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ORIGINAL ARTICLE

Radiology

Hepatic Artery and Portal Vein Hemodynamics in Nonalcoholic Fatty Liver Disease in Adult Saudi Patients: A Doppler Ultrasound Study

Abdullah Sulaiman Alshehri[1], Moawia Gameraddin[2,3*], Yousef Saeedullah[1], Marwan Hamid Alaeinbawi[1], Bilal Rabah Altamimi[1], Awadia Gareeballah[2,3], Suliman Salih[4], Moa'ath Abdullah Sindi[1]

[1]Medical Imaging Department, King Fahad Hospital Madinah, King Saudi Arabia
[2]Department of Diagnostic Radiologic Technology, College of Applied Medical Sciences, Taibah University, Al-Madinah, King Saudi Arabia
[3]Faculty of Radiological Sciences and Medical Imaging, Alzaiem Alazhari University, Khartoum, Sudan
[4]Radiology and Medical Imaging Department, Fatima College of Health Sciences, Abu Dhabi, UAE

Abstract

Background: Nonalcoholic fatty liver disease (NAFLD) is a growing public health problem. With the growing severity of NAFLD, there are considerable alterations in the hemodynamics of the hepatic circulation that might affect the prognosis of the condition, according to numerous reports written to assess the vasculature of the liver in patients affected with fatty liver disease. The aim of the study was to examine hemodynamic alterations in the hepatic artery (HA) and portal vein (PV) in NAFLD patients and determine how they relate to the severity of the condition, and to classify patients into various categories of NAFLD and connect the results to liver size and body mass index (BMI).

***Methods and Results*:** One hundred and six diagnosed NAFLD patients who attended the Imaging department at King Fahad Hospital from December 2019 to January 2020 were retrospectively studied. The mean age of the patients was 45.75±15.6 years, with a range of 10-79 years. The patients were examined by a TOSHIBA Xario, SSA-660A ultrasound system utilizing a multifrequency convex transducer (2–5 MHz) for all sonographic exams. B-mode assessed the liver parenchyma, and spectral Doppler estimated the HA and PV. The US appearance of hepatosteatosis, according to the severity of echogenicity, was graded (0-3**).** Most participants were asymptomatic (76.4%), and diabetes and diabetes with hypertension were diagnosed in 12.3% and 11.3%, respectively. It was observed that grade 1 hepatosteatosis was more prevalent than the other grades: 54 cases versus 41 cases for grade 2 and 11 cases for grade 3. The mean values of liver size and BMI in grade 3 were higher than in grade 1 (P=0.0033 and P=0.0054, respectively). A Spearman test found that the liver size (R=0.19, P=0.05) and BMI (R=0.26, P=0.01) had weak positive, but statistically significant, correlations with the severity of the hepatosteatosis grade. Doppler indices of the HA and PV in NAFLD patients did not differ significantly in hepatosteatosis grades 1-3. Only the PSV and EDV of the main PV showed a significant decrease in the hepatosteatosis grade 2 compared to grade 1 (P=0.0065 and P=0.0234, respectively). Despite the insignificant differences, the Doppler flow parameters of the HA decreased with the severity of hepatic steatosis; for example, the hepatic artery resistive index (HARI) was 0.77±0.16 in grade 1, 0.72±0.16 in grade 2, and 0.75±0.10 in grade 3, respectively. The hepatic artery pulsatility index (HAPI) was 1.62±49 in grade 1, 1.63±.68 in grade 2, and 1.74±0.77 in grade 3. There was also a trend toward a decrease in PSV and end-diastolic velocity (EDV) of HA with the severity of hepatosteatosis.

Conclusion: The severity of hepatic steatosis is significantly correlated with liver size and BMI. The blood flow parameters of PV and HA decrease with the severity of hepatic steatosis except for the pulsatility index. (**International Journal of Biomedicine. 2023;13(2):259-264.**)

Keywords: NAFLD • body mass index • hepatosteatosis • hepatic circulation

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Abbreviations

BMI, body mass index; **EDV**, end-diastolic velocity; **HA**, hepatic artery; **HARI,** hepatic artery resistive index; **HAPI,** hepatic artery pulsatility index; **NAFLD**, nonalcoholic fatty liver disease; **PV**, portal vein; **PI**, pulsatility index; **PSV**, peak systolic velocity; **RI**, resistive index; **VPI,** venous pulsatility index.

