Ain Shams University
Faculty of Medicine
Department of Internal Medicine

# Assessment of Omentin-1 as an Adipokine in obese male and females with and without fatty liver disease

*A Thesis submitted for Partial Fulfillment of Master Degree in Internal Medicine*

**By**

**Amal Muatafa Ali Mustafa Eid Aboreziq**

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**Under supervision of**

**Prof. Dr. Mohammed Ali Marei Makhlouf**

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

**Dr. Gina Gamal**

**Lecturer of Internal Medicine**
**Faculty of Medicine**
**Ain Shams University**

**Dr. Ahmad Magdy**

**Lecturer of Internal Medicine**
**Faculty of Medicine**

**Faculty of Medicine**
**Ain Shams University**
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بسم الله الرحمن الرحيم
قَالوُاسُبحَانَك لاَعلِمَ لنَا إلا مَاعَلمتَناَ
إنكَ أَنتَ العَلِيمُ الحَكِيمُ
صدق الله العظيم
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*Amal Mustafa Ali Mustafa Eid Aboreziq*

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## LIST OF ABBREVIATIONS

| Abb | Full Term |
|---|---|
| NAFLD | Non-alcoholic fatty liver disease |
| HCC | hepatocellular carcinoma |
| NAFL | non-alcoholic fatty liver |
| PCOS | Polycystic ovarian syndrome |
| OSA | Obstructive sleep apnea |
| HTAG | hepatic triacylglycerol |
| ALD | alcoholic liver disease |
| SAT | subcutaneous adipose tissue |
| VAT | visceral adipose tissue |
| WA | white adipocytes |
| BA | brown adipocytes |
| WAT | white adipose tissue |
| DM | diabetes mellitus |
| MetS | metabolic syndrome |
| OSAS | obstructive sleep apnoea syndrome |
| CRP | C-reactive protein |
| TNF-a | tumour necrosis factor-a |
| IL-6 | interleukin-6 |
| FFA | free fatty acid |
| T2DM | type 2 diabetes mellitus |
| mRNA | Omentin messenger ribonucleic acid |
| IGT | impaired glucose tolerant |
| IR | insulin resistance |
| NASH | nonalcoholic steatohepatitis |
| BMI | body mass index |
| ASP | Acylation-stimulating protein |
| C5L2 | chemoattractant receptor-like protein |

# ABSTRACT

**Background;** Omentin- 1 and chemerin have been identified as interesting novel adipokines that may modulate insulin action. Also, they have been suggested to be linked to obesity- induced insulin resistance, **Aim and objectives;** To evaluate the assessment of omentin-1 as an adipokine in obese male and females with and without fatty liver disease, **Subjects and methods;** This is a comparative case control study, was carried out at outpatients clinics of internal medicine department of Ain Shams University,on 40 patients divided into two groups: Group (A): 20 patient with fatty liver 10 of them obese and 10non obese Group (B):20 not have fatty live 10obese and 10 non obese, from November 2019 till May 2020, **Results**: there was high statistically significant difference between the four studied subgroups as regard Triglycerides and statistically significant difference as regard Cholesterol and LDL.C, **Conclusion**; Our results suggest that serum omentin levels are raised in patients with NAFLD regardless of potential confounders and represent an independent predictor of hepatocyte ballooning. Also, decreased omentin levels have a close association with metabolic syndrome in women with morbid obesity, **Keywords; Adipokines, enzyme-linked immunosorbent assay, liver fibrosis, nonalcoholic fatty liver disease.**

# INTRODUCTION

*Omentin-1 (intelectin-1,IS new adipocytokine COMPOSED OF of 313 aminoacids, described in 2003expressed in plasma ,visceral fat and other va.it is plays crucial roles in diabetic , insulin resistance, obesity and inflammation produced. Plasma levels of omentin-1 are decreased in obesity and other insulin-resistant states, also OMENTINE1contributes to the changes of cholesterol synthesis and absorption. OMENTIN-1may be use as biomarker to heart disease, poly cystic overy syndrome, bone metabolism, Inflamotry disease, cancer, sleep apnea syndrom and preeclampsia, coronary heart disease and peripheral heart disease also play arole in these disease many research done to discover these role ometrin levels were significantly higher in patients with NAFLD than in controls but more studay need tobe done to confirm this relation shipe.*

However, its role in the liver pathogenesis and in the metabolic consequences of the liver disorders is not fully elucidatedincrease level of omentine- 1in obese fatty liver patient.also need to be observed in non obese fatty liver disease.

We need to studay about the relation of serum omentin-1 with fatty liver in obese and non obese.Study show that with control of hypertension, Weight loss, OLIVE OIL RICH diet, aerobic exersize training, aorvastatine, antidiabetic drugs treatment, are effectiveway of increasing serum omentine -1level.

Obesity is associated with a spectrum of liver abnormalities, known as nonalcoholic fatty liver disease (NAFLD), characterized by an increase in intrahepatic triglyceride (IHTG) content (i.e. steatosis) with or without inflammation and fibrosis (i.e. steatohepatitis). NAFLD has become an important public health problem because of its high

prevalence, potential progression to severe liver disease, and association with serious cardiometabolic abnormalities, including type 2 diabetes mellitus (T2DM), the metabolic syndrome and coronary heart disease.

