Original Article

Frequency of Hemodynamic Variations in Hepatic Artery according to Grades of Non-Alcoholic Fatty Liver Disease on Doppler Ultrasound

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Abstract

Background: Non-alcoholic fatty liver disease is an important cause of hepatic related morbidity and mortality due to its spectrum from simple hepatic steatosis to fibrosis/cirrhosis; latter alter the hepatic vascular hemodynamics particularly of hepatic artery.

Objective: To evaluate the hemodynamic variations in Hepatic artery in subjects with non-alcoholic fatty liver disease (NAFLD) on Doppler Ultrasound and correlate it with different grades of NAFLD.

Methods: This hospital based observational study was done in the Department of Radiology, Dr Ruth K.M. Pfau Civil Hospital Karachi from September 2023 to August 2024. This study enrolled 139 subjects of either gender between 18-55 years of age with NAFLD according to study criteria. Then ultrasound was performed to grade the NAFLD and measure the liver span followed by Doppler ultrasound of hepatic artery to calculate resistive index (HARI).

Results: There were 90 (64.7%) males and 49 (35.3%) females with mean age of 43.7 ± 9.9 years. Grade I fatty liver was more common seen in 70 (50.4%) subjects followed by grade II in 53 (38.1%) and grade III in 16 (11.5%) subjects. Liver span was increased with raising severity of fatty liver seen in 32 (23%) subjects. Hepatic artery Resistive Index decreased as the grades of fatty liver increased; HARI was 0.77 ± 0.05 in grade I, 0.72 ± 0.05 in grade II and 0.68 ± 0.03 in grade III.

Conclusion: Hepatic artery RI decreases with the severity of fatty liver so Doppler ultrasound is reliable and cost effective imaging modality to assess the hemodynamic changes in hepatic artery in NAFLD patients.

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Introduction

Non-alcoholic fatty liver disease (NAFLD) is one of the common health problem worldwide with an estimate of 25% of the population being affected by it.[1,2] NAFLD is by definition a liver with greater than 5% fat weight in the absence of excessive alcohol intake.[3] It become even more adverse when combined with obesity, diabetes, dyslipidemia and increased age.[3,4] Previously it was considered a benign entity due to asymptomatic nature and subtle onset but its prolonged course increased the disease burden of NAFLD so now regarded as a major cause of hepatic associated complications.[4,5] The exact prevalence of NAFLD in Pakistan is not known. A hospital based study done on medical

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OPD patients demonstrated fatty liver on ultrasound with a frequency of 21.7%.[6]

The disease spectrum in NAFLD extending from simple hepatic steatosis to nonalcoholic steatohepatitis to fibrosis and cirrhosis which ultimately lead to end stage liver disease and development of hepatocellular carcinoma.[3,4,7] So accurate assessment of grades of NAFLD is essential for therapeutic decisions and surveillance of this chronic condition. The gold standard method to diagnose NAFLD is the hepatic biopsy but due to an invasive procedure it has certain flaws like error in sampling, high cost and procedural associated complications varying from just pain to lethal hemorrhage.[8,9] This resulted in seeking out of non-invasive morbidity-free imaging methods for diagnosis and grading of NAFLD. Gray scale ultrasound is a radiation-free, non-invasive, cheap and easily available imaging modality to detect fatty liver and assess the stages of NAFLD but its sensitivity is decreased in mild fatty liver, and it is neither sensitive to assess fibrosis.[10,11] Doppler ultrasound is another easily available non-invasive imaging technique to evaluate the hepatic vasculature via calculation of resistance and pulsatility indices as fatty infiltration alter the hepatic hemodynamics.[4,9] Among these the resistive index of hepatic artery (HARI) is the commonest and important Doppler parameter which is significantly altered due to inflammation / fibrosis.[8,10,11] Other imaging modalities like computed tomography (CT) and magnetic resonance imaging (MRI) despite their pros and cons, do not provide information regarding hemodynamic effect by fatty infiltration on the hepatic vascular system.[8]

The incidence of NAFLD is on rising pattern in our population and once it diagnosed it should be monitored. Though liver biopsy is gold standard but it is not realistic to perform liver biopsies on all NAFLD patients. Various studies are done to assess the hepatic vascular hemodynamics in patients with NAFLD and correlate these parameters with different grades of NAFLD as well as can determine the prognosis of the disease.[9,11-13] but there is no published local data or information available so the current study is planned to evaluate hemodynamic variations in hepatic artery in non-alcoholic fatty liver disease on Doppler Ultrasound and to correlate it with different grades of severity of NAFLD.

Methods

It was an analytic observational hospital based study conducted at the Department of Radiology, Dr. Ruth K.M. Pfau Civil Hospital, Karachi from September 2023 to August 2024 by using non probability consecutive sampling technique. Subjects of either gender between 18-55 years of age referred to Radiology Department for ultrasound abdomen due to non-specific signs/symptoms and diagnosed with fatty liver based on ultrasound findings were considered eligible for the study. Patients were excluded if they had history of viral hepatitis, chronic liver disease of any cause, alcohol consumption, hepatic malignancy or vascular liver disease.

