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Triglycerides and Cholesterol Associated with Nonalcoholic fatty liver disease

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Abstract :

Background: NAFLD is the most common chronic liver disease that linked to dyslipidemia, hyperglycemia and insulin resistance. The present study show increase cholesterol, Triglyceride, LDL, HbA1c, ALP, AST, and ALT in NAFLD patients that as compared to control at *p-value <0.05*. Furthermore this study show increase LDL in female as compared with male that were (155.95 ±6.77, 141.61 ±5.26) respectively, at *P-value P≤0.05*. In addition decrease mean ±SD of AST in NAFLD patients their age <40 as compared with NAFLD patients their age >40 that were (26.88 ±2.04, 29.94 ±1.94) respectively, at *P-value P≤0.05*. This study concluded increase cholesterol, triglyceride, LDL, HbA1c, ALP, AST, and ALT in NAFLD and decrease HDL. Also this study show no differences in cholesterol, triglyceride, HDL, HbA1c, ALP, AST, and ALT when regarding to gender in NAFLD patients. The prevalence of fatty liver disease has been increasing. There is a correlation between it and dyslipidemia, and the prevalence of dyslipidemia rises sharply when other risk factors, including diabetes.

Keywords: NAFLD, Lipid profile, , liver function test.

الدهون الثلاثية والكولسترول المرتبطان بمرض الكبد الدهني غير الكحولي

مستخلص:

الخلفية: يعتبر مرض الكبد الدهني غير الكحولي الأكثر شيوعا التي ترتبط بخلل في الشحوم ، ارتفاع السكر في الدم ومقاومة الأنسولين. وتظهر الدراسة الحالية زيادة الكولسترول ، الدهون الثلاثية ، الكولسترول الضار ، وزيادة في نسبة انزيمات الكبد في مرضى الكبد الدهني بالمقارنة مع السيطرة في قيمة <0.05. وعلاوة على ذلك تظهر هذه الدراسة زيادة البروتين الدهني منخفض الكثافة في الإناث بالمقارنة مع الذكور التي كانت (155.95 ±6.77 ، 141.61 5 5.26) على التوالي .

بالاضافة الى ذلك انخفض متوسط الانحراف المعياري لانزيم ناقل الامين الاسبارتات في مرضى الكبد الدهني غير الكحولي الذين تقل اعمارهم عن 40 عاما مقارنه بمرضى الكبد الدهني غير الكحولي التي تزيد اعمارهم عن 40 عاما والذين كانوا (26.88 ± 2.04، 29.94 ± 1.94) على التوالي عند قيمة 0.05 . وخلصت هذه الدراسة الى زيادة الكولسترول والدهون الثلاثية ، والكولسترول الضار ، ومعدل السكر التراكمي وانزيمات الكبد فيما يتعلق بالجنس في مرضى الكبد الدهني غير الكحولي ، زيادة في مرضى الكبد الدهني غير الكحولي وكانت هناك علاقة بين شحوم الدم والعوامل الاخرى التي تزيد من خطر الاصابة بها في ذلك مرض السكري .

الكلمات المفتاحية: مرض الكبد الدهني غير الكحولي، فحوصات الدهون، اختبار وظائف الكبد.

1-Background

Fatty liver disease is often classified into two categories: nonalcoholic and alcoholic fatty liver disease. Nonalcoholic fatty liver disease (NAFLD) encompasses a range of liver conditions that resemble alcoholic liver disease but occur in individuals who do not consume excessive amounts of alcohol [1]. NAFLD is categorized into grades I, II, and III based on histological characteristics. Grade I (simple steatosis) is characterized by elevated hepatic echogenicity and visible periportal and diaphragmatic echogenicity on ultrasonography. In grade II, there is a change in the liver's echo pattern that is distinguished by lobule inflammation with steatosis and liver cell ballooning. Elevated hepatic echogenicity, undetectable periportal echogenicity, diaphragm obstruction (lobule inflammation with steatosis, liver cell ballooning, and Mallory hyaline fibrosis) are ultrasonic characteristics associated with grade III [2]. It basically goes from steatosis, or the accumulation of fat, to cirrhosis or fibrosis (steatohepatitis) [3].

