Hepatic vein spectral doppler waveform in patients with fatty liver changes - a study from Western Nepal

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\textbf{Abstract}

\textbf{Background}

Spectral Doppler waveform interpretation of hepatic vein is of considerable importance as it mirrors cardiac and hepatic physiology. The aim of this study was to evaluate the flow velocity waveform pattern in patients with different grades of fatty infiltration of liver and compare them with normal individuals.

\textbf{Methods}

This was a prospective study carried out in 213 patients, taking 100 patients as “control” groups; and 113 “cases” with varying degree of fatty liver graded by ultrasonography. The patients included asymptomatic individuals with no history of cardiac, hepatic disease or alcohol intake. The study also excluded cases with any medical disease such as ascitis that could influence the outcome of hepatic Doppler measurement. The Doppler hepatic waveform of the right hepatic vein was taken and classified as triphasic, biphasic and monophasic.

\textbf{Results}

All except one of the control group had normal triphasic pattern. Patients with severe grade of hepatic steatosis (Grade III) showed monophasic flow in 72.2\% of the cases with sensitivity and specificity amounting to 83.3 and 87.7 respectively. A significant difference was observed in distribution of Doppler waveform pattern ($p= 0.00001$).

\textbf{Conclusion}

Triphasic waveform pattern was seen in majority of normal individuals with no cardiac or hepatic disease, while, in patients with increasing grade of hepatic steatosis, the waveform changed to biphasic and monophasic pattern due to decreased compliance of the hepatic veins.

\textbf{Key words}

Doppler ultrasound, fatty liver, hepatic vein waveform.
Background

Spectral Doppler waveform interpretation of hepatic vein is of considerable importance as it mirrors cardiac and hepatic physiology. The hepatic vein Doppler waveform generally shows a triphasic pattern which includes two hepatofugal phases corresponding to atrial and ventricular diastoles, along with a short phase of retrograde hepatopetal flow caused due to the increase in pressure in the right atrium during atrial systole [1, 2]. Triphasic pattern shows 3 waves – A, S and D wave, the A wave corresponds to atrial contraction. During ventricular systole the tricuspid annulus moves towards the cardiac apex creating a relative negative pressure in the atrium. This causes antegrade blood flow out of the liver and into the heart during the S wave. The V wave corresponds to atrial overfilling. The peak of V wave may be below, at or above the base line. The term “triphasic” does not include the V wave, perhaps because this wave represents only transitional phase [3]. Tricuspid valve opening is represented by the D wave. C wave is a normal variant which can cause a small retrograde spike following the A wave [4].

Ultrasonography is often used in the diagnosis of fatty liver, considering its non-invasiveness, wide availability and low cost [5 – 7]. Fatty liver disease commonly occurs in obese subjects [8]. The hepatocytes, containing fat droplets and abundant endoplasmic reticula in their cytoplasm, become swollen and lead to impaired sinusoidal microcirculation and narrowed hepatic sinusoidal lumens. The ischemia induces hepatic fibrinogenesis, which, if persists for a long period, may progress to liver cirrhosis [9]. It has been described that the hepatic vein pulsatility decreases in fatty infiltration of liver, from triphasic to biphasic and eventually to monophasic flow pattern where no oscillation in the flow velocity waveform is identified at pulsatile Doppler [10]. The objective of our study is to evaluate the flow velocity waveform pattern in normal individuals and in patients with different grades of fatty infiltration of liver.

Material and Methods

Study design, participants and collection of data

It was a prospective hospital based study conducted in the Department of Radiology, Gandaki Medical College, Pokhara, Nepal between June 2012 to June 2013. 100 subjects were selected as ‘control’ group while 113 (cases) were included with varying degrees of fatty liver as graded by ultrasonography. BMI was calculated for those with fatty liver (formula BMI = weight/height^2 (kg m^-2). 43.2% of cases were males while 56.8% cases were females. The mean age was 39.5 with youngest individual age 18 and eldest aged 78.

The Doppler ultrasound was performed with Toshiba Accuvix with 2.0- 4.0 MHz convex probe. Each individual was examined after overnight fasting in supine/50-600 left lateral position. Any case with space occupying lesion in the liver was excluded. The sample gate was positioned approximately 4-6 cm from the hepatic vein confluence within the right hepatic vein. The subjects were asked to hold their breath at the end of shallow inspiration and the spectral analysis was recorded over a period of five seconds. Fatty infiltration of liver has been classified on USG as Normal, Grade I, II and III and correlated with the Doppler waveform pattern Figs 1, 2 and 3.
Waveform tracing showing monophasic waveform. No oscillations seen.