Sample size was calculated by taking 10% frequency of grade III-NAFLD,[14] 5% margin of error and 95% confidence interval with the help of WHO sample size calculator. The total calculated sample size was 139. Written informed consent was obtained from each subject and permission was sought from Institutional Review Board (IRB-3095/DUHS/Approval/2023/338).

Demographic data including age, gender, height, weight and body mass index were calculated. All subjects had undergone hepatic ultrasound with six hour fasting to measure the liver span and grade the severity of NAFLD using Toshiba Diagnostic Ultrasound system (Japan) with a convex 3.5MHz trans-abdominal transducer by an experienced radiologist followed by Doppler ultrasound of the hepatic artery at the level of porta hepatis with patient lying in the supine position to measure the resistive index (RI).[9,15] Then measured indices were analyzed and correlated with the severity of the NAFLD.

Liver span is measured as largest longitudinal extension of right lobe, taking normal < 150mm.[16] Severity of fatty liver is labelled as grade I if the hepatic echogenicity is mildly increased with normal visualization of portal vein wall and diaphragm, grade 2 if the hepatic echogenicity is moderately increased with impaired visualization of portal vein wall and diaphragm, and grade 3 if the hepatic echogenicity is markedly increased with poor visualization of the portal vein wall and diaphragm.[2,9,15] HARI was calculated in the main hepatic artery at the level of porta hepatis with the subject in the suspended respiration by obtaining the peak systolic velocity (PSV) and end diastolic velocity (EDV) via the formula (HARI=PSV – EDV / PSV).[15]

Collected data was analyzed using SPSS Version 26.0. Quantitative data such as patients' age, weight, height, BMI, liver span and Doppler indices of hepatic artery (HARI) were expressed as means and standard deviations while qualitative data were calculated as frequencies and percentages for gender, obesity, diabetes mellitus, dyslipidemia and grades of fatty liver on ultrasound. A p-value of < 0.05 was reflected as statistically significant.

Results

A total of 139 subjects with NAFLD were enrolled in the study to evaluate hemodynamic variations in hepatic artery on Doppler Ultrasound. Out of 139 subjects, 90 (64.7%) were males and 49 (35.3%) were females in the range of 18-55years with an overall mean age of 43.7 ± 9.9 years. The NAFLD was most prevalent in subjects aged >40 years. The mean weight of the subjects was 69.3 ± 10.3 kg and had a height of 1.62 ± 0.38m, resulting in BMI of 27.3 ± 5.6 kg/m2. Table 1 shows the clinico-demographic profile of subjects with NAFLD. It was observed that grade I – NAFLD was more prevalent than other grades constituted 50.4%. The mean liver span measured 150.05 ± 11.3mm with majority of subjects had normal liver span (<150mm) while it was increased in 32 (23%) subjects. Doppler indices of HA decreased with raising grades of NAFLD; HARI was measured 0.77±0.05 in grade I, 0.72±0.05 in grade II and 0.68 ± 0.03 in grade III. Table 2 shows relationship between grades of fatty liver, liver span and HARI.

Table 1: *Clinico-demographic profile of subjects with NAFLD (n=139)*

Variables		Mean ± SD / %
Age (years)		43.7 ± 9.9 years
Weight (kg)		69.3 ± 10.3kg
Height (m)		1.62 ± 0.38m
BMI (kg/m^2)		27.3 ± 5.6 kg/m^2
Gender	Male	90 (64.7%)
	Female	49 (35.3%)
Obesity	Yes	56 (40.3%)
	No	83 (59.7%)
Dyslipidemia	Yes	52 (37.4%)
	No	87 (62.6%)
Diabetes Mellitus	Yes	35 (25.2%)
	No	104 (74.8%)

Table 2: *Relationship between the grades of fatty liver, liver span and HARI (n=139)*

Grades of fatty liver	Number of patients (%)	Liver Span (mm)	HARI (Mean ± SD)
Grade I	70 (50.4%)	145.69 ± 7.0	0.77 ± 0.05
Grade II	53 (38.1%)	150.47 ± 11.7	0.72 ± 0.05
Grade III	16 (11.5%)	167.7 ± 7.7	0.68 ± 0.03

Discussion

The current study was designed to investigate the hemodynamic variation in hepatic artery (HARI) in NAFLD subjects and to correlate this with grades of NAFLD in order to describe the effect of fatty infiltration on hepatic artery compliance. The majority of subjects were aged > 40years with mean age of subjects was 43.7 ± 9.9 years and mean BMI of 27.3 ± 5.6 kg/m^2 in the current study. The significant association was noted between BMI and severity of NAFLD in current study with highest BMI in subjects having grade III - NAFLD, also reported in literature.[12,15,17,18]

