EVALUATION OF THE RISK OF ATHEROSCLEROSIS IN CHRONIC HEPATITIS C PATIENTS

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By

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ABSTRACT

HCV infection is associated with increased common carotid intima-media thickness (IMT) and carotid-artery plaques in some but not all studies. The aim of this study is to evaluate the relationship between chronic hepatitis C virus (HCV) infection, clearance of HCV and atherosclerosis. It was found that chronic HCV is associated with favourable lipid profile (significant lower serum levels of total cholesterol, TGs and LDL-c). It was also associated with significant higher mesenteric fat thickness and non significant increase in the carotid IMT.

(Key Words): **Chronic hepatitis C – Atherosclerosis – Intima media thickness.**

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ALT	**Alanine transaminase**
AST	**Aspartate transaminase**
ALP	**Alkaline Phosphatase**
Apo A1	**Apolipoprotein A1**
Apo B	**Apolipoprotein B**
CHD	**Coronary Heart Disease**
CMV	**Cytomegalo Virus**
CP	**Chlamydia Pneumonia**
CRP	**C reactive protein**
DICOM	**Digital Imaging and Communication in Medicine**
ELISA	**Enzyme Linked Immunosorbant Assay**
ETR	**End of Treatment Response**
HAI	**Hepatic Activity Index**
HBV	**Hepatitis B Virus**
HCV	**Hepatitis C Virus**
HCC	**Hepatocellular Carcinoma**
HDL	**High Density Lipoprotein**
HP	**Helicobacter Pylori**
HSP	**Heat Shock Protein**
IFN	**Interferon**
IMT	**Intima Media Thickness**
IMT f	**Intima Media Thickness of the far wall**
IMT n	**Intima Media Thickness of the near wall**
IR	**Insulin Resistance**
LD	**Lumen Diameter**
LDL	**Low Density Lipoprotein**
LPS	**Lipopolysaccharide**
MTP	**Microsomal Triglyceride Transfer Protein**
NAFLD	**Non Alcoholic Fatty Liver Disease**
NASH	**Non Alcoholic Steatohepatitis**
NCD	**Non Communicable Disease**
NCEP	**National Cholesterol Education program**

ORF	**Opening Reading Frame**
PCR	**Polymerase Chain Reaction**
SVR	**Sustained Virological Response**
TC	**Total Cholesterol**
TGs	**Triglycerides**
TIFF	**Tagged Image File Format**
TMR	**Transcription Mediated Amplification**
TNF	**Tumour Necrosis Factor**
VEGF	**Vascular Endothelial Growth Factor**
VLDL	**Very Low Density Lipoprotein**
WHO	**World Health Organization**

INTRODUCTION

The incidence of noncommunicable diseases (NCDs) such as cardiovascular disease (CVD), diabetes, cancer, renal, genetic and respiratory diseases is rising significantly in the Eastern Mediterranean Region. Currently, 47% of the Region's burden of disease is due to NCDs and it is expected that this will rise to 60% by the year 2020. The modifiable risk factors—smoking, unhealthy diet and physical inactivity, expressed as diabetes, obesity and high lipids—are the root causes of the global epidemic in NCD. In Egypt noncommunicable diseases account for about 42% of the total deaths while CVD accounts for about 22% ***(WHO, 2004).***

In 1999, CVD and diabetes ranked highest in the league of years of life lost due to premature mortality. In men, these accounted for 23.7% of total years of life lost (YLLs), compared with the second most common cause of premature death, injuries, accounting for 11.7%. CVD and diabetes also accounted for the greatest number of YLL in women ***(National Information Center for Health & Population, 1999).***

Hepatitis C is a major cause of liver-related morbidity and mortality and represents a major public health problem in Egypt and worldwide ***(Alberti and Benvegnu, 2003).***

Egypt has the highest hepatitis C virus (HCV) prevalence in the world (overall prevalence of HCV antibody is 12% in the general population, reaching 40% in persons over age 40 in rural areas) ***(Medhat et al, 2002).***

HCV is the predominant cause of chronic liver disease (CLD) in Egypt and there is a large underlying reservoir of HCV-caused liver disease ***(Strickland et al., 2002).***

In Egypt, HCV is the main cause of hepatocellular carcinoma which occurs in older patients, nearly all of them have advanced fibrosis and cirrhosis ***(El-Sahhar, 2004).***

The countries of the Eastern Mediterranean Region are, therefore, suffering from a double burden of both communicable and noncommunicable diseases ***(WHO, 2004).***

The link between communicable and noncommunicable diseases could exist. In some studies, chronic infections have been found to be associated with atherosclerosis ***(Leinonen and Saikku, 2002).***

Inflammation plays a central role in the initiation and progression of atherosclerotic disease ***(Hansson, 2005).*** It was suggested that infection burden was associated with prevalence of coronary atherosclerosis, and it was particularly important when C-reactive protein was elevated. The high level infection burden could predict vulnerable plaque ***(Niu et al, 2005).***

The possible association between HBs Ag positivity and carotid atherosclerosis was investigated. Findings suggest a possible role of chronic hepatitis B infection in the pathogenesis of carotid arteriosclerosis ***(Ishizaka et al, 2002).*** Other pathogens were found to be associated with atherosclerosis include chlamydia pneumoniae, cytomegalovirus, herpes simplex virus, helicobacter pylori and respiratory infections ***(Smeeth et al, 2004).***

But whether prior infection causes atherosclerosis is unclear. Pathogens could plausibly promote the development of atherosclerosis in a number of ways, including pro-inflammatory and pro-thrombotic effects, disturbances of lipid metabolism, endothelial dysfunction, and increased vulnerability to Plaque rupture ***(Shah, 2001).***

It is possible, but unproven, that hepatitis C (HCV) infection accelerates atherosclerosis. It was concluded that donor hepatitis-C virus seropositivity is an independent risk factor for increased mortality and for the development of accelerated allograft vasculopathy after cardiac transplantation. These observations may have implications for the use of HCV-positive donors in heart transplant recipients ***(Haji et al, 2004).***

By analyzing the data of subjects who had undergone general health-screening tests, a possible association between carotid atherosclerosis and seropositivity of antibody against hepatitis C virus (HCV) has been reported ***(Ishizaka et al, 2003).***

A pilot study was done to assess the atherosclerosis risk factors among those with chronic HCV infection. The lower blood pressure, as well as the better lipid profile, suggests a lower risk of CVD in the group chronically infected with HCV compared to others. But fasting glucose levels were higher among those with chronic HCV infection compared to those not infected ***(Schwarzinger et al, 2004) and (Arafa et al, 2005).***

Chronic hepatitis C is a recognized risk factor for type 2 diabetes and it could be implicated into the pathogenesis of atherosclerosis. The role of hepatitis C virus (HCV)-related steatosis in these epidemiological associations remains to be determined ***(Adinolfi et al, 2005).***

Data regarding the association between atherosclerosis and HCV are controversial. HCV infection is associated with increased common carotid intima-media thickness (IMT) (which is a marker of early atherosclerosis, its anatomic extent and progression) and carotid-artery plaques in some ***(Vassalle et al, 2004)***, but not all studies ***(Volzke et al, 2004).***