CORRELATION OF PORTAL VEIN PULSATILITY PATTERN AND SEVERITY OF LIVER DISEASE IN PATIENTS WITH CIRRHOSIS AND PORTAL HYPERTENSION

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Abstract:

***Objective*:** To correlate the portal vein pulsatility pattern with severity of liver disease in patients with cirrhosis of liver and portal hypertension.

***Subjects and methods*:** Doppler signals from the main portal vein of 36 healthy adults and 52 cirrhotic patients with portal hypertension were studied. Severity of liver disease was graded using modified Child-Pugh classification. Pulsatility of portal flow was quantified using portal venous pulsatility index and complete spectral widening was defined as absence of window below the wave base. The Doppler findings were correlated between the study groups.

***Results*:** The mean pulsatility index value in control group was 0.37+0.10 and in cirrhotic patients was 0.17+0.03 (Child A- 0.21+0.02, Child B- 0.18+0.02, Child C- 0.14+0.03). The difference between control and cirrhosis group, as well as the difference within different Child classes were statistically significant ($P<0.05$). None of the patients in control group had complete spectral widening while 76.92% of cirrhotic patients had complete spectral widening (28.5% of Child A, 66.6% of Child B and 100% of Child C). The difference in distribution of complete spectral widening between control and cirrhotic group as well as within the cirrhotic group was statistically significant ($P<0.05$).

Conclusion: Portal vein pulsatility index and spectral widening can reflect the early hemodynamic changes in cirrhotic patients. These changes become more pronounced with increasing severity of liver disease.

Key words: portal vein pulsatility pattern, cirrhosis, portal hypertension

Introduction:

Cirrhosis is defined by World Health Organization (WHO) as a diffuse process characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules.[1] Progressive hepatic fibrosis causes several regional hemodynamic changes like hepatic venous outflow obstruction, changes in hepatic artery resistance and development of portal hypertension with increasing sinusoidal resistance. These hemodynamic changes influence the degree of portal hypertension and liver dysfunction.[2,3]

Ultrasonography is the most commonly used imaging modality for diagnosis and follow up of patients with cirrhosis. The diagnosis usually relies on late findings of volume redistribution, irregularity of liver surface and secondary findings of portal hypertension. However, B-mode sonography is incapable of examining patients of cirrhosis without these late findings.[2]

Doppler sonography is a non-invasive diagnostic modality based on hemodynamic parameters. Hemodynamic changes might have developed even in cases with normal findings on B-mode sonography.[4] Therefore assessment of these alterations has importance for early diagnosis and for close follow up of previously diagnosed cases.[2] Hepatic venous Doppler changes have been described in cirrhosis; however these changes are not specific for cirrhosis and can even be seen in cases of steatosis.[5]

Alterations of portal vein hemodynamics in cirrhosis have been observed in various studies. With recent interest in analysis of portal vein pulsatility pattern in relation to cirrhosis of liver, different measures of pulsatility of portal waveform have been studied. Simple parameters like portal vein pulsatility index and spectral widening were found, in some studies, to reflect the early changes in portal hemodynamics in relation to the severity of liver disease.[6] Though extensive studies regarding their usefulness is lacking in literature, these early changes can serve as valuable indicators of presence of cirrhosis when other imaging findings are equivocal or negative. These parameters can be of value in assessment of severity of liver disease and the follow up of patient as well. [6]

Despite wide variation, there are in general two pulsatility patterns in normal conditions; (a) the more common slight fluctuation pattern with a PI between 0.2 to 0.5, and (b) the less common pronounced pulsatility pattern with a PI > 0.5. A PI value > 1 (severe pulsatility), a situation defined by systolic flow interruption or reversal, suggests presence of cardiac disease whereas PI value below 0.2 (almost non-pulsatile or flat wave envelope) is considered to represent presence of chronic liver disease. [6] Spectral width changes, esp. complete spectral widening also suggests presence of chronic liver disease.

