

Assessment of Doppler waveform patterns and flow velocities of hepatic veins in children with acute viral hepatitis

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PURPOSE

To evaluate hepatic vein flow patterns and velocities in children with acute viral hepatitis and to compare the findings to a group of healthy children, with duplex sonography.

MATERIALS AND METHODS

Forty children with acute viral hepatitis were enrolled in group 1 and forty healthy children were enrolled in group 2 (control group). Both groups underwent gray scale and duplex sonography. Hepatic venous Doppler flow patterns were categorized as triphasic, biphasic, or monophasic. Peak systolic velocities of hepatic veins were recorded.

RESULTS

In group 1, hepatic venous flow was triphasic in 61.6%, monophasic in 26.6%, and biphasic in 11.6% of the patients. These figures were 88.3%, 8.3%, and 3.3%, respectively, for the controls in group 2. Group 1 had fewer patients with only a triphasic flow pattern, but had a higher percentage of monophasic and biphasic flow patterns. There was a triphasic flow pattern in all three hepatic veins in 50% of group 1 and in 80% of group 2. Differences in flow patterns of hepatic veins between the groups were found to be significant according to the student t-test ($p < 0.01$), and this was independent of age, gender, feeding status, and activity.

CONCLUSION

Similar to reports of chronic liver disease or diffuse liver disease, significant differences in the flow patterns of hepatic veins were found in children with acute viral hepatitis. Hepatic vein flow patterns were frequently monophasic or biphasic in group 1, especially when accompanied by change in hepatic echogenicity. There was no significant difference in the flow velocities of the hepatic veins between group 1 and group 2.

Key words: • children • acute viral hepatitis • duplex sonography

Hepatic veins drain blood from low-pressure hepatic sinusoids to the inferior vena cava. In duplex sonography (DS), flow in hepatic veins is normally pulsatile due to changes occurring in right heart flow during the cardiac cycle (1, 2). The normal liver is compliant and can adapt easily to the pressure changes (3), and triphasic flow occurs due to reversal of flow in the inferior vena cava during atrial systole. This triphasic flow pattern is evident in fetuses in the second trimester of gestation (1-5).

During some conditions, such as cirrhosis or rejection of liver transplantation, the liver parenchyma becomes less compliant, which often results in loss of the triphasic venous flow pattern (1, 2, 4-6). Whether or not hepatic parenchymal abnormality can be diagnosed or suspected based on evaluation of the hepatic veins with DS is a matter of debate. Some authors claim that DS is insufficient in this respect, while others argue that DS has high sensitivity and specificity in the diagnosis of cirrhosis and rejection of liver transplantations (1-6).

Flow pattern changes in hepatic vein waveforms in patients with chronic viral hepatitis have been demonstrated with DS examination (4-7). One could hypothesize that flow changes are expected in the acute form of the disease as well. The purpose of this study was to evaluate, with DS, the flow patterns of hepatic veins in children with acute viral hepatitis (AVH).

Materials and methods

We prospectively evaluated 40 consecutive children presenting to our hospital with AVH between February 2001 and August 2001. Group 1 was composed of these 26 males and 14 females whose ages ranged from 1.5 to 14 years. Diagnosis of AVH was based on clinical and laboratory findings. The criteria for the diagnosis of AVH included elevated hepatitis A viral titers, hepatic enzymes and icterus. None of the patients included in group 1 presented with any clinical evidence of heart and chronic liver diseases. Patients were excluded from participating in the study if they had undergone any abdominal or thoracic surgery. Group 2 was the control group, and was comprised of 19 male and 21 female healthy volunteers aged 2 to 16 years. None of the children in group 2 had a known or suspected disease. Hepatic enzymes were normal and viral titers were absent in group 2. Written consent was obtained from all the children's parents (group 1 and group 2).

The cases in group 1 were divided into three age groups: 1-5 years, 5-11 years, and 11-16 years. Their gender, feeding status (fasting or postprandial), and activity were recorded. The minimum duration of fasting was 4 hours. The age, gender, feeding status, and activity distribution of children in group 1 and 2 is shown in Table 1.

