Evaluation of Serum Levels of Adiponectin in Egyptian Patients with Hepatitis C Related Chronic Liver Disease

THESIS
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ABSTRACT

Introduction:

Adipose tissue secretes a number of biologically active adipokines one of them is Adiponectin. However there is no data about the secretion of adiponectin during hepatitis C infection, some studies revealed that in chronic HCV patient's hypoadiponectinemia is significantly associated with the development of liver steatosis. Adiponectin may be an attractive therapy for fatty liver disease.

Aim of the work:

The aim of this study is to define a potential role of adiponectin in patients with chronic hepatitis C virus infection in Egypt and to investigate its role in HCV-related steatosis.

Subjects and Methods:

The present study was conducted on forty-fore patients suffering from chronic hepatitis C and sixteen healthy volunteers served as controls. The subjects selected from the National Research Institute for Tropical Medicine and Liver Disease.

Results:

The significant finding of this study is that the chronic HCV patients have reduced circulating adiponectin levels than healthy controls (12.7± 8.2 for HCV vs. 19.5 ± 11.6 for control, P = 0.04). The results of the present study suggest that there is no significant correlation seen between adiponectin and steatosis as well as the grades of steatosis as mean adiponectin level is 9.00 ± 7.45 in steatosis < 30% while it is 14.50 ± 2.12 in steatosis > 30% (P = 0.29).

Conclusion:

In conclusion, this study demonstrates that hypoadiponectinaemia in HCV-infected patients did not correlate with hepatic steatosis.

Key words*:* Adiponectin, HCV, Steatosis

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LIST OF ABBREVIATIONS

- ACC : Acetyl co-enzyme A
- Acrp 30 : Adipocyte complement- related protein 30.
- Adipo R1 : Adiponectin receptor 1.
- Adipo R2 : Adiponectin receptor 2.
- ALT : Alanine transferase.
- AMPK : Adenosine monophosphate kinase.
- APM1 : Adipose most abundant gene transcript 1.
- AST : Aspartate transferase.
- BMI : Body mass index.
- CAMP : Cyclic adenosine monophosphate.
- EIA : Enzyme immunoassay
- ELISA : Enzyme linked immunosorbant assay.
- FFA : Free fatty acids.
- GPCRs : G protein- coupled receptors.
- HCV : Hepatitis C virus.
- HCC : Hepatocellular carcinoma.
- HSc : Hepatic stellate cells.
- HSF : Highly saturated fats.
- HMW : High molecular weight.
- IGF-1 : Insulin like growth factor 1
- IL-10 : Interluekin 10
- IRES : Internal ribosomal entry site.
- KDa : Kilodalton: unified atomic mass unit.
- LDLR : Low density lipoprotein receptor.
- LMW : Low molecular weight.
- NAFLD : Non alcoholic fatty liver disease.
- NTR : None translated region.

- ORF : Open reading frame.
- PI : Phosphatidyle inositol.
- PPARα : Peroxisome proliferators activated receptor alpha ligand
- Pref-1/dlk1: Preadipocyte factor 1 / delta-like 1
- RIBA : Recombinant immunoblot assay.
- RT-PCR : Reverse transcriptase – polymerase chain reaction.
- SR-B1 : Scavenger receptor class B type 1.
- SREBP-1C: Sterol regulatory element-binding protein 1C
- T 1/2 : Half life.
- TG : Triglycerides.
- TNF-α : Tumour necrosis factor alpha
- 7 TM : Seven -transmembrane receptor.
- WAT : White adipose tissue.

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INTRODUCTION

INTRODUCTION

Approximately 200 millions people are chronically infected with hepatitis C virus (HCV) in the world **(Liagpunsakul& Chalasani, 2004)**. HCV accounts for 20% of cases of acute hepatitis, 70% of cases of chronic hepatitis, 40% of cases of end stage cirrhosis, 60% of cases of hepatocellular carcinoma (HCC) and 30% of liver transplantation. It is the most frequent indication for hepatic transplantation **(Consensus, 1999).**

About 85% of those infected with HCV will not clear the virus and will develop chronic hepatitis of varying severity **(Marcellin, 1999).** In approximately 1/3 of patients, ALT is normal despite detectable HCV RNA in serum. Hepatic histology shows only mild disease, hepatic fibrosis progression and activity are also lower **(Jamal, 1999; Marcellin, 1999)** in the remaining 2/3 ALT is elevated usually 2 – 10 times. Mild chronic hepatitis affects 50%, moderate or severe chronic hepatitis is seen in about 50% of newly diagnosed patients. Liver biopsy remains the most accurate way of distinguishing mild from moderate or severe chronic hepatitis **(Barkhuizen et al., 1999).**

Chronic hepatitis C is characterized by several histological features ranging from bile duct damage, lymphoid follicles, steatosis and fibrosis. Although up to 30% of patients with chronic hepatitis C may develop cirrhosis, little is known about factors that determine increasing fibrosis and progressive disease in an individual (**Piche et al., 2004).**

Adipose tissue has traditionally been considered as an energy storage organ but over the last decade, a new role has emerged as an important endocrine organ **(Ahima et al., 2000).**

Adipose tissue secretes a number of biologically active adipokines which is a variety of hormones including Leptin, Resistin, Ghrelin and Adiponectin. The protein leptin, a satiety hormone, regulates appetite and energy balance of the body. Increased Resistin concentration might cause insulin resistance and thus could link obesity with type 2 diabetes. Ghrelin is produced in the stomach and involved in short term regulation of feeding and long term regulation of energy metabolism and lastly adiponectin could suppress the development of atherosclerosis and liver fibrosis and might play a role as an anti inflammatory hormone. These hormones directly influence other organ systems including the brain, liver and skeletal muscle and are significantly regulated by the nutritional status **(Ursula& Axel, 2004).**

Leptin is a highly hydrophobic 16 KDa protein hormone composed of 167 amino acid residue polypeptide. It is encoded by a gene called the obese gene. It is expressed predominantly in adipocytes. Smaller amounts also secreted by stomach and placenta **(Zhang, 1997).**

Leptin exhibiting many important effects; as an adipostat and body weight regulator, glucose homeostasis through antagonizing insulin signaling in hepatocytes leading to increased glycogenolysis and gluconeogenesis and it has angiogenic activity as it induces neovascularization. Leptin plays a crucial role in liver fibrosis. Activated, but not quiescent, hepatic stellate cells express