بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

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MONA MAGHRABY

Study of IL-10 serum marker and its association with NAFLD in adult Egyptian patients

Thesis Submitted For Partial Fulfillment of Master Degree
In Gastroenterology

By

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Bishoy Refaat Rassmy Harown

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LIST OF ABBREVIATIONS

Abb	Full Term
ALT	alanine aminotransferase
AST	aspartate aminotransferase
BMI	body mass index
CRF2	cytokine receptor family
CSIF	cytokine synthesis inhibitory factor
CT	computed tomography
FF	free fatty
FFA	free fatty acids
GGT	Gamma glutamyl transferase
GIP	glucose-dependent insulin tropic polypeptide
GLP-1	glucagon-like peptide-1
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HDL	High-density lipoprotein
HNE	4-hydroxy-2-trans-nonenal
HSI	Hepatic Steatosis Index
IFN	interferon
IL	interleukin
IR	insulin resistance
LFTs	Liver function tests
LPS	lipopolysaccharide
LT	liver transplantation
MTP	The microsomal triglyceride transfer protein
NAFL	nonalcoholic fatty liver
NAFLD	nonalcoholic fatty liver disease
NASH	Nonalcoholic steatohepatitis
NK	Nuclear kappa
PPARα	Peroxisome proliferator-activated receptors
ROS	reactive oxygen species
SNPs	single nucleotide polymorphisms
TGF	transforming growth factors
Th2	T-helper cell clones

TNF	tumor necrosis factors
VLDL	very low-density lipoprotein

ABSTRACT

Background;Non-alcoholic fatty liver disease (NAFLD) is commonly associated with obesity and diabetes, and is characterized by insulin resistance (IR) Cytokines and adipocytokines (i.e. mediators mainly derived from adipose tissue) play a major role in the orchestration of inflammatory processes throughout the body, **Aim and objectives;** To evaluate the relation between serum levels of IL-10 and NAFLD in Egyptian patients, **Subjects and methods;** This study is A randomized case control cross sectional study, was carried out at Eldemrdash University Hospital, Internal medicine departments, on patients above 18 years old with Hepatic Steatosis Index (HSI) and NAFLD, duration of study about 6 months, **Result;** There was high statistically significant difference between studied cases as regard IL-10, **Conclusion**; high IL-**10 levels limiting the effects of the inflammatory response that is, by** counter regulating the effects of pro-inflammatory cytokine so that the protective function of IL-10 in steatotic liver relies on suppression of TNF-a production. Morbidly obese patients with increased age and elevated levels of LDL, fasting glucose, HOMA-IR, and TNF-a, in combination with low circulating levels of IL-10, seem to be at higher risk to develop severe-NAFLD and should be clinically monitored,
Keywords; Non-alcoholic fatty liver disease; Tumor necrosis factor alpha; Interleukin-10; Steatohepatitis.

INTRODUCTION

In the last decade, there has been a remarkable scientific effort to improve our understanding of the pathogenesis, diagnosis, and treatment of non-alcoholic fatty liver disease (NAFLD). Clinical studies revealed dramatically high prevalence of NAFLD worldwide *[Chen SH et al, 2011- Andersen T et al,1994]*. Worrying data on the prevalence of NAFLD in children and adolescents was also revealed *[Manco M et al, 2008]*. Importantly, in American adolescents followed in the National Health and Nutrition Examination Survey between 1999 and 2004, serum elevation of hepatic enzymes [i.e. (AST), (ALT)] was observed in 6% to 11% of subjects (depending of ethnicity) *[Fraser A et al, 2007]*. Furthermore, serum ALT increase was positively associated with waist circumference and insulin resistance, suggesting that NAFLD might be considered as the hepatic manifestation of other epidemic diseases, such as metabolic syndrome and obesity *[Chen SH et al, 2011- Andersen T et al,1994]*. In fact, in obese children and adolescents, NAFLD affects about 20% to 74%, indicating that this disease might start early during life, providing more time for its deleterious evolution *[Strauss RS et al, 2000 - Chan DF et al, 2004]*. Although NAFLD has been described as an increased hepatic accumulation of fat (steatosis), a recent scientific consensus defined it as a complex spectrum of diseases, ranging from asymptomatic steatosis with possible aminotransferase alterations to non-alcoholic steato-hepatitis (NASH), cirrhosis, and also hepatocellular carcinoma *[Adams LA et al, 2005 - Angulo P et al, 2002]*. Whether these conditions are different stages of a common progressive disease or should be considered as different entities, is still an open question.

Thus, additional pathophysiological studies on improved animal models are needed to clarify this issue. Indeed, NAFLD is often underestimated, under diagnosed, and not treated in the current medical practice; therefore, its pathophysiological history is at risk of remaining a mystery for several years.

At present, the most suitable area for improving our knowledge of the pathophysiology of NAFLD is represented by the chronic inflammation that underlies all NAFLD entities/stages *[Tarantino G et al, 2010]*. Soluble cytokines and chemokines, regulating inflammatory cell function and survival, could be considered as very promising candidates. On the other hand, hormonal axes, adipocytokines, and growth factors have also received attention from NAFLD scientists..

*Aim of the Wor*k

Aim of The Work was to evaluate the relation between serum levels of IL-10 and NAFLD in Egyptian patients

Chapter (1)

NAFLD history and pathogenesis

Definition and spectrum:

Pseudoalcoholic hepatitis, alcohol-like hepatitis, fatty liver hepatitis, steatonecrosis, and diabetic hepatitis are also used to describe nonalcoholic fatty liver disease (NAFLD). NAFLD is the term used to describe the alcohol-like liver injury that occurs in the absence of alcohol abuse and embraces the range of histological abnormalities including simple steatosis or fatty liver (NAFL), non-alcoholic steatohepatitis (NASH) and NAFLD induced cirrhosis **(Figure 1)** ***(Byrne & Targher, 2015).***

Although various conditions such as hepatitis C infection, starvation, alcohol abuse and drug toxicity may cause fatty infiltration of the liver, the term NAFLD is reserved for the liver manifestation associated with the metabolic syndrome ***(Younossi et al., 2018).***

Two major factors are responsible for the rapid increase in prevalence of this condition; namely increasing obesity and the practice of measuring parameters of liver function before starting statin therapy. Although NAFLD is undoubtedly a common condition, it is still under-recognized and under-diagnosed with much unknown about its natural history, pathogenesis and treatment ***(Cusi et al., 2017).***

NAFLD is subdivided into:

- **Nonalcoholic fatty liver (NAFL):** in which hepatic steatosis is present without evidence of significant inflammation