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Serum Hepcidin Levels in Relation to Serum Iron and Ferritin in Obese Women with Non-Alcoholic Fatty Liver Disease (NAFLD)

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ABSTRACT

Background: Non-alcoholic fatty liver disease, the most common hepatic illness globally, (NAFLD), is accompanied by obesity, insulin resistance, and metabolic syndrome. Since increased iron reserves may raise the likelihood of hepatic inflammation and fibrosis, they may be of pathogenic significance in NAFLD. By destroying ferroprotein, the only known iron exporter in mammals, hepcidin regulates iron release from spleen macrophages and hepatic cells in addition to controlling dietary iron absorption from enterocytes.

Objective: This study aimed to evaluate serum hepcidin levels and its relation to serum iron and ferritin in obese female patients with NAFLD.

Patients and Methods: Fifty obese women with a body mass index (BMI) ≥ 30 kg/m^2 and diagnosed as NAFLD and 30 healthy normal-weight women, with a BMI of 23.05 ± 1.85 were enrolled in the study. Serum hepcidin levels were measured and were compared to the control populations.

Results: The mean level of hepcidin in obese women with NAFLD was 28.38 ± 13.66, which was significantly higher than that of controls (14.03 ± 2.85) and its levels were correlated with lipid profile [(negatively with cholesterol (r_s: -0.290) and triglyceride (r_s: -0.326) and positively with HDL (r_s: 0.309)], but didn't correlate with iron profile.

Conclusion: The current study revealed that in obese women with NAFLD, serum hepcidin values were significantly increased than in healthy females with normal weight and its levels were correlated with lipid profile (negatively with cholesterol and triglyceride and positively with HDL), but didn't correlate with iron profile. So, in NAFLD patients with iron overload, hepcidin may make significant contributions to the early diagnosis and therapy choices.

Keywords: NAFLD, Serum Hepcidin, Ferritin.

INTRODUCTION

Different types of liver failure that result in gradual destruction and regeneration of the hepatic parenchyma, inducing cirrhosis, are considered chronic liver disease (CLD). The last stage of liver fibrosis, cirrhosis, frequently results in portal hypertension and liver failure [(1)]. NAFLD has emerged as a main cause of CLD in the West owing to the rising the possibility of both obesity and insulin resistance (IR) [(2)]. A fatty liver in an adult without clear reasons, such as autoimmune hepatitis, viral hepatitis, or a history of alcohol use, is referred to as NAFLD [(3)].

One of the main characteristics of NAFLD is the buildup of fat in the liver, which happens in the absence of major alcohol intake. According to studies, the factors that cause excessive hepatic lipid accumulation include IR, lipid metabolism dysregulation, and an imbalance between the formation and elimination of lipids [(4)].

Serum ferritin is a measure of the body's iron reserves and has been considered as an acute phase reactant. A transitional metal like iron is quickly oxidised and serves as an oxidant. By locking iron into the cavity of the ferritin protein shell, ferritin restricts the availability of iron, which is one of its key functions throughout the acute phase responses [(5)].

Diabetes is a result of oxidative stress damage to hepatocytes and pancreatic cells brought on by excessive systemic iron [(6)].

The liver is the primary location of iron deposition and plays a crucial part in maintaining iron homeostasis by controlling the generation of hepcidin [(7)]. Hepcidin, a 25 amino acid peptide, which prevents iron absorption in the stomach and iron recycling from macrophages, hence lowering iron values in plasma and controls the body's iron equilibrium [(8)].

By destroying ferroprotein, the only identified iron exporter in mammals, hepcidin regulates iron release from macrophages and hepatic cells as well as dietary iron absorption from intestine [(9)].

Hepcidin affects cellular iron transfer to plasma and extracellular fluid through altering ferroprotein. Hepcidin's receptor. Ferroprotein, is also the sole identified cellular iron exporter in the context of vertebrates. The body's professional iron handlers, including the duodenal enterocytes that absorb dietary iron, the liver and spleen macrophages that recycle old erythrocyte, the hepatic cells that store iron, and the placental trophoblasts that transport iron to the fetus throughout pregnancy, express ferroprotein [(10)]. This study aimed to assess serum hepcidin, the iron regulatory protein, levels and its relation to serum iron and ferritin in obese female patients with NAFLD.

