شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم

HANAA ALY

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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

يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

HANAA ALY

STUDY OF THE RELATION BETWEEN SERUM LIPOPROTEIN-ASSOCIATED PHOSPHOLIPASE A2 (LP-PLA2) LEVEL AND NONALCOHOLIC FATTY LIVER DISEASE (NAFLD)

Thesis

Partial fulfillment Submitted for master degree and in

Internal medicine, Gastroenterology and Hepatology

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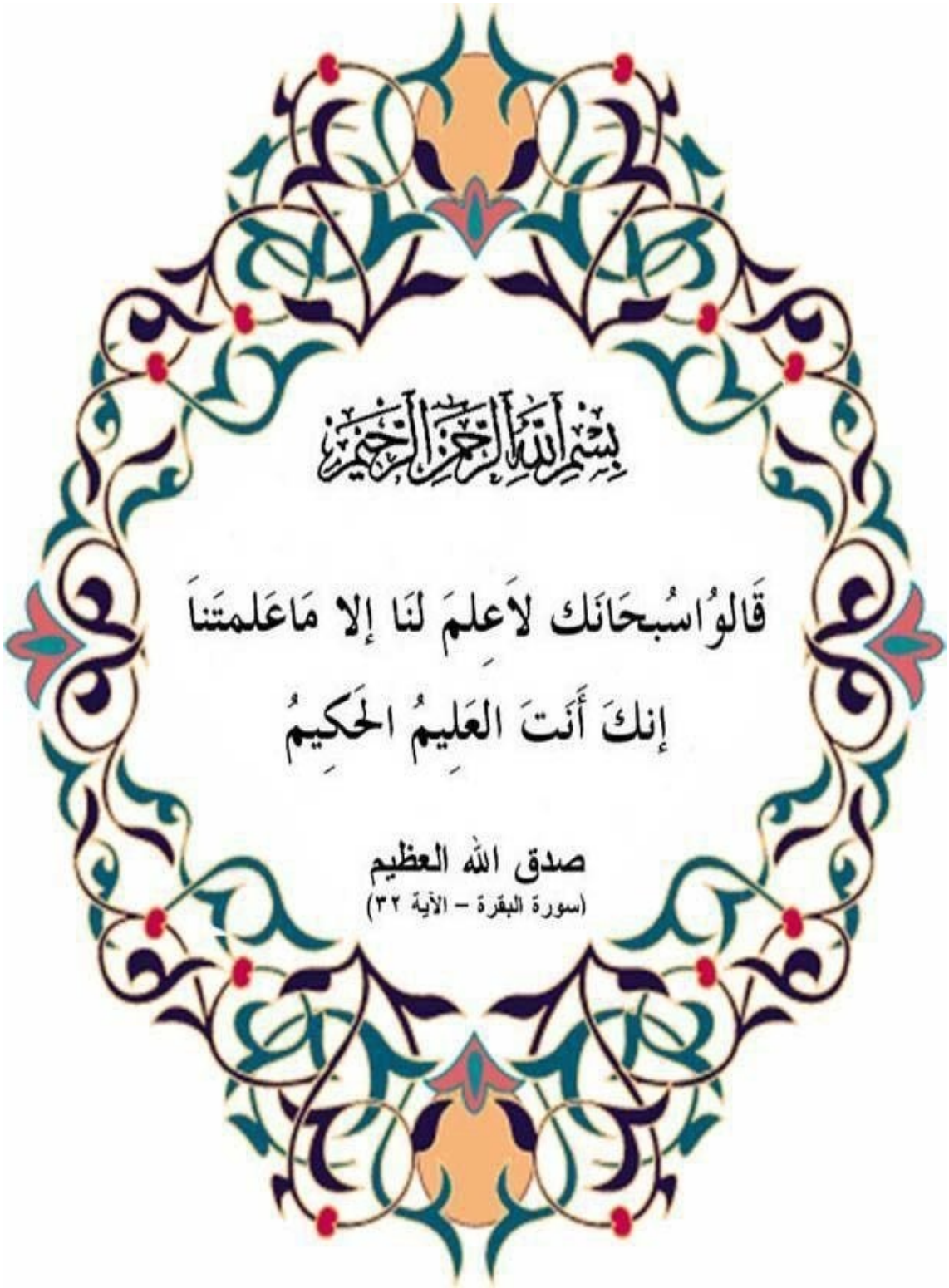
بسم الله الرحمن الرحيم
قَالوُاسُبحَانَك لاَعلمَ لنَا إلا مَاعَلمتَناَ
إنكَ أَنتَ العَلِيمُ الحَكِيمُ
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ARFI	acoustic wave force impulse
AUROC	area under receiver operating characteristic
BBB	blood-brain barrier
BMI	body mass index
BRB	blood-retinal barrier
CAP	Controlled attenuation parameter
CAVD	calcific aortic valve disease
CCR2	chemokine ligand receptor 2
CNS	central nervous system
CP	Chronic periodontitis
CRN	Clinical Research Network
CT	computed tomography
CVDs	cerebrovascular diseases
DGAT	diacylglycerol acyltransferase
DM	diabetes mellitus
ECs	endothelial cells
ER	endoplasmic reticulum
F1	fibrosis
FFAs	free fatty acids
FLI	Fatty Liver Index
FS	Fat Score
FXR	farsinoid X receptor
GSK	GlaxoSmithKline
HCC	hepatocellular carcinoma
Hh	hedgehog
HSCs	hepatic stellate cells
IL	interleukin
IQR	interquartile range
KCs	Kupffer cells
Lp-PLA2	Lipoprotein-associated phospholipase A2
LPS	lipopolysaccharide
lysoPC	lysophosphatidylcholine
MBOAT7-TMC4	membrane bound O-acyltransferase domain-containing 7 gene and transmembrane channel-like 4 gene
MCP	monocyte chemotactic protein
MTP	microsomal transfer protein
NAFL	nonalcoholic fatty liver
NAFLD	Nonalcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
NF	nuclear factor
NFS	NALFD Fibrosis Score
NICE	National Institute for Health and Care Excellence
NPDR	nonproliferative stage
oxNEFAs	oxidized nonesterified fatty acids
PAF-AH	platelet-activating factor acetylhydrolase

