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مسئولية عن محتوى هذه الرسالة.

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FIBRO-SCAN BASED SCORE AND NOVEL NONINVASIVE SERUM MARKER, FGF-21, TO ASSESS LIVER FIBROSIS IN MORBIDLY OBESE PATIENTS

Thesis

**Submitted for partial fulfillment of Master's degree In
gastroenterology and Internal medicine**

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**النتيجة المعتمدة على المسح الليفى مع استخدام (FGF-21)
كأحدث تحليل لتقييم التليف الكبدي في مرضى السمنة المفرطة
المصابين بمرض الكبد الدهني**

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CONTENTS

Title	Page
• List of Abbreviations	V
• List of Table	VII
• List of Figures.....	IX
• Introduction	1
• Aim of the work	4
• Review of literature.....	
Chapter (1): Non-Alcoholic Fatty Liver Disease	5
Chapter (2): Obesity	55
Chapter (3): Fibroblast growth factor 21	82
Chapter (4): Fibro-scan Based Score and novel non-invasive serum marker, FGF-21, to assess Liver Fibrosis in Morbidly Obese Patients.....	102
• Subjects And Methods	117
• Results	125
• Discussion.....	143
• Conclusion	155
• Recommendations	156
• Summary.....	157
• References	162
• الملخص العربي	180

LIST OF ABBREVIATIONS

Abb.	Full term
ALT	Alanine aminotransferase
APRI	AST-to-Platelet Ratio Index
AST	Aspartate aminotransferase
AUC	Area under the curve
cAMP	Cyclic adenosine monophosphate
CK-18	Cytokeratin 18
ECM	Extra ceullular matrix
ELF	Enhanced liver fibrosis
FGFRs	Fibroblast growth factor receptors
GGT	Gamma-glutamyl transferase
HA	Hyaluronic acid
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HDL	High density lipoproteins
HSCs	Hepatic stellate cells
IASL	International Association of the Study of the Liver
IL	Interleukin
IQR	Interquartile range
LDL	Low density lipoproteins
LFTs	Liver function tests
MASH	Metabolic associated steatohepatitis
MMPs	Matrix metalloproteinase
MRE	Magnetic resonance elastography
MRE	Magnetic resonance elastography
MS	Metabolic syndrome
NAFLD	Nonalcoholic fatty liver disease
NASH	Nonalcoholic steatohepatitis
OELF	Original ELF
PBC	Primary biliary cirrhosis
PCOS	Polycystic ovarian Syndrome
PKA	Protein kinase A
ROC	Receiving operating characteristic
TE	Transient elastography

List of Abbreviations

Abb.	Full term
TIMP	Tissue inhibitor of metalloproteinase
VLDL	Very-low-density lipoprotein

LIST OF TABLE

Table No	Subjects	Page
Table (1):	Non-alcoholic fatty liver disease activity scoring system	30
Table (2):	Steatosis, activity, and fibrosis scoring system.....	31
Table (3):	Brunt grading and staging of nonalcoholic steatohepatitis	32
Table (4):	Histologic comparison of non-alcoholic fatty liver disease/non-alcoholic steatohepatitis and alcoholic liver disease	34
Table (5):	Factors to be assessed in the evaluation of a patient with suspected non-alcoholic fatty liver disease	42
Table (6):	The International Classification of adult underweight, overweight and obesity according to BMI	56
Table (7):	Adult Treatment Panel definition of the metabolic syndrome.....	77
Table (8):	Serum level, absolute and normalize, of FGF21 regarding the transgenic mice, reported into the literature.....	91
Table (9):	Distribution of the studied cases according to demographic data (n=50).....	125
Table (10):	Distribution of the studied cases according to examination (n =50).....	127
Table (11):	Distribution of the studied cases according to Co-morbidity (n=50).....	128
Table (12):	Distribution of the studied cases according to lab investigation (n=50)	129
Table (13):	Distribution of the studied cases according to fibrosis grade (n=50).....	131
Table (14):	Distribution of the studied cases according to non-invasive markers (n=50)	132
Table (15):	Relation between fibrosis grades with demographicdata	132

List of Table

Table No	Subjects	Page
Table (16):	Relation between fibrosis grades with examination.....	134
Table (17):	Relation between fibrosis grades with lab investigation.....	136
Table (18):	Relation between fibrosis grades with lab investigation"continue.....	138
Table (19):	Relation between fibrosis grades with Non-invasive markers	140
Table (20):	Correlation between Fibrosis grade and different parameters (n= 50)	142