# AIM OF THE WORK

The aim of this study is the assessment of omentin-1 as an adipokine in obese male and females with and without fatty liver disease.

# Chapter **(1)**

# Non-Alcoholic Fatty Liver Disease

## I. INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is an umbrella term and encompasses the simple deposition of adipose tissue in the liver to more progressive steatosis with associated hepatitis, fibrosis, cirrhosis, and in some cases hepatocellular carcinoma (HCC). For the sake of terminology, NAFLD is comprised of non-alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH). NAFL is characterized by steatosis of the liver, involving greater than 5% of parenchyma, with no evidence of hepatocyte injury. Whereas, NASH is defined by histologic terms that is a necroinflammatory process whereby the liver cells become injured in a background of steatosis. Although the natural history of NAFLD remains incompletely characterized, what is clear from the published data is a risk of progression to cirrhosis and HCC (**Lebeaupin et al., 2018).**

However, whether there is a clear progression of NAFL to NASH is under active investigation, but early evidence suggests this could be the case. In terms of epidemiology, several studies have tried to quantify the true worldwide incidence of NAFL/NASH; however, due to extreme variations in study parameters and available testing, a clear and reliable occurrence rate is not currently available. With that being said, estimates have been posited suggesting the incidence of NAFLD to be 20%-30% in Western countries and 5%-18% in Asia. It is no surprise that the prevalence of NAFLD is increasing worldwide with each passing year, given the current trends in dietary irresponsibility and preponderance of a sedentary lifestyle (**Bellentani, 2017).**

Additionally, there has been a linear rise of NAFLD with that of diabetes and metabolic syndrome. In one study from the United States, it was shown that

the incidence of NAFLD was 10% higher in overweight individuals compared to lean persons. In fact, NAFLD has been projected, within the next 20 years, to become the major cause of liver related morbidity and mortality as well as a leading indication for liver transplantation. As it currently stands, NAFLD represents the second most common reason to be listed for a liver transplant Additionally, not only does NAFLD place a strain on the medical system and its resources, it also is associated with a 34%-69% chance of dying over the next 15 years when compared with the general population. The pathogenetic processes that underscore NAFLD typically lead to death by cardiovascular disease with liver related mortality only accounting for 5% in these individuals (**Buzzetti et al., 2016).**

In this **chapter**, we will provide context for how and why NAFLD develops, current genetic proposals, histologic criteria, differential diagnoses, and prognosis of this very important disease affecting not only the United States but much of the world.

## II. RISK FACTORS AND ETIOLOGY

### 1. Metabolic syndrome and type 2 diabetes mellitus

Metabolic syndrome is a conglomerate of cardiovascular risk factors which predispose a person to developing type Ⅱ diabetes and cardiovascular disease. The current diagnostic criteria require having 3 of 5 of the following factors: Triglycerides 150 mg/dL or greater, high-density lipoprotein-cholesterol of less than 40 mg/dL in men and less than 50 mg/dL in women, hyperglycemia (fasting glucose of 100 g/dL or greater), an increased waist circumference (defined by population specific data), and hypertension (systolic blood pressure of 130 mmHg or greater or diastolic blood pressure of 85 mmHg or greater).

### 2. Ethnic differences

The rate at which NAFLD develops has been shown to be greatest in Hispanic patients. Also, NAFLD in the Asian population has been increasing, and interestingly, can be seen in those who have a normal body mass index. In a United States based study, the investigators found a lower degree of steatosis in African Americans when compared to whites and also showed a higher degree of NAFLD findings in Asians and Hispanics. The Hispanic population also has been shown to have a higher occurrence of steatohepatitis and cirrhosis, while those who are African American enjoy a decreased chance of developing liver failure. With further genetic investigation by genome wide association, it was noted that Hispanics had a twofold higher liver fat content if they possessed the homozygous PNPLA3 allele (patatin-like phospholipase domain-containing protein 3 rs738409). The PNPLA3 gene family has been shown to affect lipid metabolism and patients who harbor this polymorphism were found to have increased hepatic fat content, triglyceride stores, and inflammation. In fact, the mutation of PNPLA3 rs738409 gene (encoding I148M) has revealed more severe histologic features of NAFLD in those carrying the mutation. More information on the genetic basis for NAFLD can be found under the "genetics" heading (**Rotman and Sanyal, 2017).**

### 3. Gender and age

Unfortunately, the role of gender in the development of NAFLD has been met with differing conclusions in the literature. Several studies provide data to suggest a higher prevalence in males while others proposed the opposite. However, according to Lonardo et al epidemiological review, NAFLD is more common in men and has been shown to increase in those who are younger to middle aged with a decline noted after the age of 50-60 years. In contrast, NAFLD has been shown to spare those women who are pre-menopausal and then a rise in incidence occurs after the age of 50 with a peak at 60-69 years,