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Role of Doppler ultrasonography of the splenoportal system in diagnosing early hepatic dysfunction in non-alcoholic fatty liver disease patients

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ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) has emerged as a global and national epidemic. This is due to a sedentary lifestyle, unhealthy food habits, obesity, and metabolic syndrome prevailing among young and middle-aged individuals. Clinical diagnosis of NAFLD is difficult as most of the patients are asymptomatic. NAFLD can be assessed using an imaging system. Ultrasonography is the most widely used first-line initial imaging modality of choice. **Aims and Objectives:** To assess the role of Doppler ultrasonography of the splenoportal system in NAFLD patients. **Materials and Methods:** It is a hospital-based single-center cross-sectional study that collects data on patients who meet the inclusion criteria. A diagnosis of NAFLD will be made based on clinical and ultrasound workup. Then, Doppler Ultrasonography examination of the abdomen of the selected patient was done and assessed for different parameters. **Results:** It was observed that there was a significant decrease in portal vein velocity and its pulsatility index, a decrease in hepatic artery resistive index and pulsatility index, a reduction of hepatic vein phasicity, an increase in liver size and portal vein diameter with increasing severity of fatty liver. It is inferred that apart from assessing the hemodynamic changes in the portal circulation, we can also predict early portal hypertension and hepatic fibrosis. **Conclusion:** Doppler ultrasonography of the splenoportal system can be used to predict early fibrosis, portal hypertension, and thus cirrhosis.

Key words: Non-alcoholic fatty liver disease; Doppler ultrasonography; Fatty liver; Steatosis

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INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in India and worldwide. It has slowly become an epidemic in India and the world, especially in Western nations. This is due to the increased prevalence of obesity, unhealthy eating habits (e.g., fast foods and oily foods), and a sedentary lifestyle. Studies also say that epigenetic factors (genetic polymorphisms) also influence the development of NAFLD.[1]

NAFLD refers to a group of disorders that range from basic hepatic steatosis (fatty infiltration of the liver) to end-stage liver disease.[2-4] It is a serious issue among individuals referred for testing for abnormally high circulating levels of liver enzymes. Hepatic steatosis or steatohepatitis (fatty liver with inflammation) is suspected in up to 70% of this referral population.[5] It has a broad spectrum ranging from simple fatty infiltration of the liver (steatosis) and inflammation (steatohepatitis) to the end spectrum of cirrhosis and Hepatocellular carcinoma, per recent studies. As per the expert's prediction, it has become a leading cause of liver transplantation in the United States in 2020. The gold standard for diagnosing NAFLD, including steatosis, non-alcoholic steatohepatitis, and cirrhosis, has been liver biopsy for a long time.[6] However, it is invasive and not feasible for all patients.

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Ultrasonography is the initial best imaging modality to diagnose fatty liver and its severity. It is non-invasive, easily available, has no associated radiation risk, and is less time-consuming. When coupled with Doppler ultrasonography, we can assess the hemodynamic changes in the liver as recent studies say significant hemodynamic abnormalities progress with increasing severity of NAFLD.

However, literature regarding the disease, its progression, its complications, and its outcome using non-invasive imaging modality is very limited in India. NAFLD has become a global burden, with people developing complications such as cirrhosis, portal hypertension, and hepatocellular carcinoma. Limited literature was available about NAFLD from India. Hence, this study decided to be conducted to detect NAFLD early.

Aims and objectives

This study aims to assess the role of Doppler ultrasonography of the splenoportal system in NAFLD patients.

MATERIALS AND METHODS

This hospital-based single-center cross-sectional study was conducted from June 2019 to July 2020 in the ultrasonogram room of the Department of Radiodiagnosis, Tirunelveli Medical College.

240 Patients diagnosed to have NAFLD based on clinical history and ultrasonography evaluation were included in this study. Males and females over the age of 20 diagnosed with fatty liver disease based on an abdominal ultrasound visit to the general outpatient department were included in the present study.

Patients consuming alcohol, pregnant women and children, patients diagnosed with chronic liver disease, Hepatitis B and C infection, critically ill or hemodynamically unstable patients, patients on drugs causing steatosis (e.g., tamoxifen, steroids, and amiodarone) and patients not willing for the study were excluded from the study.

