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# تقييم الاومنتين-1 و بعض المتغيرات الكيمياوية في مصل مرضى الكبد الدهني الغير كحولي

رسالة مقدمة الى مجلس كلية العلوم / جامعة ديالى مجلس كلية العلوم الكيمياء وهي جزء من متطلبات نيل درجة الماجستير في علوم الكيمياء

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# بِسْمِ اللَّهِ الرَّحْمَانِ الرَّحِيمِ

يَرْفَعِ اللّهُ الَّذِينَ آمَنُوا مِنْكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ ۚ وَاللّهُ بِمَا تَعْمَلُونَ خَبِيرٌ

صدق الله العظيم سورة المجادلة الاية (١١)

## Dedication: -

To the one who gave me everything he has, so that I can achieve my dream, To whom was my refuge and sense of safety (my great father).

To which I shed my weak tears in her bosom, and made me stronger (My mother).

The most beautiful and best brothers and sisters

To all The reason of what I become today, thanks for your support and continuous care.



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Haneen Hassan

### **SUMMARY**

Non-alcoholic fatty liver disease (NAFLD) is one of the most prevalent diseases in the world as a result of the absence of symptoms on the person with the disease. Now it is recognized fatty tissue, not only as a place to store excess energy derived from food intake but also act to secretion a number of biologically active substances, known as adipokines or adipocytokin. Unregulated production or secretion of these adipokines resulting from increased adipose tissue may contribute to the development of non-alcoholic fatty liver disease. In this study, we focused on altered omentin-1 levels and some biochemical parameters associated with nonalcoholic fatty liver disease.

The study was conducted at Muqdudia General Hospital / Diyala Governorate , during the period 1-October-2021 to 30-Decamber-2021 and was collected through which (90) blood samples were collected after being diagnosed by the specialist doctor (by ultrasound), where the study included (60) patients with non-alcoholic fatty liver disease and an average age of (30-70) years . The patients were compared with (30) healthy people as a control group and an average age of (30-70) years . The ELISA Kit was used to detection serum omentin-1. A rapid quantitative assay HS-INSULIN-CHECK-1 is used to estimate of insulin. The CRP-latex is a slide agglutination test for the quantitive and semi-quantitive detection of C-reactive protein (CRP) in human serum. Liver function ,Lipid profile ,Total protein , Albumin , Globulin and Random blood Sugar tests were assessed using an Semi automated spectrophotometer (Humalyzer Primus).

The results of the study showed:

- 1-There was a significant increase (p < 0.05) in the level of omentin-1.
- 2-There was a significant increase (p <0.05) in the level of Alanine aminotransferase (ALT), Aspartate aminotransferase (AST) , Triglyceride (TG) , Total Cholesterol (T.C), low-density lipoprotein cholesterol (LDL-C) , Very Low density lipoprotein cholesterol (VLDL-C) , C-reactive protein (CRP) , Age , Body Mass Index (BMI) and waist .
- 3-There was a increase in the value of Alkaline phosphate (ALK), Insulin, Total Protein and Globulin but no significant difference (p > 0.05).
- 4-There is a decrease in the value of high-density lipoprotein, Albumin and Random Blood Sugar but no significant difference (p>0.05).
- 5- omentin-1 , Alanine aminotransferase, Aspartate aminotransferase, Total Cholesterol, Triglyceride, Very Low density lipoprotein cholesterol, cholesterol and globulin parameters showed a highest sensitivity compared to Alkaline phosphate, RBS and high-density lipoprotein, with high significant different (p<0.05).
- 6-Depending on specificity, Alkaline phosphate and high-density lipoprotein parameters showed a highest specificity compared to globulin, insulin, Aspartate aminotransferase, Total Cholesterol and Very Low density lipoprotein cholesterol parameters with high significant difference (p<0.05).
- 7-There are no significant correlation between omentin-1 and other parameters but no significant difference (p>0.05) .

