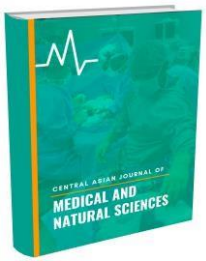

CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES
https://cajmns.centralasianstudies.org/index.php/CAJMNS
Volume: 05 Issue: 03 | July 2024 ISSN: 2660-4159

Article

Study of Erythropoietin and Lipid Profile and Some Trace Elements in Patients with Fatty Liver Disease in Thi-Qar Province, Iraq

Muna Hameed Kazem[1], Jamal Harbi Hussein Alsaadi[2]

1. Department of Chemistry, College of Science, University of Thi-Qar, Thi-Qar, Iraq
* Correspondence: Muna.hameed@utq.edu.iq
2. Department of Chemistry, College of Science, University of Thi-Qar, Thi-Qar, Iraq
* Correspondence: jamal.saadi@sci.utq.edu.iq

Abstract: Non-alcoholic fatty liver disease (NAFLD) is an increasing worldwide health issue marked by fat buildup in more than 5% of liver cells. This disease is primarily caused by the obesity epidemic and affects approximately 25% of the world's population. NAFLD might lead to various degrees of cirrhosis in a persistent liver illness. Lastly, NAFLD could result in the development of cancer of the liver. This review aims to describe and estimate erythropoietin levels and lipid levels (TG, TC, HDL, LDL, V-LDL) and some trace elements (Selenium (Se), Iron(Fe)) in patients with fatty liver disease. Serum erythropoietin and lipid levels (triglycerides (TG), cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), very low-density lipoprotein (V-LDL)) and selenium and iron levels were determined in 96 volunteers from men and women: 73 patients and 23 healthy control group. Patients were diagnosed by an internist medicine specialist. Inclusion Criteria: The cases included in this study are patients with non-alcoholic fatty liver disease, diabetes, and hypertension. Exclusion Criteria: The cases excluded from this study are patients with alcoholic fatty liver disease or fatty liver with other diseases such as heart and kidney disease. An important increase in focus of erythropoietin in fatty liver in the DM also fatty liver in the DM and HTN cohorts compared to fatty liver and controls groups ($p \leqslant 0.05$), An important increase in focus of TC in patients cohorts compared in the controls groups ($p \leqslant 0.05$), An important increase in focus of TG and VLDL in patients groups compared to controls groups ($p \leqslant 0.05$), An important increase in focus of LDL in patients groups compared to controls groups ($p \leqslant 0.05$),and An important decrease in focus of HDL in patients groups compared to controls groups ($p \leqslant 0.05$). An important increase in focus of Se in patients groups compared to controls groups ($p \leqslant 0.05$). An important increase in focus of Fe in patients groups compared to controls groups ($p \leqslant 0.05$). The study indicated that there was an increase in the levels of erythropoietin, as well as an increase in the level of (TG, TC, LDL, V-LDL), Se, Fe, and a decrease in the level of (HDL) in patient's fatty liver.

Keywords: Non-alcoholic fatty liver disease (NAFLD), erythropoietin, lipid Profile, triglycerides (TG), cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), very low-density lipoprotein (V-LDL), Selenium (Se), Iron (Fe)

Citation: Kazem, M. H., & Al-saadi, J. H. H. Study of Erythropoietin and Lipid Profile and Some Trace Elements in Patients with Fatty Liver Disease in Thi-Qar Province, Iraq. Central Asian Journal of Medical and Natural Science 2024, 5(3), 701-710.

Received: 6th June 2024
Revised: 13th June 2024
Accepted: 20th June 2024
Published: 27th June 2024

1. Introduction

Non-alcoholic fatty liver disease (NAFLD) is an increasing problem for world health due to its link to insulin-resistant metabolic diseases [1]. It can lead to cardiovascular disease and liver-related problems, including cirrhosis and hepatocellular cancer. NAFLD is marked by a large buildup of obesity, insulin resistance, and hepatic lipid. It is a broad

group of diseases, including cirrhosis, liver fibrosis, hepatocellular carcinoma, non-alcoholic steatohepatitis, and simple hepatic steatosis [2]. Despite its increasing prevalence, only 5% of NAFLD patients are aware of it, compared to 38% of those with viral hepatitis [3]. Lean individuals may still develop NAFLD, with a global incidence of 13.11%. However, metabolic dysfunction is weight-related and less common in lean individuals than in obese or overweight individuals.