Simple steatosis is characterized by the accumulation of fats as TG within the hepatic cells; non-alcoholic steatohepatitis is characterized by lipid deposition in the liver cells in addition to signs of inflammation, fibrosis (of varying degrees), and liver cell damage [4]. These conditions can vary from simple accumulation of fat in the liver (steatosis) to inflammation and liver damage (steatohepatitis) and eventually, advanced scarring of the liver (cirrhosis) [5]. NAFLD is becoming more widely acknowledged as a significant contributor to liver-related illness and death [6], as well as a risk factor for type 2 diabetes [7, 8], chronic kidney disease [9], and cardiovascular disease [10]. Much recent scientific evidence confirms the existence of a relationship between NAFLD and various metabolic diseases, such as obesity, dyslipidemia, and diabetes. Insulin resistance is a significant contributor to the development of NAFLD [5] . Research conducted in recent years has demonstrated that consuming alcohol in moderation can help reduce the development of fatty liver disease [11].

Despite this, there is a dearth of research that investigates the impact of various forms of dyslipidemia on the course of NAFLD, and the findings of the studies that have been conduct-

ed are inconclusive. According to the findings of Sun *et al*., having levels of low-density lipoprotein cholesterol (LDL-C) that are within the normal range poses a high risk of developing NAFLD. Previous research has also demonstrated that patients with non-alcoholic fatty liver disease had considerably elevated levels of oxidized LDL-C12]]. To validate the substantial relationship between NAFLD and high levels of triglycerides (TG) and high-density lipoprotein cholesterol (HDL-C) in outpatient school students aged 6 to 18 years old, a hospital-based cross-sectional study was carried out in Alexandria [13]. An observational study conducted on a population of 6814 individuals between the ages of 45 and 84 has revealed that NAFLD is linked to elevated levels of fasting TG and decreased levels of HDL-C, but no significant change in total cholesterol (TC) or LDL-C [14]. However, there has been a dearth of a comprehensive explanation about whether the passage of time impacts the relationship between different aspects of dyslipidemia and NAFLD in adults during the previous few decades. In relation to NAFLD, the metabolic abnormality parameters remain unknown. Therefore, in the present study, we performed a cross-sectional study to determine the lipid profile, liver function test, and correlation between them in Iraqi population.

2-Methodology

2.1 Subjects

There were a total of 60 samples collected for the study, with 45 people presenting with NAFLD and 15 healthy people serving as the control group. The participants ranged in age from twenty to seventy years old, and members of both sexes were included in the study. During the period beginning in December 2023 and ending in February 2024, specimens were collected from outpatient clinics.

2.2 Sample Collection

Ten milliliters of blood was obtained from each individual after a period of fasting of at least 12 hours by venous puncture using disposable syringes. Two milliliters of blood were placed in a tube containing EDTA anticoagulant to measure the Hb1AC percentage. The remaining 8 ml of blood were placed in a gelatinous tube. Centrifugation was performed at 3000 rpm for 10 minutes, which led to the separation of the serum. The samples were preserved at -20 °C until they were required for

examination. Prior to assessing the biochemical parameters, such as T.C., HDL, T.G., LDL, VLDL, ALT, AST, and ALP, the samples were thawed at room temperature [15].

2.3 Assessment of biochemical test

1. The fasting blood glucose was measured using the BIOLABO reagents kit, which is specifically designed for glucose analysis.

2. HbA1c is a diagnostic test that evaluates the percentage of glucose-bound hemoglobin in erythrocytes. HbA1c measures blood glucose stability during 8–12 weeks, the usual lifespan of red blood cells. Analytical methods were used to analyze red blood cells that respond to glycated hemoglobin, resulting in a 470 nm color. The American company Acon's On Call A1c HBA1c examination kit was used.

3. The levels of AST and ALT in the serum were determined using a colorimetric approach (Reitman and Frankel) by adhering to the protocol of the Randox kits that are available for purchase and are supplied by Randox Laboratories Ltd. (UK). ALP was determined using a colorimetric approach in accordance with the protocol of the Diasys kit that is available for commercial use and is supplied by Diasys Diagnostic System GmbH in Holzheim, Germany. An enzyme-based method was utilized to assess the levels of lipid profile, which included cholesterol, triglycerides, and HDL. The colorimetric test was carried out in accordance with the protocol of the kits that were made available by linear chemicals, Spain. LDL and VLDL levels were determined using the Friedewald equation as the basis for the calculation [15].

2-4 Statistical Analysis:

The data are presented as the Mean ± SEM. A unpaired t-test was utilized to compare the findings of research parameters between patients and control groups. The statistical studies were conducted using the SAS (2018) software package [16].