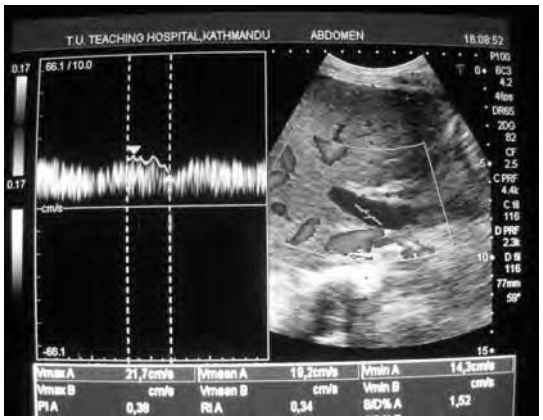


Fig 1. Normal pulsatile portal vein waveform with presence of window below the wave base.

Cirrhosis is a common problem with significant morbidity and mortality. No such study regarding alteration in portal vein pulsatility pattern in cirrhosis and portal hypertension has been done in past in Nepal. This study could highlight the role of duplex Doppler in recognizing the disease in early stage as well as in assessing the severity of the disease.

Objectives:

General objective:

- To correlate the portal vein pulsatility pattern with severity of liver disease in patients with cirrhosis of liver and portal hypertension.

Specific objectives:

- To find the mean portal vein pulsatility index (PI) value and distribution of complete spectral widening (CSW) in healthy population.
- To find the mean portal vein PI value and distribution of CSW in patients with cirrhosis and portal hypertension.
- To compare portal vein PI and presence of CSW between healthy control group and the patients with cirrhosis of liver.
- To evaluate the relation of portal vein PI and CSW to the severity of cirrhosis

of liver as determined by modified Child-Pugh classification.
- To evaluate the relation of portal vein PI and CSW to the individual Child-Pugh Variable.

Materials and methods:

It was a non randomized, case-control study carried out from November 2006 to July 2007. The study was carried out in department of radiology and the department of internal medicine, Tribhuvan University Teaching Hospital (TUTH), Kathmandu, Nepal. Convenient sampling method was used for data collection. A total of 52 patients with cirrhosis of liver and portal hypertension along with 36 healthy subjects constituted the study groups.

Patients suspected of having cirrhosis of liver admitted under or attending the department of internal medicine, TUTH, irrespective of age and sex, after obtaining informed consent, were subjected to full clinical workup, laboratory investigations, upper gastrointestinal endoscopy, and ultrasound examination and pulsed Doppler study of main portal vein.

Diagnosis of cirrhosis of liver was based on combination of clinical data, laboratory data and ultrasound data. Presence of portal hypertension was based on presence of esophageal varices in upper gastrointestinal endoscopy. Severity of liver disease was assessed with modified Child-Pugh classification.

Exclusion criteria:
- Patients with grade III-IV encephalopathy.
- Patients taking drugs altering the portal hemodynamics.
- Patients with previous sclerotherapy or band ligation.
- Patients with portal vein thrombosis.
- Patients with portal vein flow reversal or bidirectional portal flow.

Portal vein pulsed Doppler examination was performed with a 3.5 MHz probe in a commercially available ultrasound system (SONOACE 8000 LIVE) with Doppler facility. The transducer was kept along the longitudinal axis of main portal vein in an oblique para-median plane. The point of measurement was midway between the confluence of splenic & superior mesenteric vein and bifurcation of portal vein, the Doppler angle always being <60 degree. The sample volume was adjusted to include as much of the lumen as possible without including the vessel wall. The flow waveform was recorded, for patients as well as healthy subjects. All measurements were performed on fasting with patient breathing quietly.

A matching control group of healthy individuals coming to department of radiology for general health check up examination were also subjected to Doppler study of main portal vein.

Portal vein pulsatility was expressed as the Pulsatility index (PI) which was calculated as: (maximum peak velocity - minimum peak velocity)/ maximum peak velocity.

Complete spectral widening (CSW) was said to be present if no window was visible under the wave base.

