CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES

https://cajmns.casjournal.org/index.php/CAJMNS

Volume: 06 Issue: 04 | October 2025 ISSN: 2660-4159

Article

The Significance of CK18 and Azonulin when Evaluating Nonalcoholic Fatty Liver Diseases in the Iraqi Community

Asst. Prof. Dr. Nawal Abdullah Murtadha (PhD)

1. College of Science, University Of Kirkuk, Iraq
* Correspondence: nawalabbdullah@uokirkuk.edu.iq

Abstract: Nonalcoholic fatty liver disease (NAFLD), which impacts over twenty-five percent of the worldwide population, has emerged as an important issue for the public. This prevalent liver disease is characterized by excess fat buildup after hepatic steatosis, with or without hepatocyte loss, various types of inflammatory cells infiltration, nonalcoholic steatohepatitis, and, in rare instances, cirrhosis and cancer of the liver. Cytokeratin 18 (CK18), which is a marker of apoptosis and overall cell death, is an excellent biomarker for NAFLD. Liver fat accumulation in NAFLD triggers the activation of caspases, which increases the CK18 cleavage and its release into the blood. CK18 can help diagnose different stages of NAFLD, especially the nonalcoholic steatohepatitis (NASH) stage. CK18 is important for assessing the success of NAFLD treatment and forecasting the risk of NAFLD-related illnesses. The zonulin test can detect intestinal permeability among individuals with nonalcoholic fatty liver disease (NAFLD), which is typically elevated.

Keywords: Nonalcoholic fatty liver disease, cytokeratin 18, zonulin

1. Introduction

The purpose of this study was to examine serum levels of CK-18, enzyme levels in the liver, and lipid profile in individuals with NAFLD in Iraqi young adults, Assess zonulin as an indicator and predictive indicator for nonalcoholic fatty liver disorders in individuals. . A case-control study was conducted in Kirkuk Teaching Hospital from February to December, 2024. This study had 90 contributors, 60 patients (30 female and 30 male) Ages vary between 20 to 60 years. The observer group consisted of 30 incredibly healthy individuals (15 girls and 15 men) varying in age from twenty to fifty years of age old. The serum CK-18 levels, liver function enzymes (AST, ALT, GGT), and lipid profile (LDL, VLDL, Cholesterol, TG, HDL) were examined and compared to the control groups. Serum CK-18 levels were determined using the competitive enzyme-linked immunosorbent assay (ELISA) technique (Elk Biotechnology, USA). While AST, ALT, GGT, TG, Cholesterol, and HDL were calculated by Colorimetric Kit (Linear chemicals, Spain) by Spectrophotometer method. An ELISA approach was utilized to quantify human zonulin quantities in plasma, serum, and tissues homogenates. The kit was supplied by MyBioSource (San Diego, CA, USA). The average serum levels of GGT, ALT, and AST in NAFLD patients compared to those in the control group were significantly increased (P≤0. 05). NAFLD patients showed a significant increase (P≤0. 05) in serum CK-18 concentration as compared to control. Patients with NAFLD reported significantly higher (P≤0. 05) serum zonulin concentrations compared to controls. lipid profile (LDL,

Citation: Murtadha, N. A. The Significance of CK18 and Azonulin when Evaluating Nonalcoholic Fatty Liver Diseases in the Iraqi Community. Central Asian Journal of Medical and Natural Science 2025, 6(4), 2501-2509

Received: 15th Sept 2025
Revised: 30th Sept 2025
Accepted: 10th Oct 2025
Published: 30nd Oct 2025

VLDL, TG, Cholesterol) and liver enzyme significantly increased (P≤0. 05) while serum concentration of HDL significantly decreased as they were when compared with healthy people.

Based on the results regarding inflammatory markers, our findings show that most individuals participating in this research, serum CK-18 in NAFLD patients significantly increased. Greater zonulin concentration is linked to the existence of liver steatosis in nonalcoholic individuals who have liver disease.