All the patients/relatives obtained oral consent after fully explaining the study's purpose and protocols and (absence of) risk to the patients/relatives. Then, Doppler ultrasonography examination of the abdomen of the selected patient was done to assess for different parameters such as the size of the liver, grading of the severity of fatty liver based on echogenicity, the diameter of portal vein at the hilum, portal vein flow, portal vein thrombosis, type of flow in hepatic vein, resistive index (RI) of the hepatic artery, the diameter of the splenic vein and liver vascular index.

RESULTS

Of 240 patients in the present study, 24.6% (n=59) were from the age group of 31–40 years, followed by 21.3% (n=51) from 41 to 50. 20.8% (n=50), 17.9% (n=43), and 15.4% (n=37) were from age group 51–60, >60, and 21–30, respectively.

Among the 240 patients, 60.4% (n=145) were male and 39.6% (n=95). 52.9% (n=127) patients showed Grade 1 fatty liver severity grade followed by 28.3% (n=68) showed Grade 2, and 18.8% (n=45) showed Grade 3.

3.8% (n=9) patients showed monophasic hepatic vein flow, 12.1% (n=29) patients showed biphasic hepatic vein flow, 19.2% (n=46) patients showed triphasic hepatic vein flow and 65.0% (n=156) showed tetraphasic/pentaphasic hepatic vein flow.

It was statistically significant when fatty liver severity grading was compared with hepatic vein flow type ($P<0.0001$). However, when the age group was compared with fatty liver severity grading, it was statistically non-significant ($P=0.016$). Furthermore, when gender was compared with fatty liver severity grading, it was statistically non-significant ($P=0.194$).

The mean liver size of Grade 1 patients was found to be 14.82 ± 0.78, Grade 2 was found to be 15.45 ± 0.78, and Grade 3 was found to be 16.94 ± 0.43. These findings were found to be statistically significant ($P<0.0001$). The mean diameter of the portal vein of Grade 1 was found to be 10.19 ± 0.61, Grade 2 was found to be 11.74 ± 0.83, and Grade 3 was found to be 14.36 ± 0.61. These findings were also statistically significant ($P<0.0001$).

The mean peak maximum velocity of portal vein flow of the Grade 1 group was 15.01 ± 0.60, Grade 2 group was 11.80 ± 0.56, and Grade 3 was found to be 10.11 ± 0.46, which was found to be statistically significant. ($P<0.0001$) The mean peak minimum velocity of portal vein flow of the Grade 1 group was 9.84 ± 0.36, Grade 2 group was 8.66 ± 0.25, and Grade 3 was found to be 9.92 ± 0.1, which was found to be statistically significant ($P<0.0001$).

The vein pulsatility index in the portal vein was 0.34 ± 0.02 for Grade 1, 0.27 ± 0.03 for Grade 2 and 0.22 ± 0.01 for Grade 3. These values were found to be statistically significant ($P<0.0001$). When the hepatic artery RI was correlated with fatty liver severity, it was statistically significant with $P<0.0001$. It was 0.77 ± 0.04 for Grade 1, 0.68 ± 0.04 for Grade 2, and 0.58 ± 0.03 for Grade 3. The hepatic artery pulsatility index was 1.31 ± 0.06 for Grade 1, 1.17 ± 0.08 for Grade 2, and 1.00 ± 0.03 for Grade 3 ($P<0.0001$).

When splenic vein diameter was correlated with the severity of fatty liver, it was statistically significant. For Grade 1, it was 5.34±0.61. For Grade 2, it was 5.37±0.85; for Grade 3, it was 5.98±1.06. The liver vascular index of Grade 1, Grade 2, and Grade 3 patients were 9.49±0.63, 8.77±0.71, and 9.04±0.53, respectively. Table 1 shows the correlation of different parameters with the severity of fatty liver.

DISCUSSION

Of many patients, 240 were found to have NAFLD based on ultrasonographic evaluation, clinical history, and inclusion and exclusion criteria mentioned in this study methodology. In addition, different demographic parameters, such as age and sex, were studied amongst 240 patients. More patients in the age group between 31 and 40 years were found to have NAFLD, with the next age group with the prevalence of NAFLD being 41–60. This lends credence to the fact that NAFLD is more prevalent among young adults, probably due to a sedentary lifestyle and unhealthy food habits.

