AL-QADISIYAH MEDICAL JOURNAL , QAD.MED.J. 21 (1): JANUARY-JUNE 2025
WWW.qmj.qu.edu.iq

REVIEW ARTICLE

The association between type 2 diabetes mellitus , hypertension & severity of fibrosis in patients with non alcoholic fatty liver disease

Huda Jabbar Dibby[1],Zahraa Abdulaali Al-Mudhaffer[2]

1M.B.Ch.B./ M.Sc. physiology / Department of physiology/ College of Medicine/ University of Al-Qadisiyah /Iraq

2 PhD , Medical Physiology/ professor / Department of physiology/ College of Medicine/ University of Kufa./ Iraq

*Corresponding author: E-mail: huda.budairy@qu.edu.iq

Abstract:

Background: Non-alcoholic fatty liver disease (NAFLD) is considered one of the most common chronic liver disorders worldwide. In the context of non-alcoholic steatohepatitis (NASH), hepatic steatosis is associated with lobular inflammation and cellular apoptosis, which can progress to fibrosis and cirrhosis. NAFLD is highly prevalent among patients with type 2 diabetes (T2DM) and hypertension. However, the identification of patients at higher risk for developing more severe fibrosis remains unclear in clinical practice.

Aim of the study: This study aims to assess the severity of non-alcoholic fatty liver disease in a sample of Iraqi patients using FibroScan and correlate the severity of liver fibrosis with type 2 diabetes and hypertension

Patients and methods: This cross-sectional study included 124 patients with clinical, laboratory, and imaging evidence of NAFLD, diagnosed by an experienced hepatologist. All patients had hypertension and/or T2DM and were recruited from the Gastroenterology Center at Al-Diwaniyah Teaching Hospital in Al-Diwaniyah, Iraq, between February 2023 and April 2024. Liver fibrosis and steatosis were assessed using FibroScan (FibroScan 530 compact, Echosens, Paris, France), with a highly trained gastroenterologist performing the evaluations.

Results: The distribution of patients by fibrosis stage was as follows: 26 patients (21.0%) had normal fibrosis (Fibrosis score 0), 44 patients (35.5%) had mild fibrosis (Fibrosis score 1), 23 patients (18.5%) had moderate fibrosis (Fibrosis score 2), and 31 patients (25.0%) had severe fibrosis (Fibrosis score 3). Regarding hypertension and T2DM, a significant association was found between diabetes mellitus and the severity of fibrosis ($p < 0.001$), while no significant relation was observed between hypertension and fibrosis severity ($p = 0.380$).

Conclusion: The degree of liver fibrosis, as assessed by FibroScan, was significantly higher in patients with NAFLD and T2DM. The findings suggest that diabetes is a major risk factor for more severe liver fibrosis in patients with NAFLD.

Keywords: hypertension, type 2 diabetes, hepatic fibrosis, NAFLD.

Introduction

Non-alcoholic fatty liver disease (NAFLD) represents a prevalent etiology of chronic liver disease on a global scale. NAFLD encompasses a spectrum of the disorder characterized by hepatic steatosis in the absence of identifiable alternative etiologies for secondary hepatic fat deposition (e.g., excessive alcohol consumption) (1). The continuum of NAFLD extends from the comparatively benign condition of non-alcoholic fatty liver (NAFL) to non-alcoholic steatohepatitis (NASH), which resides at the more severe end of this spectrum. NAFLD has the potential to advance to fibrosis and cirrhosis (2, 3). In the context of NAFLD, hepatic steatosis occurs without any indication of inflammation, whereas in NASH, hepatic steatosis is accompanied by lobular inflammation and apoptosis, which may culminate in fibrosis and cirrhosis (4, 5). The incidence of liver disease (NAFLD) has escalated rapidly on a global scale, with an estimated worldwide prevalence of 25%. NAFLD is increasingly recognized as a common chronic liver disease, particularly among individuals with central obesity, type 2 diabetes mellitus (T2DM), dyslipidemia, and metabolic syndrome (6).