Erythropoietin, a pleiotropic cytokine, is a circulatory growth factor and glycoprotein primarily produced in the kidneys [4]. It is released when tissue hypoxia is present, and it functions by attaching to the membrane erythropoietin receptors (EPOR), present in a variety of cells. EPO is a crucial regulator of erythropoiesis [5]. And has been shown to protect against metabolic diseases [6]. It stimulates brown fat-like properties in white adipose tissue from obese mice [7]. reduces adipose tissue mass and partially ameliorates steatosis in liver tissues by activating protein kinase B in a PPARγ-dependent manner [8]. In vivo studies have shown that EPO and SIRT1 cross-talk occur in liver tissue, with SIRT1 controlling the effects of EPO in the liver and reducing hepatic ER stress and lipid deposition in hepatocytes [9]. This method indicates a novel mechanism by which EPO, in a SIRT1-dependent manner, decreases ER stress in liver steatosis. Hepatokine FGF21 promotes browning of white adipose tissue, brown fat tissue thermogenesis, and hepatitis fatty acid oxidation, has been seen as a potentially effective therapeutic treatment. In vitro and in vivo, hepatic FGF21 expression may be enhanced by EPO, but enhanced expression of FGF21-targeted cells is less affected by EPO's production when SIRT1 impairment is present [10].

Cholesterol is a lipid sterol produced and transported throughout the circulatory system in eukaryotes, playing a crucial role in cell signaling, hormone production, and membrane structure [11]. It is produced and transported by lipoproteins, which are submicroscopic particles bonded together by noncovalent interactions [12]. Triglycerides are fatty acid esters derived from glycerol, the most prevalent kind of lipid in the body. They are created with more calories and stored in fat cells, converted into tri-glycerides and released into tissues when needed [13]. One of the main groups of serum lipoproteins, high-density lipoproteins (HDL), reverses the movement of cholesterol from peripheral cells to the liver [14]. The liver convert HDL into bile acids, which are then eliminated down the biliary tract and into the intestinal tract. Because there is a negative association between blood HDL-cholesterol levels and the risk of developing atherosclerosis, measuring HDL-cholesterol levels is crucial for therapeutic purposes [15].

Low-density lipoproteins (LDLs) have a major part in the development of atherosclerotic and coronary sclerosis [16]. VLDL is produced by the liver, combining lipoproteins, triglycerides, and cholesterol to produce VLDL [17]. The byproducts of its conversion in the blood flow are low-density lipoprotein (LDL) and intermediate-density lipoprotein (IDL). Selenium, a trace element in human nutrition, was first discovered in 1817 as a byproduct of sulfuric acid production [18]. It is essential for combating oxidizing and forms a portion of the catalysis core of many antioxidant selenium proteins [19]. Selenium plays crucial biological functions in the body, such as immunity control, thyroid gland metabolism, immunological response modulation, oxidative stress management, and oxidation/antioxidant ratio modification [20]. Iron is essential for mammalian enzymes and processes, including the citric acid cycle, mitochondrial respiration, oxygen sensing, and DNA biosynthesis [21]. Hepatic iron overload could support the pathophysiology of the pathophysiology of non-alcoholic fatty liver disease (NAFLD), as too much free iron triggers the Fenton reaction [22].

2. Materials and Methods

The research was carried out at the (University of Thi-Qar) Biochemistry Laboratory at the College of Science and Al-Nasiriyah Teaching Hospital and Private laboratories. This was during the period between November (2023) to February (2024). The current study included 96 Volunteers from men and women and divided into four groups: 73patients and 23healthy control group. Patients were diagnosed by an internist medicine specialist. 96 cases were considered and divided in to four groups: 1. Fatty Liver: includes (28) patients; 2. Fatty Liver with DM: includes (22) patients; 3. Fatty Liver with DM and HTN: includes (23) patients; 4. Controls: includes (23) healthy.

Collect blood sample

After the disease is detected by the ultrasound deviceA 5 ml blood sample is obtained. from men and women intravenously. Place in a gel tube for separation Serum. The blood was Permitted for solidification at the surrounding temperature, and then the serum was left Separated by centrifugation to divide it at a speed of 3000 revolutions per minute (rpm). The serum specimens were separated for 10 minutes, after which they were kept at -20°C (for future chemical indicator testing, unless utilized right away).

Statistical analysis

The findings of the statistical analysis, which was conducted with SPSS V 23, were presented as mean ± standard deviation (mean ± SD). Subgroups were compared using a one-way ANOVA. The link between the current research parameters was ascertained by using Pearson's correlation. P-values indicating statistical significance (P≤0.05) were used.

3. Results

General Characteristics the Groups Under Study's

Table 1 displays a general summary of patient characteristics including age and BMI.