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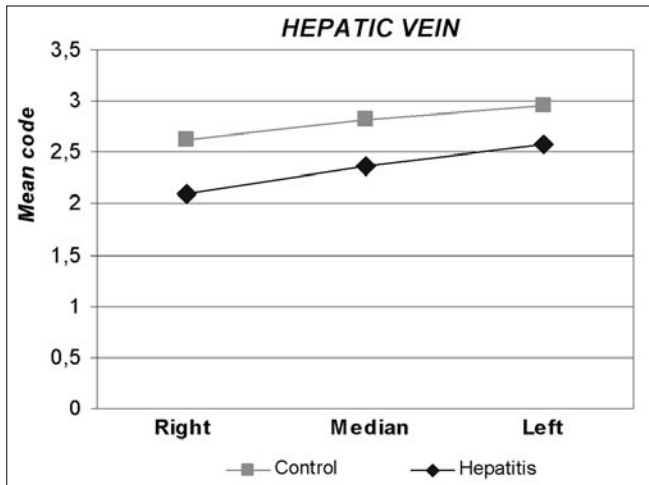


Figure 1. Plot of the means of hepatic vein flow patterns of each hepatic vein. Coding flow as monophasic flow = 1; biphasic flow = 2; triphasic flow = 3. Flow pattern differences between the groups are significant ($p < 0.01$).

Both study groups underwent DS examination with a 3.75 MHz convex probe and 7.5 MHz linear probe (Toshiba 140 A, Tokyo, Japan). All DS examinations were performed by one radiologist who was aware of the case diagnoses and none of the cases required sedation. When possible, cases were examined in a supine position during inspiration. In order to exclude unexpected intercurrent disease, in addition to evaluating the hepatic parenchyma and hepatic vasculature, we also evaluated the gallbladder, the

periportal area, kidneys, pancreas, para-aortic space, spleen, and the peritoneal space with gray scale ultrasonography. All abnormal findings were recorded. Subsequently, in the position where the right, middle, and left hepatic veins could best be seen, we placed the sample gate within the vein, and sampled Doppler flow patterns and measured the peak systolic flow velocity (V maximum: Vmax). The insonation angle was between 40° and 60°. In some instances, in young, uncooperative children, Dop-

pler angle correction was made after freezing the image and then measurement of Vmax was performed. We recorded, on hard copy film, the flow patterns and Vmax flow velocities of each case.

In order to prevent flow measurements from excessively being affected by cardiac motion, the Doppler gate was positioned at least 3-4 cm distal to the opening of the hepatic veins into the inferior vena cava (6-8).

If there was return of flow below the baseline, the flow pattern was regarded as triphasic, with the exception the presence of changes related to respiration; if there were no modulations in the flow pattern, it was considered monophasic, and if there were modulations that did not reach the baseline, the flow pattern was classified as biphasic (1, 2).

The results are presented as a plot of means of the codes of the hepatic vein flow pattern:

- 1 = monophasic flow,
- 2 = biphasic flow,
- 3 = triphasic flow.

Statistical analysis

Statistical analysis of flow pattern and velocity differences between the groups was made with the student t-test. Age, gender, feeding status, and activity differences between the groups were analyzed with the chi-square test (SPSS for Windows, version 9.0 statistical package). P values < 0.05 were regarded as significant.

Results

In group 1, a triphasic flow pattern was present in 61.6% of the 120 hepatic veins sampled, whereas a monophasic flow pattern was observed in 26.6% and a biphasic flow pattern in 11.6%. In group 2, a triphasic flow pattern was observed in 88.3% of the 120 hepatic veins sampled, a monophasic flow pattern was noted in 8.3%, and a biphasic flow pattern in 3.3%. The hepatic vein flow patterns of group 1 and group 2 are shown in Table 2.

When comparing both groups, the incidence of triphasic flow patterns in group 1 was less, while the incidence of monophasic and biphasic flow patterns was greater. The differences in the flow patterns of the hepatic veins of the two groups were found to be significant according to the student t test ($p < 0.01$) (Figure 1).

Table 1. Age, gender, feeding status, and activity distribution of the group with AVH and the control group.