Hence, most people are in the age group 30–60 years of age. This was correlated with the study conducted by Perumpail et al.,[7] mentioned that the prevalence of NAFLD was common among people in the age group of 30–70 years and was in concordance with that study. Most patients affected by NAFLD are males, which concord with studies conducted by Ballestri et al.,[8,9] where it was inferred that men are more commonly affected. Women are affected only in the elderly due to hormonal imbalances and menopause. By analyzing the liver size along with statistical significance ($P<0.0001$) among the different grades of fatty liver and also between the individual grades of fatty liver, which also had a statistical significance ($P<0.0001$).

Table 1: Distribution of patient's characteristics

Parameters	Frequency	Percent
Age group		
21–30	37	15.40
31–40	59	24.60
41–50	51	21.30
51–60	50	20.80
>61	43	17.90
Gender		
Male	145	60.40
Female	95	39.60
Fatty liver severity grading		
Grade 1	127	52.90
Grade 2	68	28.30
Grade 3	45	18.80
Hepatic vein flow type		
Monophasic	9	3.80
Biphasic	29	12.10
Triphasic	46	19.20
Tetraphasic/Pentaphasic	156	65.00

Our study shows that liver size increases with increasing grades of fatty liver severity. Compared with the single-center-based study by Khanal et al.,[10] our study concurred with their study with an even more accurate correlation of increasing liver size with increasing severity of fatty liver. The normal flow pattern of hepatic veins is a triphasic/tetraphasic/pentaphasic flow pattern. From the data collected on hepatic vein flow pattern, it is found that the severity of fatty liver is inferred that with increasing severity of fatty liver from grade 1 to grade 3, hepatic vein flow phasicity progressively decreases with progression. This was in concordance with the study conducted by Solhjoo et al.,[11] Although the study population was less, it was concluded that hepatic vein flow dampened with increasing severity. The change in portal vein diameter between grade 1, grade 2, and grade 3 fatty changes in the liver was statistically significant ($P<0.0001$) in our study.

With reference values of portal vein diameter <13 mm as per literature, recent studies, and standard textbooks,[12] there was not much change in portal vein diameter among grade 1 and grade 2 fatty changes in the liver. However, patients with grade 3 fatty changes in the liver showed mild portal vein dilatation. Few patients had a portal vein diameter of more than 15.5 mm, which is the criteria for diagnosing portal hypertension. When comparing our data collected on portal vein diameter, it is observed that grade 3 fatty liver patients had a mean value of 14.36 mm and, therefore at risk of developing fibrosis and portal hypertension. With increasing severity of fatty liver, portal vein diameter was increasing. When correlating the peak maximum velocity of portal vein flow (Vmax in cm/s) with fatty liver severity, there was statistical significance ($P<0.0001$) between the various grades of fatty liver and peak maximum velocity of the portal vein with increasing severity and also statistical significance was there ($P<0.0001$) while comparing the mean difference in peak maximum velocity of the portal vein between each grade of fatty liver. When correlating the peak minimum velocity of portal vein flow (Vmin in cm/s) with fatty liver severity, There was statistical significance ($P<0.0001$) between the various grades of fatty liver and portal vein peak minimum velocity with increasing severity of fatty liver and also statistical significance was there ($P<0.0001$)while comparing the mean difference of portal vein peak minimum flow velocity between each grade of fatty liver. There was statistical significance ($P<0.0001$) between the various grades of fatty liver and Portal vein pulsatility index with increasing severity of fatty liver and also statistical significance was there ($P<0.0001$) while comparing the mean difference of Portal vein pulsatility index between each grade of fatty liver. Hence, in our study, the peak maximum velocity, peak minimum velocity, and vein pulsatility index decrease with increasing severity of fatty liver. This implies a slowing blood flow within the portal venous system, and the flow pattern