Nonalcoholic fatty liver disease (NAFLD) is the leading cause of chronic liver disease worldwide, and it is linked to an increased risk of hepatic-related morbidity and mortality, as well as type 2 diabetes (T2D), overweight and obesity, and cardiovascular disease [1]. The initial symptom of NAFLD is the accumulation of extra fat in the liver (>5%) in the absence of drug or alcohol consumption. These anomalies include a broad range of the hepatic clinic pathologic spectrum that have no medical history, from simple steatosis to non-alcoholic steatohepatitis (NASH), a condition called liver cirrhosis, and finally hepatocellular cancer [2]. The term nonalcoholic fatty liver disease has been replaced with the new concept of metabolic dysfunction-associated fatty liver disease (MAFLD), which was proposed in 2020 and does not need the exclusion of viral hepatitis or alcoholic liver disease. For those who have dysmetabolism and fatty liver, this name is more appropriate. MAFLD, which affects 25% of individuals globally, is well recognized as the leading cause of chronic liver disease in both Europe and the United States [3]. The diagnosis is based on the patient's medical history, physical examination, liver steatosis, evaluation of metabolic risk factors, liver biochemistry, and, in certain cases, a liver biopsy. To adjust treatment for each patient, patients should have a non-invasive liver fibrosis examination. Most individuals can be treated in a primary care setting, however, patients who are suspected of having concurrent secondary liver disease or who are at elevated risk of advanced disease should be referred to a specialist [4][5]. The only treatment options available at the moment for end-stage disease are liver transplantation and lifestyle modifications aimed at weight loss, as there are currently no approved medications. New pharmaceutical substances should be licensed soon. Only in Non-alcoholic Steatohepatitis (NASH) monitoring for HCC is advised [6]. Screening of NAFLD with liver biopsy is impractical. There should be noninvasive alternatives to tackle this issue and to distinguish between steatosis, steatohepatitis, and fibrosis. 90% of NASH patients had elevated levels of the liver enzymes aspartate aminotransferase (AST) and the aminotransferase alanine (ALT) [7]. The most prevalent abnormal outcome in patients with NAFLD is modestly increased blood amino transferase levels. Nevertheless, liver enzyme values may be normal in up to 78% of NAFLD patients [8]. Other investigations found that people with NAFLD frequently have higher levels of the enzyme Gamma-glutamyl transferase (GGT) in their blood. Alkaline phosphatase (ALP) occasionally rises in NAFLD; thus, liver function tests cannot provide reliable data for diagnostic reasons [9]. Cytokeratin-18 is the most common intermediate filament protein discovered in liver cells and is essential for hepatocyte integrity. It is formed after the death of damaged hepatocytes caused by obesity-related degeneration, and caspase-cleaved CK18 components enter the bloodstream. CK18 components in the bloodstream will differ from steatohepatitis and ordinary steatosis, since apoptotic does not occur in basic steatosis [10]. Of tremendous attention and inquiry. Several potential biomarkers have been identified and researched. For example, the existence of CK18 fragments was investigated in patients with NAFLD who were identified via liver biopsy. CK18 is a class I cytokeratin. Keratin 8 works well with partner. It generates filaments, which are the most common intermediate filament gene products. Therefore, these chemicals can be found in a single layer of epithelial tissues in the human body [11]. Individuals with NASH showed significantly greater amounts of CK18 fragments in plasma (P<0. 001) compared to those with steatosis or normal findings. Others conducted additional investigations based on similar findings. A meta-analysis research found that the CK18 fragment test has a sensitivity and specificity

of 78% and 87%, respectively, for steatohepatitis and NAFLD [12]. Aida *et al.* were able to differentiate between NAFLD stages by using plasma CK18 fragment, which was considered a medically valuable biomarker. In another study, serum CK18 has shown a great specificity for NAFLD and fibrosis; nevertheless, its narrow sensitivity made screening examination for NAFLD staging inadequate. Whether or not performing CK18 tests with additionalbiomarkersorlaboratorytestsmaydemonstratebeneficialresults requires additional research. It has been reported that hepatocellular carcinoma can be tested through CK18 biomarkers instead of alpha-fetoprotein [13]. There are several approaches for evaluating intestinal permeability. Plasma zonulin concentrations, easily measured by blood testing, are commonly used to assess the permeability of the gut. The protein regulates permeability in the gut in a reversible mechanism. Zonulin promotes the attachment of intestinal epithelial cells to each other [14].

2. Materials and Methods

The study aimed at comparing the serum levels of Cytokeratin-18 and Zonulin, liver enzymes, and lipid profile of NAFLD patients to those of control groups.