Age groups	# patients	Male	Female	Postprandial	Fasting	Calm	Asleep	Agitated
1-5	10	6 (3)	4 (7)	4 (3)	6 (7)	6 (5)	2 (2)	2 (3)
5-11	22	16 (12)	6 (10)	6 (6)	16 (16)	20 (22)	1 (0)	1 (0)
11-16	8	4 (4)	4 (4)	2 (3)	6 (5)	8 (8)	0 (0)	0 (0)

Numbers in parentheses are values of the control group.

Table 2. Hepatic vein flow patterns of the group with AVH and the control group.

Hepatic Vein	Flow pattern and percentages (%)					
	Monophasic		Biphasic		Triphasic	
	#	%	#	%	#	%
Right	17 (7)	42.5 (17.5)	2 (1)	5 (2.5)	21 (32)	52.5 (80)
Middle	9 (2)	22.5 (5)	7 (3)	17.5 (7.5)	24 (35)	60 (87.5)
Left	6 (1)	15 (2.5)	5 (0)	12.5 (0)	29 (39)	72.5 (97.5)
Total	32 (10)	26.6 (8.3)	14 (4)	11.6 (3.3)	74 (106)	61.6 (88.3)

Numbers in parentheses are values of the control group.

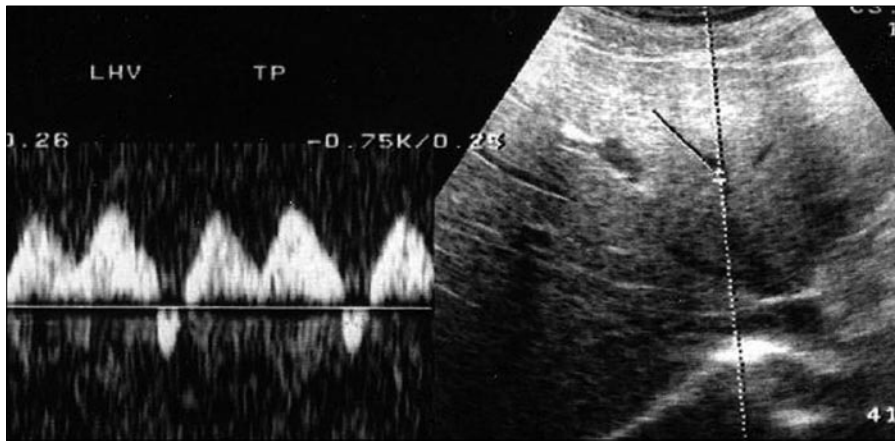


Figure 2. A 10-year-old boy with acute viral hepatitis. Doppler sonographic image shows triphasic flow pattern within left hepatic vein.

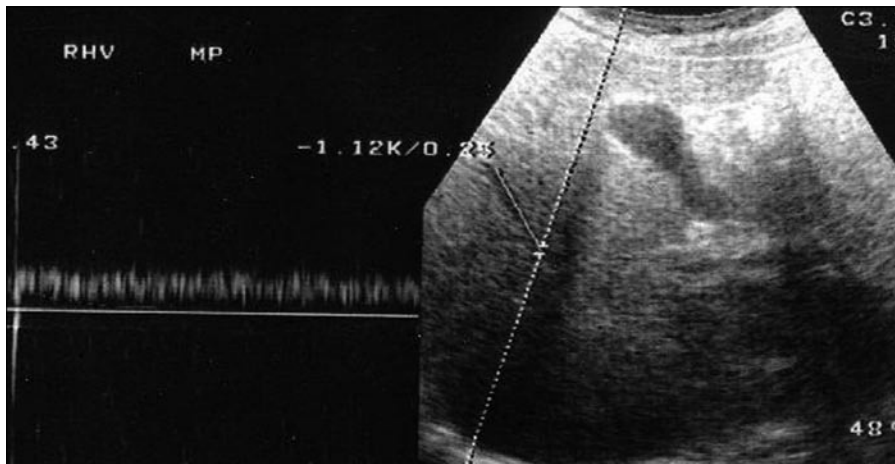


Figure 3. A 7-year-old girl with acute viral hepatitis. Doppler sonographic image demonstrated monophasic flow pattern within the right hepatic vein.

