THE VALUE OF SERUM RETINOL-BINDING PROTEIN 4 LEVELS FOR DETERMINING INSULIN SENSITIVITY IN PATIENTS WITH CHRONIC HEPATITIS C VIRUS INFECTION

Thesis

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٢٠١٢


بسم الله الرحمن الرحيم
وَأَنْزَلَ اللهُ
عَلَيْكَ
الْكِتَابَ
والْحِكْمَةَ
وَعَلَّمَكَ مَا
لَمْ تَكُنْ تَعْلَمُ
وَكَانَ فَضْلُ
اللهِ عَلَيْكَ
عَظِيمًا

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INTRODUCTION

Hepatitis C virus (HCV) infection is one of the principle causes of cirrhosis and hepatocellular carcinoma and has a strong impact on public health worldwide***(Elzanaty et al., 2008).***

HCV currently infects ≈2% of the world's population. Collectively, among all nations, the percentage positive for HCV ranges from 0.01% in Scandinavia to 3% in North Africa, with a single unique exception, Egypt. The prevalence of HCV in Egypt was reported to be 10.8% among first-time blood donors. For more than a decade, Egypt has been widely regarded as having an epidemic, with the highest recorded prevalence of HCV in the world. HCV is currently the most significant public health problem in Egypt the recently published Egyptian Demographic Health Survey (EDHS) in 2009 was a national probability sample of the resident Egyptian population. This report estimated an overall anti-HCV antibody prevalence of 14.7%. The number of Egyptians estimated to be chronically infected was 9.8% ***(Elzanaty et al., 2008).***

RBP4 is the specific transport protein for retinol in the blood, and alterations of retinol intake and vitamin A status affect hepatic release of RBP4 and circulating RBP4,It is well known that the liver is the major source of circulating RBP4 in humans, and therefore the hepatic biosynthetic capacity may greatly influence serum RBP4 ***(Tacke et al., 2008).***

RBP4 is secreted mainly by hepatocytes (80%) but also by adipose tissue (20%), and RBP4 secretion from visceral adipos tissue is increased in patients with obesity and type 2diabetes, which is the reason why this protein is regarded as an adipokine. Circulating RBP4 levels in patients with chronic liver disease are probably dependent on liver protein synthesis capacity and effective hepatic blood flow. In fact, in a recent study that measured hepatic RBP4 production in vivo in patients with cirrhosis, blood concentrations of RBP4 were associated with hepatic production of RBP4 and correlated with circulating levels of albumin, cholinesterase, and coagulation factors ***(Bahr et al., 2008).***

Serum retinol binding protein4 is identified as novel adipokines mediating systemic insulin resistance also hyperinsulinemia and glucose intolerance are present in nearly all patients with liver cirrhosis, and insulin resistance is an established risk factor for disease progression and survival in patients with chronic liver diseases (CLD) ***(Eray et al., 2007).***

AIM OF THE WORK

The aim of our study to investigate the role of serum retinol-binding protein 4 in insulin resistance in patients with chronic hepatitis C infection.

C*hapter 1*

HEPATITIS C VIRUS

Characteristics of hepatitis C virus

It became apparent after the discovery of the hepatitis A and B viruses in the late 1960s and early 1970s that a large proportion of cases of acute and chronic hepatitis could not be explained by either of these agents. Another viral agent was suspected, and patients infected with this suspected agent were said to have non-A, non-B hepatitis. The agent was finally identified in 1989 when the genome of the virus was cloned and the agent was designated the hepatitis C virus ***(Choo et al., 1989)***

**** HCV Genome:***

HCV is an enveloped positive–stranded RNA molecule of approximately 9600 nucleotides, it belongs to the Flaviviridae family and is classified in the genus Hepacivirus. The viral genome is approximately 10 kb in length and encodes 10 viral gene products that are functionally divided into structural and non structural genes. The structural genes include Nucleocapsid (core) and envelop (E1 and E2) genes and are located on the 5` one third of the genome. The non structural genes include p7, NS2, NS3, NS4A, NS4B, NS5A,

and NS5b and are located on the 3` two thirds of the genome ***(Thio et al., 2000).***

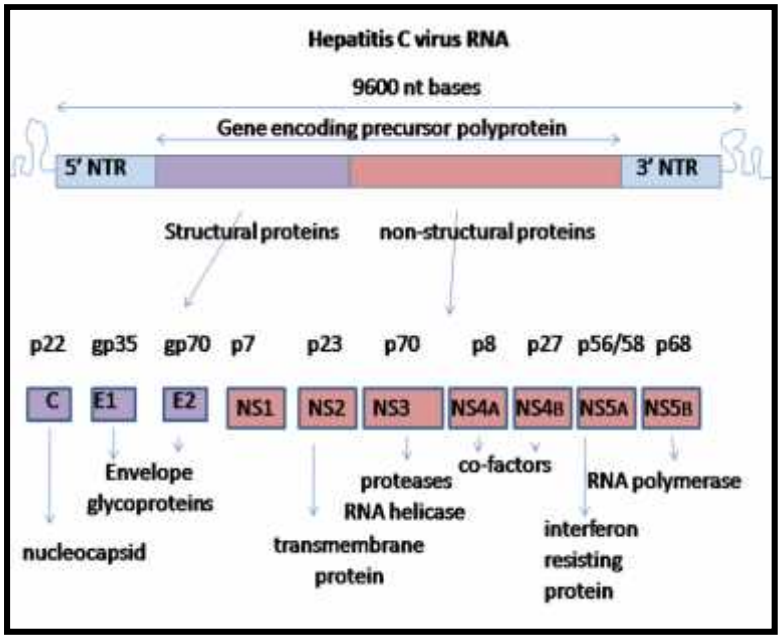

Figure (1): Genome organization of Hepatitis C virus ***(Kato, 2000)***.

Any of the proposed functions of HCV gene products appear to be relevant to potential mechanisms of malignant transformation. The core gene product has been implicated to interact with the pathways related to apoptosis, signal transduction, transcriptional activation, and transformation ***(Lai and Ware., 2000).***

HCV core has also been proposed to have immunosuppressive activities through its interaction with the complement receptor C1qR on T cells, which may contribute to chronic infection Other structural proteins also may play important roles in chronicity and malignant transformation. The structural protein, E2, has been shown to interfere with interferon action in vitro by inhibition of protein kinase R, an important intermediate of interferon effect ***(Kittlesen et al., 2000)***.