Introduction

Nonalcoholic fatty liver disease (NAFLD) is a growing public health problem. A quarter to a third of the world's population is currently affected by NAFLD, which is rising due to the high incidence of diabetes and obesity.[1-3] An important liver-related complication in NAFLD is the development of steatohepatitis, cirrhosis, and hepatocellular carcinoma.[4,5] Global prevalence of NAFLD is 25.24% (95% CI: 22.10-28.65) with highest prevalence in the Middle East and South America and lowest in Africa.[6] NAFLD is the most frequent cause of aberrant liver enzyme levels in Eastern and Western nations.

The gold standard for the detection of hepatic steatosis is liver biopsy. However, liver biopsy is invasive, sometimes painful, and has rare but potentially serious complications.[7] Ultrasound is the most frequently used primary imaging modality for evaluating liver disease. The basic sign of steatosis is the increased echogenicity of the liver parenchyma in comparison to the cortex of the right kidney. Calculation of the hepatorenal index based on B-Mode ultrasound images showed in a some studies excellent diagnostic accuracy, even for the diagnosis of mild steatosis.[8-10] Doppler ultrasound imaging is a non-invasive technique for evaluating the hepatic blood supply and various diseases of the liver parenchyma.[11] Due to alterations impacting vascular compliance in the liver, Doppler can provide more details about the degree of disease severity and parenchymal damage.[12]) With the growing severity of NAFLD, there are considerable alterations in the hemodynamics of the hepatic circulation that might affect the prognosis of the condition, according to numerous reports written to assess the vasculature of the liver in patients affected with fatty liver disease.[13,14] There is little information on this problem in Saudi literature.

The aim of the study was to examine hemodynamic alterations in the hepatic artery (HA) and portal vein (PV) in NAFLD patients and determine how they relate to the severity of the condition, and to classify patients into various categories of NAFLD and connect the results to liver size and body mass index (BMI).

Materials and Methods

One hundred and six diagnosed NAFLD patients who attended the Imaging department at King Fahad Hospital from December 2019 to January 2020 were retrospectively studied. The mean age of the patients was 45.75±15.6 years, with a range of 10-79 years. The BMI was determined for each patient. The data was collected from the PACS system and patients' records. Exclusion criteria were cardiovascular diseases, acute or chronic hepatic disease, acute or chronic kidney disease, alcohol consumption, use of any medications that negatively affect the liver, and a history of thoracic or abdominal surgery.

Sonographic procedure

The patients were examined by a TOSHIBA Xario, SSA-660A ultrasound system utilizing a multifrequency convex transducer (2–5 MHz) for all sonographic exams. All eight liver segments were carefully scanned, and subjects with vascular malformations or hepatic masses (cyst or hemangioma) were excluded. B-mode assessed the liver parenchyma, and spectral Doppler estimated the HA and PV. The US appearance of hepatosteatosis, according to the severity of echogenicity, was graded as follows:[15] grade 0, normal echogenicity; grade 1 (mild): a slight diffuse increase in fine echoes in liver parenchyma with normal visualization of the diaphragm and intrahepatic vessel borders; grade 2 (moderate): a moderate diffuse increase in fine echoes with slightly impaired visualization of intrahepatic vessels and diaphragm; grade 3 (severe): a marked increase in fine echoes with poor or no visualization of the intrahepatic vessel borders, diaphragm, and posterior right lobe of the liver.

Three measurements of the Doppler parameters were taken at the same location, and the mean value was used in the final analysis. The PV measurements were all done in the left lateral decubitus position with breath held in inspiration; the measurements were taken at the level of the main PV before the bifurcation. The Doppler angle was always < 60°. The maximum velocity (V max), minimum velocity (V min), mean flow velocity (MFV), and portal vein diameter were measured. The portal venous pulsatility index (VPI) was calculated according to the following equation: VPI = Vmax – Vmin/ Vmax.[16] The HA indices were measured at the level of porta hepatis with the patient lying in the supine position. The main hepatic artery resistive index (HARI) was obtained with the patient in suspended respiration [(HARI = [PSV − EDV]/ PSV)]. Hepatic artery pulsatility index (HAPI) was calculated according to the following equation: HAPI = (peak systolic velocity − end diastolic velocity)/mean velocity. A designed data collection sheet was used to gather the data.

Statistical analysis was performed using statistical software package SPSS version 23.0 (SPSS Inc, Armonk, NY: IBM Corp). For descriptive analysis, results are presented as mean (M) ± standard deviation (SD). Multiple comparisons were performed with one-way ANOVA with Tukey's pairwise comparisons. Spearman's rank correlation coefficient (R) was calculated to measure the strength and direction of the relationship between two variables. A probability value of $P<0.05$ was considered statistically significant.