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List of Abbreviations		
Abbreviations	Full Name	
AC	Alcoholic Cirrhosis	
AFLD	Alcoholic fatty liver disease	
ALB	Albumin	
ALK,ALP	Alkaline phosphate	
ALT	Alanine aminotransferase	
AMPK/eNOS	Adenosine monophosphate kinase-endothelial nitric oxide synthase	
AST	Aspartate aminotransferase	
BMI	Body mass index	
CG	Control group	
CIMT	Carotid intima-media thickness	
CRP	C-reactive protein	
CT	Computed tomography	
CVD	Cardiovascular disease	
DNL	De novo lipogenesis	
ELISA	Enzyme-Linked ImmunoSorbent Assay	
FA	Fatty acid	
НСС	Hepatocellular carcinoma	
HDL-C	high-density lipoproteins- cholesterol	

IR	Insulin resistance
LDL-C	low density lipoprotein -cholesterol
MetS	Metabolic Syndrome
MRI	Magnetic resonance imaging
NAD <sup>+</sup>	Nicotinamide adenine dinucleotide
NADH <sup>+</sup>	Nicotinamide adenine dinucleotide dehydrogenase
NAFLD	Nonalcoholic fatty liver disease
NASH	Non-Alcoholic SteatoHepatitis
p38/JNK	protein kinase/Jun N-terminal kinase
PBC	Primary biliary cholangitis
PPARa	Peroxisome proliferator-activated receptor a
RBP4	Retinol-binding protein 4
RBS	Random blood sugar
RGT	Reagent
SREBP-1c	Sterol regulatory element-binding protein le
STD	Standard
T2D	Type 2 diabetes
TAG	Triacylglycerol
TC	Total cholesterol
TG	triglycerides
TNF-a	Tumor necrosis factor alpha

VCAM-1	vascular cell adhesion molecule 1
VLDL	Very low density lipoprotein
WAT	White adipose tissue

#### 1.1 Introduction

Nonalcoholic fatty liver disease (NAFLD) is the most common liver disease worldwide (1). In the absence of a large consumption of alcohol, it leads to the formation of fat in the liver, as it begins to accumulate simple triglycerides in the liver cells without accompanying inflammation or damage to cells of liver, phenotype called non-alcoholic fatty liver (NAFL)(2). Fatty liver disease, if not diagnosed in its early stages, will continue to cirrhosis of the liver and thus lead to death. Non-alcoholic fatty liver disease is associated with diabetes, high blood pressure, obesity, metabolic syndrome and cardiovascular disease (3). In patients with NAFLD, insulin capacity to limit glucose production is compromised, resulting in moderate hyperglycemia, which promotes insulin secretion and leads to hyperinsulinemia. Fasting hyperglycemia and hyperinsulinemia are thus side effects of hepatic insulin resistance and they are linked to the liver fat, even when BMI is not taken into account (4). Pro-inflammatory cytokines play an important role in the development of fatty liver disease (5). Multiple regulatory proteins, known as adipokines, are secreted molecules with a variety of local, peripheral and central functions and are derived from adipose tissue (6). These adipokines have an important role in fatty liver disease (7). These adipokines are at different levels in patients with fatty liver disease compared to the control group. Omentin-1 was secreted from visceral adipose tissue (8). Omentin-1 is a circulating adipokine that has been identified as an adipokine that could help with insulin sensitivity. Reduced omentin-1 expression has been linked to a number of chronic inflammatory disorders (9). Omentin-1 is made up of 313 amino acids(35 kDa) (10). Associated with metabolism, immunity and inflammation (11). Omentin-1 is considered as adipokine effective in obesity and obesity-related disorders (12). It also increases insulin sensitivity and glucose uptake (11). Omentin-1 helps in the metabolism of fat (13).

### 1.2 Literature Review

Yilmaz and et al, in (2011) studied the association of Serum omentin-1 in patients with nonalcoholic fatty liver disease. They found that levels of the omentine-1 serum are higher in patients with non-alcoholic fatty liver disease compared to controls (14).

The Study of Montazerifar and et al,. (2017) included finding the relationship between Serum omentin-1, vaspin, apelin levels and central obesity in patients with nonalcoholic fatty liver disease and it was found that only apelin was different from adipokines analyzed in patients with non-alcoholic fatty liver disease compared to control groups so apelin could be considered a more appropriate diagnostic marker to predict non-alcoholic fatty liver disease (15).

The researchers Arslan and et al, in (2017) studied the comparative effectiveness of diet alone and diet plus metformin treatment on omentin-1 levels in type 2 diabetes patients with nonalcoholic fatty liver disease. They were measured omentin-1 levels in type 2 diabetics who suffered from non-alcoholic fatty liver disease and were treated in two ways; only diet and diet plus metformin therapy and it was found that levels of omentine-1 decreased in the second group by metformin treatment and were more beneficial to patients Type 2 diabetes with non-alcoholic fatty liver disease (16).