A case and control research was conducted at Kirkuk Teaching Hospital from February to December, 2024. This study included 90 participants: 60 patients (30 female and 30 male) Ages vary between 20 to 50 years. The control group consisted of 30 normally healthy individuals (15 girls and 15 men) ranged in age from twenty to fifty years old. Serum CK-18levels, liver function enzymes (AST, ALT, GGT), and lipid profile (LDL, VLDL, Cholesterol, TG, HDL) were measured and compared to the control groups. Serum CK-18levels was estimated by competitive-enzyme-linked immunosorbent assay (ELISA) technique (Elk biotechnology, U. S. A.). While AST, ALT, GGT, TG, Cholesterol, and HDL were calculated by Colorimetric Kit (Linear chemicals, Spain) by Spectrophotometer method. An ELISA approach was utilized to quantify human zonulin quantities in plasma, serum, and tissues homogenates. The kit was supplied by MyBioSource (San Diego, CA, USA).

A sterile throwaway syringe was used to collect about 8ml of venous blood from each patient, which was then transferred to two gel tubes. Blood in a gel tube was allowed to coagulate at room temperature before being centrifuged at 4000 rpm for 10 minutes; serum was collected and divided into two Eppendorf tubes for each sample, then stored at -20C in a deep freezer until the time of analysis.

All test results and questionnaire data were compiled into a datasheet. Data analysis was conducted using IBM SPSS version 28. 0 and Real Statistics Resource Pack for Excel 2016.

3. Results

Table 1 shows that the mean serum GGT in NAFLD patients had considerably greater levels ($p< 0. 05$) compared to the control group, it also observed substantial ($p< 0. 05$) difference in serum ALT level among NAFLD patients and those in the comparison group, the mean serum AST level in NAFLD patients was significantly higher ($p < 0. 05$) than the control group. It also shows that the patients with NAFLD had a considerable rise ($p < 0. 05$) in serum CK-18 concentration as compared to control. Patients with NAFLD had a considerable rise ($p < 0. 05$) in serum Zonulin concentration as compared to control.

Table 1. Levels of GGT, ALT, AST, CK-18 and Zonulin in patients with NAFLD

Parameters	Study groups	Mean	SD	P value
GGT (IU/ L)	Patient	279. 87	17. 94	0. 001
	Control	52 .09	5. 12	
ALT (IU/ L)	Patient	46. 14	5. 98	0. 002
	Control	2 .169	1 .28	
AST (IU/ L)	Patient	48. 81	2 .33	0. 001
	Control	18. 01	2 .25	
CK-18 (mIU/mL)	Patient	530. 86	2 .289	0. 000
	Control	167. 92	0 .115	
Zonulin (ng/mL)	Patient	398. 91	16. 29	001 .0
	Control	84. 52	10. 8	
Duration of NAFLD ((years) (mean ± SD) = 3. 26 ± 97 .1				

P < 0. 05 Significant

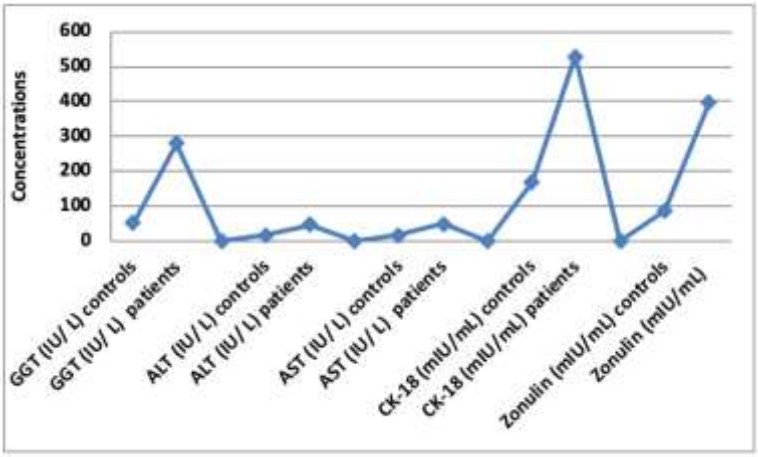

Figure 1. Concentrations of GGT, ALT, AST, CK-18 and Zonulin in patients with NAFLD

Table 2 demonstrates that patients with NAFLD had considerably higher ($p < 0.05$) serum lipid profiles (TG, VLDL, LDL, cholesterol) and significantly lower ($p < 0.05$) HDL concentrations compared to controls.