Table 1. Overall Features the Groups Under Study's

Groups	BMI(Kg/m²) Mean ±SD	Age (Years)
Fatty Liver	31.38±4.82	44.53±13.81
Fatty Liver with DM	32.64±5.19	50.00±7.69
Fatty Liver with DM and HTN	35.66±3.6.88	56.82±12.48
Controls	28.24±4.85	51.65±12.38

DM: Diabetic mellitus
HTN: Hypertension
BMI: Body mass index
SD represents the Standard deviation

Serum Levels of Erythropoietin Concentration

Table 2 and Figure 1 indicate a notable rise in the value of erythropoietin in the fatty liver with DM and fatty liver with DM and HTN groups in comparison with the fatty liver and control groups (p≤0.05). There was no difference in the level of erythropoietin between fatty liver and control groups (p≤0.05).

Table 2. Serum Erythropoietin levels of control and patient's groups

Groups	NO.	Erythropoietin (U/Ml) Mean ±SD
Fatty Liver	28	62.31±9.39 c
Fatty Liver with DM	22	68.91±7.66 b
Fatty Liver with DM and HTN	23	75.04±10.56 a
Controls	23	56.37±11.42 c
LSD		4.37

No represents the Number of subjects.
LSD represents the Least Significant Difference
(a, b, c) indicates having various letters in same column have been significantly differed (P <0.05) The different letters refer to a significant difference. The same letters refer to a non-significant difference.

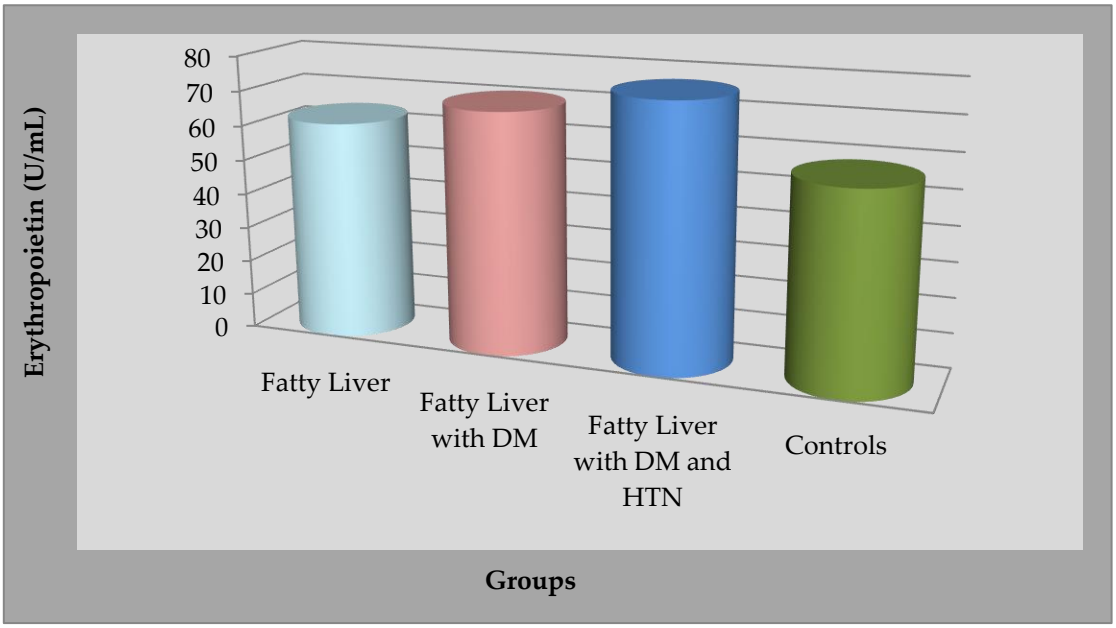

Figure 1. Serum Erythropoietin concentrations of control and patient's groups

Serum Levels of Lipid Profile concentrations

Table 3 and Figure 2 indicate a notable rise in the value of TC in patients groups in comparison with controls groups (p≤0.05). There was no difference in the level of TC between fatty liver and fatty liver with DM groups (p≤0.05).

Also this table and figure indicate a notable rise in the value of TG and VLDL in patients groups in comparison with controls groups (p≤0.05). There was no difference in the level of TG and VLDL between fatty liver with DM and fatty liver with DM and HTN groups (p≤0.05).

The same table and figure indicate a notable rise in the value of LDL in patients groups in comparison with controls groups (p≤0.05). There was no difference in the level of LDL between fatty liver and fatty liver with DM groups (p≤0.05).

While this table and figure indicate a notable drop in the level of HDL in patients groups in comparison with controls groups (p≤0.05). There was no difference in the level of HDL between fatty liver and fatty liver with DM groups (p≤0.05).

