

**SERUM FERRITIN VERSUS INTERLEUKIN-10 (IL-10) AS
PREDICTORS OF RAPID VIROLOGICAL RESPONSE
(RVR) IN PATIENTS RECEIVING ANTI- HEPATITIS
C VIRUS (HCV) TREATMENT**

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَأَنْزَلَ اللَّهُ عَلَيْكَ
الْكِتَابَ وَالْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ تَكُنْ
تَعْلَمُ وَكَانَ فَضْلُ
اللَّهِ عَلَيْكَ عَظِيمًا

صدق الله العظيم

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LIST OF CONTENTS

Title	Page No.
Introduction.....	1
Aim of the work.....	4
<u>Review of Literature</u>	
• Natural history and treatment of HCV.....	5
• Interleukin-10 and HCV	33
• Ferritin and HCV	42
Patients and methods	52
Results.....	56
Discussion.....	100
Summary and Conclusion.....	110
Recommendations.....	111
References.....	112
Arabic Summary	——

LIST OF TABLES

Tab. No.	Title	Page No.
Table (1):	Definitions of treatment response	30
Table (2):	Predictors of Response to standard Therapy for HCV Infection	31
Table (3):	Side effects of interferon and ribavirin	32
Table (4):	Metavir score system	54
Table (5):	Age distribution among the studied groups	57
Table (6):	Gender distribution among the studied groups	58
Table (7):	BMI of the studied groups	59
Table (8):	Comparison between the two groups as regards Hb. Level.	60
Table (9):	Comparison between the two groups as regards RBCs.....	61
Table (10):	Comparison between the two groups as regards WBCs 62	62
Table (11):	Comparison between the two groups as regards platelets.....	63
Table (12):	Comparison between the two groups as regards Free T3.....	64
Table (13):	Comparison between the two groups as regards Free T4.....	65
Table (14):	Comparison between the two groups as regards TSH.....	66
Table (15):	Comparison between the two groups as regards Total bilirubin.....	67
Table (16):	Comparison between the two groups as regards Serum Albumin.....	68
Table (17):	Comparison between the two groups as regards Prothrombin time.....	69

LIST OF TABLES (Cont...)

Tab. No.	Title	Page No.
Table (18):	Comparison between the two groups as regards Prothrombin activity.....	70
Table (19):	Comparison between the two groups as regards Total cholesterol.....	71
Table (20):	Comparison between the two groups as regards Triglycerides.....	72
Table (21):	Comparison between the two groups as regards LDL.....	73
Table (22):	Comparison between the two groups as regards HDL.....	74
Table (23):	Comparison between the two groups as regards Blood urea.....	75
Table (24):	Comparison between the two groups as regards Serum creatinine.....	76
Table (25):	Comparison between Group B and Controls as regards Serum IL-10.....	77
Table (26):	Comparison between Group A and Controls as regards Serum Ferritin.....	78
Table (27):	Comparison between 1 ST and 2 ND PCR in group A.....	79
Table (28):	Comparison between 1 ST and 2 ND PCR in group B.....	80
Table (29):	Comparison between group A and group B as regards 1 st PCR.....	81
Table (30):	Comparison between group A and group B as regards 2 ND PCR.....	82
Table (31):	Comparison between group A and group B as regards RVR.....	83
Table (32):	The change in Hb level before treatment and after 4 weeks.....	84
Table (33):	The change in RBCs count before treatment and after 4 weeks.....	85
Table (34):	The change in serum bilirubin before treatment and after 4 weeks.....	86

LIST OF TABLES (Cont...)

Tab. No.	Title	Page No.
Table (35):	The effect of Age and BMI on RVR.	87
Table (36):	Relation between sex and RVR.	88
Table (37):	Relation between Liver enzymes and RVR.....	89
Table (38):	The effect of DM on RVR.	90
Table (39):	The effect of hepatomegaly on RVR.	91
Table (40):	The effect of splenomegaly on RVR.	92
Table (41):	The relation between presence of Abs for schistosoma and RVR.	93
Table (42):	The relation between pesense of living bilharizial ova in rectal snip and RVR.	94
Table (43):	Comparison between the effects of elevated serum IL-10 and Ferritin on RVR.	95
Table (44):	Correlation between Serum Ferritin, serum IL-10 and response with Age.....	96
Table (45):	Ranges of Serum IL-10 and Serum Ferritin as measured in both groups.....	97
Table (46):	ROC curve for Serum Ferritin.	98
Table (47):	ROC curve for Serum IL-10.....	99

