CORRELATION BETWEEN THE SERUM LEVELS OF TRANSAMINASES AND THE FIBROSE STAGE OF THE LIVER IN CHRONIC HEPATITIS

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Keywords: *chronic hepatitis, liver fibrosis, percutaneous liver biopsy, ALAT, ASAT*

Abstract: *Fibrogenic reaction is a consequence of immunological mechanisms that have developed in the presence of the virus influencing fibrogenesis. The aim of this study is to observe whether there is any correlation between histological changes and high ALAT and ASAT values. All patients included in our study presented some degree of fibrosis, a fact that may be explained by the easy subjective symptomatology of the disease and the lack of reliable tests, except liver biopsy, for the detection of fibrosis. The ASAT / ALAT report has been <1 in all cases. According to the results we have obtained, the histological activity index may be correlated with the degree of fibrosis, and the ASAT and ALAT serum values are significant in relation to the degree of fibrosis; therefore they may be used for the purpose of monitoring the treatment of fibrosis regression during therapy.*

Cuvinte cheie: *hepatita cronică virală, fibroza hepatică, puncție biopsie hepatică, ALAT, ASAT*

Rezumat: *Reacția fibrogenică este consecința mecanismelor imunologice desfășurate în prezența virusului care are influență asupra fibrogenezei. Scopul studiului a fost de a observa dacă există o legătură între modificările histologice şi valorile crescute ale ALAT şi ASAT. În acest studiu toți pacienții au avut un anumit grad de fibroză, fapt explicat prin simptomatologia subiectivă uşoară a bolii şi lipsa unor teste fiabile pentru descoperirea fibrozei în afară de biopsia hepatică. Raportul ASAT/ALAT a fost <1 la toate cazurile. Conform rezultatelor obținute indicele de activitate histologică este în corelație cu gradul de fibroză, valorile serice ASAT şi ALAT sunt semnificative în raport cu gradul de fibroză, ele putând fi recomandate în urmărirea tratamentului de regresie a fibrozei sub tratament.*

INTRODUCTION

Hepatic viral infections are one of the major causes for the development of liver fibrosis. It is still uncertain why human beings are not able to eliminate the infection with B and C hepatitis viruses (1). Once in the body, 40-50% of the hepatic viruses latently evolve towards a chronic form; in a relatively long period, of 20 to 30 years, 20% of these viruses evolve to cirrhosis. 1-4% of the patients with cirrhosis will present hepatocellular carcinoma.

Fibrosis is a dynamic process, which depends on the transcriptional gene and the extra-cellular matrix that synthesizes the proteoglycans and organizes them into a three-dimensional structure.

Experimental models (2) contributed to defining the mechanisms whereby hepatic fibrosis is induced. Fibrogenic reaction is a consequence of immunological mechanisms that have developed in the presence of the virus influencing fibrogenesis.

PURPOSE OF THE STUDY

The purpose of this study is to investigate the correlation between the histological activity index (HAI) and the degree of fibrosis to the serum levels of alanin-aminotransferase (ALAT) and aspartatamino-transferase (ASAT), in patients with chronic hepatitis of B and C viral etiology, taking as reference standards the histological results obtained from the material collected by liver biopsy.

MATERIAL AND METHOD

This study is based on the observation of 140 patients with chronic viral hepatitis (type B, C and B + C) at whom percutaneous liver biopsy (PLB) was performed in Oradea County Hospital, between March 2009 - March 2010.

The criterion for inclusion in the study was the absence of antiviral therapy in patients with chronic hepatitis.The distribution of cases by sex, age and etiology is shown in Table I

The histological diagnosis was based on the material obtained by liver biopsy. Tissue samples were placed in 10% formaldehyde solution.

The processing was performed in paraffin blocks of which 5µ slices were cut and colored in standard hematoxylin and eosin staining, Masson Trichrome staining and the reticulin method.

The histopathological changes observed were the parenchymal lesions of the liver, as well as the size and composition of the port space, the changes in Kupffer cells, biliary canalicula and others.