PDR	proliferative stage
PGx	pharmacogenetic
PNPLA3	patatin-like phospholipase domain-containing protein 3
PPAR	peroxisome proliferator-activator receptor
SFAs	saturated fatty acids
SMCs	smooth muscle cells
SREBP1c	sterol-regulatory element binding protein 1c
TAGs	triacylglycerols
TE	transient elastogrpahy
TLR	toll-like receptor
TNF	tumor necrosis factor
UKPDS	UK Prospective Diabetes Study
US	ultrasonography
VLDL	very low-density lipoprotein
WHR	waist–hip ratio

ABSTRACT

Background; Nonalcoholic fatty liver disease (NAFLD) is the hepatic manifestation of metabolic syndrome and is one of the most common causes of chronic liver disease, worldwide. Lipoprotein-associated phospholipase A2 (Lp-PLA2) was recently characterized as a novel inflammatory biomarker that is correlated with several components constituting the metabolic syndrome, **Aim and objectives** to study serum levels of Lp-PLA2 in patients with NAFLD to detect its relation to the incidence and severity of NAFLD, **Subjects and methods;** This is Case Control cross -sectional clinical Study, was carried out at Internal Medicine and Hepatology outpatient clinic at Ain Shams University Hospital on 80 persons were divided into 2 groups: (Group-I): 40 patient with NAFLD as a study group, (Group-II): Forty(40) healthy subjects as a control group, **Result;** There was high statistically significant difference between the studied groups as regard Lp-PLA2, **Conclusion**; The clinical use of Lp-PLA2, a biomarker for NAFLD, requires the standardization of analytical methods, characterization of analytical features, assessment of performance characteristics, incremental yield of different markers for given clinical indications, and demonstration of cost-effectiveness,
Keywords; NAFLD; NASH; LP-PLA2.

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) now refers to a spectrum of liver diseases that rangs from steatosis (i.e., fatty infiltration of the liver) to Non-alcoholic steatohepatitis (NASH) ie, steatosis with inflammation and hepatocyte necrosis, to fibrosis and cirrhosis with increased risk of hepatocellular carcinoma ***(Angulo, 2002)***. NAFLD is the most common cause of cryptogenic cirrhosis, which is cirrhosis that cannot be explained by hepatitis, alcohol abuse, toxin exposure, autoimmune disease, congenital liver disease, vascular outflow obstruction, or biliary tract disease ***(Clark and Diehl, 2003).***

Global prevalence of NAFLD is 25.24% with highest prevalence in the Middle East and South America and lowest in Africa. Metabolic comorbidities associated with NAFLD included obesity (51.34%), type 2 diabetes (22.51%), hyperlipidemia (69.16%), hypertension (39.34%), and metabolic syndrome (42.54%). HCC incidence among NAFLD patients was 0.44 per 1,000 person ***(Younossi et al., 2016).***

The mechanism of the liver injury in NAFLD is currently thought to be a “multiple-hit process” where the first “hit” is represented by an increase in liver fat, followed by multiple additional factors that trigger inflammatory activity which leads As a consequence to mitochondrial dysfunction with oxidative stress and production of reactive oxygen species and endoplasmic reticulum (ER) stress-associated mechanisms are activated ***(Buzzetti et al., 2016).***

NAFLD shares the same etiologic factors with metabolic syndrome, such as obesity, diabetes, and dyslipidemia. These are also major cardiovascular risk factors. Several epidemiological studies

indicate that NAFLD, especially in its more severe forms, is linked to an increased risk of cardiovascular disease, and this increased risk is independent from underlying cardio-metabolic risk factors Furthermore, in recent studies, NAFLD itself has been shown as an atherosclerotic risk factor ***(Targher et al., 2010).***

Lipoprotein-associated phospholipase A2 (Lp-PLA2) was recently characterized as a novel vascular-specific inflammatory biomarker correlated with several components constituting the metabolic syndrome and implicated in atherosclerosis and used for cardiovascular risk assessment. Several clinical epidemiological studies have been published demonstrating the relationship between serum Lp-PLA2 levels and increased risk of cardiovascular disease ***(Wang et al., 2017).***

Oxidative stress is regarded as a major leading cause of NAFLD, and the anti-oxidative property of Lp-PLA2 has been well addressed by several studies However, few studies were performed to explore the relationship between Lp-PLA2 and NAFLD occurrence ***(Rosenson, and Stafforini, 2012).***