Ultrasound frequently demonstrates a hyperechoic texture or an illuminated liver due to widespread fatty infiltration (7). The sensitivity and specificity of ultrasound are, respectively, 89% and 93% in the identification of enhanced fibrosis and steatosis (8). Nevertheless, ultrasound is the most economical

SUBMITTED: 11/ OCTOBER /2024 | ACCEPTED: 18/JANUARY/2025 | PUBLISHED: 30/JUNE/2025

technique and has become the predominant modality utilized in clinical practice. The sensitivity of ultrasound is diminished in individuals with obesity (9, 10). The ultrasound exhibiting hyperechogenic liver tissue in comparison to the echogenicity of the spleen or kidney is indicative of steatosis. However, the sensitivity of ultrasound in these circumstances is merely 60–94% (11).

Vibration-controlled transient elastography constitutes the most prevalent and credible technique among noninvasive methodologies for measuring liver stiffness. The FibroScan device, which is the most frequently utilized, extensively researched, and rigorously validated VCTE apparatus, is widely recognized (12). The utilization of FibroScan received approval from Europe and the Food and Drug Administration (FDA) in the years 2003 and 2013, respectively, for the assessment of liver stiffness. It was initially documented by Yoneda in 2007 that this system can ascertain the degree of fibrosis in nonalcoholic fatty liver disease (NAFLD) (13).

with the growing number of publications, recently It has been proved that NAFLD is not limited to liver related morbidity and mortality, but it is a multisystemic disease involving many extrahepatic system & become the leading cause for development of many health problems like type 2 diabetes mellitus, cardiovascular diseases(CVD) and chronic kidney disease(CKD) & other chronic illnesses (14).

NAFLD also is considered to be hepatic manifestation of metabolic syndrome , such association between NAFLD and metabolic disorders led researchers to updating the term NAFLD , as it might be unsuitable nomenclature , because it describe only liver pathology without its metabolic dysfunctional association & it is difficult to reflect what is the disease & its severity for its patients. For such purposes metabolic-dysfunction-Associated Fatty Liver Disease' (MAFLD) projected to be the more suitable term reflecting disease pathogenesis & the approach for its management. A metanalysis has been shown that an increased mortality up to 57% is due to liver & cardiovascular diseases. (16).

The metabolic disorders in NAFLD patients like obesity , T2DM, dyslipidemia , insulin resistance are a risk factors for many CVD& it has been shown in many studies an association between the severity of hepatic disease & cardiovascular disorders like coronary atherosclerosis ,accumulation of toxic lipid in the liver induces inflammation & oxidative stress contributing the development of CVD ,also the production of proinflammatory mediators in NAFLD is elevated & are considered as risk factors for CVD.

The exact mechanism of renal damage induced by NAFLD is not clear but enhanced atherogenesis is the possible cause also enhanced stimulation of angiotensin-aldosterone system (RAAS) that is associated with NAFLD will cause increase hepatic fibrosis & renal damage , association of NAFLD & CKD is attributed by many researchers to metabolic abnormalities like diabetes and hyperuricemia (14, 17) .

Patients and methods

Patients

This cross-sectional study included 124 individuals diagnosed with Non-Alcoholic Fatty Liver Disease (NAFLD) based on clinical, laboratory, and imaging findings, as confirmed by an experienced hepatologist. The participants were recruited from the gastroenterology center at Al-Diwaniyah Teaching Hospital in Al-Diwaniyah, Iraq, between February 2023 and April 2024. Ethical approval was granted by the Ethical Approval Committee of Kufa College of Medicine, University of Al Kufa, as well as the medical research ethical committee of the Al-Diwaniyah Department of Health. All participants provided informed consent after a thorough explanation of the study.The patients selected were seeking routine medical evaluations. The criteria for inclusion were defined as follows: Adult individuals, regardless of gender, diagnosed with NAFLD were eligible for participation in the study. However, pregnant women, smokers, individuals who consume alcohol, and those with other underlying health conditions were excluded from this research endeavor.

Methods

1.Biochemical analysis :

All the patients with NAFLD who are included in this study sent for fasting blood glucose (FBG), glycated hemoglobin (HbA1c), lipid profile including; Total cholesterol (TC), High-density lipoprotein cholesterol (HDL), Low-density lipoprotein cholesterol (LDL) and Triglyceride (TG)) , liver enzymes including; alanine aminotransferase (ALT), aspartate aminotransferase (AST)) and total serum bilirubin .