PATIENTS AND METHODS

Fifty obese women, with a BMI ≥ (30 kg/m^2) diagnosed as NAFLD, were enrolled in the current study as an obese women group and 30 healthy normal-weight women, with a BMI ranging from 18 to 25 kg/m^2 were included as a control group. Diagnosis of NAFLD was based on liver assessment both by laboratory investigations and by U/S obtained for both groups. The current study started from the beginning of June 2022 to the end of December 2022 and was conducted in the

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clinical pathology department of Al-Azhar University Hospital, Assiut.

Exclusion criteria:

1. Taking hormone replacement treatment or drugs known to cause hepatic steatosis concurrently.
2. History of hepatotoxic drugs or alcohol intake.
3. Patients using lipid-lowering drugs.
4. Postmenopausal women and people who use contraception.
5. Patients with hemochromatosis, biliary illness and anaemia, or decreased renal function. Patients with viral or autoimmune hepatitis.
6. Present-day proof of inflammatory disorders, either acute or persistent.
7. Malignant diseases.

All participants were subjected to the following:

1. A thorough physical examination and history taking to collect demographic information, such as age, sex, and related personal and family background, a thorough history was obtained (current acute or chronic inflammation, history of liver disease in details, kidney disease, medications, alcohol consumption, previous viral hepatitis infection, malignancy etc….). Thorough clinical examination (hepatosplenomegaly, lymphadenopathy, anemia etc…...). The subjects were just wearing their pants when their weight and height were assessed. Weight (kg) divided by height (m^2) was used to compute BMI.
2. Laboratory testing such as (CBC, LFTs, KFTs, RBG & glycated Hb (Hb A1c), viral hepatitis markers, iron profile (Serum iron, TIBC, transferrin saturation and ferritin) and the lipid profiles (cholesterol, TG, LDL-c and HDL-c) following a 12-hour overnight fast.
3. Estimation of serum hepcidin level: It was done by enzyme-linked immunosorbent assay using ELISA kit (Quantikine® ELISA), by Bio-Techne China Co., Ltd., Shanghai). The assay employed a quantitative solid-phase sandwich ELISA. The wells of the provided microplate have been precoated with a target-specific antibody. These wells were subsequently filled with samples, standards, or controls, which bind to the mobilized antibody. The sandwich is created by adding the second antibody after washing away any unbound material. A substrate solution was then added, which interacts with the enzyme-antibody-target combination to provide a quantifiable signal. The amount of target present in the original specimen directly relates to how strong this signal is.

Ethical approval: The Ethics Committee of Al Azhar University's Faculty of Medicine granted the study approval. All participants signed informed consents after a thorough explanation of the goals of the study. The Helsinki Declaration was followed throughout the study's conduct.

Statistical Analysis

Using IBM SPSS V. 20.0, a statistical tool for social sciences, the gathered data were examined. Quantitative data were expressed using the range (minimum and maximum), mean ± standard deviation (SD), median, and interquartile range (IQR). The qualitative data were described in terms of numbers and percentages. To confirm that the distribution was normal, the Shapiro-Wilk test was used. At a 5% level, the significance of the obtained results was evaluated. Two sets of quantitative data that are regularly distributed were compared using the Students t-test. To compare two groups with abnormally distributed quantitative variables, the Mann-Whitney test was used. The correlation between two quantitative variables with erroneous distributions is known as the Spearman coefficient. The acceptable margin of error was set at 5%, and the confidence interval was set at 95%. A P value ≤ 0.05 was deemed significant.

RESULTS

The current study was a case control study that was conducted in the clinical pathology department of Al-Azhar University Hospital, Assiut. The study included a total of 80 participants. Among them, 50 obese women who were diagnosed as NAFLD, with a BMI greater than 30 kg/m^2, as an obese women group and 30 normal-weight women, with a BMI more than 18 and less than 25 kg/m^2, as a control group. The mean age of obese women group was 38.28 ± 4.93 years and the mean age of the control group was 35.87 ± 4.52 years with statistically significant difference between both groups (p=0.032). The mean BMI of the obese women group was 34.78 ± 2.1 kg/m^2 while the mean of the control group was 23.05 ±1.85 kg/m^2 with a high statistically significant difference between both groups ($p<0.001$) (table 1).

Table (1): Demographic data.