Table 2: Serum levels of lipid profile in patients with NAFLD

Variable	Groups	Mean	SD	P value
TG (mg/dL)	Patient	213. 12	14. 55	0. 000
	Control	146. 88	9. 22	
Total Cholesterol (mg/dL)	Patient	199. 39	24. 55	0. 003
	Control	151. 87	28. 39	
HDL (mg/dL)	Patient	30. 32	4. 12	0. 001
	Control	39. 85	6. 51	
LDL (mg/dL)	Patient	121. 88	14. 40	0. 004
	Control	89. 05	9. 18	
VLDL (mg/dL)	Patient	39. 20	3. 11	0. 001
	Control	33. 14	1. 89	

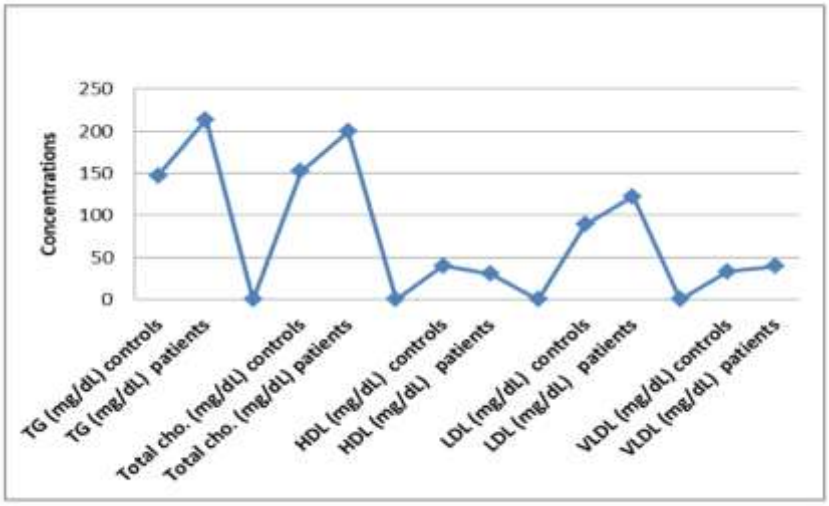

Figure 2: Concentrations of lipid profile in patients with NAFLD

The correlation coefficient was used for determining linear relationships among biochemical markers in patient groups compared to the control group. It was found that all biomarkers CK-18, Zonulin, GGT, AST, and ALT were risk factors and had highly statistically significant differences. An odd ratio of less than one implies a higher frequency of occurrence. An odd ratio greater than one implies a lower probability of a certain event (protective exposure) as presented in Table 3.

Table 3: Odd ratio for CK-18, Zonulin, GGT, AST, and ALT in NAFLD patients compared to the control group

Variable	OR	P value
CK-18 (mIU/mL)	7. 23	0. 001
Zonulin (ng/mL)	8. 45	0. 001
GGT (U\L)	8. 32	0. 001
AST (U\L)	2. 78	0. 016
ALT (U\L)	3. 61	0. 011
p<0. 05 considered significantly different- [S]= Significant, [NS]= Non significant, OR= odd ratio		

Table 3: Odd ratio for CK-18, Zonulin, GGT, AST, and ALT in NAFLD patients compared to the control group

Variable	OR	P value
CK-18 (mIU/mL)	7. 23	0. 001
Zonulin (ng/mL)	8. 45	0. 001
GGT (U\L)	8. 32	0. 001
AST (U\L)	2. 78	0. 016
ALT (U\L)	3. 61	0. 011
p<0. 05 considered significantly different- [S]= Significant, [NS]= Non significant, OR= odd ratio		

Table 1 shows that the mean serum GGT in NAFLD patients had considerably greater levels ($p < 0.05$) compared to the control group, it also observed substantial ($p < 0.05$) difference in serum ALT level among NAFLD patients and those in the comparison group, the mean serum AST level in NAFLD patients was significantly higher ($p < 0.05$) than the control group. It also shows that the patients with NAFLD had a considerable rise ($p < 0.05$) in serum CK-18 concentration as compared to control. Patients with NAFLD had a considerable rise ($p < 0.05$) in serum Zonulin concentration as compared to control.