2.Anthropometric measurements:

For each patient blood pressure measurements (BPM) in mmHg ,were done including systolic blood pressure(SBP) and diastolic blood pressure (DBP) , the circumference of waist (WC) measured at the midpoint between the costal margin and iliac crests, for the calculation of body mass index (BMI) the weight in kilogram (kg) divided by the height (m) squared (Eknoyan G. ,2008).

3.ultrasonographic evaluation of NAFLD :

Abdominal Ultrasound Examination by using a Sonoscap P15 , Digital color doppler US made in China by curvilinear multifrequency(3 - 5 MHz) transducer , was performed by a skilled and well trained radiologist , strongminded in following the suitable procedures for obtaining the images of liver during the scanning and using unique sonographic features for the existence of fat, standardization of instrument setting for the imaging of all patients were done , the images were taken while the patient lie in supine and right decubitus situation raising the right arm overhead , the probe tip covered with US gel, to prevent the shadowing on liver image which caused by ribs or bowel an intercostal scanning was performed .Some parameters where used for diagnosis of NAFLD like hepatic parenchymal brightness, liver to kidney echogenicity, hepatic and portal veins distortion is demonstrated as loss of identification of intrahepatic vessels margins with narrowed lumen which resulted from the attenuation of acoustic wave and vascular remodeling, attenuation of the structures image within a depth of 4-5 cm causing difficult interpretation of the deeper structures, and gallbladder wall definition, in addition increased subcutaneous tissue thickness which is the distance between skin and liver surface (18).

4.Fibroscan :

Fibroscan was done for each patient in this study by well-trained gastroenterologist for measuring liver fibrosis and steatosis by using Fibroscan touch compact 530 (Echosens Paris, France) with 3.5 MHz, M+ probe . examination performed with patients instructed to fast at least 6 hours prior the test , scanning the patient with lying in supine or right decubitus position raising the right arm over the head . Ultrasound gel was then used to

cover the probe tip. Ten or more measurements in the same location were taken while scanning the right side of their liver via an intercostal gap, For measuring the success rate, the number of times a measurement was successful was divided by the total number of times. When the success ratio is 60% or higher as well as median or interquartile range is 30% or below, the result is deemed trustworthy (Caussy et al., 2018). After suitable positioning of the patient, small piston located on the tip of the probe induce which hits the skin surface and according to the velocity and attenuation of these waves the patient's data that will proceed and displayed on the screen as the liver stiffness measurement (LSM) or elasticity (E) and controlled attenuation parameter (CAP). Those measurements which were ineffective, ignored automatically and the message "invalid measurement" was displayed , (CAP) was used for steatosis measurement ,expressed in decibels per meter (dB/m) while (LSM) or elasticity (E) for fibrosis in kilopascals (kPa) , the cut off values for steatosis and fibrosis were adapted from the study by Kamali et al. as shown in table(1)

Table 1: grading of steatosis & fibrosis according to fibroscan measurements (20)

Steatosis score	Cut off value	Fibrostatic score	Cut off value
S0 (No)	< 237 dB/m	F0 (no)	Less than 5.5
S1 (mild)	237– 259 dB/m	F1 (mild fibrosis)	5.5 to 8.0
S2 (moderate)	259 – 291 dB/m	F2 (moderate fibrosis)	8.1 to 10.0
S3 (sever)	291 – 400 dB/m	F3 (severe fibrosis)	10.1 to 16.0

Statistical analysis

The data were subjected to statistical analysis utilizing SPSS version 20.0. The data were ultimately presented as the mean value ±the standard deviation (SD). The relationship between parameters was evaluated using analysis of variance (ANOVA), followed by post-hoc testing to compare variables between each group of patients. In this investigation, a significance level of 0.05 or less was used as the threshold for determining statistical significance.