	Obese women (n = 50)	**Control (n = 30)**	**T**	**P**
Age (years)				
Min. – Max.	25.0 – 46.0	27.0 – 45.0		
Mean ± SD.	38.28 ± 4.93	35.87 ± 4.52	2.185*	0.032*
Median (IQR)	39.50 (35.0 – 42.0)	36.0 (33.0 – 38.0)		
Weight (kg)				
Min. – Max.	78.0 – 117.0	50.0 – 73.0		
Mean ± SD.	92.26 ± 9.25	63.23 ± 7.19	14.715*	<0.001*
Median (IQR)	91.0 (84.0 – 98.0)	64.50 (58.0 – 69.0)		
Length (cm)				
Min. – Max.	157.0 – 172.0	157.0 – 173.0		
Mean ± SD.	162.7 ± 4.94	165.4 ± 4.64	2.450*	0.017*
Median (IQR)	161.5 (158.0 – 167.0)	166.5 (163.0 – 169.0)		
BMI (kg/m^2)				
Min. – Max.	31.23 – 40.96	18.59 – 25.04		
Mean ± SD.	34.78 ± 2.10	23.05 ± 1.85	25.232*	<0.001*
Median (IQR)	34.50 (32.95 – 36.14)	23.74 (21.56 – 24.45)		

Comparison between the two studied groups regarding CBC parameters revealed that there was no statistically significant difference between both as regards RBCs, Hb, WBCs, and PLT (p values were 0.873, 0.814, 0.0.553 and 0.132 respectively). We observed a high statistically significant difference between obese women group and control group as regard glycemic control parameters; random bl glucose (RBG) and HbA1c with (p<0.001) for both parameters (Table 2).

Table (2): Comparison between the two studied groups according to glycemic control

	Obese women (n = 50)	**Control (n = 30)**	**T**	**P**
RBG (mg/dl) Mean ± SD.	110.7 ± 22.24	93.60 ± 16.61	3.928*	<0.001*
HbA1c (%) Mean ± SD.	5.27 ± 0.24	4.95 ± 0.30	5.196*	<0.001*

We also found that there was a highly significant difference between the studied groups as regards lipid profile (TG, Cholesterol, LDL, and HDL) with (p<0.001) for the four parameters (Table 3).

Table (3): Comparison between the two studied groups according to lipid profile

	Obese women (n = 50)	**Control (n = 30)**	**T**	**P**
TG (mg/dl) Mean ± SD.	241.4 ± 51.31	106.2 ± 25.42	10.862*	<0.001*
Cholesterol (mg/dl) Mean ± SD.	199.4 ± 43.36	156.5 ± 35.59	4.566*	<0.001*
LDL (mg/dl) Mean ± SD.	108.3 ± 26.90	73.29 ± 18.01	3.401*	0.001*
HDL (mg/dl) Mean ± SD.	42.76 ± 8.47	61.97 ± 7.27	10.338*	<0.001*

Regarding the iron profile, the study showed a statistically significant difference between both groups as regards serum iron (p=0.029), and high statistically significant difference regarding TIBC (p=0.003) and ferritin (p<0.001). However, there was no statistically significant difference between the two studied groups as regards transferrin saturation (p=0.364) (Table 4).

Table (4): Comparison between the two studied groups according to iron profile

	Obese women (n = 50)	**Control (n = 30)**	**Test of Sig.**	**P**
Serum Iron (ug/dl) Mean ± SD.	96.28 ± 23.75	83.03 ± 19.56	U= 530.50*	0.029*
TIBC (ug/dl) Mean ± SD.	311.9 ± 62.95	276.3 ± 42.0	t= 3.030*	0.003*
Transferrin saturation (%) Mean ± SD.	30.64 ± 4.27	29.81 ± 3.28	t= 0.913	0.364
Ferritin (ng/ml) Mean ± SD.	274.2 ± 71.91	96.30 ± 23.94	U= 0.000*	<0.001*

In the same way, comparison between both groups regarding liver function tests (ALT, AST, Total bilirubin, direct bilirubin, albumin, and ALP), there was high statistically significant difference between the two studied groups (obese women and control group) with (p<0.001) for all tests. (Table 5).

Table (5): Comparison between the two studied groups according to liver function tests

	Obese women (n = 50)	**Control (n = 30)**	**Test of Sig.**	**P**
ALT (U/L) Mean ± SD.	100.9 ± 24.82	29.57 ± 7.01	t= 16.988*	<0.001*
AST (U/L) Mean ± SD.	78.98 ± 19.41	24.57 ± 8.98	t= 15.577*	<0.001*
Total bilirubin (mg/dl) Mean ± SD.	0.78 ± 0.18	0.46 ± 0.11	t= 6.711*	<0.001*
Direct bilirubin (mg/dl) Mean ± SD.	0.19 ± 0.03	0.08 ± 0.02	U= 157.0*	<0.001*
Albumin (g/dl) Mean ± SD.	3.60 ± 0.28	4.56 ± 0.41	U= 15.00*	<0.001*
ALP (U/L) Mean ± SD.	116.1 ± 24.00	71.47 ± 15.79	t= 8.809*	<0.001*

In regard to the serum creatinine level, our study revealed that there was a statistically significant difference (p=0.008). The present study revealed a high statistically significant difference between both groups (obese women group and normal healthy women group) as regard hepcidin. The mean level of hepcidin was 28.38 ± 13.66 ng/ml in the obese women group and 14.03 ± 2.85 ng/ml in the control groups (P < 0.001) (Table 6).