3- Result

These results obtained for this study showed there is significant increase in mean ±SD values of cholesterol, triglyceride, LDL, HbA1c, ALP, AST, and ALT in NAFLD patients that were (344.29±22.12, 187.7±35.14, 174.7±22.07, 5.95±0.35 120.7±21.82, 28.04±7.08, 28.29±5.90) respectively as compared with control that were (160±19.32, 154.7± 22.73, 100.2±1.11, 4.47 ±0.47, 97.3±2.79, 17.24±0.61,

17.24±0.61), at *P-value P<0.05*. While the mean ±SD of HDL in NAFLD patients decreased as compared with controls, which were 33.18±4.24 and 42.1 ±0.86 respectively, at *P-value P≤0.05*, as shown in Table (1).

Table 1: Comparison between NAFLD patients and control in regarding to lipid profile and liver function test

Parameters	NAFLD patients		*P-value*
	Control	Patient	
Cholesterol (mg/dl)	160±19.32	344.29±22.12	(P≤0.05)
Triglyceride (mg/dl)	154.7± 22.73	187.7±35.14	(P≤0.05)
HDL (mg/dl)	42.1 ±0.86	33.18±4.24	(P≤0.05)
LDL (mg/dl)	100.2±1.11	174.7±22.07	(P≤0.05)
HbA1c (%)	4.47 ±0.47	5.95±0.35	(P≤0.05)
ALP (U/L)	97.3±2.79	120.7±21.82	(P≤0.05)
AST (U/L)	17.24±0.61	28.04±7.08	(P≤0.05)
ALT (U/L)	17.7±0.37	28.29±5.90	(P≤0.05)

As shown in Table 2, there is no statistical differences in mean ± SD in regarding to gender of cholesterol, triglyceride, HDL, HbA1c, ALP, AST, and ALT in NAFLD patients that were (233.39 ±12.89, 187.32 ±7.58, 34.40 ±1.28, 5.90 ±0.10, 119.53 ±6.01, 27.84 ±1.72, 29.14 ±0.I7) respectively in male as compared with female that were (240.96 ±16.20, 188.30 ±13.07, 32.02 ±0.85, 6.02 ±0.07, 122.36 ±6.23, 29.17 ±2.36, 27.12 ±2.42), at *P-value P>0.05*. While increase mean ±SD of LDL in female as compared with male that were (155.95 ±6.77, 141.61 ±5.26) respectively, at *P-value P≤0.05*.

Table 2: Effect of Gender in Patient Parameter Studies

Parameters	Gender		T-test
	Male	Female	
Cholesterol (mg/dl)	233.39 ± 12.89	240.96 ± 16.20	NS 33.61
Triglyceride (mg/dl)	187.32 ± 7.58	188.30 ± 13.07	NS 29.567
HDL (mg/dl)	34.40 ± 1.28	32.02 ± 0.85	NS 3.514
LDL (mg/dl)	141.61 ± 5.26	155.95 ± 6.77	* 12.655
HbA1c (%)	5.90 ± 0.10	6.02 ± 0.07	NS 0.286
ALP (U/L)	119.53 ± 6.01	122.36 ± 6.23	NS 18.205
AST (U/L)	27.84 ± 1.72	29.17 ± 2.36	NS 6.028
ALT (U/L)	29.14 ±0.I7	27.12 ± 2.42	NS 4.924
* (P≤0.05), NS: Non-Significant.			

As for Table 3, there are no statistical differences in mean ±SD in regard to age of cholesterol, triglyceride, HDL, LDL, HbA1c, ALP, and AST in NAFLD patients that were (249.58 ±34.05, 192.40 ±14.57, 33.92 ±5.42, 148.46 ±11.37, 5.99 ±0.42, 116.93 ±8.31, 28.38 ±1.67) respectively in NAFLD patients their age <40 as compared with NAFLD patients their age >40 that were (237.10 ±35.02, 180.27 ±8.73, 32.55 ±3.78, 146.42 ±7.09, 5.87 ±0.35, 126.80 ±14.02, 28.43 ±2.06), at *P-value P>0.05*. While the mean ±SD of AST decreased in NAFLD patients their age <40 as compared with NAFLD patients their age >40 that were (26.88 ±2.04, 29.94 ±1.94), respectively, at *P-value P≤0.05*.