The data obtained were compiled and analyzed using standard statistical analysis. SPSS 12 was utilized for the data analysis and presentation. Results were expressed as mean+standard deviation for Pulsatility Index values. Differences in the mean Pulsatility Index values between control and cirrhotics as well as within the cirrhotic group were analyzed using Independent t-test, Anova test and Bonferroni test. Differences in the distribution of complete

Spectral Widening were analyzed with Chi-Square test and Fisher's-Exact test. Probability values of <0.05 were considered significant.

Results:

Age Distribution in control and cirrhosis groups:

The mean age of patients with cirrhosis was 49.63+14.73, minimum age being 18 years and maximum being 79 years. The mean age of subjects in control group was 48.44+14.92, minimum and maximum age being 19 years and 84 years respectively.

Sex distribution in control and cirrhosis groups:

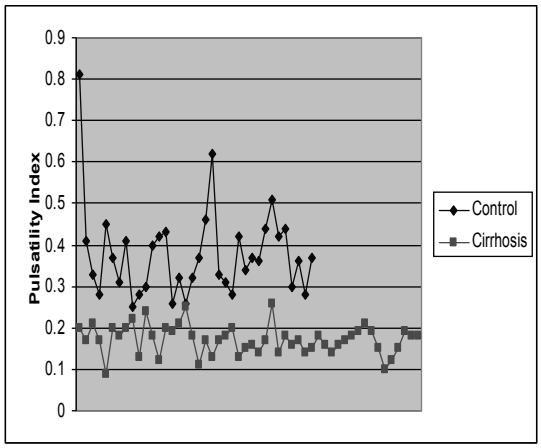
In cirrhosis group, 19 patients (36.54%) were female and 33 patients (63.46%) were male. Similarly in control group, 14 patients (38.89%) were female and 22 patients (61.11%) were male.

Distribution of patients in different Child-Pugh classes:
The total number of patients in cirrhosis group was 52. 13.46% (7) of them were in Child-Pugh class A, 40.38% (21) in class B and 46.15% (24) in class C.

Pulsatility Index in control and cirrhosis groups:

In our study, PI values were between 0.25 to 0.81 in control group, the mean value being 0.377+0.108. 91.66% (33 of 36) healthy individuals had PI between 0.2 – 0.5 and 8.33% (3 of 36) had pronounced pulsatility >0.5. However none of the individuals had PI >1 or <0.2.

Chart 1: Pulsatility Index in cirrhosis and control groups



The PI values in cirrhosis group were between 0.9 to 0.26, mean pulsatility index value being 0.171+0.035. The mean value in control group was 0.377+0.108. Independent t-test for equality of means showed the difference to be highly significant with P value of 0.000.

The mean PI in Child-A was 0.215+0.025, in Child-B 0.181+0.023 and in Child-C was 0.149+0.030. This shows that the PI becomes lower with increasing severity of cirrhosis. The differences of mean PI values within the Child classes were statistically significant. (P=0.017 between Child A & B), (P=0.001 between Child B & C) and (P=0.000 between Child A & C).

Spectral Widening in control and cirrhosis groups

Complete spectral widening (CSW) was present in 76.92 % of patients with cirrhosis (40 of 52) and none of healthy subjects in control group (0 of 36). The difference between distribution of CSW in control and cirrhosis group had high statistical significance (P=0.000 by Chi-square test and Fisher's exact test).
Complete spectral widening was present in all the patients in Child-C while it was present in only 2 of 7 patients in Child-A and 7 of 14 patients in Child-B. 28.57% of Child-A patients, 66.66% of Child-B patients and 100% of Child-C patients had complete spectral

widening. The difference of presence of CSW within Child classes was significant.(P=0.000)

Age and Pulsatility Index/CSW in control and cirrhosis groups

The difference of mean PI values in different age groups was not statistically significant in both control group (P=0.205) and cirrhosis group (P=0.234).

Since none of the healthy individuals had complete spectral widening, there was no relation at all between age of the individual and CSW in control group. All the cirrhotic patients in 51-60 yrs age group had complete spectral widening, the majority of patients in rest of the age groups also having CSW. The difference of presence of complete spectral widening in cirrhotic patients of different age groups was not statistically significant (P=0.453).