Table (6): Comparison between the two studied groups regarding hepcidin

	Obese women (n = 50)	**Control (n = 30)**	**U**	**P**
Hepcidin (ng/ml) Mean ± SD.	28.38 ± 6.98	14.03 ± 2.85	112.0*	<0.001*

A correlation study between hepcidin level and different parameters in obese women group was done and revealed that there was a positive correlation between hepcidin and RBCs (r=o.353, p=0.012), RBG (r=o.362, p=0.010), HDL (r=o.309, p=0.029) and creatinine (r=o.293, p=0.039). There was a negative correlation concerning TG (r= - o.326, p=0.021) and cholesterol (r= - 0.290, p=0.041). While, there was no correlation between hepcidin and Hb, platelets, WBCs reticulocyte count, HbA1c, LDL, iron profile parameters (serum iron, TIBC, ferritin and transferrin saturation) and liver function tests (Table 7).

Table (7): Correlation between hepcidin with different parameters in obese women group:

Hepcidin (ng/ml) vs.	r_s	P
Age (/years)	0.078	0.590
Weight (kg)	0.102	0.479
Length (cm)	0.054	0.711
BMI (kg/m^2)	0.007	0.962
RBCs (×10^6/UL)	0.353	0.012*
Hb (g/dl)	0.156	0.280
WBCs (×10^3/UL)	-0.100	0.489
PLT (×10^3/UL)	-0.191	0.185
RBG (mg/dl)	0.362	0.010*
HbA1c (%)	0.014	0.925
TG (mg/dl)	-0.326	0.021*
Cholesterol (mg/dl)	-0.290	0.041*
LDL (mg/dl)	-0.246	0.086
HDL (mg/dl)	0.309	0.029*
ALT (U/L)	0.111	0.443
AST (U/L)	0.071	0.626
Total bilirubin (mg/dl)	0.068	0.641
Direct bilirubin (mg/dl)	-0.014	0.925
Albumin (g/dl)	0.121	0.401
ALP (U/L)	-0.177	0.220
Creatinine (mg/dl)	0.293	0.039*
Serum Iron (ug/dl)	0.057	0.696
TIBC (ug/dl)	-0.112	0.439
Transferrin saturation (%)	0.257	0.071
Ferritin (ng/ml)	0.015	0.919

DISCUSSION

Since hepcidin synthesis may be increased by both fat and diabetes, it is challenging to understand hepcidin levels in NAFLD. For instance, hepcidin is produced from adipose tissue in morbidly obese individuals, which might result in anaemia and iron trapping in reticuloendothelial cells. Accordingly, it is unclear from the available evidence in NAFLD whether hepcidin primarily connects with body iron storage, metabolic syndrome traits, or the hepatic inflammation found in nonalcoholic steatohepatitis (NASH) [(11)].

In general, iron reserves, inflammation, and endoplasmic stress increase hepcidin expression whereas anaemia, hypoxia, and oxidative stress decrease it. Hepcidin has lately gained more attention as a biomarker for a systemic inflammation as a result of its elevation by cytokines. Hepcidin is largely expressed in the liver, although some investigations have shown that it is also present, albeit at considerably lesser levels, in the context of adipose tissue [(12)]. Therefore, we aimed to assess serum hepcidin levels and its relation to serum iron and ferritin in obese females with NAFLD.

The current study compared data of both groups regarding demographic data as age, weight, length, BMI. Iron profile, lipid profile, CBC parameters, liver and kidney function tests and hepcidin levels. Finally, a correlation study between hepcidin levels and different parameters in obese women group was done.

The control group's mean age was 35.87 ± 4.52 years, whereas the obese women's mean age was 38.28 ±4.93 years, with a statistically significant difference between the two groups (p=0.032). The control group's mean BMI was 23.05 ± 1.85 kg/m^2, whereas the mean of the obese women group was 34.78 ± 2.1 kg/m^2, with a significant difference between both groups in terms of BMI (p<0.001).

