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RESEARCH ARTICLE

EVALUATION OF SERUM FERRITIN IN NON-ALCOHOLIC

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ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) is a clinical condition that comprises a wide spectrum of liver damage, ranging from simple steatosis to steatohepatitis, advanced fibrosis and cirrhosis in patients with normal or elevated serum alanine transaminase enzyme (ALT). NAFLD tends to develop in people who are overweight or obese or have diabetes, high cholesterol or high triglycerides.

Methods: The study is a case control study conducted on 50 patients who were diagnosed to have fatty liver assessed by ultrasonography and 25 controlled healthy individuals with matched age and sex. All the study persons underwent full clinical assessment and laboratory investigations including ALT and AST-, serum albumin, prothrombin time and INR, complete blood count (CBC), fasting plasma glucose (FPG), (HbAiC) and fasting lipid profile including, serum total cholesterol, triglyceride (TG), low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) and serum ferritin and iron.

Results: The study shoed high statistically significant difference between patients group and control group as regards serum ferritin level p value (<0.001) , and there was high statistically significant positive correlation between serum ferritin level and BMI, TG, AST, ALT, Fasting Plasma Glucose, HBA1C , serum uric acid , LDL, serum IRON ,TIBC with p value (<0.001) .

Conclusion: Serum ferritin can be used as a useful marker for evaluation of the presence of NAFLD and useful marker for evaluation of associated dyslipidemia , diabetes and presence of metabolic syndrome.

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INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is a clinical condition that comprises a wide spectrum of liver damage, ranging from simple steatosis to steatohepatitis, advanced fibrosis and cirrhosis in patients with normal or elevated serum alanine transaminase enzyme (ALT). NAFLD and non-alcoholic steatohepatitis (NASH) are highly prevalent diseases, and is estimated that a quarter of the adult population currently has NAFLD. Furthermore, 20- 30% of patients with NAFLD will develop NASH that may progress to cirrhosis, end stage liver disease and hepatocellular carcinoma (Nascimbeni *et al.,* 2013). The Diagnostic Challenge NAFLD is most often diagnosed in asymptomatic (ortired) persons after the detection of raised aminotransferases during routine screening, or abnormal hepatic ultrasonography performed for another purpose. Alternatively, hepatomegaly may be detected during routine physical examination when liver tests are normal (Mofrad *et al.,* 2003), the presence of symptoms, usually nonspecific, does not appear related to disease severity; there can be improvement with modest weight reduction (Hickman *et al.,* 2004). Non-alcoholic fatty liver disease (NAFLD) is the build up of extra fat in liver cells that is not caused by alcohol. It is normal for the liver to contain some fat. However, if more than 5% - 10% percent of the liver's weight is fat, then it is called a fatty liver .NAFLD tends to develop in people who are overweight or obese or have diabetes, high cholesterol or high triglycerides. Rapid weight loss and poor eating habits also may lead to NAFLD. However, some people develop NAFLD even if they do not have any risk factors. Serum ferritin may reflect increased disease severity in NAFLD either due to increased ongoing hepatic or systemic inflammation or increased body iron stores, or a combination of these factors (Dongiovanni *et al.,* 2011).

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There is a need for biomarkers that reliably discriminate NASH from bland steatosis. An earlier suggestion that highly specific C-reactive protein may be valuable has not been confirmed (Hui *et al.,* 2004). Serum ferritin is elevated in approximately60% of patients with NASH, probably reflecting hepatocyte injury and liver inflammation rather than an increase in hepatic iron stores. Thus, although a possible role for iron in exacerbating NAFLD (particularly fibrogenesis) has been debated (Chitturi *et al.,* 2002). Hepatic Imaging. Increased echogenicity ("bright" scan) with ultrasonography or increased radiolucency with computerized tomography (compared with kidney) provide supportive evidence of steatosis. One study reported sensitivity of ultrasonography for steatosis was 89% with specificity of 93%; this compared with 77% and 89%, respectively, for fibrosis (Joseph *et al.,* 1991). Few studies compare ultrasound and computed tomography for diagnostic accuracy in NAFLD or NASH. In one such study, the sensitivity of both tests was 75% to 80% when appreciable (33% hepatocytes with stainable fat) steatosis was present (Saadeh *et al.,* 2002).

The aim of the current study was to: examine the relationship of serum ferritin to clinical, and laboratory data in adult patients with NAFLD diagnosed by ultrasonograhpic examination.