Sex and Pulsatility Index/CSW in control and cirrhosis groups

The difference of mean PI values in male and female group was not statistically significant (P=0.884 in control group and P=0.222 in cirrhosis group).

Since none of the healthy individuals had CSW, there was no relation at all between sex and CSW. 72.72% (24 of 33) of cirrhotic male patients had CSW, while 84.21% (16 of 19) of cirrhotic females had CSW. The difference of presence of CSW in male and female groups was not statistically significant (P=0.344)

Relation of Pulsatility Index and Spectral Widening with Child-Pugh variables.

The PI values were lower with increasing grades of all five variables (ascites, encephalopathy, albumin, Bilirubin and PT prolongation), the difference between the lowest and highest grades being statistically significant. However the statistically significant increase in presence of CSW was noted only with increasing values of Bilirubin and PT prolongation.

Discussion:

The normal portal vein demonstrates an undulating hepatopetal flow. Mean portal venous velocity is approximately 15 to 18 cm/sec. Normal portal venous flow rates vary in the same individual: they increase after a meal, decrease after exercise or when the patient is upright. It also varies with respiration.(10,11) As portal hypertension develops, the flow in the portal vein loses its undulatory pattern and becomes progressively flattened. As the severity of portal hypertension increases, flow becomes biphasic and finally hepatofugal. [6,7]

Various measurements and indices have been used by different authors to study the portal hemodynamics and used it as indicators of hepatic morphological changes. They include measures of portal flow and measures of pulsatility pattern.

There are number of measures of portal flow such as congestion index, modified hepatic index, hepatic vascular index and portal blood flow. However these composite measures of portal flow are difficult to calculate, hindering their widespread use and their reliability too is yet to be proved.[2] Unreliability of measures of portal vein flow was also noted in a study by Haktanir A et al.[2] The studies evaluating interobserver difference in the portal flow measurements found that acceptable interobserver agreement was not found between the observers.[8,9]

Pulsatility pattern is measured using measures like pulsatility ratio[10], pulsatility score[11] and pulsatility index. Pulsatility ratio and pulsatility score both describe the same measure that is quantified as the minimum peak velocity/

maximum peak velocity, which increases with progressive loss of pulsatility. Portal vein pulsatility index on the other hand was preferred by other authors as a high or low index directly expresses the corresponding situation, i.e., high or low portal vein pulsatility. [6] In this study also portal vein pulsatility index was used for the same reason.

Mean PI values in healthy individuals:

The mean PI value in healthy individuals in our study was 0.377+0.108. The PI values found by different authors are 0.39+0.1 (Barakat M) [6], 0.48+0.31 (Gallix BP et al)[12], 0.22 (Chou LS et al)[13]. Duerinkx et al[14] and Wachsberg et al[11] found PI values in healthy individuals to be <0.61 and <0.54 respectively.

In our study 91.66% (33 of 36) healthy individuals had PI between 0.2 – 0.5 and 8.33% (3 of 36) had pronounced pulsatility >0.5. However none of the individuals had PI >1 or <0.2. Barakat M[6] had found that 77.6% of healthy individuals had PI between 0.2 - 0.5 and 22.4% had pronounced PI >0.5, while none had PI >1 or <0.2. These findings are consistent with the general agreement that portal vein pulsatility index values in healthy adults are within 0.2 to 0.5 range.

Mean PI values in cirrhotic patients:

The mean PI value in patients with cirrhosis and PH in this study was 0.17+0.03. The difference of PI value between the control and cirrhosis group was statistically significant.

In a study involving 157 patients, Barakat M[6] had found PI of 0.23+0.08 in cirrhotic patients. The lower PI value in our study was partly due to less number of patients in Child-Pugh class A (13.4% in our study vs. 38.2% in study of Barakat M.). The less number of Child-A patients in our study was due to the fact that liver biopsy was not included as a diagnostic criteria for cirrhosis, which is invaluable in ascertaining the presence of cirrhosis in early disease with minimal clinical, laboratory and morphological changes.