In group 1, US of the abdomen was unremarkable in 12 cases (30%) and abnormal in 28 cases (70%). In group 2, all (100%) were normal. $P=0.000$ was regarded as significant (chi-square test).

Some of the cases from group 1 with abnormal sonography findings had

more than one abnormal sonography finding. In group 1, 17 cases (42.5%) showed changes in parenchymal echogenicity. Extrahepatic findings such as splenomegaly, thickening of the gallbladder wall and edema, sludge in the gallbladder, lymphadenopathy (LAP), ascites, and pleural effusion were accep-

ted as abnormal sonographic findings, and the patients from group 1 with these findings made up the 70% (n=28) with abnormal sonographic findings.

In the 28 cases in group 1 with abnormal sonographic findings, decreased echogenicity of the liver parenchyma was present in 10, heterogeneity of the liver parenchyma in 5, coarsened echogenicity of the liver parenchyma in 2, increased periportal echogenicity in 7, thickening of the gallbladder wall and edema in 4, sludge in the gallbladder in one case, hepatomegaly in 19, splenomegaly in 11, periportal-paraortic-paracaval-mesenteric LAP in 4, ascites in 2, and pleural effusion in one case.

Of the 28 cases (84 hepatic veins) in group 1 that also had an abnormal gray scale US of the liver, 55.9% of them had a triphasic flow pattern, 28.5% had a monophasic flow pattern, and 15.4% had a biphasic flow pattern. Of the 17 cases in group 1 having changes in liver parenchyma echogenicity, eleven had monophasic and/or biphasic flow patterns in all 3 of their hepatic veins (Table 3).

In group 1, the cases with unremarkable gray scale ultrasonographic examinations of the abdomen did not have simultaneous monophasic or biphasic flow patterns in all 3 of their hepatic veins. Of 12 cases in group 1 with normal gray scale ultrasonographic findings of the abdomen, a triphasic flow pattern was observed in 75% of the 36 hepatic veins, a monophasic flow pattern in 22.2% of them, and a biphasic flow pattern in 2.8% of them. The abdominal sonography results and hepatic vein flow patterns of group 1 are shown in Table 3.

When compared with the overall percentages of flow pattern incidences in group 1, in the cases having abnormal sonographic findings of the liver, the incidence of the triphasic flow patterns was lower and the incidence of monophasic and biphasic flow patterns was higher. When compared with the overall incidences of flow patterns, the differences between the two groups are more evident. The distribution of the hepatic vein flow patterns of the groups is shown in Table 4.

In 50% of the cases in group 1 and in 80% of the controls in group 2, triphasic patterns were observed in all of three hepatic veins. A triphasic pattern was seen in only two hepatic

Table 3. Abdominal ultrasonography results and hepatic vein flow patterns of the cases in the group with AVH.

Abdomen ultrasonography results	# cases	Hepatic vein		
		Right M -B -T	Middle M -B -T	Left M -B -T
Normal	12	5-0-7	3-1-8	0-0-12
Abnormal	28	12-2-14	6-6-16	6-5-17
*Decreased echogenicity	10	5-2-3	3-2-5	1-3-6
*Heterogenous echogenicity	5	5-0-0	1-4-0	3-2-0
*Coarsened echogenicity	2	2-0-0	2-0-0	2-0-0

M: Monophasic B: Biphasic T: Triphasic
* Cases that had echogenicity changes in liver parenchyma.