Table 3. Serum Lipid Profile levels of control and patient's groups

Groups	NO.	TC (mg/dL) Mean ±SD	TG (mg/dL) Mean ±SD	HDL (mg/dL) Mean ±SD	LDL (mg/dL) Mean ±SD	VLDL (mg/dL) Mean ±SD
Fatty Liver	28	204.23±17.85 b	187.93±38.18 b	45.01±6.50 b	121.63±20.76 ab	37.58±7.63 b
Fatty Liver with DM	22	206.66±27.48 b	221.65±21.44 a	42.55±6.70 bc	119.77±30.11 b	44.33±4.22 a
Fatty Liver with DM and HTN	23	219.88±32.20 a	226.81±38.68 a	40.45±11.50 c	134.06±34.18 a	45.36±7.73 a
Controls	23	174.11±31.40 c	105.47±19.97 c	71.09±12.60 a	81.92±29.94 c	21.09±3.99 c
LSD		12.34	13.69	4.31	12.94	2.73

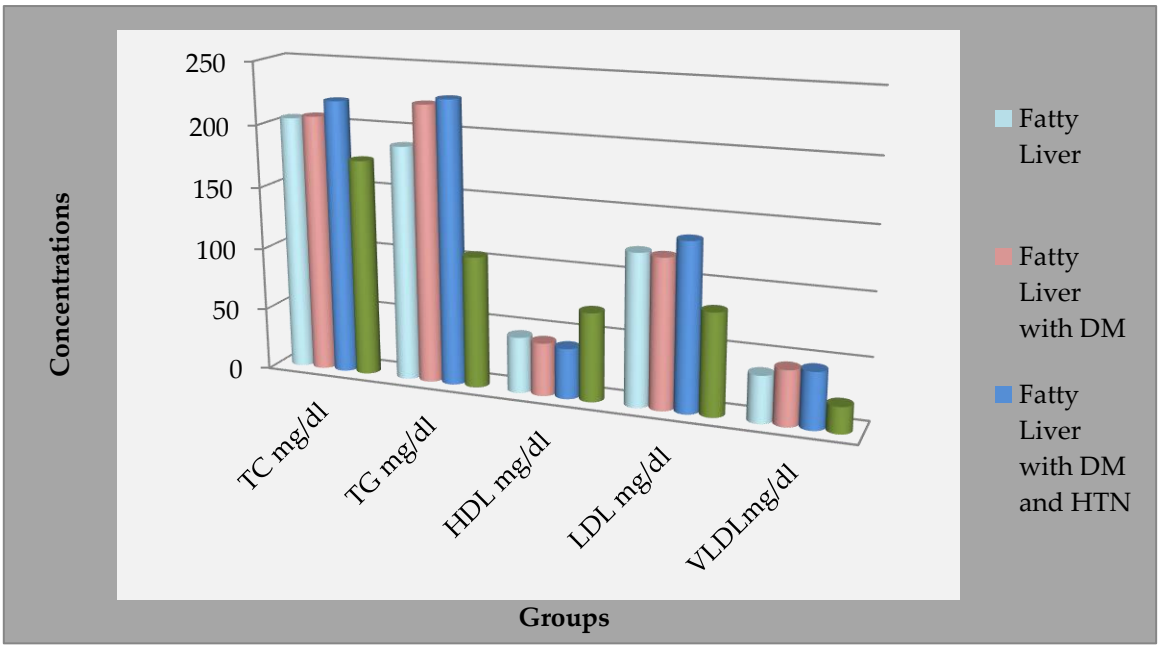

Figure 2. Serum Lipid Profile concentrations of control and patient's groups

Serum Levels of trace elements concentrations

a) Serum Levels of Se concentrations

Table 4 and Figure 3 indicate a notable rise in the value of Se in patients groups in comparison with controls groups (p≤0.05). There was no difference in the level of Se between fatty liver with DM and fatty liver with DM and HTN groups (p≤0.05).

Table 4. Serum Se levels of control and patient's groups

Groups	NO.	Se (μ mol\L) Mean ±SD
Fatty Liver	28	3.84±1.08 b
Fatty Liver with DM	22	3.31±0.76 c
Fatty Liver with DM and HTN	23	3.30±0.68 c
Controls	23	6.16±1.53 a
LSD		0.47

