PROGNOSTIC VALUE OF HCV SEROTYPING IN THE EVALUATION OF INTERFERON THERAPY

Thesis
Submitted in Partial Fulfillment of
M.D Degree In Clinical and Chemical Pathology

By

Shereen Mohamed Fahim

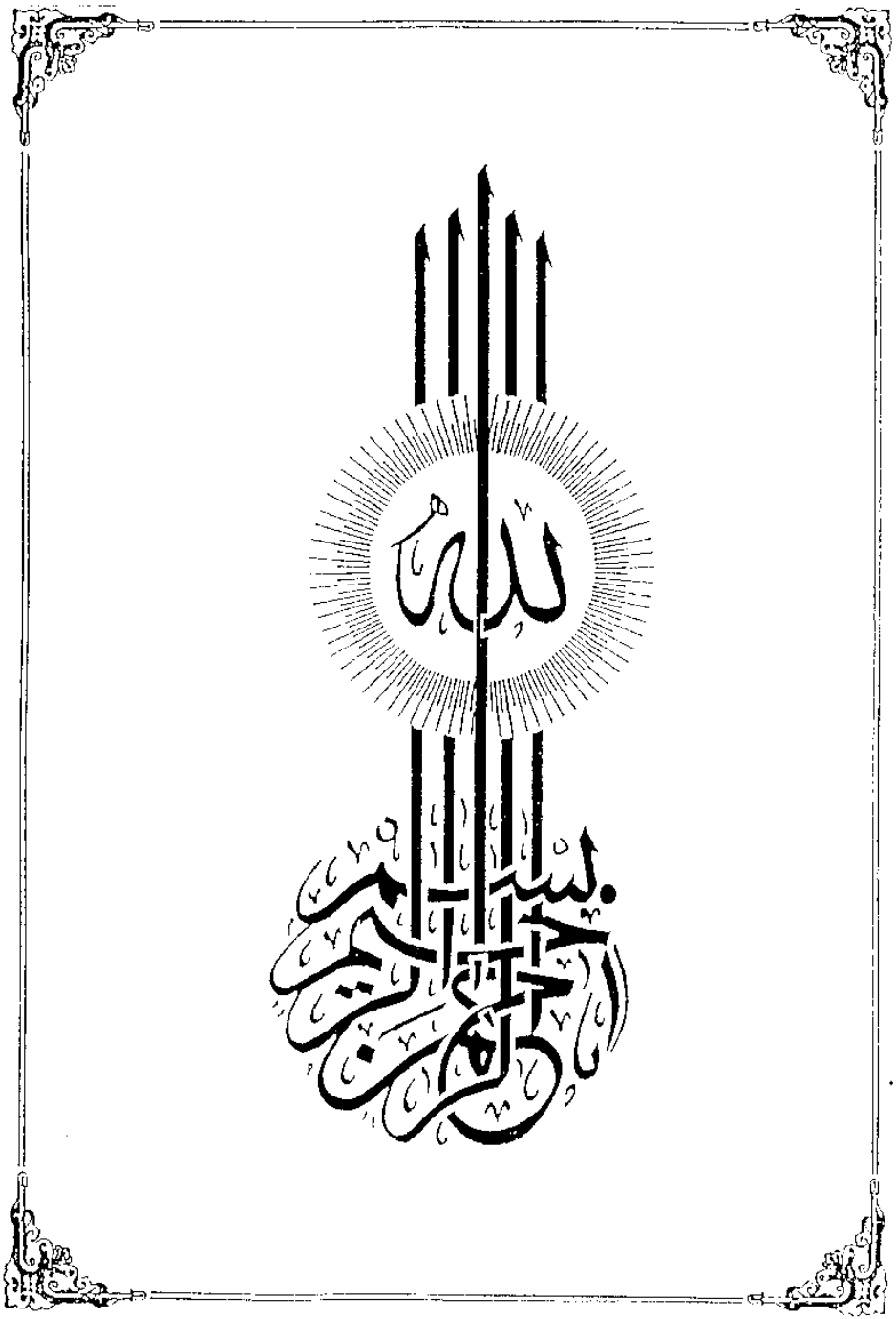
Supervisors

Prof. Dr. **AMANI IBRAHIM SALEH**
Professor of Clinical Pathology
Prof. Dr. **MOHAMED ALY MADWAR**
Professor & Head of tropical Medicine
Prof. Dr. **MONA MOHAMED RAFIK**
Professor of Clinical Pathology
Dr. **NAHLA MOHAMED ZAKARIA YOUSEF**
Lecturer of Clinical Pathology
Dr. **HANAA AHMED AMER**
Lecturer of Clinical Pathology

Faculty of Medicine
Ain Shams University
1998

Central Library - Ain Shams University

Central Library - Ain Shams University



Central Library - Ain Shams University

Central Library - Ain Shams University

Central Library - Ain Shams University

ACKNOWLEDGEMENT

I wish to express my deep appreciation and gratitude to **Prof. Dr. AMANI IBRAHIM SALEH,** Professor of Clinical Pathology, Faculty of Medicine, Ain Shams University, for her meticulous supervision, sincere effort and outstanding assistance through every step of this study.

I would like to express special thanks and gratitude to **Prof. Dr. MOHAMED ALY MADWAR,** Professor and Chairman of Tropical Medicine Department, Faculty of Medicine, Ain Shams University, for his supervision, kind help, valuable observation and generous support.

I would like to express my deep thanks and sincere appreciation to **Prof. Dr. MONA MOHAMED RAFIK,** Professor of Clinical Pathology, Faculty of Medicine, Ain Shams University, for her valuable suggestions and continuous encouragement.

I wish to express my deep thanks to **Dr. NAHLA M. ZAKARIA YOUSEF,** Lecturer of Clinical Pathology, Faculty of Medicine, Ain Shams University, for her devotion all the time and effort she sacrified and valuable friendship she offered me in order to start and complete this work.