**Inclusion criteria**
Only patients referred for ultrasonography of abdomen, from different departments in our hospitals were included in the study.
The patient selection criteria included subjects > 18 years of age and absence of cardiac or liver diseases.

**Exclusion criteria**
Pregnant subjects, patient with previous history of abdominal or thoracic surgery, those consuming more than 40gm of alcohol/day and those taking medication for cardiac disease or medications which would affect the liver were excluded from the study as such conditions could influence the hepatic vein waveforms.

**Ethical committee approval**
Prior permission had taken from the Institutional ethical committee. All the guidelines and ethics followed for the human experimentation in this research work.

**Data management and statistical analysis**
The statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 17 (SPSS Inc; Chicago, IL, USA) software.
The comparison between different variables was tested using the t test. Unpaired t test done among the subjects. A p value less than 0.05 was considered statistically significant.

**Results**
The spectral Doppler pattern was observed in all cases. The different pattern of wave form observed in normal, grade I, II and III fatty changes are listed in Table 1.

| Doppler Studies | Control Group (n=100) | Case Group with Fatty liver (n=113) |
|-----------------|-----------------------|-------------------------------------|
| Monophasic      | 1(1%)                 | 2(6.6%) 8(12.3%) 13(72.2%)          |
| Biphasic        | 99(99%)               | 3(10%) 10 (15.3%) 2(11.1%)          |
| Triphasic       |                       | 25 (83.3%) 47 (72.3%) 3 (16.6%)     |
| Total           | 100                   | 30 65 18 113                        |

**Table – 2: Sensitivity and Specificity Analysis of Doppler against the three grades of fatty liver**

| Doppler                  | Grade I Fatty Liver | Grade II Fatty Liver | Grade III Fatty Liver |
|--------------------------|---------------------|----------------------|-----------------------|
| Sensitivity              | 16.7                | 27.7                 | 83.3                  |
| Specificity              | 81.4                | 85.8                 | 87.7                  |
| Negative Predictive Value| 85.6                | 73.0                 | 98.3                  |
| Positive Predictive Value| 12.8                | 46.2                 | 38.5                  |

The sensitivity and specificity analysis of Doppler against the three grades of fatty liver is given in Table 2.
The area under the ROC curve with confidence interval and p value is presented in Figs 4,5 and 6.

**Discussion**
Inspection of the hepatic vein Doppler waveform adds to the examination time insignificantly. The right hepatic vein is preferred as pulsatility is greater in left and middle hepatic veins due to cardiac motion [11]. Our study was limited to asymptomatic cases with no history of cardiac or liver diseases to avoid any erroneous wave form pattern. As in study done by Pedersen J F et al, there was no association between the hepatic flow pattern and age, sex or BMI. However in the present study, majority of the obese patient with BMI ≥ 30 had moderate to severe hepatic steatosis [12].

In the control group, healthy individuals with triphasic wave form was observed in all except one who had biphasic wave form which is consistent with observations made by Bolondi, 1 Pedersen J F12  and O’Donohue [13].
Our data revealed monophasic flow pattern in 20.3% of patients with fatty liver, of which 6.6% was with Grade I, 12.3% with grade II and 72.2% with grade III fatty liver. This percentage is slightly lower as compared to the study done by Herbay et al [14] who reported the pattern to be detected in 27% of the patients with fatty liver. Karabulut et al reported monophasic flow in 74% of obese subjects with fatty liver which is almost consistent with our findings of 72.2% of patients with grade III fatty liver [15]. Reformation of the hepatic waveform has been attributed to impaired hepatic compliance caused by intrahepatic fat deposition within the hepatocytes [16, 17].

A statistically significant observation was seen in subjects with severe steatosis (p = 0.00001) which corresponds well with observation made by Borges et al who reported monophasic flow pattern in severe steatosis to be 60% with p value < 0.01. [18]. The sensitivity and specificity of Doppler was higher in grade III hepatic steatosis corresponding to 83.3% and 87.7% respectively. The sensitivity was decreasing with lesser degree of fatty infiltration of liver however the specificity remained significant.
Conclusion

Our findings suggest that triphasic waveform is observed in majority of individuals without fatty infiltration of liver while with increasing grade of hepatic steatosis the waveform shifts from triphasic to monophasic due to decrease in vascular elasticity.

Study limitations and future scope

Sample size of the present study is less and multicentric study with larger sample size is welcome to explore more information.

Abbreviations

Body mass index [BMI]

Competing interest

Authors do not have any competing interest.

Authors’ contribution

MKS collected the data. BS prepared statistical analysis. MKS, DGM, AG, BS participated in planning study design, collating the data, writing the manuscript and editing the final version.

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