



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم



MONA MAGHRABY



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شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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MONA MAGHRABY



Usefulness 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

Dina Morsy Ahmed Mohamed

*M.Sc., of Internal Medicine
Faculty of Medicine – Ain Shams University*

Under Supervision of

Prof. Dr. Mohamed Abdel-Fattah El Malatawy

*Professor of Internal Medicine
Faculty of Medicine – Ain Shams University*

Asst. Prof. Dr. Ossama Ashraf Ahmed

*Assistant Professor of Internal Medicine
Faculty of Medicine – Ain Shams University*

Asst. Prof. Dr. Hany Haron Kaiser

*Assistant Professor of Internal Medicine
Faculty of Medicine – Ain Shams University*

Dr. Doaa Mohamed Abdel Aziz

*Lecturer of Clinical Pathology
Faculty of Medicine – Ain Shams University*

**Faculty of Medicine- Ain Shams University
2021**

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سببنا أنك لا تعلم لنا
إلا ما علمتنا أنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgment

*First and foremost, I feel always indebted to **ALLAH**, the Most Kind and Most Merciful.*

*I'd like to express my respectful thanks and profound gratitude to **Prof. Dr. Mohamed Abdel-Fattah El Malatawy**, Professor of Internal Medicine, Faculty of Medicine – Ain Shams University for his keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.*

*I am also delighted to express my deepest gratitude and thanks to **Asst. Prof. Dr. Ossama Ashraf Ahmed**, Assistant Professor of Internal Medicine, Faculty of Medicine – Ain Shams University, for his kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.*

*I am deeply thankful to **Asst. Prof. Dr. Hany Haron Kaiser**, Assistant Professor of Internal Medicine, Faculty of Medicine – Ain Shams University, for his great help, active participation and guidance.*

*I wish to introduce my deep respect and thanks to **Dr. Doaa Mohamed Abdel Aziz**, Lecturer of Clinical Pathology, Faculty of Medicine – Ain Shams University, for her kindness, supervision and cooperation in this work.*

I would like to express my hearty thanks to all my family for their support till this work was completed.

Last but not least my sincere thanks and appreciation to all patients participated in this study.

Dina Morsy Ahmed Mohamed

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List of Abbreviations

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

List of Abbreviations (Cont...)

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

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.