FACTORS PREDICTING THE RESPONSE TO ALPHA INTERFERON THERAPY IN PATIENTS WITH CHRONIC HEPATITIS "C"

Thesis

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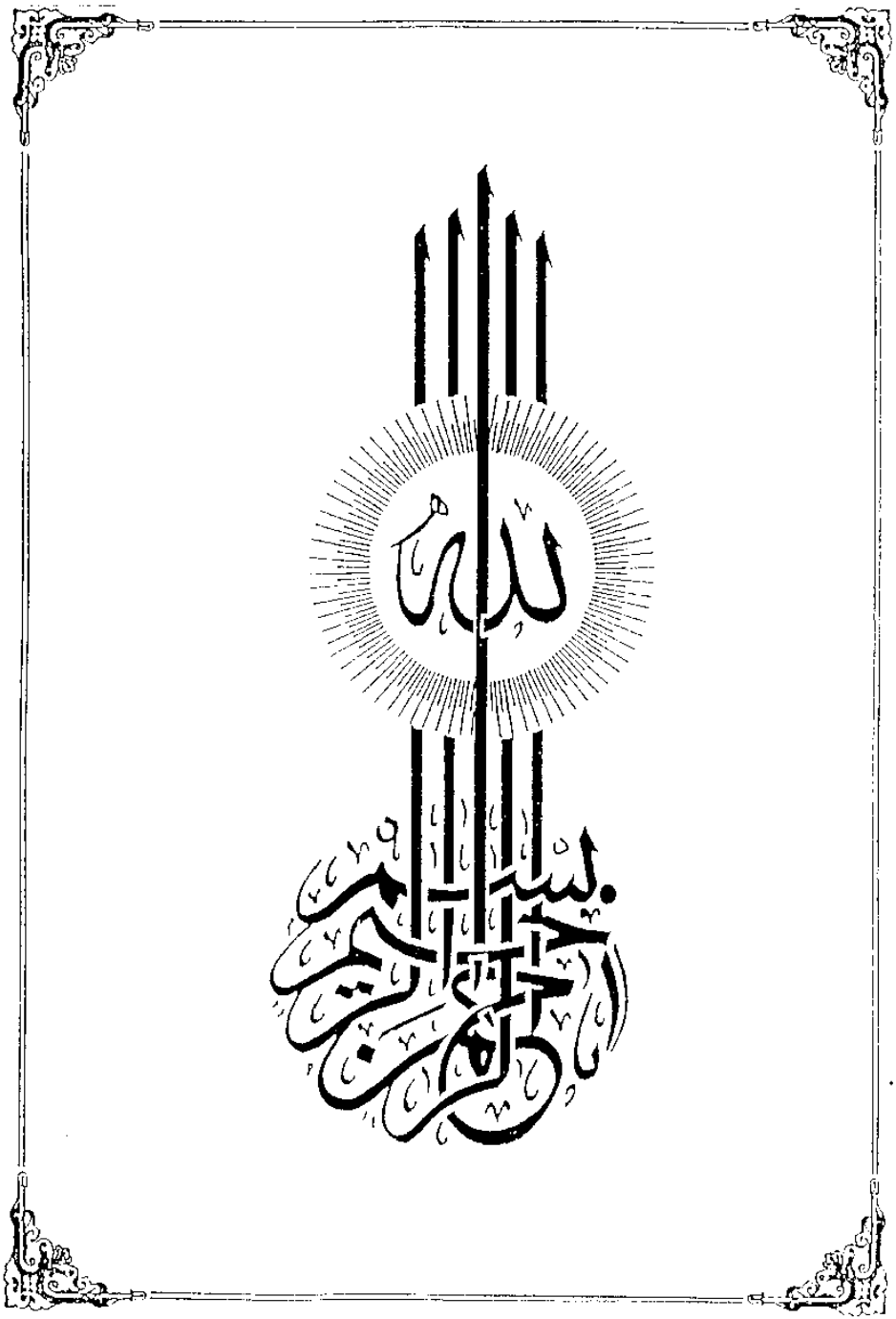

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LIST OF ABBREVIATIONS

3-MU	: Three millions unit
ADCC	: Antibody-dependent cell-mediated cytotoxicity
AIDS	: Acquired immunodefeciency syndrome
ALK-ph	: Alkalin phopshatase
ALT	: Alanine aminotransferase
AST	: Aspartate aminotransferase
CAH	: Chronic active hepatitis
CDC	: Center disease control
CLH	: Chronic lobular hepatitis
CML	: Chronic myelogenous leukemia
CPH	: Chronic persistent hepatitis
E	: Envelope
ELISA	: Enzyme linked immunosorbent assay
EMC	: Essenteal mixed cryoglobulinaemia
GGT	: Gama glutamile transaminase
HBV	: Hepatitis B virus
HCC	: Hepatocellular carcinoma
HCV	: Hepatitis C virus
HIV	: Human immunodeficiency virus
HS	: High significant
IDu	: Injecting drug users
IFN	: Interferon
IHD	: Ischaemic heart diseases
IVDU	: Intravenous drug use
LDH	: Lactic acid dehydrogenase
LKMI	: Liver and kidneey microsomal antibodies

LIST OF ABBREVIATIONS(Cont.)