Patients and methods

This study included 50 Patients with fatty liver by ultrasonography and 25 normal persons(control group) of same age and sex. The cases were 12 males (24%) and 38 females (76%) with mean age of 46.46 ± 9.20 years (rang from 45 to 65 years) and the control group were 22 females (88.00%) and 3 males (12.0%). All the patients were subjected to detailed medical history and clinical examination. Full physical examination was performed including measurement of weight, height and body mass index (BMI), systolic and diastolic blood pressures (SBP and DBP, respectively), abdominal examination. Abdominal ultrasonographic procedure were carried on to detect fatty liver and exclusion of other hepatic or abdominal problems. Routine laboratory tests including liver function tests (liver enzymes -ALT and AST-, serum total bilirubin, albumin, prothrombin time and INR), complete blood count (CBC), fasting plasma glucose (FPG), (HbAiC) and fasting lipid profile including serum total cholesterol, triglyceride (TG), low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) were performed. Serum ferritin and iron were determined.

Principle of ferritin test

The Ferritin Quantitative Test is based on a solid phase enzyme-linked immunosorbent assay (ELISA). The assay system utilizes one rabbit anti-ferritin antibody for solid phase (microtiter wells) immobilization and a mouse monoclonal anti-ferritin antibody in the antibody-enzyme (horseradish peroxidase) conjugate solution. The test sample is allowed to react simultaneously with the antibodies, resulting in the ferritin molecules being sandwiched between the solid phase and enzyme-linked antibodies. After a 45-minute incubation at room temperature, the wells are washed with water to remove unbound-labeled antibodies. A solution of TMB Reagent is added and incubated at room temperature for 20 minutes, resulting in the development of a blue color. The color development is stopped with the addition of Stop Solution, and the color is changed to yellow and measured spectrophotometrically at 450 nm. The concentration of ferritin is directly proportional to the color intensity of the test sample. Male: 20-250 ng/ml and Female: 10- 120 ng/ml.

Statistical Methods

Data were statistically described in terms of mean and standard deviation for quantitative data and frequencies (number of cases) and relative frequencies (percentages) for qualitative data. Comparison of quantitative variables was done using unpaired t test. For comparing categorical data, Chi square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency is less than 5. Correlations were done to test for linear relations between quantitative variables by Pearson correlation coefficient. All statistical calculations were done using SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 21. P-value is considered significant if < 0.05*.

RESULTS

This study included 50 Patients have fatty liver and 25 age and sex matched normal person.

Table 1 shows: descriptive statistics of demographic data of patients.

Table 1. Descriptive statistics of demographic data of patients

Variables	Patients	
	Mean	Standard Deviation
Age ys	46.46	9.20
Duration of disease (years)	8.15	4.58
Weight (kg)	100.30	15.84
Height (cm)	162.94	11.14
BMI (kg/m2)	36.94	4.32
SBP(mmhg)	137.38	14.83
DBP(mmhg)	88.10	8.01

Table 2 shows : comparative study of laboratory data between patients and control showed high stastistically difference between patient and control (p value < 0.001) as regards weight, BMI, fasting plasmaglucose, HBA1C, cholesterol,TG, LDL, seum Iron,TIPC, serum uric acid and there were stastistically difference between patient and control (p value <0.01) as regards systolic blood pressure and diastolic blood pressure.

Table 3 shows: correlation between serum ferritin and other studies parameters showed highly stastically siginificant (p value < 0.001) as regard weight, BMI, TG, AST, ALT, Fast Plasma Glucose, HBA1C , LDL, serum IRON ,TIBC and it showed stastically siginificant value (p value <0.02) as regard cholesterol

Table 4 shows : Comparison between Patients and control Group as regards serum ferritin and it showed highly statistically significant p value (<0.001)

Table 2. Comparative study of laboratory data between patients and control

Variables	Group				
	Patients		Control		P value
	Mean	Standard Deviation	Mean	Standard Deviation	
Age(ys)	46.46	9.20	49.36	4.97	0.081
Weight(kg)	100.30	15.84	67.28	4.20	<0.001
Height (cm)	162.94	11.14	163.40	5.11	0.807
BMI(kg/cm2)	36.94	4.32	24.92	1.26	<0.001
SBP(mmhg)	137.38	14.83	114.40	6.66	<0.001
DBP(mmhg)	88.10	8.01	74.00	5.77	<0.001
Gamma GT(U/L)	50.38	8.05	43.96	3.76	<0.001
Alkaline Phosphatase(U/L)	75.40	19.61	64.08	9.13	0.001
Albumin(gm/dl)	4.09	.64	3.99	.47	0.489
ALT(U/L)	35.62	4.07	23.12	2.55	<0.001
AST(U/L)	24.02	4.40	17.56	2.10	<0.001
Fast Plasma Glucose(mg/dl)	173.80	91.32	106.00	3.77	<0.001
HBA1C %	6.13	1.00	4.78	.57	<0.001
Cholesterol(mg)	333.10	16.96	194.00	8.54	<0.001
TG(mg/dl)	252.40	13.45	141.08	7.46	<0.001
HDL(mg/dl)	35.66	3.89	35.56	3.58	0.915
LDL(mg/dl)	259.60	15.51	126.76	4.70	<0.001
Serum Iron(µg/dL)	175.26	12.18	121.16	4.96	<0.001
TIPC(µg/dL)	236.40	5.89	211.56	6.57	<0.001
Serum Uric Acid (mg/dl)	5.87	.61	5.47	.37	0.001