Results

The general characteristics of patients enrolled in this study are shown in table 2. The age was ranging between 26 and 60 years and it averaged 47.06 ±9.71 years. The study enrolled 74 (59.7 %) males and 50 (40.3 %) females. The body mass index (BMI) was ranging from 22.66 -34.5 kg/m2 and the mean BMI was 31.81 ±3.47 kg/m2. The waist circumference was in the range of 90 -127 cm and the mean was 107.73 ±10.89 cm. Regarding serum lipids, serum triglyceride was in the range of 68 -420 mg/dl and its mean was 182.52 ±82.13 mg/dl, serum total cholesterol was in the range of160-470 mg/dl and the mean was 234.89 ±67.47 mg/dl, serum HDL was in the range of 15 -55 mg/dl and the mean was 35.79 ±7.39 mg/dl, serum LDL was in the range of 90 -265 mg/dl and the mean was 162.70 ±35.97 mg/dl.

With respect to liver function, AST level was in the range of 15 -67 IU/L and the mean was 47.81 ±12.34 IU/L, ALT level was in the range of 10 -116 and the mean was 52.56 ±27.06 IU/L and the TSB level was ranging between 0.7 -4.7 mg/dl and the mean was 2.20 ±1.15 mg/dl. Regarding pulmonary function test, FEV1 was in the range of 1.21 -4.4 and the mean was 3.14 ±0.65. The mean FVC was 3.96 ±0.90 with a range between 1.64 -5.3 and the mean FEV/FVC% was 79.82 ±7.66 and its range was between 58.59 -98.32. Out of all enrolled patients, 36 (29 %) were hypertensive and 53 (42.7 %) were diabetic.

The results of fibroscan are shown in figure 1 and table 3. Patients were distributed as following: 26 patients had Normal (Fibrosis score 0) accounting for 21.0 %; 44 patients had Mild (Fibrosis score 1) accounting for 35.5 %; 23 patients had Moderate (Fibrosis score 2) accounting for 18.5 % and 31 patients had Severe (Fibrosis score 3) accounting for 25.0 %. Comparison of adiponectin levels in non-alcoholic fatty liver disease (NAFLD) according to results of fibroscan is shown in table 4. With respect to mean serum adiponectin, there were significant differences across various stages of fibrosis ($p < 0.001$); in general the level was lower with increasing degree of fibrosis, 5.15 ±1.03, 4.82 ±0.73, 3.47 ±0.47 and 1.61 ±0.20 in stages F0, F1, F2 and F3, respectively, as shown in figure 2.

The relation between diabetes mellitus and hypertension with severity of fibrosis in patients with NAFLD shown in table 4, there was significant relation between diabetes mellitus and severity of fibrosis ($p < 0.001$) , but no significant relation between hypertension and severity of fibrosis ($p = 0.380$) .

Table 2: The general characteristics of patients enrolled in this study

Characteristic		Result	Characteristic		Result
Number of cases	n (%)	124 (100.0 %)			
Age (years)	Mean± SD	47.06 ±9.71	LDL (mg/dl)	Mean± SD	162.70 ±35.97
	Range	26 -60		Range	90 -265
Sex	Male, n (%)	74 (59.7 %)	AST (IU/L)	Mean± SD	47.81 ±12.34
	Female, n (%)	50 (40.3 %)		Range	15 -67
Weight (kg)	Mean± SD	88.73 ±13.42	ALT (IU/L)	Mean± SD	52.56 ±27.06
	Range	71 -114		Range	10 -116
Height (m)	Mean± SD	166.67 ±8.42	TSB (mg/dl)	Mean± SD	2.20 ±1.15
	Range	155 -180		Range	0.7 -4.7
BMI (kg/m^2)	Mean± SD	31.81 ±3.47	FEV1	Mean± SD	3.14 ±0.65
	Range	22.66 -34.5		Range	1.21 -4.4
WC (cm)	Mean± SD	107.73 ±10.89	FVC	Mean± SD	3.96 ±0.90
	Range	90 -127		Range	1.64 -5.3
TG (mg/dl)	Mean± SD	182.52 ±82.13	FEV/FVC%	Mean± SD	79.82 ±7.66
	Range	68 -420		Range	58.59 -98.32
Cholesterol (mg/dl)	Mean± SD	234.89 ±67.47	Hypertension	Yes, n (%)	36 (29 %)
	Range	160-470		No, n (%)	88 (71 %)
HDL (mg/dl)	Mean± SD	35.79 ±7.39	Diabetes	Yes, n (%)	53 (42.7 %)
	Range	15 -55		No, n (%)	71(57.3 %)

n: number of cases; SD: standard deviation; BMI: body mass index; WC: waist circumference; TG: triglyceride; HDL: high density lipoprotein; LDL: low density lipoprotein; AST: aspartate transaminase; ALT: alanine transaminase; TSB: total serum bilirubin; FEV1: forced expiratory volume; FVC: forced vital capacity