mRNA	: Messenger RNA
NAE	: Necrolytic acral erythema
NANB	: Non-A Non-B hepatitis
NCR	: Non-coding region
Ns	: Non structural
OAS	: Oligoadenylate synthetase
ORF	: Open reading frame
PCR	: Polymerase chain reaction
PCT	: Porphyria cutanea tarda
PGE_2	: Prostaglandins E_2
PKP1	: Protein kinase P1
RIBA	: Recombinant immunoblot assay
RNA	: Ribonucleic acid
RT	: Reserve transcription
S	: Significant
SGOT	: Serum glutamic oxaloacetic transaminase
SGPT	: Serum glutamic pyruvate transaminase
TAM	: Transfusion-associated hepatitis
UK	: United Kingdom
USA	: United State of American

INTRODUCTION AND AIM OF THE WORK

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Introduction:

Hepatitis C is a viral infection. The distribution is about 1% to 2% of the world population. In some areas such as Egypt the prevalence is high as 15%.

This Virus is notorious for evolving into Chronic Hepatitis once one acquires the disease.

Over time there is a spectrum of histologic involvement that ranges any where from mild to severe *(Tong et al., 1995)*, Chronic Hepatitis C occurs in 50-80% of patients with post-transfusion hepatitis C which is the most common cause of chronic hepatitis.

The diagnosis is confirmed by anti-HCV by immuno-assay enzymes in cases of suspected chronic hepatitis C but -ve enzyme immunoassay, the diagnosis be confirmed by +ve (RIBA) or detection of hepatitis C virus RNA in serum of polymerase chain reaction, the liver biopsy confirm the presence of chronic hepatitis *(Alter, 1994)*.

It is quite clear that interferon-α major advance in treatment of chronic viral hepatitis C.

It has been demonstrated that patients who are treated with interferon-α fare better in termination of their biochemical, histological and viral response than those who are not treated

with interferon-α. Although interferon-α is the only affective treatment for chronic hepatitis C. Up to 50% of patients who respond to interferon-α therapy subsequently relapse. Much research has therefore been directed to identifying predictors of long-term response to interferon-α *(Congress abstract review January 1996, Madrid, Spain); (Saracco et al., 1993; De Salvo, Noventa-Chemellol et al., 1995).*

Aim of the Work:

The aim of the work is to identify the factors predicting the response to alpha interferon therapy in patients with chronic hepatitis C.

REVIEW OF LITERATURE

Chapter I

HEPATITIS

The term hepatitis is applied to a broad category of clinicopathological conditions, that result from the damage produced by viral, toxic, pharmacological, or immune-mediated attack upon the liver, and that share common pathological features in the form of hepatocellular necrosis, and inflammatory cell infiltration of the liver *(Bass and Van Dyke, 1990).*

Acute Hepatitis:

It implies a self-limiting episode of liver-cell damage, in which variable numbers of hepatocytes undergo necrosis. These episodes are largely due to infective or toxic agents *(Richmond and Finlayson, 1987).* They are commonly asymptomatic, lasting less than six months, culminating either in complete resolution of the liver damage with return to normal liver function and structure or in rapid progression of the acute injury toward extensive necrosis and fatal outcome *(Bass and Van Dyke, 1990).*

The most important infective causes of acute hepatitis are the hepatitis viruses. Less frequently non-viral agents such as leptospira icterohaemorrhagicae (Weil's disease), Toxoplasma gondii (Toxoplasmosis) and Coxiella burneti (Q fever) may cause acute hepatitis. Bacteria usually produce a liver abscess rather than an acute hepatitis *(Richmond and Finalyson, 1987).* Rickettsial, mycoplasma and systemic fungal infections cause liver damage as part of generalized organ involvement.

Other less frequent causes of acute hepatitis include poisons e.g. carbon tetrachloride, vinyl chloride, and ethylene glycol and similar solvents (glue sniffing) *(Rubenstein and Wayne, 1991)*. Alfatoxin and Amantia phalloides (mushrooms) *(Clark and Kumar, 1990)*. It also include toxic drugs e.g. Alcohol (ethanol and methanol), halothane (after repeated exposures), paracetamol, PAS, isoniazid and rifampicin, methotrexate, chlorpromazine and the monoamine oxidase inhibitors. Pregnancy is another rare cause of acute hepatitis *(Rubenstein and Wayne, 1991)*.

Histological changes are essentially similar whatever the cause is Hepatocytes show degenerative changes, undergo necrosis and are rapidly removed. The distribution of these changes varies somewhat with the aetiological agent, but necrosis is usually in zone 3 *(Clark and Kumar, 1990)*. The lobules may be infiltrated with mononuclear cells. Polymorphonuclear leukocytes and fatty changes are not seen. The portal tracts are enlarged with a predominantly mononuclear cell infiltrate *(Richmond and Finalyson, 1987)*. The extent of the damage is very variable between individuals affected by the same agent, at one end of the spectrum, single and small groups of hepatocytes die (spotty or focal necrosis), while at the other end whole lobules are destroyed (massive hepatic necrosis) resulting in fulminant hepatic failure *(Clark and Kumar, 1990)*. Between these extremes one sees confluent necrosis of hepatocytes with collapse of the reticulin framework, particularly between the central veins and portal tracts which become linked to one another, this is known as bridging or subacute hepatic necrosis *(Richmond and Finlayson, 1987)*.