The liver lesions were categorized and scored using the Metavir and the Knodell scores (3.4). Such forms of evaluation are essential for diagnosing, treatment choice, prognosis estimation, and the clinical observation of these pathologies.

The serum levels of ALAT and ASAT were obtained by kinetic method using a Hitachi 902 Cobas-Mira device type (normal values: ASAT <38 U/L in men and <32 U/L in women, ALAT <41 U/L in men and <31 U/L in women).

For the statistical interpretation of data, the SPSS, version 17, was used for calculating the averages of parameters, the standard deviations, the median, the coefficient of variations, the variation range (min-max) and the quartila variation (5).

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Table no. 1. The distribution of subjects in relation to etiology, sex and age groups

ETIOLOGY																	
HCV						HBV						HBV+HCV					
<40 years old		40-60 years old		>60 years old		<40 years old		40-60 years old		>60 years old		<40 years old		40-60 years old		>60 years old	
M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
FREQUENCY																	
12	18	35	45	2	2	5	7	5	3	1	0	2	0	1	1	1	0
Total: 114 cases						Total: 21 cases						Total: 3 cases					
PERCENT																	
24.5	27.7	71.4	69.2	4.1	3.1	45.5	70	45.5	30	9.1	0	50	0	25	100	25	0

Table no. 2. Mean values of transaminases in chronic viral hepatitis, in relation to etiology and sex

SEX	ETIOLOGY		ALAT	ASAT
MASCULINE	HVC	Mean	94.43	82.29
		N	49	49
		Std. Deviation	18.753	18.677
	HVB	Mean	94.45	79.45
		N	11	11
		Std. Deviation	9.310	16.121
	HVC+HVB	Mean	92.25	74.00
		N	4	4
		Std. Deviation	13.817	14.213
FEMININE	HVC	Mean	90.75	77.85
		N	65	65
		Std. Deviation	21.091	15.733
	HVB	Mean	104.50	90.30
		N	10	10
		Std. Deviation	20.845	22.774
	HVC+HVB	Mean	102.00	67.00
		N	1	1
		Std. Deviation	.	.

The Student Test was used to compare the average values with the normal distribution.

RESULTS

Laboratory results were compared with the results obtained after performing liver biopsy, which constituted the reference standard for the diagnosing of liver fibrosis.

The mean values of serum transaminases (ALAT, ASAT) (see Table II) were significantly increased statistically ($p < 0.001$), as compared to normal values in both chronic hepatitis B (HBV) and in chronic hepatitis C (HCV). The highest values of ASAT and ALAT, as compared to the normal ones, were recorded in HBV, with a mean value of 84.62 U/L, respectively 99.24 U/L.

Mean transaminase values are higher in males as compared to those in females, though the differences are not statistically significant ($p > 0.05$) for both ALAT and for ASAT).

Depending on the value of the necrotic inflammatory index, the hepatitis activity was considered minimally active (METAVIR score A1F1-A1F2), moderately active (METAVIR score A2 or 3F2 or 3) and severely active (METAVIR score A3F3 or 4) (Table III)

ASAT Values

- were higher in the first category, the one with minimum active hepatitis (A1F2);
- were increased in patients with A1F2 METAVIR score (78.25±17.06)
- were higher in moderately active hepatitis, at those with A3F3 (88) activity – having no statistical significance for the present study, as there is only one case.

ALAT values:

- the highest values were recorded in the first category (minimum active hepatitis A1F2) (78.25±17.06);
- in terms of age groups, a higher value was obtained at the age group of people over 60 years old, in those with hepatitis C (117±31003), as compared to other etiological categories.

ASAT and ALAT values were consistently higher in patients with viral hepatitis C, as compared to the other categories, presenting an average value of 79.25 ±17 125 ASAT and of 92.33± 20 116 ALAT.

