Pretreatment serum ferritin as a predictor of response to pegylated interferon and ribavirin therapy in patients with chronic hepatitis C infection

THESIS
Submitted for Partial Fulfillment of Master Degree in Tropical Medicine

Presented by
Ahmed Salah El Din Hassan
M.B., B.Ch.

Under Supervision of
Professor Dr. Ahmed Abbas El-Khatib
Professor of Tropical Medicine
Faculty of Medicine
Ain Shams University

Dr. Ashraf Mohamed Al Breedy
Lecturer of Tropical Medicine
Faculty of Medicine
Ain Shams University

Faculty of Medicine
Ain Shams University
2013

بسم الله الرحمن الرحيم

قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا

عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم

سورة البقرة آية (٣٢)

First and foremost thanks to ALLAH, the most merciful.

I wish to express my deepest appreciation and sincere gratitude to **Prof. Dr.Ahmed Abbas El Khattib,** Prof. of Tropical Medicine, Faculty of Medicine, AinShamsUniversity, for his continuous encouragement, kind supervision, valuable instructions and sincere advice which have been the main factors to complete this work. It was a great honor to me to work under his supervision.

Words can never express my deepest gratitude, appreciation and greatest respect to **Dr.Ashraf Mohamed El Breedy,** Lecturer of Tropical Medicine, Faculty of Medicine, AinShamsUniversity, for his close supervision, continuous guidance, great help and indispensable advice in every step of this work. He has generously devoted much of his valuable time, experience and effort for planning and supervision of this work and for presenting it in an ideal form.

I am also delighted to express my deep gratitude and thanks to all my dear professors and my colleagues that without their help, this work could not have been completed.

Last but not least, I would like to thank my mother, her support; encouragement, quiet patience and unwavering love were undeniably the bedrock upon which the past years of my life have been built. I would like to thank my father for his unconditional support, both financially and emotionally throughout my degree.

In particular, the patience and understanding shown by him. Their tolerance of my occasional vulgar moods is a testament in itself of their unyielding devotion and love.

Table of Contents

List of tables

List of figures

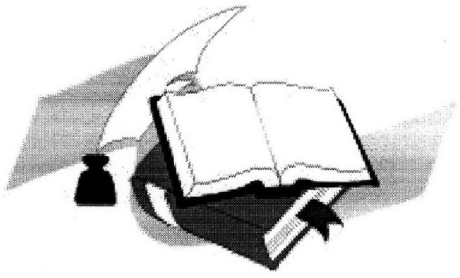
List of Abbreviations

AIH	Autoimmune hepatitis
ALT	Alanine Aminotransferese
ARFP	Alternate Reading Frame Protein
AST	Aspartate Aminotransferese
BMI	Body Mass Index
CBC	Complete Blood Count
CD	Cluster of differentiation
CHC	Chronic Hepatitis C
DC	Delta change
DNA	Deoxyribonucleic acid
ELISA	Enzyme-linked immunosorbent assay
EVR	Early virological response
FCH	Fibrosing Cholestatic Hepatitis
GGT	Gamma-glutamyl transpeptidase
HAV	Hepatitis A virus
HBV	Hepatitis B virus
HCC	Hepato cellular carcinoma
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
HLA	Human leukocyte antigen
IFN	Interferon
IRES	Internal ribosome entry site
IL	Interleukin
MELD	Model for End-Stage Liver Disease
MPGN	Membranoproliferative glomerulonephritis
NAFLD	Non-alcoholic fatty liver disease
NIH	National Institute of Health
NS	Nonstructural
PCR	Polymerase Chain Reaction
RNA	Ribonucleic acid
RVR	Rapid virological response

List of Abbreviations (cont.)

SOC	Standard of care
SVR	Sustained virological response
TGF	Transforming growth factor
Th1	T- helper cells 1
Th2	T- helper cells 2
TMA	Transcription-mediated amplification
ULN	Upper Limit of Normal
UTR	Untranslated region

Introduction



Introduction

Hepatitis C virus (HCV) infection is a worldwide major health problem. Recent estimates indicate that approximately 130–210 million individuals, i.e. 3% of the world population, are chronically infected with HCV ***(Shepard et al., 2005 and Lavanchy, 2009)***. More than 90% of HCV isolates from Egyptian patients are of the genotype 4 variant, which is significant considering that Egypt has the highest worldwide prevalence, with 9% country wide and up to 50% in certain rural areas, due to specific modes of infection ***(Kamal and Nasser, 2008)***. Eventually, 20-50% of chronic HCV patient's progress to cirrhosis and 5-7% develop hepatocellular carcinoma within 10-20 years ***(Mohamed, 2004).***

The current treatment for patients with chronic hepatitis C is the combined Ribavirin and Interferon-based therapies for 24 to 48 wk. Antiviral therapy for chronic hepatitis C has many goals; the primary goal is durable viral clearance as evidenced by the absence of HCV RNA in serum (virological response); the secondary goal is reduction of damage to the liver as determined by either persistently normal ALT levels (biochemical response) or improved liver biopsy, with the expectation that this will delay or prevent cirrhosis, HCC, the need for liver transplantation, and