I wish to extend my thanks to **Dr. HANAA AHMED AMER,** Lecturer of Clinical Pathology, Faculty of Medicine, Ain Shams University, for her sincere help and effort during this work.

Last, but not least, I would like to send my best regards and thanks to My Family for their help and continuous encouragement.

Central Library - Ain Shams University

Central Library - Ain Shams University

ABSTRACT

Hepatitis C virus commonly caused persistent infection and chronicity. HCV infection can lead to serious consequences including cirrhosis and hepatocellular carcinoma.

In this study a trial was done to determine the prevalence of HCV serotype in Egyptian patients with chronic hepatitis C infection and whether serotyping correlates with the genotyping methods. In addition, a trial was done to find out the predictors of response to IFN-alpha therapy in these patients.

This study was done on 51 cases diagnosed as having chronic HCV infection. Detection of HCV RNA was performed by qualitative PCR for all patients before and after treatment by IFN-alpha for 6 months. In addition, HCV RNA quantitation was performed for only 36 patients before treatment. HCV serotyping was performed before treatment for all patients using Murex 1-6 HCV serotyping assay.

This study revealed that serotype 4 is the prevalent serotype in Egypt (74.5%). Most of the responders are of serotype 4. Good correlation exists between both serotyping and genotyping assays. Liver transaminases are not predictors for HCV viremia. Follow up of chronic HCV patients under treatment could be done by HCV RNA.

We conclude that serotyping assays can be used as front-line typing approach in patients with chronic hepatitis C infection.