Table 3. Correlation between serum ferritin and other studied parameters among NASH

Parameters	Statistical significance	
	R	P
AGE	0.24	0.870 (n.s)
Weight	0.669	<0.001
Height	0.218	0.128 (n.s.)
BMI	0.730	<0.001
SBP	-0.97-	0.504 (n.s.)
DBP	-.044-	.764(n.s.)
Gamma GT	-0.181-	0.210 (n.s)
Cholesterol	0.430	<0.002
Triglycerides	0.835	<0.001
AST	0.536	<0.001
ALT	0.575	<0.001
Alkaline phosph.	0.80	0.581 (n.s.)
Albumine	0.071	0.625 (n.s.)
Urea	0.154	0.284 (n.s.)
Creatinine	-0.114-	0.431 (n.s.)
Hemoglobin	-0219-	0.126 (n.s.)
Fast Plasma Glucose	0.531	<0.001
HBA1C	0.765	<0.001
LDL	0.816	<0.001
Serum Iron	.788	<0.001
TIPC	.681	<0.001
Serum Uric Acid	.126	.383
Platelets count (in thousands)	.066	.647
TLC	.153	.290
total bilirubin	.191	.185
Duration of disease (years)	-.090-	.638

Table 4. Comparative study between Patients and control Group as regards serum ferritin

	Group				P value
	patients		Control		
	Mean	Standard Deviation	Mean	Standard Deviation	
Serum Ferritin(ng/ml)	226.93	43.94	45.46	20.96	<0.001

DISCUSSION

Nonalcoholic fatty liver disease (NAFLD) is a medical condition that is characterized by the buildup of fat (called fatty infiltration) in the liver. The aim of the present work is to study the relation between Serum ferritin and non alcoholic fatty liver disease (NAFLD). The study showed that the prevalence of non alcoholic fatty liver disease is more common in obese, diabetic patients and more common in patients with metabolic syndrome. These results are in agreement with Park *et al*, who showed that NAFLD based on ultrasound findings was associated with elevated serum ferritin (Park *et al.,* 2012). In agreement with our results valenti *et al.* showed elevated serum ferritin in NAFLD patients compared to control. Who studied diagnostic and therapeutic implication of the association between ferritin level and severity of NAFLD (Valenti *et al.,* 2012). That the increased serum ferritin level is an independent predictor of liver damage in patients with NAFLD and is useful to identify patients at risk of NASH. Our results were in contrast to Paul *et al*., 2002 who proved that serum ferritin levels lack diagnostic accuracy for liver fibrosis in patients with non alcoholic fatty liver disease. Our study is contrast to Natasha *et al*., 2012 who showed that serum ferritin levels do not predict the stage of underlying non alcoholic fatty liver disease. It was found that 86% of our cases were obese and above ideal body weight by 10 to 35 percent. Our results are concordant with Hsiao *et al.,* 2003, who studied 210 patients with NAFLD and found that obesity was present in 74% of cases and most of patients were 10 to 40 percent above ideal body weight. And proved that the prevalence of NAFLD was 20.5% (43/210) in obese patients**.** All our patients had bright liver on sonographic examination**.** These were in agreement with- Palmentieri *et al*., 2006, who stated that bright liver echo pattern on ultrasound B-mode examination help in the diagnosis of liver steatosis**.** Also Dasarathy *et al.,* 2009. showed that US is better in detecting macrovesicular hepatic steatosis of any degree with a sensitivity of 61% and a specificity of 100% compared with microvesicular fat with a sensitivity of 43% and a specificity of 73%**.** In contrast to our results Saverymuttu *et al*., 1986, stated that Ultrasonography is not sufficiently sensitive for the detection of lesser degrees of steatosis.

Conclusion

In conclusion our results showed that there was statistically significant difference as regard serum ferritin in patients in comparison to control and showed high statistically significant positive correlation between serum ferritin and other studies parameters (wieght, BMI, cholesterol, TG, LDL, AST , ALT, FBG, HBA1C, Serum iron, TIBC).

Compliance with ethical requirements

Mohamed Elbasel, Noha Khalil, Haytham Sameer, Dina Hassan declare that they have no conflict of interest. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Informed

consent was obtained from all patients for being included in the study.

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