شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم

HANAA ALY

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Role Of Circulating Endocan as a Biomarker in Non-alcoholic Fatty Liver Disease

A Thesis

Submitted for the Partial Fulfillment of the Requirements of Master degree In Internal Medicine & Gastroenterology

By

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Faculty of Medicine
Ain Shams University
2021

سورة البقرة الآية: ٣٢

Acknowledgement

First of all, thanks to Allah, most merciful and compassionate. Without the help of Allah, nothing could be done.

I would like to express my sincere gratitude and deep appreciation to Prof. Noha Abd EL Razek El Nakeeb Professor of Internal medicine & Gastroenterology, Faculty of Medicine, Ain Shams University, for her continuous scientific guidance. Words cannot adequately express my great thanks and gratitude to her.

I am delighted to express my deep gratitude and sincere thanks to Prof. Manal Sabry Mohamed Assistant Professor of Internal medicine & Gastroenterology, Faculty of Medicine Ain Shams University, Faculty of Medicine, Ain Shams University, for her great help, endless support, and kind supervision throughout the period of work.

I am greatly indebted to, Dr. Ahmed Mohamed ElGhandour Assistant Professor of Internal medicine & Gastroenterology, Faculty of Medicine, Ain Shams University, for his continuous interest, helpful cooperation, and effective advice throughout the entire work. He guided me patiently, provided me generously with his valuable experience, which kept me on the right way.

Ahmed Mohamed Elsaid Awad.

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List of Abbreviations

Abbreviation	Full name
NAFLD	nonalcoholic fatty liver disease
MAFLD	metabolic (dysfunction) associated fatty liver disease
T2DM	type 2 diabetes mellitus
TG	triglyceride
HDL	high-density lipoprotein
MS	metabolic syndrome
FFAs	free fatty acids
VLDLs	very low density lipoproteins
DNL	de novo lipogenesis
GLP-1	Glucagon-like insulinotropic peptide-1
FXR	farnesoid X receptor
SOD	superoxide dismutase
Gpx	glutathione peroxidase
SOD2	superoxide dismutase 2
PEMT	phosphatidylethanolamine Nmethyltransferase
FADS1	fatty acid desaturase 1
KLF6	Kruppel-like factor 6
SNP	single-nucleotide polymorphism
MRI	magnetic resonance imaging
CT	computed tomography
AAR	alanine aminotransferase ratio
HIS	Hepatic Steatosis Index
FLI	Fatty Liver Index
VAI	Visceral Adiposity index
PDFF	proton density fat fraction
MRS	Magnetic resonance spectroscopy

CAP	Controlled attenuation parameter
HFD	high-fat diet
LT	liver transplantation
HCV	hepatitis C virus
US	ultrasound
HCC	hepatocellular carcinoma

Introduction

Non-alcoholic fatty liver disease (NAFLD) has emerged as the most prevalent chronic liver disease in developed nations in recent years. It is defined as the presence of 5% steatosis in the absence of secondary causes of fat accumulation in the liver **(Arias-Loste et al., 2014)**. Prevalence of NAFLD is growing, even in the developing world, because of the global obesity epidemic **(Kabbany et al.,2017)**.

Moreover, very close association between the disease and metabolic syndrome has been identified **(Carr et al., 2016)**. The natural history of NAFLD is not well established, with significant knowledge gaps about the marked inter-individual variations in disease onset, progression, and complications. NAFLD represents a wide spectrum of clinical entities from asymptomatic hepatic steatosis to more advanced liver disease with hepatic failure or hepatocellular carcinoma **(Rinella et al ., 2015).**

The rate of disease progression in most cases is slow, although rapid development of advanced liver disease may be occasionally found. About one-third of people eventually develop NASH; however, regression of fibrosis is also noticed in about 20% of these cases. NAFLD is considered as a metabolic disorder that results from complex interaction between genetic, hormonal, and nutritional factors **(Oh et al.,2016)**.

Recent evidence suggests that several genetic risk factors predispose to the development and progression of NAFLD. NAFLD remains asymptomatic in a significant proportion of patients, and the diagnosis is often suspected when liver functions are found abnormal on biochemical testing or when hepatic imaging suggest fatty liver, when performed for some other reasons **(López-Velázquez et al.,2014)**.

NAFLD fibrosis score (NFS) using clinical and biochemical parameters to predict the severity of liver involvement is the most validated non-invasive tool to assess the disease. NFS is based on age, body mass index, aspartate transaminase (AST), ALT, platelets, albumin, and presence or absence of impaired fasting glucose **(Angulo et al., 2007)**.

There is no single intervention that is proven to be fully effective in the treatment and cure of NAFLD. The main goals of treatment are to improve steatosis and to prevent progression of the disease. Intense lifestyle modification and treatment of the risk factors are the cornerstones of disease management. Medical and surgical interventions serve as second-line treatments, or adjuvants. As a result, there has been increased recognition of the need to assess and closely monitor individuals for risk factors of components of NAFLD and NASH, as well as the severity of these conditions using biomarkers **(Verma et al.,2013).**

Endocan, previously called endothelial cell specific molecule-1 is a novel endothelium derived soluble dermatan sulfate proteoglycan. It has the property of binding to a wide range of bioactive molecules associated with cellular signaling and adhesion and thus regulating proliferation, differentiation, migration, and adhesion of different cell types in health and disease. An increase in tissue expression or serum level of endocan reflects endothelial activation and neovascularization which are prominent pathophysiological changes associated with inflammation and tumor progression **(Kali et al.,2014)**.

New insights and diagnostic improvements in NAFLD such as transient elastography and FibroScan are trending. However, focusing on noninvasive, cheap, and useful biomarkers in clinical practice is mandatory. In this way, the role of circulating biomarkers related to

endothelial dysfunction and the severity of underlying liver disease need to be investigated.

It is suggested that there is a role of endocan in vascular contribution to organ-specific inflammation and in endothelium-dependent pathological disorders including many disorders such as systemic inflammatory syndrome. Endocan is not investigated thoroughly in different stages of liver diseases, such as NAFLD **(Erman et al.,2020)**.