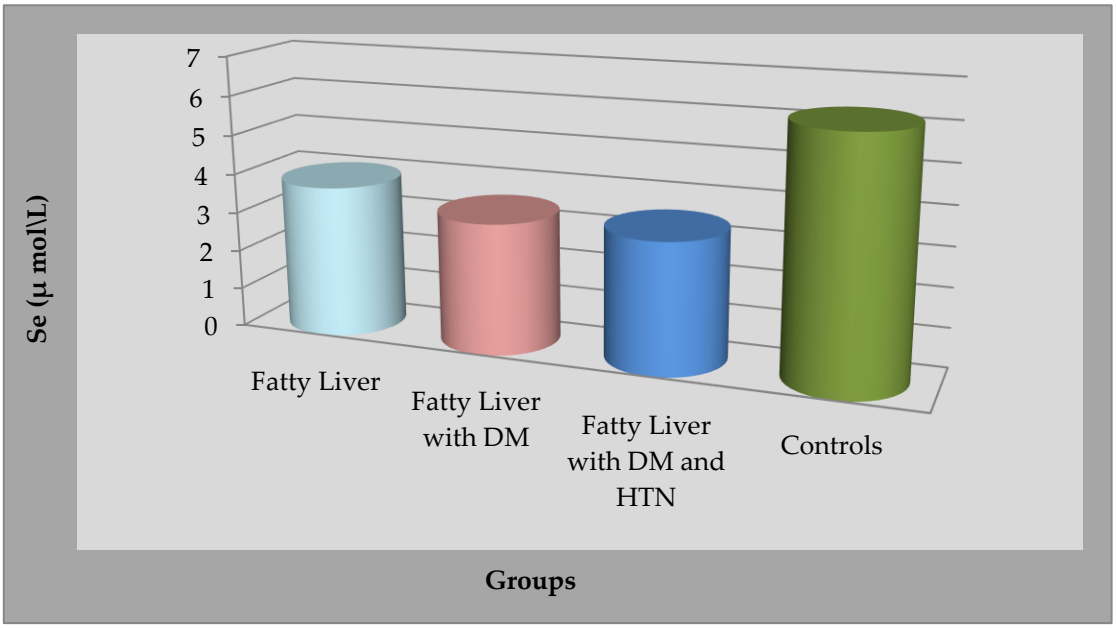

Figure 3. Serum Se concentrations of control and patient's groups

b) Serum Levels of Fe concentrations

Table 5 and Figure 4 indicate a notable rise in the value of Fe in patients groups in comparison with controls groups ($p \leq 0.05$). There was no difference in the level of Fe between fatty liver with DM and fatty liver with DM and HTN groups ($p \leq 0.05$).

Table 5. Serum Fe levels of control and patient's groups

Groups	NO.	Fe (µ mol\L) Mean ±SD
Fatty Liver	28	1.50±0.30 b
Fatty Liver with DM	22	0.95±0.21 c
Fatty Liver with DM and HTN	23	1.02±0.16 c
Controls	23	1.65±0.33 a
LSD		0.11

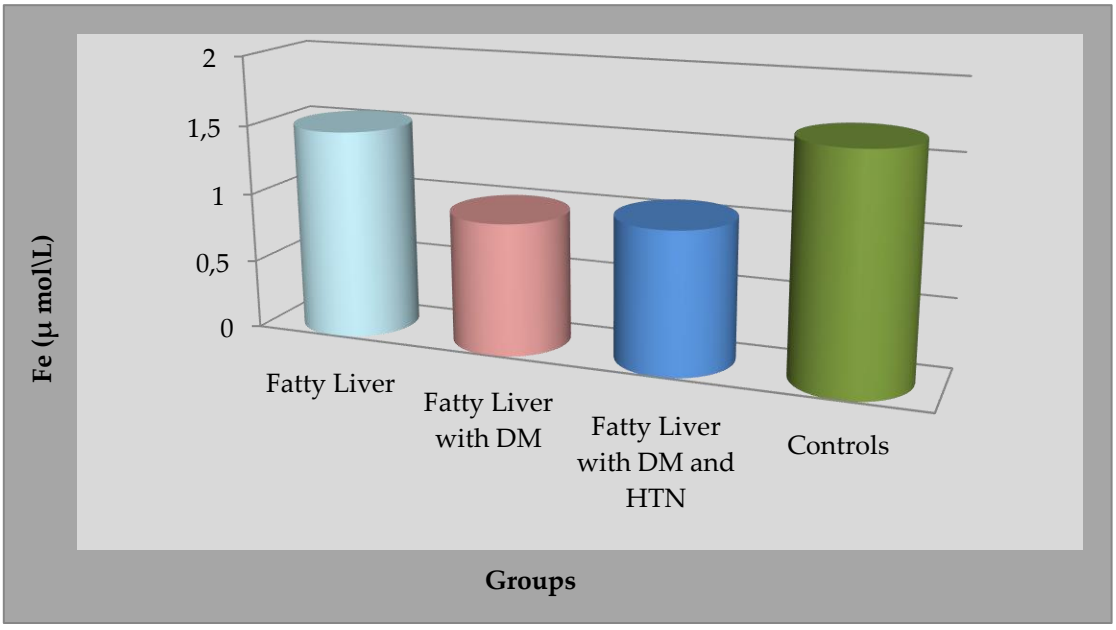

Figure 4. Serum Fe concentrations of control and patient's groups

4. Discussion

Serum Levels of Erythropoietin Concentration

EPO production and secretion are primarily sourced from kidney peritubular interstitial cells. but other organs like the liver, uterus, and cerebral also play a role. EPO expression is regulated by oxygen tension, not red blood cell concentration [23]. Hypoxia-inducible factor 1 (HIF-1) can regulate EPO expression and the EPO receptor (EPOR), increasing EPO synthesis [24]. Higher disability may be correlated with elevated EPO blood levels during brain maturation [25]. The human hemopoietic Epo receptor (Epo-R) is a member of Classes of receptors for cytokines class I and binds to the Epo-R dimer, causing cytoplasmic Janus kinases 2 (JAK2) to phosphorylate the tyrosine residues of the Epo-R and other internal proteins. Inflammation may be the source of EPO hyporesponsiveness in non-alcoholic fatty liver disease (NAFLD), as it impairs the body's ability to respond to medicines that stimulate erythropoiesis [26].