Table 2: Fatty liver severity grading with hepatic vein flow type

Parameters	Hepatic vein flow type				Total	P-value
	Monophasic	Biphasic	Triphasic	Tetraphasic/Pentaphasic		
Fatty liver severity grading						
Grade 1	0	0	1	126	127	<0.0001
Grade 2	2	0	36	30	68	
Grade 3	7	29	9	0	45	
Total	9	29	46	156	240	

Table 3: Fatty liver severity grading with age group and gender

Parameters	Fatty liver severity grading			Total	P-value
	Grade 1	Grade 2	Grade 3		
Age group					
21–30	28	8	1	37	0.016
31–40	31	19	9	59	
41–50	23	19	9	51	
51–60	24	10	16	50	
>61	21	12	10	43	
Gender					
Male	70	46	29	145	0.194
Female	57	22	16	95	

Table 4: Fatty liver severity grading with outcome of the study

Parameter	Grade 1	Grade 2	Grade 3	P-value
Liver size (cm)	14.82±0.78	15.45±0.78	16.94±0.43	<0.0001
Portal vein diameter (mm)	10.19±0.61	11.74±0.83	14.36±0.61	<0.0001
Peak maximum velocity of the portal vein (Vmax in cm/s)	15.01±0.60	11.80±0.56	10.11±0.46	<0.0001
Peak minimum velocity of the portal vein (Vmax in cm/s	9.84±0.36	8.66±0.25	9.92±0.1	<0.0001
Vein pulsatility index	0.34±0.02	0.27±0.03	0.22±0.01	<0.0001
Hepatic artery RI	0.77±0.04	0.68±0.04	0.58±0.03	<0.0001
Hepatic artery PI	1.31±0.06	1.17±0.08	1.00±0.03	<0.0001
Splenic vein diameter (mm)	5.34±0.61	5.37±0.85	5.98±1.06	<0.0001
Liver vascular index	9.49±0.63	8.77±0.71	9.04±0.53	<0.0001

PI: Pulsatility index, RI: Resistive index

becomes less pulsatile. These results concordance with the study conducted by Baikpour et al.,[13] A retrospective study was done on biopsy-proven cases of NAFLD and portal vein pulsatility was assessed and the values were assessed in the mean of 0.19 for high-risk NAFLD patients. There was statistical significance (P<0.0001) between the various grades of fatty liver and hepatic artery RI HARI with increasing severity of fatty liver, and also statistical significance was there (P<0.0001) while comparing the mean difference of hepatic artery RI HARI between each grade of fatty liver. There was statistical significance (P<0.0001) between the various grades of fatty liver and hepatic artery pulsatility index HAPI with increasing severity of fatty liver, and also statistical significance was there (P<0.0001) while comparing the mean difference of hepatic artery pulsatility index HAPI between each grade of fatty liver. Hence it is inferred that both hepatic artery RI and hepatic artery pulsatility index decrease with increasing severity of fatty liver, which is in concordance with the study conducted by Tana et al.,[14] where hepatic artery RI was correlated with NAFLD fibrosis score and was found that NAFLD patients showed low hepatic artery RI when compared to normal individuals. No correlation between NAFLD patients and splenic vein diameter, splenic vein thrombosis, and liver vascular index could be established.

Limitations of the study

The study has a limitation in that the amount of fibrosis cannot be quantified, resulting in a qualitative assessment. Another limitation is the potential for subjective variation when distinguishing between a normal liver and grade 1 hepatic steatosis. Additionally, ultrasound diagnosis of steatosis requires at least 20% of hepatocytes to be affected, which may not be suitable for individuals with higher levels of obesity due to the early attenuation of the ultrasound beam. These limitations can be overcome by ultrasound elastography, which offers techniques such as strain elastography and shear wave elastography to accurately measure liver stiffness and detect the degree of fibrosis. However, it is important to note that the gold standard for assessing hepatic fibrosis remains liver biopsy, despite its invasive nature and potential for sampling errors due to limited tissue sampling.

CONCLUSION

This study was conducted on 240 NAFLD patients using Doppler ultrasonography of the splenoportal system. All the observations show that it is possible to predict early fibrosis, portal hypertension, and hence cirrhosis through Doppler ultrasonography of the splenoportal system.

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