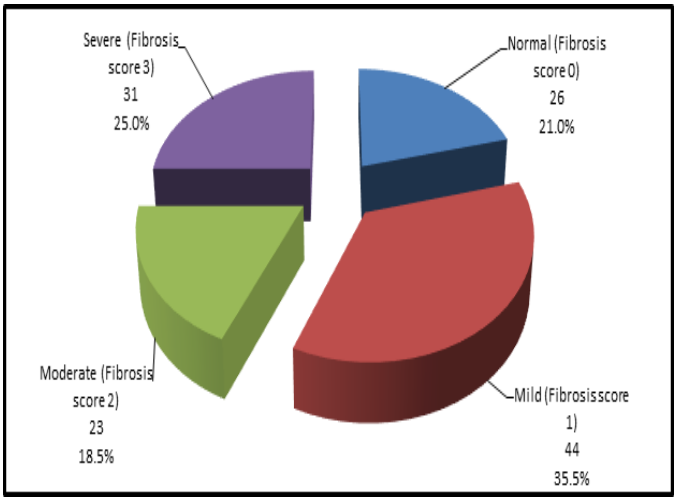

Figure 1: Pie chart showing the frequency distribution of enrolled patients according to results of fibroscan

Table 3: The results of fibroscan

Fibrosis score	Number of cases	Mean ±SD	Range
Normal (Fibrosis score 0)	26	4.21 ±0.63	3.2 -5
Mild (Fibrosis score 1)	44	6.91 ±0.67	5.8 -7.8
Moderate (Fibrosis score 2)	23	8.72 ±0.36	8.2 -9.2
Severe (Fibrosis score 3)	31	11.56 ±0.80	10.6 -12.8
Total	124	7.84 ±2.67	3.2 -12.8

SD: standard deviation

Table 4.: The relation between diabetes mellitus and hypertension with severity of fibrosis in patients with NAFLD

Characteristic	Fibrosis score 0 n = 26	Fibrosis score 1 n = 44	Fibrosis score 2 n = 23	Fibrosis score 3 n = 31	P value
Hypertension					
Yes, n (%)	6 (23.1 %)	10 (22.7 %)	8 (34.8 %)	12 (38.7 %)	0.380
No, n (%)	20 (76.9 %)	34 (77.3 %)	15 (65.2 %)	19 (61.3 %)	
Diabetes mellitus					
Yes, n (%)	2 (7.7 %)	21 (47.7 %)	11 (47.8 %)	19 (61.3 %)	< 0.001 ***
No, n (%)	24 (92.3 %)	23 (52.3 %)	12 (52.2 %)	12 (38.7 %)	

***: significant at p ≤0.001

Discussion

In this investigation, FibroScan was employed to assess hepatic status in individuals diagnosed with NAFLD due to its superior advantages compared to traditional ultrasound evaluations. Given its extensive accessibility and economical nature, abdominal ultrasonography continues to be the most prevalently utilized imaging technique for the detection of hepatic steatosis in patients with MAFLD (20). Nevertheless, its clinical efficacy in identifying mild-to-moderate steatosis (<30%) is restricted, and more sensitive modalities—such as the controlled attenuation parameter obtained from FibroScan—are recommended (21) . An additional merit of FibroScan over abdominal ultrasonography is that it allows for the concurrent acquisition of data regarding both steatosis and fibrosis. Ultimately, FibroScan findings exhibit a high concordance with liver biopsy results across varying stages of fibrosis (22, 23).