The study conformed to the principles outlined in the Declaration of Helsinki and was approved by the Scientific Ethics Committee of the local hospitals. Informed consent was obtained from patients before collecting the data. All identifiable information about patients was removed, and the data were coded to ensure anonymity.

Results

Most participants were asymptomatic (76.4%), and diabetes and diabetes with hypertension were diagnosed in

12.3% and 11.3%, respectively (Table 1). The prevalence of NAFLD among different age groups was assessed (Table 2). It was most prevalent in the age group of 40-49 years, followed by the 30-39 years. The age group of 40-49 years showed a more frequent incidence of grade 1 hepatosteatosis (n=14), followed by grade 2 (n=9) and grade 3 (n=5), while the age group of 30-39 years showed almost the same frequency of grade 1 (n=13) and grade 2 (n=12); grade 3 was found only in two cases (Table 2).

Table 1.

Demographic characteristics of the study sample

Variable	n	%
Gender		
Males	55	51.9
Females	51	48.1
Age group, years		
10-19	8	7.5
20-29	7	6.6
30-39	26	24.5
40-49	29	27.5
50-59	15	14.1
60-69	17	16.0
70-79	4	3.8
Clinical history		
Asymptomatic	81	76.4
Diabetes mellitus	25	23.6
Average age: 45.75±15.6, years		
Average BMI: 27±4.02, kg/m^2		

Table 2.

Distribution of hepatosteatosis grade among different age groups.

Age group, years	Grade 1	Grade 2	Grade 3
10-19	5	2	1
20-29	7	0	0
30-39	13	12	2
40-49	14	9	5
50-59	6	6	3
60-69	7	10	0
70-79	2	2	0
Total	54	41	11
100%	51%	38.6%	10.4%

Considering the 15 cm cut-off point for liver size, the results showed that 22.6% of the participants had an enlarged liver (16-18.99 cm [n=20] and 19-22.99 cm [n=4], respectively) (Figure 1). It was observed that grade 1 hepatosteatosis was more prevalent than the other grades: 54 cases versus 41 cases for grade 2 and 11 cases for grade 3 (Figure 2).

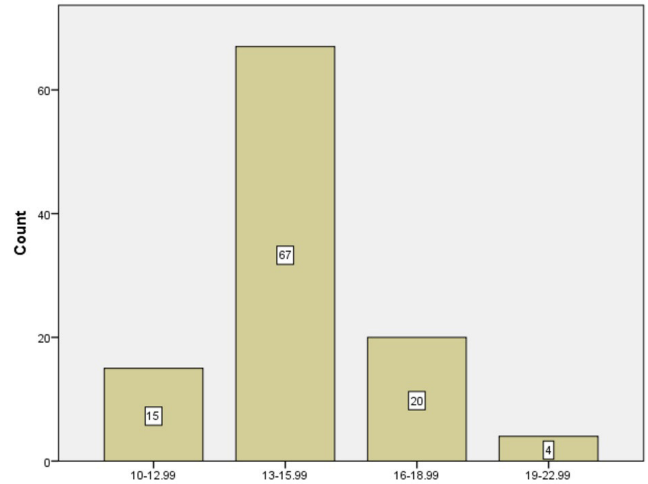


***Fig. 1**. Liver size (cm).*

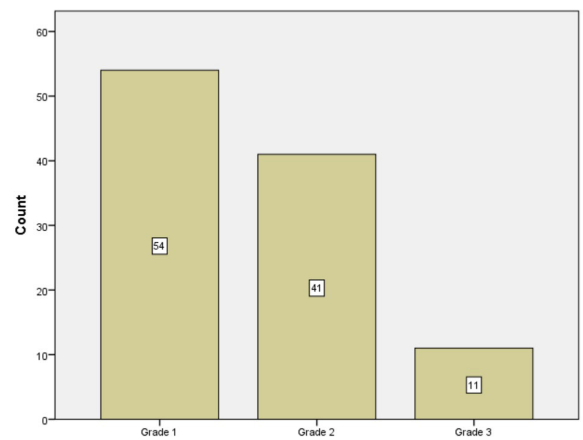


***Fig. 2**. Hepatosteatosis grade.*

The rising hepatosteatosis grade significantly correlated with liver size and BMI. However, the PV diameter increased with the severity of fatty liver infiltration without a statistically significant difference (P=0.9347). The mean values of liver size and BMI in grade 3 were higher than in grade 1 (P=0.0033 and P=0.0054, respectively) (Table 3, Figure 3). A Spearman test found that the liver size (R=0.19, P=0.05) and BMI (R=0.26, P=0.01) had weak positive, but statistically significant, correlations with the severity of the hepatosteatosis grade (Table 3).