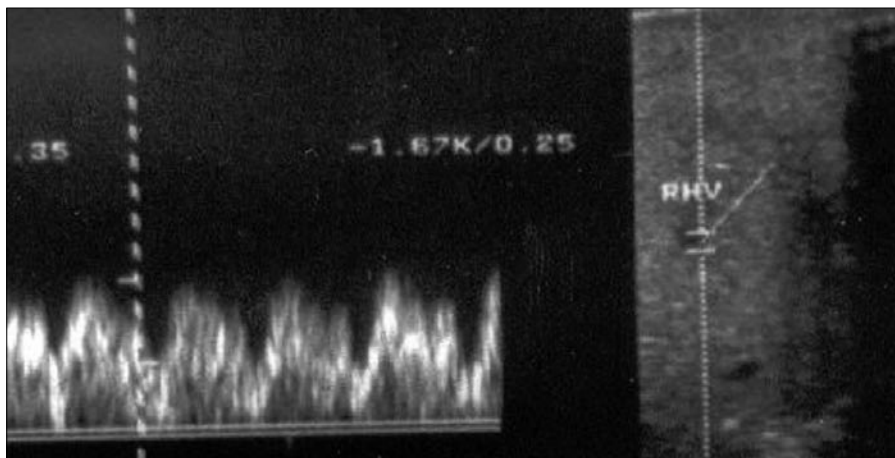


Figure 4. A 6-year-old boy with acute viral hepatitis. Doppler sonographic image shows biphasic flow pattern within the right hepatic vein.

veins in 10% of the cases in group 1 and in 7.5% of the controls in group 2. In 15% of the cases in group 1 and in 10% of the controls of group 2, there was a triphasic pattern in only one hepatic vein (Figure 2).

A monophasic pattern was observed (Figure 3) in all of three hepatic veins in 10% of the cases in group 1 and in 2.5% of the controls in group 2. While there was a biphasic pattern in all of the hepatic veins in 2.5% of cases in group 1, none of the controls in group 2 had a biphasic pattern in any of the hepatic veins. (Figure 4).

In both groups, among three main hepatic veins, a triphasic flow pattern

was observed most commonly in the left hepatic vein, a monophasic flow pattern in the right hepatic vein, and a biphasic flow pattern in the middle hepatic vein (Table 2).

In both groups, the hepatic vein flow velocities (V_{max}) were highest in the left hepatic veins followed by the middle hepatic veins, whereas the lowest mean velocity was found in the right hepatic veins. The flow velocity distribution of the hepatic veins in group 1 and 2 is shown in Table 5.

There was no significant difference ($p > 0.05$) in the flow velocities of the hepatic veins of groups 1 and 2 when an in-between group analysis was per-

formed; however, in each group, the flow velocity differences between the right hepatic veins and middle hepatic veins, the right hepatic veins and left hepatic veins, and the middle hepatic veins and left hepatic veins were statistically significant ($p < 0.05$).

In both groups, there was no statistically significant difference between flow patterns and velocities of the hepatic veins relative to age, gender, feeding status, and activity.

Discussion

The effects of cardiac function, and both intraabdominal and intrathoracic pressure on hepatic vein flow patterns have been reported (1). These influence not only the velocity of hepatic vein flow, but also its pulsatility. Pulmonary venous hypertension and increased right heart pressure will cause an increase in hepatic vein pulsatility, while increased thoracic pressure (Valsalva maneuver) decreases the venous return to the right heart and decreases hepatic vein pulsatility (1, 4, 5, 7).

The liver is more compliant in children as compared to adults (9). Normally, due to the reversal of flow that occurs during atrial systole, a triphasic flow pattern is observed in hepatic veins. When the liver is rigid, as in instances of hepatic diseases or masses, obesity, and the presence of ascites or increased intraabdominal pressure, a depression occurs in the Doppler wave (biphasic flow pattern), or normal pulsations disappear entirely (monophasic flow pattern) (1, 3-5, 7).

After eating, the flow in hepatic veins does not change (1, 8). Following physical exercise, the maximum hepatic vein flow velocity increased (8). Gender, exercise, and food intake do not change hepatic vein flow patterns (2). In the present study, we found no relationship between age, gender, feeding status, and activity, and the flow patterns or flow velocities of the hepatic veins in both groups.

Based on a study of 100 healthy children, Jequier et al. (1) emphasized that no significant differences were seen in hepatic vein flow patterns of children who were hungry or in children who had just eaten. Among children who were agitated or calm, or even sleepy, no significant differences were seen in hepatic vein flow patterns. However, age was found to be highly significant in most of the newborns

Table 4. Percentile distribution of hepatic vein flow patterns of the two groups.

	# patients	# hepatic veins	Flow pattern (%)		
			Monophasic	Biphasic	Triphasic
Group 1	40	120	26.6	11.6	61.6
Group 1-A	12	36	22.2	2.8	75
Group 1-B	28	84	28.5	15.4	55.9
Group 2	40	120	8.3	3.3	88.3

Group 1: patients with AVH Group 1-A: group 1 patients with normal abdominal US
Group 1-B: group 1 patients with abnormal abdominal sonography Group 2: control group

Table 5. Distribution of hepatic veins flow velocities of group 1 (AVH) and group 2 (controls).