Table 3: Effect of Age groups in parameters study of patients

Parameters	Age groups (year)		T-test
	<40 yr.	≥40 yr.	
Cholesterol (mg/dl)	249.58 ±34.05	237.10 ±35.02	36.118 NS
Triglyceride (mg/dl)	192.40 ±14.57	180.27 ±8.73	30.037 NS
HDL (mg/dl)	33.92 ±5.42	32.55 ±3.78	3.569 NS
LDL (mg/dl)	148.46 ±11.37	146.42 ±7.09	17.919 NS
HbA1c (%)	5.99 ±0.42	5.87 ±0.35	0.290 NS
ALP (U/L)	116.93 ±8.31	126.80 ±14.02	18.487 NS
AST (U/L)	28.38 ±1.67	28.43 ±2.06	6.122 NS
ALT (U/L)	26.88 ±2.04	29.94 ±1.94	2.971 *
* (P≤0.05), NS: Non-Significant.			

As shown in Table (4), the result of the present study demonstrated that there was a positive correlation between liver enzymes (ALP, AST, and ALT) with HbA1c in patients with NAFLD (r = 0.53), (r = 0.36), (r = 0.31)

Table 4: The coefficient of correlation between HbA1c and Liver enzymes in patients group

Parameters /Liver enzymes	Correlation coefficient-r with HbA1c	*P-value*
ALP	0.53 **	0.0048
AST	0.36 *	0.0352
ALT	0.31 *	0.0496
* (P≤0.05), ** (P≤0.01).		

As shown in Table (5), the result of the present study demonstrated that there was a positive correlation between liver enzymes (ALP, AST, and ALT) with cholesterol in patients with NAFLD (r = 0.68), (r = 0.61), (r = 0.70).

Table 5: Correlation coefficient between Cholesterol and Liver enzymes in patients group

Parameters /Liver enzymes	Correlation coefficient-r with Cholesterol	*P-value*
ALP	0.68 **	0.0001
AST	0.61 **	0.0009
ALT	0.70 **	0.0001
** (P≤0.01).		

As shown in Table (6), the result of the present study demonstrated that there was a positive correlation between liver enzymes (ALP, AST, and ALT) with triglyceride in patients with NAFLD (r = 0.62), (r = 0.36), (r = 0.61).

Table 6: Correlation coefficient between Triglyceride and Liver enzymes in patients group

Parameters /Liver enzymes	Correlation coefficient-r with Triglyceride	*P-value*
ALP	0.62 **	0.0007
AST	0.36 *	0.0352
ALT	0.61 **	0.0009
* (P≤0.05), ** (P≤0.01).		

As shown in Table (7), the result of the present study demonstrated that there was a negative correlation between liver enzymes (ALP and ALT) with HDL in patients with NAFLD (r = -0.32), (r = -0.35) and no correlation between AST with HDL in patients with NAFLD (r = 0.008). Furthermore no correlation between liver enzymes (ALP, AST, and ALT) with LDL in patients with NAFLD (r = 0.09), (r = 0.19), (r = 0.18).

Table 7: Correlation coefficient between HDL, LDL with Liver enzymes in patients group

Parameters /Liver enzymes	Correlation coefficient-R			
	HDL		LDL	
	Correlation	P-value	Correlation	P-value
ALP	-0.32 *	0.0487	0.09 NS	0.644
AST	0.008 NS	0.966	0.19 NS	0.336
ALT	-0.35 *	0.0422	0.18 NS	0.353
* (P≤0.05), NS: Non-Significant.				

4- Discussion

The present study attempted to describe the abnormality of lipid levels among the patients of NAFLD and influences of the liver on triglyceride and cholesterol levels. This proves that the liver plays a crucial function in maintaining a healthy balance of fats in the body. Treatment of non-alcoholic fatty liver disease, which involves removing excess fat from the liver, can lower blood sugar levels, triglyceride percentages, and cholesterol levels.

In present study, results obtained showed there is significant increase in mean ±SD values of cholesterol, triglyceride, LDL, HbA1c, ALP, AST, and ALT in NAFLD patients as compared with control. This is consistent with the results of several other studies that have found an elevated lipid profile in individuals with NAFLD. In a cross-sectional study conducted by Cholongitas *et al*., in the USA, it was discovered that individuals with NAFLD had elevated levels of triglycerides17]]. In a separate cross-sectional study conducted in Brazil, it was found that individuals with NAFLD exhibited elevated levels of triglycerides. Nevertheless, a study conducted by Lin *et al*. revealed that 63 % of the participants with NAFLD exhibited elevated levels of cholesterol[18] .