Regarding the glycaemic control indices, RBG and HbA1c, there were highly statistically significant difference between the obese women group and the control group with (p<0.001) for both parameters. Additionally, we discovered that there was a very significant difference in TG, Cholesterol, LDL, and HDL across the examined groups, with (p<0.001) for each of the four parameters.Similar to this, comparing the results of the two groups' LFTs (ALT, AST, total bilirubin, direct bilirubin, albumin, and ALP) demonstrated a highly statistically significant difference between the two groups (obese women and the control group), with (p<0.001) for all tests.

Our research found that there was a statistically significant change in terms of the serum creatinine level (p=0.008).In relation to the iron profile, the study revealed a highly statistically significant difference concerning TIBC (p=0.003) and ferritin (p<0.001), as well as a statistically significant difference between the two groups for serum iron (p=0.029). However, there was no statistically significant difference in transferrin saturation between the two study groups (p=0.364).

We evaluated the differences in hepcidin between the study groups and discovered that there was a large statistically significant difference in hepcidin between both groups (obese women and controls) with (p<0.001).

A correlation study between hepcidin level and different parameters in obese women group was done and revealed that there was a positive association between hepcidin and RBCs (r=o.353, p=0.012), RBG (r=o.362, p=0.010), HDL (r=o.309, p=0.029) and creatinine (r=o.293, p=0.039). While, there was a negative correlation as regards TG (r= - o.326, p=0.021) and cholesterol (r= - o.290, p=0.041). Furthermore, there was no correlation between hepcidin and Hb, platelets, WBCs reticulocyte count, HbA1c, LDL, iron profile parameters (serum iron, TIBC, ferritin and transferrin saturation) and liver function tests.

In agreement with our findings, **Senates *et al.*** [13] found that NAFLD patients had considerably greater blood levels of hepcidin than age- and gender-matched controls, and that their BMI was also significantly higher.

On another point of view, in a study by **Boja *et al.*** [14], serum hepcidin values in NAFLD patients and controls were comparable (60.5 ± 31.1 versus 55.8 ± 11.9 ng/ml, p=0.285). However, compared to NAFLD patients without iron overload, those with iron overload showed substantially higher hepcidin levels (78.4 ± 35.5 versus 56.5 ± 28.9ng/ml, p=0.027). Hepcidin levels are higher in NAFLD patients who have an excess of iron. As hepcidin values in NAFLD cases without iron accumulation were comparable to hepcidin levels in controls, they came to the conclusion that the higher hepcidin values in their patients most likely represent the physiologic responses to hepatic iron buildup. Similarly, also study by **Auguet *et al.*** [15] reported that morbidly obese (MO) women had much higher amounts of hepcidin than women who were in control weight ranges. The difference between women with morbid obesity with a normal liver and those who had NAFLD, however, was not statistically significant. Therefore, they proposed that NAFLD is not connected with high hepcidin levels, rather with obesity. In the same way, **Marmur *et al.*** [16] showed no correlation between hepcidin values and the severity of NAFLD in terms of histology. Additionally, supporting the idea that in individuals with NAFLD, serum hepcidin values could be more indicative of adipose tissue mass in comparison with the degree of hepatic histopathological structure. The fact that the higher values of hepcidin in the NAFLD group have only been observed in the setting of a considerably increased BMI**.** Also**, Marmur *et al.*** [16] revealed that blood hepcidin values in NAFLD cases with dysmetabolic iron overload (DIOS) are equivalent to those reported in different CLD with iron overload (CLD-IO), with the exception of familial hemochromatosis, where individuals have congenital hepcidin deficiency. When comparing hepcidin levels to serum ferritin or the liver iron score, individuals with DIOS had usually comparable rates to those with CLD-IO, but cases with alcoholic cirrhosis and hepatitis C virus (HCV) indicated a propensity to have minimal values to some extent**.**

In the same point of view, **Uysal *et al.*** [17] saw no appreciable variation in blood hepcidin levels between NASH patients and age-matched controls (BMI was comparable between NASH and control groups)**.** Other earlier investigations have shown contradictory findings. **Barisani *et al.*** [18] (2008) reported that NAFLD patients' hepcidin production was insufficient for a given value of iron condition in comparison with the control group.