LIST OF FIGURES

Fig. No.	Title	Page No.
Figure (1):	Structure of the positive-sense ss-RNA genome of HCV	6
Figure (2):	Natural History of HCV Infection.	19
Figure (3):		21
Figure (4):	Recommendation for treatment algorithm for patients with HCV genotype 1- 4 – 6	23
Figure (5):	Recommendation for treatment algorithm for patients with HCV genotypes 2 and 3	23
Figure (6):	Graphic display of virological responses	30
Figure (7):	IL-10 family members, all share common receptor subunits.....	37
Figure (8):	Ferritin structure	47
Figure (9):	Intracellular Iron Homeostasis.	49
Figure (10):	Age distribution among the studied groups.....	57
Figure (11):	Gender distribution among the studied groups.....	58
Figure (12):	BMI of the studied groups.....	59
Figure (13):	Comparison between the two groups as regards Hb. Level.	60
Figure (14):	Comparison between the two groups as regards RBCs.....	61
Figure (15):	Comparison between the two groups as regards WBCs.....	62
Figure (16):	Comparison between the two groups as regards platelets.	63
Figure (17):	Comparison between the two groups as regards Free T3.	64
Figure (18):	Comparison between the two groups as regards Free T4.....	65

LIST OF FIGURES (Cont...)

Fig. No.	Title	Page No.
Figure (19):	Comparison between the two groups as regards TSH.....	66
Figure (20):	Comparison between the two groups as regards Total bilirubin.	67
Figure (21):	Comparison between the two groups as regards Serum Albumin.....	68
Figure (22):	Comparison between the two groups as regards prothrombin time.	69
Figure (23):	Comparison between the two groups as regards Prothrombin activity.	70
Figure (24):	Comparison between the two groups as regards Triglycerides.....	72
Figure (25):	Comparison between the two groups as regards LDL.....	73
Figure (26):	Comparison between the two groups as regards HDL.	74
Figure (27):	Comparison between the two groups as regards Blood urea.....	75
Figure (28):	Comparison between the two groups as regards Serum creatinine.	76
Figure (29):	Comparison between Group B and Controls as regards serum IL-10.	77
Figure (30):	Comparison between Group A and Controls as regards serum ferritin.	78
Figure (31):	Comparison between group A and group B as regards 1 st PCR.....	81
Figure (32):	Comparison between group A and group B as regards 2 ND PCR.....	82
Figure (33):	Comparison between group A and group B as regards RVR.	83

LIST OF FIGURES (Cont...)

Fig. No.	Title	Page No.
Figure (34):	The change in Hb level before treatment and after 4 weeks.....	84
Figure (35):	The change in RBCs count before treatment and after 4 weeks.	85
Figure (36):	The change in serum bilirubin before treatment and after 4 weeks.	86
Figure (37):	The effect of Age and BMI on RVR.	87
Figure (38):	Relation between sex and RVR.....	88
Figure (39):	Relation between Liver enzymes and RVR.....	89
Figure (40):	The effect of DM on RVR.....	90
Figure (41):	The effect of hepatomegaly on RVR.....	91
Figure (42):	The effect of splenomegaly on RVR.	92
Figure (43):	The relation between presence of Abs for schistosoma and RVR.....	93
Figure (44):	The relation between pesense of living bilharizial ova in rectal snip and RVR.	94

LIST OF ABBREVIATIONS

Abbrev.	Full term
Abs	Antibodies
AIDS	Acquired immunodeficiency syndrome
ALT	Alanine aminotransferases
APC	Antigen presenting cell
AST	Aspartate aminotransferase
BMI	Body mass index
CD4	Cluster of differentiation 4
CHC	Chronic hepatitis C
CSF	Colony stimulating factor
CSIF	Cytokine synthesis inhibitory factor
DM	Diabetes mellitus
DVR	Delayed virological response
ETR	End of treatment response
EVR	Early virological response
GSH	Glutathione
Hb	Hemoglobin
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HDL	High density lipoprotein
HIV	Human immunodeficiency virus
HLA-C1	Human leukocyte antigen C group 1
HOMA-IR	Homeostasis model assessment of insulin resistance
IDU	Intravenous drug users
IFNs	Interferons

