institute and Chairman of the biochemistry department faculty of medicine, menoufiya university for his strong support, continuous help and supervision.

Ass. Prof. Dr. Imad Fahim Abdelhalim, Ass. Professor of clinical pathology, faculty of medicine, menoufiya university for his guidance, advice and help.

Lastly I would like to express my appreciation to *Ass. Professor Dr. Mohamad Tawfik Badr*, Ass. Professor of pathology department, liver institute, menoufiya university for his help and advice.

Thanks to all my colleagues for encouragement.



INTRODUCTION

E

INTRODUCTION

Hepatitis C is a form of slowly progressive, silent and often asymptomatic hepatocellular damage. Transaminases are useful markers for measuring such damage in most cases, but not in mild cases as their activities lag behind changes in hepatocellular integrity because of their relatively long half life. {Lau et al 1993}

Moreover transaminases are located in periportal hepatocytes so their activities do not increase in mild liver damage. Thus was the need to get a better and more accurate marker than transaminases, also due to the wide fluctuation of their activity^{ity} and the presence of significant histological changes in patients with normal concentration of transaminases. {Tiainen ^{and Kallio} et al 1994}

Glutathione S-transferases (GST, EC 2.5.1.18) are a family of enzymes that catalyze the conjugation of glutathione with toxic hydrophobic molecules. α glutathione S-transferase (α GST) the basic human class of the enzyme also referred to as ligandin has a molecular weight of 50 KD, short half life of < 90 min. and present in high concentration in the cytosol of both periportal and centrilobular hepatocytes. {Hiley et al 1988}

α Glutathione S-transferase is uniformly distributed in hepatic tissue, thus elevated in both centrilobular and periportal liver damage, while ALT is elevated mainly with periportal damage. In addition α glutathione S-transferase has a shorter half life, low M.W, and high cytosolic concentration, so it is rapidly detected following hepatocellular

damage. Due to these properties α glutathione S-transferase will provide more accurate and early measure of hepatocellular damage. {Nelson et al 1995}

An enzyme immunoassay has been recently developed, and α GST has been proposed as a better and more sensitive index of hepatocellular injury than transaminases. { Ray et al 1995 }

The importance of α GST was proved in several clinical settings such as halothane hepatotoxicity , birth asphyxia, autoimmune chronic hepatitis and paracetamol poisoning. Further more it was reported that α GST in combination with ALT may improve the biochemical assessment of hepatocellular damage in chronic hepatitis C patients.

{ Vaubourdolle et al 1995 }

AIM OF THE WORK

AIM OF THE WORK

The aim of our study is to evaluate Alpha glutathione S-transferase (α -GST) as a marker of hepatocellular damage in chronic hepatitis C patients and compare it to the healthy control group to assess the clinical importance of α -GST in monitoring the disease activity in these patients.

other liver function tests namely

ALT & AST