Table no. 3. The inflammatory necrotic index and the serum levels of the transaminases

ACTIVITY	SCORE		ASAT	ALAT
MINIMALLY ACTIVE	AOF1	Mean	68.00	74.00
		N	2	2
		Std. Deviation	.000	1.414
	A1F0	Mean	71.83	87.00
		N	12	12
		Std. Deviation	11.769	17.220
	A1F1	Mean	70.55	86.65
		N	20	20
		Std. Deviation	10.570	16.516
	A1F2	Mean	78.25	94.80
		N	20	20
		Std. Deviation	17.060	22.336
MODERATELY ACTIVE	A2F1	Mean	67.00	77.60
		N	5	5
		Std. Deviation	3.317	14.153
	A2F2	Mean	84.96	94.53
		N	51	51
		Std. Deviation	18.702	18.196
	A2F3	Mean	87.20	100.92
		N	25	25
		Std. Deviation	19.205	21.629
	A3F3	Mean	88.00	116.00
		N	1	1
		Std. Deviation	.	.
	A3F4	Mean	87.00	115.00
		N	1	1
		Std. Deviation	.	.
SEVERELY ACTIVE	A2F3	Mean	70.50	99.50
		N	2	2
		Std. Deviation	3.536	4.950
	A3F3	Mean	94.00	98.00
		N	1	1
		Std. Deviation	.	.

The majority of patients included in the study presented moderately active activity, the histological activity index (HAI) ranging between 9 and 12 points, while at the 55 patients with minimally active activity, 2-7 points were obtained. The Spirman correlation coefficient was of 0.79 ($p < 0.01$) for patients with chronic hepatitis C, indicating a correlation between the HAI score and the fibrosis stage.

Table no. 4. Serum transaminase values by etiology types

Etiology/ Transaminase		No. of cases	Minimum	Maximum	Mean	Std. Deviation
HCV	**ALAT**	114	46	149	92.33	20.116
	ASAT		60	131	79.75	17.125
HBV	**ALAT**	21	76	141	99.24	16.288
	ASAT		63	135	84.62	19.853
HCV+HBV	**ALAT**	5	72	103	94.20	12.736
	ASAT		61	94	72.60	12.700

DISCUSSIONS

Several studies (6,7,8,9,10) have discussed the values of serum markers (ALAT, ASAT) in chronic viral hepatitis, especially at cases of infection with the C virus; however, the fluctuations in serum transaminase levels and their connection to inflammatory activity and the degree of fibrosis is still uncertain. Among the cases of hepatitis that have been studied so far, the ones caused by virus C raise special problems, as 20% of the cases evolve to cirrhosis and 1-4% of them develop liver-cell carcinoma each year.

The control of infection, of fibrosis progression and the therapeutic trials for the remission of fibrosis have been actively investigated lately. Recent years research on the factors that initiate and influence the development of extra-cellular matrix towards fibrosis show that these processes may be reversible (11,12,13,14).

Our aim has been to observe whether there is a correlation between histological changes and high ALAT and ASAT values. All patients included in our study presented some degree of fibrosis, a fact easily explained by the easy subjective symptomatology of the disease and lack of reliable tests for the detection of fibrosis, except liver biopsy. Although there are systems to detect serum parameters indicating liver fibrosis, these are not reliable enough and therefore are not used extensively (15), biopsy remaining the main method for detecting liver fibrosis. Performing percutaneous liver biopsy in patients with normal levels of serum transaminases is still under study (16,17,18). Our results indicate a significant correlation between the degree of fibrosis and the serum values of ALAT and ASAT. The ASAT / ALAT report is <1 in all cases, being consistent with the results of some authors (19) and inconsistent with the results of others (20). Some authors consider that increased ALAT levels might be correlated with a high degree of fibrosis progression, while the normal values of this parameter are not frequently associated with it (17.21).

CONCLUSIONS

According to the results we have obtained, the histological activity index may be correlated with the degree of fibrosis, and the ASAT and ALAT serum values are significant in relation to the degree of fibrosis; therefore they may be used for the purpose of monitoring the treatment of fibrosis regression during therapy.

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