Saleh Boja *et al.*'s [14] findings were in agreement with our findings in that age, sex distribution, haemoglobin, and transferrin saturation levels were comparable in the NAFLD and the controls for the major clinical and biochemical parameters. BMI, HOMA-IR, ALT, AST, GGT, total and LDL cholesterol, triglyceride, and ferritin values were significantly increased in the NAFLD group compared to the control group, whereas HDL cholesterol levels were significantly lower. In disagreement with our study, **Marmur *et al.*** [16]**,** demonstrated that in NAFLD patients, serum hepcidin corresponds to iron indices with or without DIOS. On the other hand, they have demonstrated that no significant correlations were detected between hepcidin and BMI, NAFLD activity score, and lipid parameters (P > 0.05). Also, in contrast to the current study, as in research by **Handa *et al.*** [19], numerous other investigations discovered a correlation between hepcidin levels and iron parameters in NAFLD and DIOS. Serum ferritin in people with metabolic syndrome who have NAFLD was found to be mostly determined by hepatic iron, as evaluated by magnetic resonance imaging. The findings showed that the iron regulatory feedback on hepcidin production was retained in such cases.

Saleh Boja *et al.* [14]**,** identified a small but positive connection between ferritin and hepcidin levels, suggesting that the rise in ferritin levels may be due to increased hepcidin production, particularly in NAFLD patients with iron overload. In the same line, **Auguet *et al.*** [15]**,** noticed that plasma hepcidin has a positive correlation with ferritin ($p < 0.001$), transferrin saturation (p=0.028), and iron (p=0.007) levels and a negative correlation with transferrin values (p=0.003) when the correlation between hepcidin levels and the biochemical parameters studied was analysed. They did discover a negative correlation between circulating hepcidin levels and HDL-C (p=0.038), which is only somewhat inconsistent with our findings. **Senates *et al.*** [13] discovered that there was a significant correlation between serum hepcidin and triglyceride and cholesterol levels, while there were no significant correlations with all iron parameters, which is totally in agreement with our findings.

Regarding, serum ferritin levels' clinical utility in fatty liver patients, according to **Mohammed *et al.*** [20]**,** hyperferritinemia is prevalent in NAFLD patients, although the degree of serum ferritin increases does not indicate the stage of the underlying condition. Ferritin has been demonstrated to be a predictor of advanced fibrosis, obesity, IR, and cardiovascular disease have all been linked to hyperferritinemia, diseases connected to NAFLD. It has been suggested that serum ferritin, but not serum iron, transferrin saturation, or hepatic iron concentration, is greater in cases with severe fibrosis compared to moderate fibrosis, but not in individuals with steatosis or inflammation, and that it can in an independent manner predict extensive fibrosis [20]**.** Similarly, according to **Kowdley and colleagues** [21]**,** there is a direct link between elevated blood ferritin levels and a higher risk of progressive fibrosis in NAFLD. In individuals with biopsy-proven NAFLD, serum ferritin levels and BMI were highly correlated

with fibrosis, portal inflammation, and lobular inflammation**. Britton *et al.* [12]** discussed a study in Southeast China and found that circulating iron levels and central obesity were associated with a significant increase in the possibility of NAFLD, whereas high hepcidin to ferritin ratios were significantly associated with a significant reduction in the possibility of NAFLD in females. Additionally, elevated blood hepcidin levels could raise the possibility that central obesity poses for NAFLD**. Yang *et al.* [22]** analyzed higher blood iron levels were linked to a decreased possibility of NAFLD, according to research on serum iron and the risk of NAFLD and advanced hepatic fibrosis in US adults. There were no discernible racial or ethnic disparities in these correlations**.**

Limitations of the present study:

Despite the promising outcomes of the current study, the primary drawback is the small sample size that restricts the capability for performing sub-analyses of different patient groups. For example, morbidly obese women in presence or absence of NAFLD, in presence or absence of DIOS, and those with other CLD are among these patient groups. The second limitation is that NAFLD was identified according to noninvasive parameters and not hepatic biopsy because of the great difficulties to arrange this and the disagreement of the majority of patients.

CONCLUSION

The current study revealed that in obese women with NAFLD, serum hepcidin level was markedly elevated than in healthy females with normal weight and its level was correlate with lipid profile (negatively with cholesterol and triglyceride and positively with HDL), but didn't correlate with iron profile.

The significant increase of hepcidin level in obese females with NAFLD than in the normal weight control group women with normal liver, with the concomitant finding of increased ferritin levels in NAFLD group (even though the correlation between hepcidin and ferritin had not been approved), is highly suggestive a physiologic response to accumulation of iron and iron stores in the liver. As a result, early identification and therapeutic modalities in NAFLD cases with iron overload may benefit from the use of hepcidin and biochemical indicators of iron metabolism in FLD.

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