According to the study by Nakahara *et al*.,[19] that showed NAFLD and hyperlipidemia occur alongside one another, It was also demonstrated about 37.5% of NAFLD patients with liver biopsies have hyper-LDL choles-

terolemia and 19.5% have hypo-HDL cholesterolemia and hypertriglycemia is present in most NAFLD patients. Ma *et al.* [20], found that TG and HbA1c are separate indicators of NAFLD using multivariate analysis on 949 retired senior employees. Gholoobi, *et al*. demonstrated a substantial correlation between fatty liver disease and type 2 diabetes and low HDL [21]. Low HDL levels have been linked to diabetes, fatty liver, and heart disease [22, 23].

In our research, every female participant and over 90% of male participants had low HDL levels. This discrepancy could perhaps be attributed to the patients' co-occurrence of fatty liver disease and diabetes. The fact that women have more subcutaneous and peripheral fat than visceral and hepatic adipose tissue, along with estrogen's protective action against NAFLD, led us to believe that women may be at a lesser risk of NAFLD than men. An increased incidence of incident fatty liver and NAFLD was associated with higher TG/HDL-C levels in a cohort study [24, 25]. Based on these findings, elevated blood lipid levels, instead of the association between NAFLD and hyper-LDL and hypo-HDL cholesterolemia is greater [26, 27].

Insulin resistance may be a mediator of the relationship between TG/HDL-C and NAFLD, however the specific pathway that contributes to this association is still unknown [28-30] have demonstrated that insulin resistance leads to an increase in the creation of bigger VLDL particles that are enriched with TG, while simultaneously leading to a decrease in the concentrations of HDL-C [30]. Insulin resistance leads to an increase in TG/HDL-C. NAFLD results from insulin resistance, which makes the liver produce TG from scratch and lipolyze TG from adipose tissue [31]. Insulin resistance may thus underlie the association between TG/HDL-C and NAFLD.

Variations in body fat distribution or the antioxidant system may be related to hereditary susceptibility in our general population. NAFLD ontogenesis requires triglycerides to be deposited in the liver cells [32]. The metabolic process that leads to the deposition of lipids in the liver cells is not fully understood, although it is hypothesized that this may be because insulin resistance modifies the pathways that lead to the consumption, production, breakdown, and release of substances during liver metabolism. Although the fundamental

mechanism of the effects leading to fat buildup is unknown, it is believed that insulin resistance causes changes in the liver's metabolic pathway pertaining to the uptake, production, deprivation, or leaking of chemicals. One prevalent factor contributing to the ontogenesis of NAFLD is insulin resistance [33]. There were notable differences in the subjects' fasting lipid profiles[34].

The majority of ALT is found in hepatocyte plasma, while the majority of AST is found in both hepatocyte plasma and mitochondria. A rise in the former often indicates damage to the hepatocyte membrane, whereas a rise in the latter indicates deterioration at the level of the organelles [35]. Another popular measure of liver health is the AST/ALT ratio, where readings below one suggest modest damage to the liver cells. The results showed that AST and ALT levels were substantially greater in those with high TG indices compared to those with low indices, suggesting that there may be some hepatocyte injury. The conflicting AST/ALT results, however, point to the possibility of early NAFLD stages and mild hepatocyte injury at that time [36].

5- Conclusion

The prevalence of fatty liver disease has been increasing. There is a correlation between it and dyslipidemia, and the prevalence of dyslipidemia rises sharply when other risk factors, including diabetes, are considered. The outcome might be accelerated atherosclerosis and a higher probability of cardiovascular disease. Additional research, focusing on patients with fatty liver disease and either diabetes or no diabetes at all, is necessary to determine the patterns of dyslipidemias and whether an increase in risk factors for dyslipidemia corresponds to an increase in the number of patients afflicted.

Availability of data and materials

The authors confirm that the manuscript contains all relevant data.

Abbreviations

NAFLD: non-alcoholic fatty liver disease.

ALP : Alkaline Phosphatase

ALT: Alanine Transaminase

LDL : Low Density Lipoprotein

HDL : High Density Lipoprotein

TG/HDL-C : Triglyceride/High-Density Lipoprotein Cholesterol

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