	Group 1		Group 2	
	Mean (cm/sec)	SD	Mean (cm/sec)	SD
Right	14.85	8.96	15.42	10.22
Middle	22.17	13.87	21.97	13.01
Left	34.20	20.76	32.05	17.10

HV: hepatic vein AVH: acute viral hepatitis

when monophasic flow was present. In the present study, we did not detect a significant correlation between age groups and hepatic vein flow patterns in either of the two groups. The difference between the results observed in group 2 of the present study and the former study are probably related to the age of the cohort. In the present study, there were no children below one month of age.

Meyer et al. (9) observed triphasic flow patterns in the hepatic veins of 89% of 27 healthy children. Jequier et al. (1) also found that in 42% of healthy children, a triphasic pattern was observed in all three hepatic veins. Among three main hepatic veins, a triphasic flow pattern was observed mostly in the middle hepatic vein. This is probably due to the fact that this vein is technically well-suited in terms of the perspective of the Doppler angle used to sample the vein. Doppler angle alone does not cause flow differences in hepatic veins. A discrepant flow pattern was most commonly observed in the right hepatic vein (1).

In a study by Jequier et al. (2), triphasic flow patterns were most commonly obtained from the left, middle, and right hepatic veins, respectively. These findings are consistent with both groups in our study. Left and middle hepatic veins are best examined in the transverse plane at the level of the xiphoid process. From this angle, the veins are almost parallel to the Doppler beam, allowing optimal reception of their signals (10). Hepatic vein flow pattern was different from one vein to another in the majority of the children; the right hepatic vein having the least triphasic flow. The right hepatic vein was the most difficult to examine both with anterior and lateral approaches. Its angle is often horizontal to the confluence of the inferior vena cava, as seen by the anterior approach, and attempting electronic angle correction could not overcome the difficulty (2).

In the present study, hepatic vein flow velocities (V_{max}) were found to be

the highest in the left hepatic veins in both groups. The lowest flow velocities were found in the right hepatic veins. These findings are consistent with the results of previous investigators (3).

Arda et al. (6) studied the Doppler analysis of the hepatic veins of 30 patients with early stage chronic liver parenchyma disease and 40 healthy patients. Triphasic patterns were observed in all of the healthy patients. In patients with liver parenchyma disease, only 26.6% had a triphasic pattern, while the remainder had biphasic or monophasic patterns. Dietrich et al. (7) also evaluated the flow pattern only in the right hepatic veins of 135 patients with chronic hepatitis C and 75 healthy volunteers. Of the patients with chronic hepatitis C, 47% had triphasic, 36% had monophasic, and 17% had biphasic flow patterns; in the healthy group, 75% had triphasic, 16% had monophasic, and 9% had biphasic flow patterns. Szekely and Kupcsulik (11) studied cases with steatosis, chronic active hepatitis, and cirrhosis, and they observed a biphasic flow. In cirrhosis, they determined that the specificity of monophasic flow was 100%, and its sensitivity was 71%.

As is evident in these reports and in the present study, when groups with hepatitis were compared to healthy groups, the incidence of a triphasic flow pattern was significantly higher, and the incidence of monophasic and biphasic flows patterns was significantly lower in the hepatitis groups.

In patients with miscellaneous causes of chronic diffuse liver disease, similar changes may be seen in hepatic vein flow patterns (4-7, 11). In the present study, particularly in the patients who had changes in liver parenchyma echogenicity, the hepatic vein flow patterns were frequently found to be either monophasic and/or biphasic.

In conclusion, the absence of a triphasic flow pattern can be seen in newborns. Therefore, when hepatic parenchymal disease is suspected and a monophasic flow pattern is found

with a Doppler study of the hepatic veins, the examiner should be careful not to mistake a normal variant for a pathological finding. It must be confirmed if the change of a previously triphasic hepatic vein flow to a biphasic or monophasic flow in a given vein should be considered as a possible sign of parenchymal liver disease in children.

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