SERUM LEVELS OF NEOPTERIN IN PATIENTS WITH HEPATITIS C VIRUS RELATED CHRONIC LIVER DISEASE

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IN THE NAME OF ALLAH
MOST MERCIFUL MOST COMPASSIONATE

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LIST OF ABBREVIATIONS

ALT	Alanin transaminase
AFP	alpha-fetoprotein
ADA	Adenosine deaminase isoenzymes isoenzymes
AST	Aspartate transaminase
ALP	Alkaline phosphatase
ANA	Antinuclear antibody
bDNA	branched chain DNA test
CTL	cytotoxic T lymphocytes cell
CMV	Cytomegalovirus
CSF	Cerebrospinal fluid
EIAs/ELISAs	enzyme-linked immunoassays
ECG	electrocardiography
ESR	Erythrocyte sedimentation ratio
FT-AT	FibroTest -ActiTest
FBS	Fasting blood sugar
GGT	gamma glutamyl transpeptidase
GTP	guanosine triphosphate
HCV	Hepatitis C virus
HBV	Hepatitis B virus
HCC	hepatocellular carcinoma
HIV	Human immune deficiency virus
HAI	Histology Activity Index
HGF	hepatocytes growth factor
HBsAg	Hepatitis B surface antigen
HCV-Ab	Hepatitis C virus antibody
HbsAb	Hepatitis B surface antibody
HbcAb	Hepatitis B core antibody
IFN	Interferon
IL	interleukin
MHC	major histocompatibility complex
NK	natural killer cells
NANBH	non-A non-B hepatitis
PCT	Porphyria cutanea tarda
PCR	polymerase chain reaction test
PPBS	2 hours postprandial blood sugar
P	propability value

RT-PCR	Reverse transcription polymerase chain reaction test
ROS	reaktive oxygen species
r	correlation coefficient
ROC	Receiver operating characteristic curve
SVR	*Sustained viral response*
SD	Standard deviation
Th	T helper lymphocytes cells
TNF	tumour necrosis factor
TMA	transcription mediated amplification test
VV	vaccinia viruses
WHO	World Health Organization

ABSTRACT

Background: Chronic hepatitis C infection and cirrhosis have slowly progressive course and accompanied by liver inflammation and fibrosis. Increased serum neopterin level has been detected in patients having Chronic hepatitis C disease. Neopterin is produced by monocytes/macrophages when activated by interferon-gamma secreted from T lymphocytes as a part of body immune response against hepatitis C viral infection.

Objectives: To assess the changes in the serum neopterin level in Egyptian patients having chronic liver disease due to hepatitis C virus infection and cirrhosis , and to correlate the neopterin levels with changes in the laboratory parameters and pathological stages of liver disease .

Methods : 85 subjects were included; 40 patients having chronic hepatitis C as group I , 30 patients having cirrhosis as group II and a control group included 15 healthy subjects as group III .

Results : Serum neopterin level was higher in patients with chronic hepatitis C disease and in patients with liver cirrhosis compared to healthy individuals. Also liver cirrhosis patients had higher serum neopterin level than patients with chronic hepatitis C disease.

Conclusion : A correlation was found between serum neopterin level and severity of chronic hepatitis C and cirrhosis as assessed by liver biopsy and Child-Pugh score.

Keywords : Serum neopterin - Chronic hepatitis C disease - Cirrhosis immune response

INTRODUCTION

The World Health Organization has declared hepatitis C as a global health problem, with approximately 3% of the world's population infected with HCV ***(WHO epidemiology report , 2002)***. Egypt contains one of the highest prevalence of hepatitis C in the world. The national prevalence rate of HCV antibody positivity has been estimated to be between 10-13% **(*Mohamed , 2004*).**

The evolution of HCV infection has been shown to be extremely slow and prognosis is very variable ***(Di-Bisceglie ,2000)***. About 15 % of infected individuals recover spontaneously, 25 % have asymptomatic disease with persistently normal alanine transaminase(ALT)**,** and a relatively high percentage (70-80%) proceeds towards chronicity ***(Sherlock and Dooley, 1997 ; Marcellin , 1999).*** Chronic HCV infection can lead to liver damage with development of cirrhosis in 10-20% of patients , and hepatocellular carcinoma (HCC) in 1-5% patients after 20-30 years and the prognosis is much worse if the patient has already developed significant fibrosis ***(Serfaty et al, 1998) .***

Infection by hepatitis C virus causes biochemical, immunological and histological changes in host immune response against the virus. The host viral interaction will determine whether a patient will clear the infection without treatment or have persistence of infection. The success of HCV in causing persistent infection is probably related to its extremely high mutation rate and its existence as multiple quasi-species, each slightly

different in sequence from the other. Many patients have a clinical course characterized by peaks and depressions of clinical and biochemical activity suggesting that HCV may be capable of down regulation in order to reduce immune pressure ***(Brechot , 1994 ; Honda et al., 1994).***

Recent attention has focused on Neopterin as a valuable biochemical marker of cellular immunity. The early innate nonspecific response of the immune system is activated by gamma interferon which activates monocytes/macrophages producing a chemical called 7,8 dihydro-neopterin and its oxidation product neopterin . Due to its chemical structure, neopterin belongs to the class of pteridines. It is excreted in an unchanged form via the kidneys ***(Berdowska et al.,2001).***

Factors that increase neopterin level in normal persons are increased age, white race and use of antihistaminics ***(Diamondstone et al., 1994).*** Elevated neopterin levels result from viral infections ***(Schuster , 1993 ; Shi ,1997)***, immune system activation, autoimmune disorders ***(Fuchs et al., 1995)***, malignant disease ***(Weiss et al., 1993)***, allograft rejection ***(Kamecka, 1994)*** cardiac and renal failure and coronary artery disease ***(Gupta et al. , 1997).*** Increased concentrations of neopterin which were reported in patients with viral infections, provides information about activation of T helper cell derived cellular immune activation***(Schuster , 1993)***.

Neopterin can also be regarded as a marker of reactive oxygen species formed by the activated cellular immune system. Therefore, by neopterin measurements not only the extent of cellular immune activation but also the extent of oxidative stress can be estimated***(Murr et al., 2002)*** .

Studies about association between chronic hepatitis C virus infection and increased neopterin concentrations in blood donors revealed a significant association between neopterin concentrations and a positive PCR result in the HCV antibody-seropositive blood donors ***(Reibnegger et al., 1986 ; Prior et al., 1987) .***

Wilmer and colleagues (1995), found higher levels of neopterin in patients with liver cirrhosis , Increased serum neopterin concentrations were found in 41% of all patients with patients in the cirrhotic stage of disease showing higher neopterin values than those in the non-cirrhotic stage ***(Wilmer et al., 1995 ; Fernandez et al., 2000).***

AIM OF WORK

This study aims to assess the changes in the serum Neopterin level in Egyptian patients having chronic liver disease due to hepatitis C virus infection and cirrhosis , and to correlate the neopterin levels with changes in the laboratory parameters and pathological stages of liver disease .