LIST OF ABBREVIATIONS

Abbrev.	Full term
IL	Interleukin
LDL	Low density lipoprotein
NK Cell	Natural killer cell
NR	Null response
PBMC	Peripheral blood mononuclear cell
PegIFN	Pegylated interferon
PR	Partial response
RBCs	Red blood cells
RBV	Ribavirin
RVR	Rapid virological response
SCF	Stem cell factor
SOC	Standard of care
SVR	Sustained virological response
TGF	Tumor growth factor
Th cell	T-helper cell
TNF	Tumor necrosis factor
TSH	Thyroid-stimulating hormone
WBCs	White blood cells
WHO	World Health Organization

INTRODUCTION

Hepatitis C is an infectious disease affecting primarily the liver, caused by the hepatitis C virus (HCV). The infection is often asymptomatic, but chronic infection can lead to scarring of the liver and ultimately to cirrhosis, which is generally apparent after many years. In most cases, those with cirrhosis will go on to develop liver failure, liver cancer or life-threatening esophageal and gastric varices (*Ghany et al., 2011*).

HCV is spread primarily by blood-to-blood contact associated with intravenous drug use, poorly sterilized medical equipment and transfusions. An estimated 130–170 million people worldwide are infected with hepatitis C. The existence of hepatitis C (originally "non-A non-B hepatitis") was postulated in the 1970s and proven in 1989 (*Ghany et al., 2011*).

The virus persists in the liver in about 85% of those infected. This persistent infection can be treated with medication: the standard therapy is a combination of peginterferon and ribavirin. Overall, 50–80% of people treated are cured. Those who develop cirrhosis or liver cancer may require a liver transplant. Hepatitis C is the leading cause of liver transplantation, though the virus usually recurs after transplantation. No vaccine against hepatitis C is available (*Hoofnagle and Seeff, 2011*).

The World Health Organization has declared hepatitis C a global health problem, with approximately 3% of the world's

population (roughly 170-200 million people) infected with HCV (*Hoofnagle and Seeff, 2011*).

Egypt contains the highest prevalence of hepatitis C in the world, where genotype 4 represents over 90% of cases. Chronic HCV infection is the main cause of liver cirrhosis and liver cancer in Egypt and indeed, one of the top five leading causes of death (*Fried et al., 2011*).

It is well known that there are many factors that affect a successful treatment outcome. When people are trying to make a decision about whether or not to be treated it is important to take many of these predictors of treatment response into consideration. However, it is also important to remember that the predictors to treatment response listed below are there to help in the decision making process; they should never be used to deny or discourage treatment for anyone. These predictors include: virus genotype, viral load, disease severity, IL28B, IL-10, serum ferritin, age, metabolic disorders like: insulin resistance, steatosis and metabolic syndrome (*Davis et al., 2012*).

High serum ferritin is a common finding in many acquired liver diseases, particularly in chronic hepatitis C (CHC) and is predictive of poorer response to antiviral therapy. Ferritin is the iron-storage protein in tissues and its serum levels correlate with total iron content; thus, it may be speculated that high serum ferritin level may be a marker of iron overload. This is usually true in the absence of chronic inflammation, with very rare exceptions, but ferritin synthesis and release are increased in

states of chronic immune stimulation and the actual meaning of hyperferritinemia in CHC has not been fully elucidated (*Distante et al., 2012*).

IL-10 is a cytokine produced primarily by monocytes and to a lesser extent by lymphocytes. This cytokine has pleiotropic effects in immunoregulation and inflammation. It down-regulates the expression of Th1 cytokines, MHC class II antigens, and costimulatory molecules on macrophages. It also enhances B cell survival, proliferation, and antibody production. Furthermore, there is strong evidence of a substantial genetic component to IL-10 production the 1082 G/G genotype is known to be related to increased IL-10 production and is associated with a high risk of inefficient HCV clearance and resistance to treatment (*Yu and Gu, 2011*).