4. Discussion

The current study shows an increase in serum GGT in NAFLD patients as compared with the control group. Our study agrees with Chen, who reported a high

level of GGT in NAFLD patients and also agrees with Mukherjee, who found GGT significantly elevated in NAFLD patients. Given that GGT is frequently associated with resistance to insulin and a higher body mass index, studies may lead to it as a test for evaluating the severity of fatty liver irrespective of etiopathogenesis [15]. Gamma-glutamyl transferase, a commonly used biomarker of liver cell damage, can predict NAFLD. It has a substantial correlation with the development of NAFLD. Furthermore, studies show that increased GGT levels are linked to a more severe histological spectrum of non-alcoholic fatty liver disease, including fibrosis and NASH [16]. GGT levels in NAFLD patients can be elevated due to oxidative stress, an inflammatory response, and increased fat accumulation in the liver. These variables are associated with impaired insulin signaling and resistance. GGT plays an important function in glutathione breakdown, which helps to maintain homeostasis in the face of oxidative stress. Earlier research has shown that serum GGT levels are associated with chronic conditions such as nonalcoholic fatty liver disease [17]. This study shows elevated serum levels of ALT in NAFLD patients when compared with healthy individuals. This study agrees with Hadinia [18] and Ali who reported a high level of ALT in the patient group as compared with control group [19]. The enzyme ALT is widely distributed in hepatocyte cytosol. In a healthy population, serum ALT levels are typically lower. However, after hepatocyte damage and apoptosis have taken place, serum ALT levels rise significantly. In patients with various chronic liver diseases, the serum ALT value is commonly used as a standard measure of liver function to indicate hepatic inflammation and liver injury. Most clinical research and tests only included participants with elevated ALT readings. Higher ALT readings were strongly correlated with a higher risk of NAFLD in the majority of earlier investigations, particularly when it was associated with NASH [20]. In clinical practice, serum ALT is one of the more typically requested biochemical tests and is crucial for the diagnosis and treatment of liver illness in patients. In addition, high ALT levels in the general population predict mortality unrelated to liver disease, the most plausible explanation for this correlation is that the primary cause of liver damage nowadays is NAFLD, which is most commonly MAFLD [21]. Serum levels of AST in NAFLD patients were significantly greater than in healthy individuals. Our study agrees with previous research done by Won, Young bin, et al, on women who have NAFLD was shown Aspartate aminotransferase levels were significantly higher in women with polycystic ovarian syndrome (PCOS), and this may indicate a more gradual development of liver damage rather than an immediate risk of NAFLD. Comparing women with PCOS to controls, there was a greater frequency of increased liver enzyme values [22]. This study also agrees with Ou, Hongjie, et al search done on NAFLD patients who made a comparison between dyslipidemia both reported high levels of AST [23]. The human body contains large amounts of AST, with the largest concentrations found in the heart, liver, skeletal muscle, kidney, brain, pancreas, spleen, lung, and erythrocytes. AST activity was discovered to be 7700 and 7000 greater in the liver and myocardium, respectively, compared to serum [24]. This study is consistent with Han, Ji Men, *et al.* , finding in their population study based on differing associations between fatty liver and dyslipidemia according to the degree of hepatic steatosis which found higher serum levels of TG, cholesterol, LDL, and decreased HDL concentration in NAFLD patient comparing to normal individual. The relationship among dyslipidemia and fatty liver differed depending on the amount of hepatic fat buildup, with those with fatty livers being more likely to acquire dyslipidemia compared to those without. The hepatocellular manifestation of the metabolic syndrome is fatty liver. Patients with fatty liver disease usually have dyslipidemia, in addition to other metabolic risk factors such as diabetes, overweight, and hypertension [25]. These analyzed chemical parameters with NAFLD and discovered that there is a substantial association between TG, LDL, TC, and VLDL, and an inverse relationship with HDL in that group, which coincides with Mansour-Ghanel, Roya, *et al* [26][27]. Since a greater number of our patients are obese