LIST OF FIGURES

Figure No	Subjects	Page
Figure (1):	Metabolic associated fatty liver disease and the influence on liver transplantation. MAFLD: Metabolic associated fatty liver disease.....	53
Figure (2):	The World Health Organization worldwide distribution of obesity.....	62
Figure (3):	Multivariate Relative Risk of Death from Cardiovascular Disease, Cancer, and All Other Causes among Men and Women Who Had Never Smoked and Who Had No History of Disease at Enrollment, According to Body-Mass Index.....	81
Figure (4):	Signaling pathways that control FGF21 expression in skeletal muscle and FGF21-mediated metabolic effect on different tissues.....	95
Figure (5):	Distribution of the studied cases according to sex.....	126
Figure (6):	Distribution of the studied cases according to mean Weight (Kg).	127
Figure (7):	Distribution of the studied cases according to Co-morbidity.....	128
Figure (8):	Distribution of the studied cases according to mean HBA1C.....	130
Figure (9):	Distribution of the studied cases according to fibrosis grade.	131
Figure (10):	Relation between fibrosis grades and sex.....	133
Figure (11):	Relation between fibrosis grades and mean Weight (Kg).	135
Figure (12):	Relation between fibrosis grades and mean Cholesterol.....	137
Figure (13):	Relation between fibrosis grades and mean GGT (U/l).	139

✍ List of Figures

Figure No	Subjects	Page
Figure (14):	Relation between fibrosis grades and mean APRI.	141

INTRODUCTION

Finding a means to noninvasive diagnosis of non-alcoholic fatty liver disease (NAFLD) and its entities has been the aim of many research efforts since recently, and seems to remain a very much needed goal among many clinicians and researchers in the field of hepatology. Why is it that way? NAFLD is today considered to be the most common liver disease in adults. The prevalence of NAFLD in general population is very high, in the range of 15%-30% according to various studies, and is even increasing, due to the rising prevalence of diabetes and obesity. **(Ratziu et al., 2009).**

Spectrum of NAFLD includes two entities with very different natural course and prognosis: simple steatosis, which mostly has a benign non-progressive course and good prognosis, and non-alcoholic steatohepatitis (NASH), which demonstrates progression of fibrosis in about 30%-40% of patients and has a proven potential to eventually lead to cirrhosis an end-stage liver disease including hepatocellular carcinoma. **(Ekstedt et al., 2006), (Matteoni et al., 1999), (Adams et al., 2005)**

NASH seems to be present in a surprisingly high proportion of NAFLD patients, including 40% to 75% of cases with elevated aminotransferase levels, those data coming from recent studies using current histological definitions and including substantial number of patients

(Ekstedt et al., 2006), (Söderberg. et al., 2010), (Fracanzani et al., 2008)

In studies of liver biopsy findings from apparently healthy living liver donor candidates, the proportion of NASH among patients with newly discovered NAFLD was about 30%. *(Minervini et al., 2008)*

Even in patients with normal aminotransferase levels, proportion of NASH among NAFLD cases seems to be almost the same, and the whole spectrum of NAFLD including advanced fibrosis and cirrhosis has been observed in patients with completely normal laboratory findings. *(Fracanzani et al., 2007), (Mofrad et al., 2002), (Sorrentino et al., 2005)*

Liver biopsy is still considered the gold standard in diagnosis and the only reliable tool for distinguishing NASH from simple steatosis and for grading and staging the disease, providing important information about severity of steatosis, lobular inflammation, hepatocellular ballooning, and degree of fibrosis. *(Neuschwander-Tetri et al., 2019)*

Minimal histological criteria for NASH include steatosis, hepatocyte injury (in the form of ballooning or apoptosis) and lobular inflammation. Similarly to other chronic liver diseases, fibrosis is usually divided histologically in four stages: perisinusoidal fibrosis (F1), perisinusoidal and periportal fibrosis (F2), bridging fibrosis

(F3) and cirrhosis (F4). Liver biopsy also has several negative aspects: it is invasive, unpleasant for patients, it usually includes hospitalization and a day or two lost at work, and the adequate interpretation of the specimen requires a pathologist with expertise in hepatopathology, which altogether makes it a costly and time-consuming procedure. Another significant drawback of liver biopsy, and in medical terms the most important one is its substantial sampling variability, which has been consistently proven for several chronic liver diseases including NAFLD. In a well-designed study by Ratziu et al. (*Ratziu et al., 2005*)

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AIM OF THE WORK

This prospective cohort study aims to develop and validate noninvasive scoring system for assessment liver fibrosis in morbidly obese patients with NAFLD.