Erythropoietin regulates erythropoiesis, impacting trophic and development characteristics, immune-related consequences, and reactions to inflammatory cytokines [27]. In the renal and to a lesser extent in other organs, Epo production rises in hypoxic situations. Our results concur with those of these earlier investigations [28]. This was valid not only in the presence of additional cytokines in DR but also in the setting of elevated glucose levels in the blood. One typical consequence of Type 2 diabetes is diabetic retinopathy [29]. In summary, erythropoietin is one of the most significant growth factors that contributes to ischemia and angiogenic processes in diabetic retinopathy, in addition to other angiogenic variables like vascular endothelium factor. This is consistent with the study [30].

Serum Levels of Lipid Profile Concentration

The study found that patients with non-alcoholic fatty liver disease (NAFLD) have increased free cholesterol concentrations, which are more pronounced in cases of the disease's progressive form, NASH. Cholesterol esters do not change in response to elevated free cholesterol, indicating a possible impairment in the function and/or expression of the enzyme that catalyzes cholesterol esterification (ACAT). This suggests that cholesterol is one of the toxic lipids that builds up in the liver during NAFL/liver damage [31]. A buildup of lipids in hepatocytes because dyslipidemia and insulin resistance leads to liver damage and an extensive response, generating hepatic inflammation and fibrosis [32]. Elevated cellular cholesterol contributes to the onset of NAFLD and the disease's progression [33]. This validates the study's findings [34]. High blood triglycerides are more associated with NAFLD, suggesting that a diet high in carbohydrate may cause liver cells to accumulate more triglycerides [35]. Triglyceride accumulation is central to the development of NAFLD, which aligns with the findings of the study [36]. To sum up, increased TG was indicative of NAFLD [37].

NAFLD prevalence increases with elevated levels of LDL-c, possibly due to its association with multiple sclerosis. Impaired LRP6 function can lead to elevated hepatic LDL deposits and blood TG and LDL levels, these are important contributors for NAFLD [38]. Insulin resistance in NAFLD reduces the response to insulin and the generation of sugar in the liver, increasing circulating LDL cholesterol levels [39]. Excessive production of free fatty acids may influence NAFLD development. That aligns with the findings of the study [40]. VLDL, a type of lipid released by the liver, can be divided into two types: VLDL1 TG-rich, big and VLDL2 thicker, lesser. By reducing the expression of apoB mRNA, insulin controls the assembly of VLDL [41]. Preventing microsomal transfer protein synthesis and encouraging autophagic apoB breakdown. That aligns with the findings of the study [42]. Low HDL levels are crucial for the development of NAFLD, possibly due to insulin resistance. Patients with NAFLD often have lower HDL levels [43]. which is characteristic of metabolic syndromes and is seen as a sign of the liver metabolic syndrome. This aligns with the findings of the study [44].

Serum Levels of trace elements (Se, Fe) Concentration

Selenium, a trace element in human health, is primarily sourced from dietary intake and is present in 25 selenium proteins [45]. Elevated selenium levels may manage hepatic insulin resistance and compromise insulin signaling, potentially contributing to hepatic fat formation [46]. High blood selenium levels have been linked to non-alcoholic fatty liver disease (NAFLD), with a rise in hyperglycemia, hyperinsulinemia, and hyperlipidemia due to increased expression of lipogenesis-associated proteins. Elevated selenium exposure may increase the expression and activity of GPxs and enhance PTP1b activity, the essential element of liver lipid synthesis and buildup is SREBP-1c [47]. This result matched the results of the study by [48]. Iron is essential for various metabolic processes, but too much can cause oxidative damage. The hormone Hepcidin controls iron release from cells, regulating body iron homeostasis [49].

Hepatic iron is crucial in nonalcoholic fatty liver disease (NAFLD) evolution, generating oxidative stress that causes cell death, DNA, lipids, and proteins damage [50]. Increased hepatic iron stores are associated with increased lipid peroxidation and stress on the endoplasmic reticulum. Mouse liver iron load increases the pathways involved in the production of cholesterol., contributing to NAFLD pathogenesis [51]. Iron stores are associated with an increased risk of type 2 diabetes due to damage to pancreatic β-cells and increased oxidative stress, leading to insulin resistance. Addressing iron stores and reducing inflammation is crucial This outcome agreed with the findings of the research of [52].