this comes true with Khan, Reenam, which informed us that greater lipolysis in adipose tissue was observed in obese NAFLD patients, which could explain 60–70% of the fat that builds up in the liver. Adipocytes' aberrant production of hormones (such as decreased adiponectin production) and adipose tissue inflammation (such as the release of pro-inflammatory cytokines) coincide with the excessive lipolysis of adipose tissue. These factors all contribute to the promotion of insulin resistance, which in turn causes ectopic fat deposition [28]. Present study, most of the cases have lipid alteration in NAFLD may be secondary to thyroid disorder this agrees with Lai, Shuiqing, *et al* stated in NAFLD, there is a decrease in thyroid hormone levels in the liver, as well as a malfunction in the expression of intrahepatic deiodinase. Thyroid hormones regulate circulating lipoprotein, TG, and total cholesterol levels, as well as hepatic TG accumulation and metabolism. Furthermore, NAFLD's apparent local hypothyroid condition may impair thyroid hormone receptor activation by lowering hepatic lipase activity, resulting in an excess of hepatic fatty acids. In-vivo studies have demonstrated that hepatic fat accumulation can be decreased by thyroid hormone injection and thyroid hormone agonists. This study found a substantial rise in serum CK-18 in NAFLD patients as compared with the control group (P = 0. 001, Table 5). This indicates that the hepatocytes are irritated or apoptotic. Pursuant to the regulations, CK-18 is a marker for steatohepatitis that separates it from simple steatosis. Qassam et al. found a significant rise in blood CK18 levels in individuals with NAFLD compared to the control group (P value ≤ 0. 05) [29]. Furthermore, there was barely any distinction between NAFLD patients and healthy individuals [30]. Feldstein et al. discovered that NASH patients had significantly higher levels of CK18 compared with patients with NAFLD (P ≤ 0. 05) [31]. They additionally observed that a 10 U/L increase in CK18 levels increased the likelihood of getting NASH by 70%. The results obtained are comparable with those of Liang et al. , who found that blood CK-18 levels were significantly greater in NASH patients than in non-NASH individuals. CK-18 found NASH in liver cell damage and hepatocyte death. Previous research has shown that plasma CK-18 concentrations rise considerably with increasing steatosis, inflammatory processes, and fibrosis. Furthermore, it was discovered that specific liver enzymes, including as dehydrogenase to alcohol 2 and 3, are more active in non-alcoholic Iraqis [32]. The current study found a significant difference in zonulin quantity, which was higher across NAFLD categories than in the control group that was healthy. Pacifco *et al.* found that people with NAFLD had greater zonulin levels, which is consistent with this findings. The extent of steatosis was linked to an increase in zonulin content in the NAFLD patient sample [33]. In a trial aiming to investigate a process that may explain the association between zonulin levels in bloodstreams and the severity of nonalcoholic fatty liver disease, researchers discovered that obese people's gastrointestinal flora affected gut permeability. This increased intestinal permeability could explain the rise in zonulin serum levels [34]. Zak-Gob et al. reported a higher intestinal permeability that demonstrated a significant relationship with the extent of liver illness for individuals with NAFLD diagnosed through biopsy, giving confidence in the belief that human serum zonulin various levels have an advantageous correlation with the likelihood of fibrosis, steatosis, and lobular inflammation in NASH [35].

5. Conclusion

The results we obtained demonstrate that serum CK-18 in NAFLD patients increased dramatically, as did lipid profile (LDL, VLDL, TG, Cholesterol) and liver enzyme, however serum HDL content reduced significantly when compared to healthy persons. There is a link between greater zonulin concentrations and the presence of nonalcoholic hepatitis patientsThe results obtained from this study clearly indicate a significant increase in the serum levels of CK-18 in patients diagnosed with non-alcoholic fatty liver disease

(NAFLD). Along with this increase, key components of the lipid profile, including LDL (Low-Density Lipoprotein), VLDL (Very-Low-Density Lipoprotein), triglycerides (TG), and cholesterol, also exhibited substantial elevation. These changes suggest an aggravated dyslipidemic state in individuals with NAFLD, highlighting the metabolic disturbances associated with this condition. Furthermore, liver enzyme levels were found to be considerably elevated in NAFLD patients, supporting the presence of liver damage or dysfunction commonly observed in this disease. These enzyme levels, which include markers such as ALT (Alanine Aminotransferase), AST (Aspartate Aminotransferase), and GGT (Gamma-Glutamyl Transferase), serve as critical indicators of hepatic injury and inflammation. The increase in these enzymes, coupled with abnormal lipid profiles, suggests a progressive deterioration of liver function in NAFLD patients. Conversely, the study also observed a significant reduction in serum HDL (High-Density Lipoprotein) content in NAFLD patients when compared to healthy individuals. This decrease in HDL, a protective lipoprotein, further emphasizes the dyslipidemic nature of NAFLD and its association with cardiovascular risk factors. Low HDL levels are often indicative of impaired lipid metabolism and increased susceptibility to atherosclerosis, underscoring the need for comprehensive cardiovascular risk management in NAFLD patients.

REFERENCES

[1] M. L. Sanyal, J. Van Natta, J. Clark, et al. , "Prospective study of outcomes in adults with non-alcoholic fatty liver disease," N Engl J Med, vol. 385, no. 17, pp. 1559-1569, 2021.