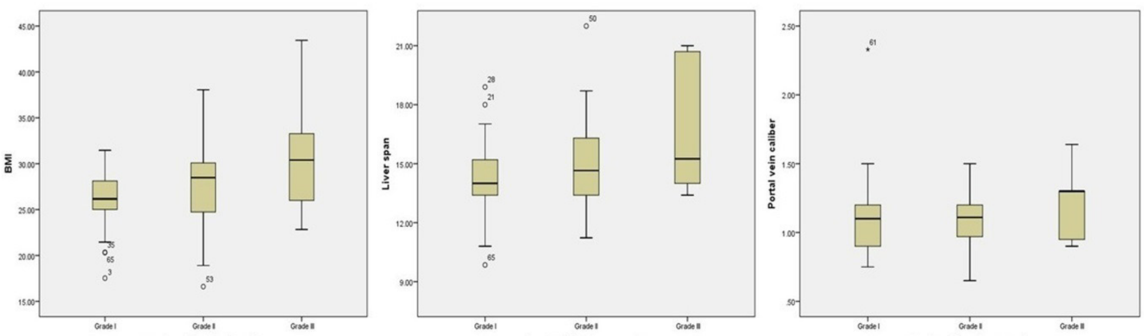
Doppler indices of the HA and PV in NAFLD patients did not differ significantly in hepatosteatosis grades 1-3. Only the PSV and EDV of the main PV showed a significant decrease in the hepatosteatosis grade 2 compared to grade 1 (P=0.0065 and P=0.0234, respectively). Despite the insignificant differences, the Doppler flow parameters of the HA decreased with the severity of hepatic steatosis; for example, the HARI was 0.77±0.16 in grade 1, 0.72±0.16 in grade 2, and 0.75±0.10 in grade 3, respectively.

Table 3.

Comparison of hepatosteatosis grade with liver size, BMI, and PV diameter.

Variable	Hepatosteatosis grade			Statistics	R
	Grade 1 (n=54)	Grade 2 (n=41)	Grade 3 (n=11)		
Liver size, cm	14.263±1.68	14.948±2.252	16.580±3.147	F=5.8422 P=0.0040 P_{1-2}=0.2591 P_{1-3}=0.0033 P_{2-3}=0.0609	0.19*
BMI, kg/m^2	26.184±2.82	27.29±4.43	30.31±6.10	F=5.2118 P=0.0070 P_{1-2}=0.3636 P_{1-3}=0.0054 P_{2-3}=0.0644	0.26**
PV diameter, cm	1.10±2.33	1.11±0.17	1.30±0.24	F=0.0676 P=0.9347 P_{1-2}=0.9948 P_{1-3}=0.9309 P_{2-3}=0.9405	0.12

*R - Spearman's rank correlation coefficient; * Correlation is significant at the 0.05 level (2-tailed);*
***Correlation is significant at the 0.01 level (2-tailed).*



A B C

Fig. 3. *Relationship between hepatosteatosis grade and the mean measurements of BMI (A), liver size (B), and PV diameter (C).*

Table 4.

Hepatosteatosis grade and Doppler flow parameters of HA and main PV.

Hepatosteatosis grade	HAPI	HARI	HA-PSV	HA-EDV	PV-PI	PV-PSV, cm/sec	PV-EDV, cm/sec
Grade 1 (n=54)	1.62±0.49	0.77±0.16	55.84±18.99	15.16±6.64	0.61±0.59	27.26±8.77	18.28±6.41
Grade 2 (n=41)	1.63±0.68	0.72±0.16	53.27±15.79	12.65±8.47	0.65±0.47	21.99±6.55	14.70±5.70
Grade 3 (n=11)	1.74±0.77	0.75±0.10	51.35±13.16	12.30±6.38	0.65±0.38	25.24±10.17	17.95±9.05
Statistics	F=0.1861 P=0.8304 P_{1-2}=0.9948 P_{1-3}=0.8182 P_{2-3}=0.8521	F=1.2100 P=0.3024 P_{1-2}=0.2697 P_{1-3}=0.9198 P_{2-3}=0.8367	F=0.4455 P=0.6417 P_{1-2}=0.7539 P_{1-3}=0.7132 P_{2-3}=0.9428	F=1.6326 P=0.2004 P_{1-2}=0.2331 P_{1-3}=0.4731 P_{2-3}=0.9893	F=0.0760 P=0.9269 P_{1-2}=0.9290 P_{1-3}=0.9715 P_{2-3}=1.0000	F=4.8876 P=0.0094 P_{1-2}=0.0065 P_{1-3}=0.7343 P_{2-3}=0.4703	F=3.7549 P=0.0267 P_{1-2}=0.0234 P_{1-3}=0.9869 P_{2-3}=0.3038

