Serum Fetuin A Level in Patients with NAFLD and Chronic HCV

Thesis

Submitted for Partial Fulfillment of MSc Degree in Internal Medicine

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2018

سورة البقرة الآية: ٣٢

Acknowledgments

In the beginning I have to thank **Allah** *who gave me power and strength to carry out this work.*

It is a great pleasure to express my sincere gratitude and highest appreciation to ***Prof. Dr.Mohamed Marie Makhlouf,*** *Professor of Gasrtoenterology and Hepatology, Faculty of Medicine Ain Shams University under whose guidance and constant supervision this work has been prepared. Actually, more and above words fail to cope with his overwhelming kindness and moral support that was a great help to me.*

I would like to express my sincere gratitude to ***Dr. Shereen Abou Bakr Saleh****, Assistant Professor of Gasrtoenterology and Hepatology, Faculty of Medicine Ain Shams University for her generous help, valuable suggestions and keen supervision and great effort to achieve this work.*

My deepest appreciations are to ***Dr. Mohamed Magdy Salama.****Lecturer of Gasrtoenterology and Hepatology, Faculty of Medicine, Ain Shams University, for his considerable help and continuous guidance.*

My special thanks and deep appreciation to ***Dr Mohamed Ali Awadeen,*** *Lecturer of Gasrtoenterology and Hepatology, Faculty of Medicine, Misr University For Science and Technology for his great support and encouragement throughout this work.*

Also great thanks to all dear ***professors*** *from whom I learned as well as my dear colleagues who supported me during this work.*

Finally, I dedicate this work to ***my family (my parents, my brothers and my husband)****who was of great help, gave me a lot of guidance and support.*

Roqaya Mahmmed

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Introduction

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Non-alcoholic fatty liver disease (NAFLD) encompasses the simple steatosis to more progressive steatosis with associated hepatitis, fibrosis, cirrhosis, and in some cases hepatocellular carcinoma.NAFLD is considered a growing epidemic, not only in the western world, but worldwide in part due to obesity and insulin resistance leading to liver accumulation of triglycerides and free fatty acids ***(Benedict and Zhang, 2017).***

NAFLD place a strain on the medical system and its resources, it also is associated with a 34%-69% chance of dying over the next 15 years when compared with the general population ***(Patel and Saxena, 2016).***

Hepatic steatosis is a feature of chronic HCV infection and a potentially finalistic condition favoring the persistence and replication of HCV thus be a useful marker for identifying those HCV patients at higher risk of liver disease progression, development of extra-hepatic diseases, and, possibly, reduced response rate to novel antivirals ***(Adinolfi et al., 2016).***

As HCV is an RNA virus with little potential for integration of its genetic material into the host genome, HCV contributes to HCC development in an indirect way, through induction of chronic inflammation, and directly, by means of viral factors. HCV-induced HCC development is a multi-step process that involves establishment of chronic HCV infection,

persistent chronic hepatic inflammation, progressive liver fibrogenesis ***(Billerbeck et al., 2013).***

Chronic infection with HCV is the leading cause of end-stage liver disease, hepatocellular carcinoma (HCC) and liver-related death in Egypt. HCV causes chronic hepatitis in 60%–80% of the patients, and 10%–20% of those patients develop cirrhosis over 20–30 years of HCV infection. About 1%–5% of the patients with liver cirrhosis may develop liver cancer and 3%–6% may decompensate during the following 20–30 years. The risk of death in the following year after an episode of decompensation is between 15% and 20% ***(Westbrook, 2014).***

Adipose tissue is now established as an active endocrine organ that has a big role in secretion of adipokines. Altered adipokine production and secretion can provide a link between adipose tissue dysfunction and obesity related disorders. as they are responsible for regulation of the whole body metabolism because they are involved in impaired insulin sensitivity or secretion, inflammation, fat distribution, satiety, and appetite, as well as endothelial dysfunction and atherosclerosis ***(Kloting and Bluher, 2014).***

Fetuin A is a glycoprotein formed by liver cells and secreted into the serum in high concentration. Fetuin A is formed during embryogenesis. It stimulates bone remodelling, regulates the process of osteogenesis and it inhibits ectopic calcification ***(Szweras et al., 2002).***

An association between insulin resistance and type 2 diabetes in individuals with high serum Fetuin A levels was reported ***(Stefan et al., 2006).***

Fetuin A is an independent risk factor for developing diabetes ***(Eraso et al., 2010).*** Additionally, further studies have emphasized that there may be an association between Fetuin A levels and peripheral arterial disease (PAD) ***(Lorant et al., 2011).***

Fetuin A is secreted into the blood stream and it is deposited as a noncollagenous protein in mineralized bones and teeth. Fetuin A acts as an important circulating inhibitor of ectopic calcification that is a frequent complication of many degenerative diseases ***(Schafer et al., 2003)***.

Human Fetuin A represents a natural inhibitor of tyrosine kinase activity of the insulin receptor. Fetuin A may play a significant role in regulating postprandial glucose disposal, insulin sensitivity, weight gain, and fat accumulation and may be a novel therapeutic target in the treatment of type 2 diabetes, obesity, and other insulin-resistant conditions ***(Rasul et al., 2012).***

Association has been proposed to exist among increased of concentration of Fetuin A, obesity andfatty liver. This is explained by the fact that fetuin A inducesInsulin resistance which is the primary abnormality leading to bothmetabolic syndrome and fatty liver disease. Accumulation off at in adipocytes leads to increased fetuin secretion ***(Reinehr and Roth, 2008).***

Fetuin A levels would associate with this early indicator of NAFLD, as well as serum liver enzymes levels circulating Fetuin A levels elevates in subjects with high liver fat and decrease in liver fat was accompanied by decrease in Fetuin A concentrations ***(Stefan et al., 2006).***

Fetuin A can be used in the diagnosis and treatment of joint arthritis as it is considered an acute phase glycoprotein, which directed scientific attention regarding its anti-inflammatory role ***(Pappa et al., 2017).***