[2] H. Chen, "Nutrient mTORC1 signaling contributes to hepatic lipid metabolism in the pathogenesis of non-alcoholic fatty liver disease," Liver Research, vol. 4, no. 1, pp. 15-22, 2020.

[3] M. Wasme, M. S. Sailh, Y. H. Tahseen, and A. K. Abdulla, "Association of some Biochemical Markers, Hepatitis B, and C Viruses with Type 2 Diabetes Mellitus in Kirkuk City/Iraq," Central Asian Journal of Medical and Natural Science, vol. 6, no. 2, pp. 578-585, 2025

[4] W. Li and W. Alazawi, "Non-alcoholic fatty liver disease," Clin. Med. (London, England), vol. 20, no. 5, pp. 509-512, 2020.

[5] S. Rana and N. Prabhakar, "Iron disorders and hepcidin," Clinica Chimica Acta, vol. 523, pp. 454-468, 2021.

[6] V. Ajmera, E. R. Perito, N. M. Bass, N. A. Terrault, K. P. Yates, R. Gill, et al. , "Novel plasma biomarkers associated with liver disease severity in adults with nonalcoholic fatty liver disease," J. Hepatol. , vol. 65, no. 1, pp. 65–77, 2017.

[7] G. Zainal, S. A. Al, and W. K. Obead, "Comparison of glycoproteins levels with some biochemical parameters in Iraqi patients with chronic liver diseases," Innovative Journal of Medical and Health Science, vol. 5, no. 2, pp. 89-93, 2012.

[8] Mikolasevic, L. Orlic, L. Zaputovic, S. Racki, Z. Cubranic, K. Anic, et al. , "The usefulness of liver test and controlled attenuation parameter in the detection of nonalcoholic fatty liver disease in patients with chronic renal failure and coronary heart disease," Wien Klin Wochenschr. , vol. 127, no. 11-12, pp. 451-458, 2015.

[9] C. E. Ruhl and J. E. Everhart, "Elevated Serum Alanine Aminotransferase and γ-Glutamyltransferase and Mortality in the United States Population," J. Gastroenterol. , vol. 136, no. 2, pp. 477-485. e11, 2009.

[10] H. H. Bragulla and D. G. Homberger, "Structure and functions of keratin proteins in simple, stratified, keratinized, and cornified epithelia," J Anat. , vol. 214, no. 4, pp. 516-559, 2009.

[11] Wieckowska, N. N. Zein, L. M. Yerian, A. R. Lopez, A. J. McCullough, and A. E. Feldstein, "In vivo assessment of liver cell apoptosis as a novel biomarker of disease severity in nonalcoholic fatty liver disease," J. Hepatol. , vol. 44, no. 1, pp. 27-33, 2006.

[12] M. ElGhandour, et al. , "Value of zonulin as a diagnostic and prognostic marker in different degrees of nonalcoholic fatty liver disease," Egyptian Liver Journal, vol. 14, no. 1, pp. 43, 2024.

[13] Y. Aida, H. Abe, Y. Tomita, T. Nagano, N. Seki, T. Sugita, et al. , "Serum cytokeratin 18 fragment level as a noninvasive biomarker for non-alcoholic fatty liver disease," Int J Clin Exp Med. , vol. 7, no. 11, pp. 4191–8, 2014.

[14] R. Kathak, R. Raihanu, et al. , "The association between elevated lipid profile and liver enzymes: a study on Bangladeshi adults," Scientific Reports, vol. 12, no. 1, pp. 1711, 2022.