5. Conclusion

The study indicated that there was an increase in the levels of erythropoietin, as well as an increase in the level of (TG, TC, LDL, V-LDL), Se, Fe, and a decrease in the level of (HDL) in patient's fatty liver.

REFERENCES

[1] K. S. Kim, S. Hong, H. Y. Ahn, and C. Y. Park, "Metabolic dysfunction-associated fatty liver disease and mortality: a population-based cohort study," *Diabetes & Metabolism Journal*, vol. 47, no. 2, p. 220, 2023.

[2] Z. M. Younossi et al., "From NAFLD to MAFLD: implications of a premature change in terminology," *Hepatology*, vol. 73, no. 3, pp. 1194-1198, 2021.

[3] S. A. P. J. M. B. R. A. T. H. L. &. Y. Z. M. Alqahtani, "Poor awareness of liver disease among adults with NAFLD in the United," *Hepatology Communications*, vol. 5, no. 11, pp. 1833-1847, 2021.

[4] J. P. Marrow, "Novel Roles of Cardiac-derived Erythropoietin in Disease," Doctoral dissertation, University of Guelph, 2024.

[5] K. M. Lappin, K. I. Mills, and T. R. Lappin, "Erythropoietin in bone homeostasis—Implications for efficacious anemia therapy," *Stem Cells Translational Medicine*, vol. 10, no. 6, pp. 836-843, 2021.

[6] J. She, Z. Yuan, Y. Wu, J. Chen, and J. Kroll, "Targeting erythropoietin protects against proteinuria in type 2 diabetic patients and in zebrafish," *Molecular Metabolism*, vol. 8, pp. 189-202, 2018.

[7] K. Kodo et al., "Erythropoietin (EPO) ameliorates obesity and glucose homeostasis by promoting thermogenesis and endocrine function of classical brown adipose tissue (BAT) in diet-induced obese mice," *PloS One*, vol. 12, no. 3, p. e0173661, 2017.

[8] T. Hong et al., "Erythropoietin alleviates hepatic steatosis by activating SIRT1-mediated autophagy," *Biochimica et Biophysica Acta (BBA)-Molecular and Cell Biology of Lipids*, vol. 1863, no. 6, pp. 595-603, 2018.

[9] T. Hong et al., "Erythropoietin suppresses hepatic steatosis and obesity by inhibiting endoplasmic reticulum stress and upregulating fibroblast growth factor 21," *International Journal of Molecular Medicine*, vol. 44, no. 2, pp. 469-478, 2019.

[10] S. Matsui et al., "Neuronal SIRT1 regulates macronutrient-based diet selection through FGF21 and oxytocin signalling in mice," *Nature Communications*, vol. 9, no. 1, p. 4604, 2018.

[11] M. S. Sekhar et al., "Physiological role of cholesterol in human body," in *Dietary Sugar, Salt and Fat in Human Health*, Academic Press, pp. 453-481, 2020.

[12] A. Taan, H. R. Faraj, and R. M. Hannon, "Clinical Study for Serum Lipid Profile and Lipid Peroxidation in Patients with Gallstones in Thi-Qar Governorate-Iraq," *University of Thi-Qar Journal of Medicine*, vol. 16, no. 2, pp. 193-199, 2018.

[13] G. S. Getz, "Lipid Transfer Proteins: Introduction to the Thematic Review," *Journal of Lipid Research*, vol. 59, no. 5, pp. 745-748, 2018.

[14] K. H. Cho, "The current status of research on high-density lipoproteins (HDL): a paradigm shifts from HDL quantity to HDL quality and HDL functionality," *International Journal of Molecular Sciences*, vol. 23, no. 7, p. 3967, 2022.

[15] M. M. Quetglas-Llabrés et al., "Status and metabolic parameters in NAFLD patients: A 24-month lifestyle intervention study," *Antioxidants*, vol. 13, no. 4, p. 480, 2024.

[16] J. G. Neels, G. Leftheriotis, and G. Chinetti, "Atherosclerosis calcification: focus on lipoproteins," *Metabolites*, vol. 13, no. 3, p. 457, 2023.

[17] K. R. Feingold, "Introduction to lipids and lipoproteins," *Endotext* [internet], 2024.

[18] N. Wang et al., "Supplementation of micronutrient selenium in metabolic diseases: its role as an antioxidant," *Oxidative Medicine and Cellular Longevity*, vol. 2017, no. 1, p. 7478523, 2017.

[19] M. L. Ojeda et al., "Binge drinking during the adolescence period causes oxidative damage-induced cardiometabolic disorders: A possible ameliorative approach with selenium supplementation," *Life Sciences*, vol. 301, p. 120618, 2022.