In a study involving 38 children (mean age 3.3 years) with end stage liver disease and portal hypertension, Westra SJ et al[15] found increased pulsatility of portal vein waveform. He had used Resistive Index (RI) as a measure of pulsatility which was calculated using the same equation that has been used in our study. Mean RI value in his study was 0.6+0.33. The reason that had been proposed for increased pulsatility in children was that in children the compliance of hepatic parenchyma is more than in adults to accommodate the arterial pressure variations.

PI in different Child-Pugh classes:

In the present study, the mean pulsatility index value was 0.21 in Child A, 0.18 in Child B and 0.14 in Child C, the differences being statistically significant. The finding that the PI value decreases with increasing severity of liver disease is consistent with the findings of Barakat M[6] who had found the mean PI value in Child A to be 0.25, in Child B 0.23 and in child C to be 0.21. However the lower mean PI value in our study in all three Child classes is difficult to explain. This could in part be related to the etiology of cirrhosis. Barakat M had not included patients with alcoholic cirrhosis in his study while majority of patients in this study had alcoholic cirrhosis. Studies evaluating the relation of portal vein PI with etiology of cirrhosis are not available in literature.

Spectral widening in control and cirrhotic patients:

In this study, none of the patients in control group had complete spectral widening while 76.92% of patients with cirrhosis and PH had complete spectral widening. This is consistent with the study of Barakat M[6] of 157 patients

with cirrhosis of liver, where 71.9% of patients with cirrhosis had complete spectral widening.

In our study, complete spectral widening was found in 28 .5% of Child A patients, 66.6% of Child B patients and 100% of Child C patients, the difference being statistically significant. In contrast, Barakat M[6] had not found any statistically significant difference in presence of complete spectral widening between different Child classes. This difference with his findings has to be further evaluated with larger studies; however this could again, in part, be due to significantly less number of patients with Child A cirrhosis (13.46% vs 38.21%) in our study.

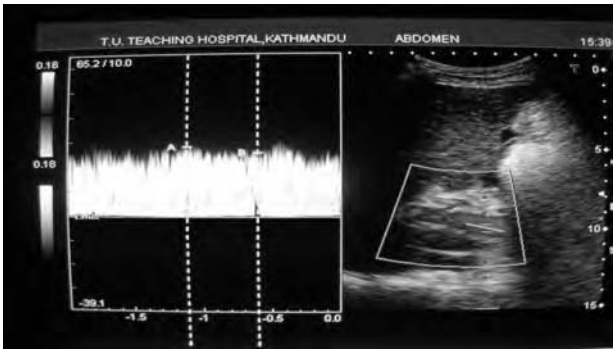


Fig 2. Portal vein wave form in a patient with Cirrhosis (Child C) with portal hypertension: flattened waveform with absent window.

Relation of Child-Pugh variables with PI and Spectral widening:

The PI values were lower with increasing grades of all five variables (ascites, encephalopathy, albumin, Bilirubin and PT prolongation), the difference between the lowest and highest grades being statistically significant. However the statistically significant increase in presence of CSW was noted only with increasing values of Bilirubin and PT prolongation. Literature is lacking regarding the relation of PI and spectral widening with the variables of Child's classification.

Conclusion:

Decrease in pulsatility index is a valuable indicator of early hemodynamic changes in cirrhotic patients with portal hypertension, changes being significantly more pronounced with increasing severity of the disease. Similarly presence of complete spectral widening is also a strong predictor of increased severity of the disease. These findings can be used as adjunctive signs to identify and monitor the hemodynamic changes in patients with cirrhosis.

The study had its own limitations. The limitations were small sample size, particularly in Child-Pugh class A, convenient sampling and limited time. TUTH being a referral centre, the patients included may not represent the patients of cirrhosis in general population. Similarly the healthy subjects included in this study were taken from General Health Check up clinic and may not represent the general population.

Further large-scale studies should be performed evaluating these parameters to establish their roles in patients with cirrhosis and portal hypertension.

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