Central Library - Ain Shams University

Central Library - Ain Shams University

LIST OF ABBREVIATIONS

ALT:	Alanine aminotransferase.
AST:	Aspartate aminotransferase.
b.DNA:	Branched deoxyribonucleic acid.
C:	Core.
CAH:	Chronic active hepatitis.
cDNA:	Complementary DNA.
DNA:	Deoxyribonucleic acid.
dNTP:	Deoxynucleotide triphosphate.
E:	Envelope.
ELISA:	Enzyme linked immunosorbent assay.
HBV:	Hepatitis B virus.
HCC:	Hepatocellular carcinoma.
HCV:	Hepatitis C virus.
HDV:	Hepatitis delta virus.
HIV:	Human immunodeficiency virus.
IFN:	Interferon.
IVD:	Intravenous drug.
LCR:	Ligase chain reaction.
LMP:	Large multicatalytic protease.
Meq:	Million equivalent.
NCR:	Non coding region.
NS:	Non structural.
r-A:	Ribonucleic adenine.
RIBA:	Recombinant immunoblot assay.
RNA:	Ribonucleic acid.
RT-PCR:	Reverse transcription polymerase chain reaction.
r-U:	Ribonucleic uracil.
STATs:	Signal-transducing transcriptional activators.
TAP:	Transporter associated with antigen presentation.

Central Library - Ain Shams University

Central Library - Ain Shams University

LIST OF FIGURES

Figures of Review of Literature:

Fig. (1): .....(6)
Organization of HCV genome.

Fig. (2): .....(33)
HCV encoded antigens used for anti-HCV antibody detection in first (1), second (2) and third (3) generation antibody tests.

Fig. (3): .....(39)
Principle of b.DNA assay.

Fig. (4): .....(41)
Accurate HCV RNA quantification by b.DNA assay.

Fig. (5): .....(44)
Ligase chain reaction.

Figures of Results:

Fig. (1): .....(86)
Frequency of the different HCV serotypes in the studied group of patients.

Fig. (2): .....(87)
Response rate to interferon therapy in the studied patients with different HCV serotypes.

Central Library - Ain Shams University

Fig. (3): .....(90)
Mean values of HCV RNA titer in different HCV serotypes.

Fig. (4): .....(94)
Mean levels of ALT and AST in responders before and after treatment (n=11).

Fig. (5): .....(95)
Mean levels of ALT and AST in non-responders before and after treatment (n=40).

Fig. (6): .....(100)
Frequency of different forms of liver affection in biopsied patients (n=45).

Fig. (7): .....(102)
Pretreatment mean values of HCV RNA in different forms of liver affection.

Fig. (8): .....(104)
Results of PCR before and after treatment.

Fig. (9): .....(109)
Mean values of HCV RNA titer in both male and female patients.

Central Library - Ain Shams University

LIST OF TABLES

Table (1): .....(56)

Table (2): .....(78)
Descriptive statistics of different parameters of all patients (n=51).

Table (3): .....(79)
Statistical presentation of different parameters of all patients.

Table (4): .....(80)
Descriptive statistics for responder group (R) (n=11).

Table (5): .....(81)
Descriptive statistics for nonresponder group (NR) (n=40).

Table (6): .....(84)
Detection of association between HCV serotyping and genotyping assays.

Table (7): .....(85)
Frequency of HCV serotypes detected in the 51 patients.

Table (8): .....(85)
Detection of the association between serotype and response to interferon-alpha treatment using the Chi-square test.

Central Library - Ain Shams University

Table (9): .....(88)
Detection of the association between serotype and histology of liver disease using the Chi-square test.

Table (10): .....(89)
Detection of association between serotype and HCV RNA quantitation (n=36).

Table (11): .....(92)
Comparison between ALT and AST before and after treatment in all patients group (n= 51).

Table (12): .....(93)
Comparison between ALT and AST before and after treatment in responder group (R) (n=11, 21.6%).

Table (13): .....(93)
Comparison between ALT and AST before and after treatment in non responder group (NR) (n=40, 78.4%).

Table (14): .....(96)
Comparison between responder (R) and nonresponder (NR) groups regarding different parameter studied.

Table (15): .....(97)
Detection of association between HCV serotype and liver enzymes (ALT & AST).

Central Library - Ain Shams University