In the current investigation, we have documented the subsequent findings: Normal, fibrosis score 0 (mean value of 4.21 ±0.63) observed in 21.0 %, mild, fibrosis score 1 (mean value of 6.91 ±0.67) noted in 35.5 %, moderate, fibrosis score 2 (mean value of 8.72 ±0.36) identified in 18.5 %, and severe, fibrosis score 3 (mean value of 11.56 ±0.80) recorded in 25.0 % of cases. According to the research conducted by Al Danaf et al. (24), 39.7 % of the cases were categorized as F0 (Normal), 17.8 % as F1 (Mild Fibrosis stage), 19.2 % as F3 (Moderate Fibrosis stage), and 23.3 % as F4 (Severe Fibrosis stage). Hence, in alignment with the findings of Al Danaf et al. (24), our data indicated that, based on Fibroscan assessments, a substantial proportion of NAFLD patients exhibited advanced stages of hepatic fibrosis. In accordance with the study by Amernia et al. (25), Fibroscan outcomes disclosed that 94 patients (45.9%) presented with F1, 67 (32.7%) with F2, 29 (14.1%) with F3, and 15 (7.3%) with F4 liver fibrosis. FibroScan, an innovative and economically viable method, is capable of offering a precise noninvasive technique for assessing and staging hepatic steatosis and fibrosis in NAFLD, particularly concerning advanced fibrosis and cirrhosis. Additional research is warranted to investigate the correlation between steatosis and fibrosis as per the same group (26).

In this study, we reported no significant association between stage of fibrosis and essential hypertension; however, higher rate of diabetes mellitus was associated with greater stage of fibrosis.

In line with current study observation, epidemiological investigation shows an approximately 49.5% NAFLD prevalence in hypertension patients, which is higher than the prevalence in the general population (27). NAFLD is associated with incident hypertension and endothelial dysfunction (28, 29) and seems to be an independent risk factor of prehypertension and hypertension (30); accumulating evidence has demonstrated

the existence of pathophysiological mechanisms including inflammation, renin-angiotensin system-sympathetic nervous system activation and insulin resistance in both hypertension and NAFLD (31, 32)

Conclusion

A significant increasing degree of liver fibrosis as indicated by fibroscan technique was present among those patients with NAFLD and T2DM .

Strengths and limitations of the Study:

The study's strength lies in its use of reliable technology to assess liver fibrosis and its focus on a clinically relevant cohort with diabetes and/or hypertension. However, limitations such as the cross-sectional design, single-center nature, and potential confounders must be acknowledged when interpreting the results. Future research should address these gaps by incorporating longitudinal designs, a more diverse population, and comprehensive control of confounding variables.

References

1.Pouwels., et al., (2022). Non-alcoholic fatty liver disease (NAFLD): A review of pathophysiology, clinical management, and the effects of weight loss. BMC Endocrine Disorders, 22(1), 63.

2.Ahmed, A., Wong, R. J., & Harrison, S. A. (2015). Nonalcoholic fatty liver disease: Review, diagnosis, treatment, and outcomes. Clinical Gastroenterology and Hepatology, 13(12), 2062–2070.

3.Machado, M. V., & Diehl, A. M. (2016). Pathogenesis of nonalcoholic steatohepatitis. Gastroenterology, 150(8), 1769–1777.

4.Nasr, P., et al., (2018). Natural history of nonalcoholic fatty liver disease: A prospective follow-up study with serial biopsies. Hepatology Communications, 2(2), 199–210.

5.Younossi ., et al.,. (2018). Global burden of NAFLD and NASH: Trends, predictions, risk factors, and prevention. Nature Reviews Gastroenterology & Hepatology, 15(1), 11–20.

6.Browning ., et al., (2004). Prevalence of hepatic steatosis in an urban population in the United States: Impact of ethnicity. Hepatology, 40(6), 1387–1395.

7.Lonardo., et al., (1995). Nonalcoholic steatohepatitis and the "bright liver syndrome": Should a recently expanded clinical entity be further extended? American Journal of Gastroenterology, 90(11), 2072–2074.

8.Hernaez ., et al., (2011). Diagnostic accuracy and reliability of ultrasonography for the detection of fatty liver: A meta-analysis. Hepatology, 54(3), 1082–1090.

9.Mottin., et al., (2004). The role of ultrasound in the diagnosis of hepatic steatosis in morbidly obese patients. Obesity Surgery, 14(5), 635–637.

10.de Moura., et al.,(2008). Fatty liver disease in severe obese patients: Diagnostic value of abdominal ultrasound. World Journal of Gastroenterology, 14(9), 1415–1418.

11.Adams, L. A., & Talwalkar, J. A. (2006). Diagnostic evaluation of nonalcoholic fatty liver disease. Journal of Clinical Gastroenterology, 40(Suppl 1), S34–S38.