Waluga M and et al,. in (2017) studied serum levels of Fibroblast growth factor-21 and omentin-1 hepatic mRNA expression in morbidly obese women with non-alcoholic fatty liver disease. The study showed that the hepatic omentin-1 mRNA levels showed a tendency to be lower in patients with advanced steatosis and hepatocyte ballooning. The FGF21 serum level was significantly higher in patients with a greater extent of steatosis (grade 2 and 3) compared to those without or with mild steatosis (grade 0 and 1) (17).

In (2018) the researchers Ebrahimi and et al,. studied the relationship between the effects of Ramadan fasting on serum concentrations of vaspin and omentin-1 levels in patients with nonalcoholic fatty liver disease. They found that fasting in Ramadan leads to a decrease in Adipokines levels such as Vaspin and omentin-1 levels compared to control groups (18).

The study of Buyukinan and et al,. in (2018) studied the association between serum vaspin and omentin-1 levels in obese children with metabolic syndrome. They found that vaspin levels were high and omentin-1 levels were low in children with obese compared to children without metabolic syndrome. These adipokines were significantly associated with elevated CRP (19).

Also in (2018) Aliasghari and et al,. studied the relationship between vaspin and omentin-1 related to insulin resistance, blood pressure and inflammation in NAFLD patients. They showed that the adipokines (Vaspin and Omentin) are associated with inflammation, insulin resistance, and blood glucose levels in patients with nonalcoholic fatty liver disease (7).

Studying the relationship between circulating omentin-1 levels and lung cancer in smokers by Ansari and et al,. in (2018) found that levels of omentine-1 have decreased significantly in patients with lung cancer, thus posing a risk factor in smokers omentine-1 can be used as an important factor in diagnosing lung cancer in smokers (20).

AHMED and et al,. in (2019) studied the association of serum omentin-1 levels with severity of nonalcoholic fatty liver disease in correlation with cardiovascular risk factors among Egyptian women. They found that levels of the omentine-1 serum are low in women with non-alcoholic fatty liver disease compared to controls (21).

Studying the relationship of omentin-1 levels in chronic liver disease by M Waluga and et al,. in (2019) found that the plasma concentration of omentin-1 level was the highest in alcoholic Cirrhosis(AC) and the lowest in control group. Post-hoc test indicated, that in the primary biliary cholangitis (PBC). group omentin is no different comparing to NAFLD group. Mean vaspin concentrations did not differ significantly between groups. The plasma concentration of irisin was the lowest in the alcoholic Cirrhosis (AC) group and the highest in the Control group (22).

In (2020) Arab and et al, studied the association between serum omentin-1 levels and bodyweight. A systematic review and meta-analysis of the study showed the omentin-1 levels were significantly lower in overweight rather than obese subjects (23).

Rothermel and et al,. in (2020) study has been included find the link between omentin-1, obesity and insulin resistance in children. They found that omentin-1 levels were low in obese people (24).

A Study of Turkkan and et al,. in (2021) found that Omentin-1 levels were decreased in obese adolescents regardless of the presence of NAFLD. However, in obese patients with NAFLD, there was a significant difference between omentin-1 and several markers of obesity and insulin resistance (25).

Çelik and et al,. study in (2021) showed that the omentin-1 levels were low in patients with high blood pressure compared to control groups (26).

Ali and et al, in (2021) studied the relationship of omentin-1 as an adipokine in obese men and women with and without fatty liver disease. Omentin-1 levels has been considered a preventive factor in assessing the incidence of non-alcoholic fatty liver disease, especially in patients with excessive obesity, and thess

Adipokines may contribute to the assessment of the incidence of non-alcoholic fatty liver disease (27).

## 1.3 The Aim of the study

The aim of this study was to determine omentin-1 serum levels and some biochemical parameters in the blood of non-alcoholic fatty liver patients. Find the relationship between omentin-1 levels with insulin and some biochemical parameters.

- 1. Measuring the level of omentin-1, insulin, liver function, lipid profile, total protein, albumin, RBS, CRP in sera of non-alcoholic fatty liver patients and control group.
- 2. Find The correlation between these parameters in sera of non-alcoholic fatty liver patients and control group.
- 3. The receiver operating characteristic (ROC) curve analysis to determine the cut off value of omentin-1, insulin, liver function ,lipid profile, total protein ,albumin , globulin , RBS,CRP in sera of non-alcoholic fatty liver patients and control group.