Although liver biopsy is the gold standard for diagnosing the NAFLD but it has drawbacks due to its invasive nature and procedural related complications. Furthermore, it is impracticable to carry out hepatic biopsies on each subject of hepatic steatosis. Hence imaging modalities like Ultrasound, Computed Tomography and Magnetic Resonance Imaging can be helpful in diagnosing NAFLD and avoiding unnecessary biopsies.[9] Among these, Ultrasound is the most common and widely available non-invasive radiation free imaging tool that not only detect and grade the severity of fatty liver but also evaluate its effect on the hepatic vasculature due to its duplex property, so the most previous studies proposing it as a useful tool to assess the severity of NAFLD.[15,16,19] Although various studies are available in the literature that showed changes in the hepatic vascular hemodynamics in patients with NAFLD and their relationship with NAFLD severity but these were performed in the west and no local data is available.[9,11-13,15,]

The current study demonstrated increased liver span in 23% subjects which was more prevalent in grade III - NAFLD showing positive correlation with increased grades of NAFLD. This was consistent with findings by Dilek et al.,[7] Balasubramanian et al.,[9] Preciado-Puga et al.,[16] and Karasin M et al.[17] In our study, we investigate the HARI to assess the impact of NAFLD on hepatic artery compliance and found that HARI was towards lower value with increasing severity of NAFLD. This was comparable with the studies done by Balasubramanian et al.,[9] Soleimantabar et al.,[10] Alkabeer et al.,[11] Sabry et al.,[12] Alshehri et al.[15] and Mohammadinia et al.[20] and who reported inverse relationship between severity of fatty infiltration and HARI. In this study, we found mean RI of 0.77 ± 0.05 in grade I, 0.72 ± 0.05 in grade II and 0.68 ± 0.03 in grade III, closely matches with study of Dilek et al.[7] and Bony et al.[8]

Sabry et al.[12] and Alshehri et al.[15] explained that with progression of hepatic steatosis, there is increased flow resistance in portal vein which reduced the hepatic portal blood flow and velocity. Consequently, there is increased hepatic artery diastolic flow as a compensatory mechanism leading to reduction of hepatic artery RI. But there is some controversy about this hypothesis that if fatty infiltration reduces portal vein flow due to increased resistance then it should also reduce the hepatic

artery flow because inside liver both vessels run in portal triad and supply same area but in a different percentage. However, this may be explained as artery is anatomically different from a vein so might respond differently in the form of vasodilatation or hypertrophy or there may be some other underlying mechanisms which need further exploration and research on larger population.

Tana et al.[13] also found lower HARI in NAFLD and inversely correlated with severity of hepatic steatosis. He also concluded that high value of HARI (>0.9) in any grade of NAFLD suggest to carry out hepatic biopsy to assess the risk of steatohepatitis while lower HARI value express low risk and does not necessitate the hepatic biopsy. In contrast, Aslan et al.,[6] Karasin et al.[17] and Bedewi et al.[21] didn't find negative relationship between HARI and NAFLD patients. These differences might be due to different Doppler techniques or site of hepatic artery, variable sample size, different population, or variation in age and gender of the study population.

HARI is not only a useful Doppler parameter for early detection of alteration in hepatic blood flow in NAFLD subjects than portal vein velocity but it also helps in assessing the effect of improvement in subject with NAFLD. Tarzamni MK et al.[19] done a study on 48 patients to assess the hemodynamic variations in response to treatment of NAFLD, and he found significant improvement in grades of fatty liver and in value of HARI after treatment of NAFLD, while no significant change in hepatic artery PI and portal vein waveform. He concluded the Doppler indexes especially hepatic artery RI contribute in monitoring the patient with NAFLD during treatment and help to prevent unnecessary health care cost by avoiding further diagnostic tests/interventions.

The main limitation of the current study is that the diagnosis as well as grading of NAFLD were done on ultrasound only, not confirmed by biopsy. Other limitations include small sample size, single center study and lastly we didn't include healthy volunteers as the control group. Further local studies should be done to evaluate the hepatic vascular Doppler indices in the NAFLD population through case-control studies on larger population to validate these findings and to look into/ better understand the pathophysiology of underlying mechanisms which might involve in decreasing portal venous flow and increasing hepatic arterial flow.

Conclusion

NAFLD represent a spectrum of hepatic parenchymal pathology that results the hemodynamic changes in liver and increases the vascular resistance. Hence it needs monitoring because NAFLD may lead to cirrhosis. Significant correlation was noted between the hemodynamic changes in hepatic artery and grades of NAFLD. Therefore, Doppler ultrasound can be used as imaging modality of choice to monitor and follow up of NAFLD.

Ethical Approval: The Institutional Review Board, Dow University of Health Sciences approved this study vide Ref: IRB-3095/DUHS/Approval/2023/338)

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Authors' Contribution:

NJ conceived, designed and did data collection, statistical analysis & manuscript writing.

RS designed, did interpretation of data and editing of manuscript.

SS reviewed critically and did final approval of manuscript.

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