بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

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قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

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تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

MONA MAGHRABY

Usefullness of a combined evaluation of the serum adiponectin level and insulin growth factor 1 to predict the early stage of nonalcoholic steatohepatitis

A Thesis

Submitted for Partial Fulfillment of **MD** Degree
in **Gastroenterology and Hepatology**

By

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Dina Morsy Ahmed Mohamed

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List of Abbreviations

Abb.	Full term
ALS	*Acid-labile subunit*
AMPK	*5-AMP-activated protein kinase*
AOX	*aldehyde oxidase*
APPL	*adaptor protein containing pleckstrin homology domain, phosphotyrosine-binding domain and a leucine zipper motif*
ARFI	*Acoustic radiation forced impulse*
BMI	*Body mass index*
CPT	*Carnitine palmitoyltransferase*
CTGF	*Connective tissue growth factor*
CVD	*Cardiovascular disease*
FAS	*Fatty acid synthase*
FFAs	*Free fatty acids*
G6P	*Glucose-6-phosphatase*
GH	*Growth hormone*
HBsAg	*Hepatitis B surface antigen*
HMW	*Highmolecular-weight*
HOMA	*Homeostatic model assessment*
HSCs	*Hepatic stellate cells*
IGFBP-3	*IGF binding protein-3*
IGFBPs	*IGF binding proteins*
IKK-b	*Inhibitor kappab kinase*
IL	*Interleukin*
IL-6	*Interleukin-6*
IR	*Insulin resistance*
IRS-1	*Insulin receptor substrate-1*
ITT	*Insulin tolerance test*
LFTs	*Liver function tests*
LMW	*Low-molecular-weight*

List of Abbreviations (Cont…)

Abb.	Full term
MetS	*Metabolic syndrome*
MMW	*Middle-molecular-weight*
MRE	*Magnetic resonance elastography*
NAFL	*Nonalcoholic fatty liver*
NAFLD	*Nonalcoholic fatty liver disease*
NAS	*NAFLD Activity Score*
NASH	*Nonalcoholic steatohepatitis*
NFκB	*Nuclear factor-kappaB*
PCOS	*Polycystic ovarian syndrome*
PEPCK	*Phosphoenolpyruvate carboxykinase*
PPAR	*Peroxisome proliferator-activated receptor*
ROMs	*Reactive oxygen metabolites*
SNPs	*Single nucleotide polymorphisms*
T2DM	*Type 2 diabetes mellitus*
TGF	*Transforming growth factor*
TGs	*Triglycerides*
TLR	*Toll-like receptor*
TNF	*Tumour necrosis factor*
TNF-a	*Tumour necrosis factor alpha*
TNF-R	*TNF receptor*

INTRODUCTION

The definition of nonalcoholic fatty liver disease (NAFLD) requires that (a) there is evidence of hepatic steatosis, either by imaging or by histology and (b) there are no causes for secondary hepatic fat accumulation such as a significant alcohol consumption, use of steatogenic medication or hereditary disorders ***(Chalasani et al., 2012).***

NAFLD is associated with metabolic risk factors such as obesity, diabetes mellitus, and dyslipidemia ***(Chalasani et al., 2012).***

NAFLD is histologically further categorized into nonalcoholic fatty liver (NAFL) and nonalcoholic steatohepatitis (NASH). NAFL is defined as the presence of hepatic steatosis with no evidence of hepatocellular injury in the form of ballooning of the hepatocytes ***(Vernon et al., 2011).***

NASH is defined as the presence of hepatic steatosis and inflammation with hepatocyte injury (ballooning) with or without fibrosis ***(Chalasani et al., 2012).***

Due to the high prevalence of NAFLD in the general population. Using routine liver biopsy to diagnose NAFLD is unreasonable as it has several limitations including its cost, invasiveness, complications, sampling variability, and inter-observer discordance ***(Gambino et al., 2011).***

Ultrasonography still represents the first-line diagnostic tool in diagnosis of NASH, compared with other imaging studies, it is widely available, convenient, safe, and relatively inexpensive ***(Bohti et al., 2011).***

Fatty liver can be diagnosed by contrast-enhanced CT if absolute attenuation is less than 40 HU, but this threshold has limited sensitivity, MRI may be useful for excluding fatty infiltration, phase-contrast imaging correlates with the quantitative assessment of fatty infiltration across the entire range of the liver ***(Knipe and Gaillard, 2015).***

Serum aminotransferase levels and imaging tests such as ultrasound, CT, and MR do not reliably assess steatohepatitis and fibrosis in patients with NAFLD, therefore, there has been significant interest in developing clinical prediction rules and non-invasive biomarkers for identifying steatohepatitis in patients with NAFLD ***(Gambino et al., 2011).***

Adiponectin is the most abundant and adipose specific adipokine and there is evidence that adiponectin decrease hepatic and systemic insulin resistance and attenuates liver inflammation and fibrosis ***(Polyzos et al., 2010).***

IGF 1 is associated with adiposity and insulin resistance ***(Runchey et al., 2014).***

In this study, we investigate whether adiponectin and IGF 1 are associated with presence of NASH or not.