12.Ozercan, A. M., & Ozkan, H. (2022). Vibration-controlled transient elastography in NAFLD: A review study. Euroasian Journal of Hepatogastroenterology, 12(Suppl 1), S41–S45. https://doi.org/10.5005/jp-journals-10018-1365

13.Yoneda, M., Fujita, K., Inamori, M., … & Kubo, S. (2007). Transient elastography in patients with non-alcoholic fatty liver disease (NAFLD). Gut, 56(9), 1330–1331.

14.Pipitone., et al., (2023). MAFLD: A multisystem disease. Therapeutic Advances in Endocrinology and Metabolism, 14, 20420188221145549.

15.Boccatonda ., et al., (2023). From NAFLD to MAFLD: Definition, pathophysiological basis, and cardiovascular implications. Biomedicines, 11(3), 883.

16.Byrne, C. D., & Targher, G. (2015). NAFLD: A multisystem disease. Journal of Hepatology, 62(1 Suppl), S47–S64.

17.Vilar-Gomez ., et al., (2017). Improvement in liver histology due to lifestyle modification is independently associated with improved kidney function in patients with non-alcoholic steatohepatitis. Alimentary Pharmacology & Therapeutics, 45(2), 332–344.

18.Khov, N., Sharma, A., & Riley, T. R. (2014). Bedside ultrasound in the diagnosis of nonalcoholic fatty liver disease. World journal of gastroenterology, 20(22).

19.Caussy, C., et al., (2018). Optimal threshold of controlled attenuation parameter with MRI-PDFF as the gold standard for the detection of hepatic steatosis. Hepatology (Baltimore, Md.), 67(4), 1348–1359.

20. Liu, X. C., et al., (2021). Quotient of waist circumference and body mass index: A valuable indicator for the high-risk phenotype of obesity. Frontiers in Endocrinology, 12, 697437.

21.Kamali., et al., (2019). Diagnostic performance of ultrasonography in detecting fatty liver disease compared to Fibroscan in people suspected of fatty liver. Advanced Biomedical Research, 8, 69.

22.Salmi., et al., (2022). Ultrasound and FibroScan® controlled attenuation parameter in patients with MAFLD: Head-to-head comparison in assessing liver steatosis. Endocrine, 78(2), 262–269.

23.Yilmaz, Y., Ergelen, R., Akin, H., & Imeryuz, N. (2013). Noninvasive detection of hepatic steatosis in patients without ultrasonographic evidence of fatty liver using the controlled attenuation parameter evaluated with transient elastography. European Journal of Gastroenterology & Hepatology, 25(11), 1330–1334.

24.Siddiqui., et al., (2019). Vibration-controlled transient elastography to assess fibrosis and steatosis in patients with nonalcoholic fatty liver disease. Clinical Gastroenterology and Hepatology, 17(1), 156–163.e2.

25.Aykut., et al., (2014). A comparison of FibroMeter™ NAFLD score, NAFLD fibrosis score, and transient elastography as noninvasive diagnostic tools for hepatic fibrosis in patients with biopsy-proven non-alcoholic fatty liver disease. Scandinavian Journal of Gastroenterology, 49(11), 1343–1348.

26.Al Danaf., et al.,. (2022). Correlation between Fibroscan and laboratory tests in non-alcoholic fatty liver disease/non-alcoholic steatohepatitis patients for assessing liver fibrosis. World Journal of Hepatology, 14(4), 744–753.

27.Amernia ., et al (2021). FIB-4, APRI, and AST/ALT ratio compared to FibroScan for the assessment of hepatic fibrosis in patients with non-alcoholic fatty liver disease in Bandar Abbas, Iran. BMC Gastroenterology, 21(1), 453.

28.Xu, X., Jin, J., & Liu, Y. (2023). Performance of FibroScan in grading steatosis and fibrosis in patients with nonalcoholic fatty liver disease: A meta-analysis. Arab Journal of Gastroenterology, 24(4), 189–197.

29.Lorbeer., et al., (2017). Association between MRI-derived hepatic fat fraction and blood pressure in participants without history of cardiovascular disease. Journal of Hypertension, 35(4), 737–744.