[20] J. H. Alsaadi and R. N. Altaiee, "A Clinical Investigative Study for Homocysteine and Some Trace Elements Levels in Pregnant with Preeclampsia and Premature BI," *Türk Fizyoterapi ve Rehabilitasyon Dergisi/Turkish Journal of Physiotherapy and Rehabilitation*, vol. 32, no. 3, pp. 5111-5120, 2024.

[21] L. Lin et al., "Nanomedicine targets iron metabolism for cancer therapy," *Cancer Science*, vol. 113, no. 3, pp. 828-837, 2022.

[22] S. Altamura et al., "Iron aggravates hepatic insulin resistance in the absence of inflammation in a novel db/db mouse model with iron overload," *Molecular Metabolism*, vol. 51, p. 101235, 2021.

[23] K. Maiese, "Novel applications of trophic factors, Wnt and WISP for neuronal repair and regeneration in metabolic disease," *Neural Regeneration Research*, vol. 10, no. 4, pp. 518-528, 2015.

[24] K. Nishimura et al., "The effect of hemin-induced oxidative stress on erythropoietin production in HepG2 cells," *Cell Biology International*, vol. 38, no. 11, pp. 1321-1329, 2014.

[25] S. J. Korzeniewski et al., "Elevated endogenous erythropoietin concentrations are associated with increased risk of brain damage in extremely preterm neonates," *PLoS One*, vol. 10, no. 3, p. e0115083, 2015.

[26] N. Ueda and K. Takasawa, "Impact of inflammation on ferritin, Hepcidin and the management of iron deficiency anemia in chronic kidney disease," *Nutrients*, vol. 10, no. 9, p. 1173, 2018.

[27] L. Toro et al., "Erythropoietin induces bone marrow and plasma fibroblast growth factor 23 during acute kidney injury," *Kidney International*, vol. 93, no. 5, pp. 1131-1141, 2018.

[28] H. Zou, R. S. Wong, and X. Yan, "Erythropoietin hyporesponsiveness in non-alcoholic fatty liver disease," *Clinical and Experimental Pharmacology and Physiology*, vol. 51, no. 6, p. e13869, 2024.

[29] J. H. Alsaadi, N. H. Alrikabi, and H. M. Younis, "Clinical Study of Changes Selenium, Zinc, Lead and Lipid Profile in Serum with Retinopathy Diabetic Patients in Thi Qar Governorate," *History of Medicine*, vol. 9, no. 1, pp. 1038-1047, 2023.

[30] S. Davidović et al., "Serum erythropoietin concentration and its correlation with stage of diabetic retinopathy," *BMC Ophthalmology*, vol. 19, pp. 1-8, 2019.

[31] P. Puri et al., "A lipidomic analysis of nonalcoholic fatty liver disease," *Hepatology*, vol. 46, no. 4, pp. 1081-1090, 2007.

[32] H. Chatrath, R. Vuppalanchi, and N. Chalasani, "Dyslipidemia in patients with nonalcoholic fatty liver disease," *Seminars in Liver Disease*, vol. 32, no. 1, pp. 22-29, 2012.

[33] T. P. Johnston et al., "Apolipoprotein E expression and its role in the pathogenesis of dyslipidemia, obesity, and insulin resistance: Insights from experimental models," *International Journal of Molecular Sciences*, vol. 22, no. 12, p. 6421, 2021.

[34] S. Petersen and K. D. Shulman, "Etiology of insulin resistance," *The American Journal of Medicine*, vol. 119, no. 5, pp. 10-16, 2006.

[35] A. R. Saltiel, "Insulin resistance in the pathogenesis of dyslipidemia," *Current Diabetes Reports*, vol. 15, no. 4, p. 41, 2015.

[36] Y. Wang et al., "Endoplasmic reticulum stress is associated with inflammation in obese women with polycystic ovarian syndrome," *Endocrine*, vol. 54, no. 3, pp. 731-738, 2016.

[37] K. A. Bradshaw, "Insulin signaling in health and disease: novel insights from lipidomics," *Trends in Endocrinology and Metabolism*, vol. 27, no. 3, pp. 235-247, 2016.

[38] E. Marwaha et al., "The role of adipose tissue in metabolic dysregulation in nonalcoholic fatty liver disease," *Metabolism*, vol. 64, no. 8, pp. 1066-1074, 2015.

[39] B. A. Neuschwander-Tetri, "Efficacy and safety of dietary supplements in nonalcoholic fatty liver disease," *Clinics in Liver Disease*, vol. 18, no. 1, pp. 115-133, 2014.

[40] G. P. Aithal, "Treating non-alcoholic fatty liver disease," *BMJ*, vol. 362, p. k2734, 2018.