The HAPI was 1.62±49 in grade 1, 1.63±.68 in grade 2, and 1.74±0.77 in grade 3. There was also a trend toward a decrease in PSV and EDV of HA with the severity of hepatosteatosis (Table 4).

Discussion

In the study, participants' average age was 45.75±15.6 years and BMI was 27±4.02 kg/m^2. The study found a significant difference in BMI among the grades of fatty liver infiltration, with the highest BMI (30.31±6.10 kg/m^2) at grade 3 hepatosteatosis. Abangah et al.[17] also detected a significant association between hepatosteatosis grades and BMI. Doppler US is an important non-invasive method in evaluating hepatic vasculature in NAFLD, as diffuse fatty infiltration in the liver alters hemodynamics in the PVB as well as HA resistance.[18,19] In our study, we investigated the characteristic flow parameters of the PV and HA to assess the impact of NAFLD on hepatic vascular compliance. Several reports show that the PV flow velocity,[20-22] HARI,[23-25] and HAPI[26] correlate negatively with NAFLD severity. Solhjoo et al.[27] showed that patients with NAFLD had a high rate of abnormal hepatic vein Doppler waveform patterns, and decreased VPI is suggestive of reduced vascular compliance in the liver. We found that only PV-PSV statistically significantly decreased with the severity of hepatosteatosis. HA Doppler velocities and HARI showed a tendency toward lower values with increasing hepatosteatosis severity. Our Doppler finding is consistent with Balasubramanian, [25] Sabry et al., [28] and Tana et al.(29) who reported that the Doppler indices were significantly lower in NAFLD and inversely associated with the severity of fatty infiltration. Mihmanli et al.[18] also found that HARI decreases as the severity of diffuse fatty infiltration increases. Another Iranian study [24] found that HARI was 0.75 in patients with grade 1 fatty liver, 0.68 in grade 2, and 0.64 in grade 3. There was an inverse relationship between HARI and different grades of fatty liver in NAFLD patients (P=0.001). In contrast, a study by Aslan et al.[30] did not find characteristic changes in HARI in NAFLD patients.

The study revealed a significant positive correlation between the changes in liver size with the severity of fatty infiltration: The liver size increased significantly as the grading of fatty infiltration increased (P=0.005). Similar to this finding, Khan et al.[31] found a significant correlation between rising grades of fatty liver, liver size, and BMI.

The current study showed that the liver size and BMI had weak, but statistically significant, positive correlations with the severity of the hepatosteatosis grade. Aslan et al.[30] also found that liver size was increased significantly with the degree of fatty infiltration (P<0.001). In a study by Khanal et al.,[31] 22.9% of patients with NAFLD had increased liver size, and a significant association between increasing grades of fatty liver was found with increasing liver size (P=0.001) and BMI (P=0.045).

In conclusion, the severity of hepatic steatosis is significantly correlated with liver size and BMI. The blood flow parameters of PV and HA decrease with the severity of hepatic steatosis except for the PI.

This study has significant limitations, notwithstanding our findings—first, the study's 1-year duration and small sample size of participants; the second factor is the absence of liver biopsy, the gold standard for diagnosing NAFLD. However, liver biopsy is an invasive procedure, and most patients decline to do it. Last, we did not use healthy volunteers as the control group. Further evaluating hepatic vascular Doppler indices in the NAFLD population is advocated through case-control studies with bigger sample sizes and longer follow-up intervals.

Competing Interests

The authors declare that they have no competing interests.

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***Corresponding author**: Dr. Moawia Gameraddin, Ph.D., Department of Diagnostic Radiologic Technology, College of Applied Medical Sciences, Taibah University, Al-Madinah, King Saudi Arabia. E-mail: gameraldinm@gmail.com*

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