[15] Q. Li, et al. , "Gamma-glutamyl transferase to high-density lipoprotein cholesterol ratio has a non-linear association with non-alcoholic fatty liver disease: A secondary prospective cohort study in non-obese Chinese adults," Front. Med. , vol. 9, pp. 995749, 2022.
[16] L. W. Chen, et al. , "Gamma-glutamyl transpeptidase elevation is associated with metabolic syndrome, hepatic steatosis, and fibrosis in patients with nonalcoholic fatty liver disease: A community-based cross-sectional study," Kaohsiung J. Med. Sci. , vol. 37, no. 9, pp. 819-827, 2021.
[17] Hadinia, et al. , "Circulating levels of pro-inflammatory cytokines in patients with nonalcoholic fatty liver disease and non-alcoholic steatohepatitis," Iranian J. Immunol. , vol. 16, no. 4, pp. 327-333, 2019.
[18] Ali, et al. , "Frequency of non-alcoholic fatty liver disease (NAFLD) and its associated risk factors among Type-2 diabetics," Pakistan J. Med. Sci. , vol. 38, no. 1, pp. 28, 2022.
[19] X. Ma, et al. , "Proportion of NAFLD patients with normal ALT value in overall NAFLD patients: a systematic review and meta-analysis," BMC Gastroenterol. , vol. 20, pp. 1-8, 2020.
[20] T. Wong, R. J. Wong, and R. G. Gish, "Diagnostic and treatment implications of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis," Gastroenterology & Hepatology, vol. 15, no. 2, pp. 83, 2019.
[21] Y. B. Won, et al. , "Non-alcoholic fatty liver disease in polycystic ovary syndrome women," Sci. Rep. , vol. 11, no. 1, pp. 7085, 2021.
[22] H. Ou, et al. , "Association between smoking and liver fibrosis among patients with nonalcoholic fatty liver disease," Can. J. Gastroenterol. Hepatol. , 2019.
[23] G. Ndrepepa, et al. , "Aspartate aminotransferase and mortality in patients with ischemic heart disease," Nutr. Metab. Cardiovasc. Dis. , vol. 30, no. 12, pp. 2335-2342, 2020.
[24] M. Han, et al. , "Differing associations between fatty liver and dyslipidemia according to the degree of hepatic steatosis in Korea," J. Lipid Atheroscler. , vol. 8, no. 2, pp. 258-266, 2019.
[25] R. Mansour-Ghanaei, et al. , "Biochemical markers and lipid profile in nonalcoholic fatty liver disease patients in the PERSIAN Guilan cohort study (PGCS), Iran," J. Fam. Med. Prim. Care. , vol. 8, no. 3, pp. 923-928, 2019.
[26] R. S. Khan, et al. , "Modulation of insulin resistance in nonalcoholic fatty liver disease," Hepatology, vol. 70, no. 2, pp. 711-724, 2019.
[27] N. N. Noori and N. A. Murtadha, "Uncontrolled type 2 diabetes mellitus modulated plasma levels of lipid catabolic proteins," Georgian Med. News, no. 7-8, pp. 352-353, 2024.
[28] S. Q. Lai, et al. , "Sensitivity to thyroid hormone indices are closely associated with NAFLD," Front. Endocrinol. , vol. 12, pp. 766419, 2021.
[29] S. A. Qassam, Z. K. Ahmed, and S. Z. Nada, "The role of biochemical markers in the assessment of non-alcoholic fatty liver disease in young Iraqi people," Iraq Med. J. , vol. 3, no. 2, pp. 2019.
[30] M. M. Maher, W. A. Ibrahim, S. A. Saleh, L. Shash, H. Abou Gabal, M. Tarif, and M. Gamal, "Cytokeratin 18 as a non-invasive marker in diagnosis of NASH and its usefulness in correlation with disease severity in Egyptian patients," Egypt J. Med. Hum. Genet. , vol. 16, no. 1, pp. 41–46, 2015.
[31] E. Feldstein, N. Alkhouri, R. De Vito, A. Alisi, R. Lopez, and V. Nobili, "Serum cytokeratin-18 fragment levels are useful biomarkers for nonalcoholic steatohepatitis in children," Am J Gastroenterol, vol. 108, no. 9, pp. 1526–1531, 2013.
[32] Liang, F. Liu, F. Wang, T. Han, L. Jing, Z. Ma, and Y. Gao, "A noninvasive score model for prediction of NASH in patients with chronic hepatitis B and nonalcoholic fatty liver disease," BioMed Res. Int. , 2017, pp. 2017.
[33] Pacifco, E. Bonci, L. Marandola, S. Romaggioli, B. S. Bascetta, and C. Chiesa, "Increased circulating zonulin in children with biopsy-proven nonalcoholic fatty liver disease," World J. Gastroenterol. , vol. 20, no. 45, pp. 17107, 2014.
[34] Zhu, S. S. Baker, and C. Gill, "Characterization of gut microbiomes in nonalcoholic steatohepatitis (NASH) patients: a connection between endogenous alcohol and NASH," Hepatology, vol. 57, no. 2, pp. 601–609, 2013.
[35] Zak-Gołąb, P. Kocełak, M. Aptekorz, M. Zientara, L. Juszczyk, G. Martirosian, et al. , "Gut microbiota, microinfammation, metabolic profile, and zonulin concentration in obese and normal weight subjects," Int. J. Endocrinol. , vol. 2013, article 674106, 2013.