

ON THE ACTIVITY OF SOME ENZYMES IN ALCOHOLIC AND NON-ALCOHOLIC HEPATIC STEATOSIS

ANCA-MIRELA AMARIEI¹, GABRIELA DUMITRU¹, ELENA CIORNEA^{1*}

Key words: hepatic steatosis, alkaline phosphatase, alanine- and aspartate-aminotransferase, γ -glutamyl-transferase

Abstract: The study, developed on a series of patients - both women and men - of various ages, suffering from non-alcoholic and alcoholic hepatic steatosis, was devoted to the activity of some enzymes, bearing important implications in the evaluation of the health condition of the hepatic tissue, such as alanine- and aspartate-aminotransferase, γ -glutamyl-transferase and alkaline phosphatase. The results obtained evidence significant differences both between men and women, and between the categories of age under study, in most cases the values recorded being distinctly higher than the reference interval viewed as physiologically normal.

INTRODUCTION

The extent of affection of the hepatic cells, known as increasing the permeability of the hepatocyte membrane, although not necessarily lysis or necrosis of such cells, is usually detected by the increased amounts of some cellular enzymes in the serum (Abdelmack *et al.*, 1995; Angulo, 2002). The seric level of such enzymes varies with the number of affected hepatocytes, with the lesion extent of each cell, with the speed at which the lesions had been produced and speed at which the involved enzymes are eliminated from the serum (Cojocaru, 1997; Cojocaru *et al.*, 2007).

Consequently, in various liver diseases, various spectra of the activity of the lesion-producing enzymes may be observed, as a function of the etiology and evolution stage of hepatopathy (Pâslaru, 2004).

The enzymes employed for the evaluation of the hepatic function are the aspartate-aminotransferase (ASPT, GOT) and alanine-aminotransferase (ALAT, GPT), also known as transaminases, as well as alkaline phosphatase (AF, ALP) and γ -glutamyl-transferase (GGT, γ -GT). Generally, such enzymes do not represent specific markers of the hepatic disfunction, with the exception of the hepatic isoenzyme of the alkaline phosphatase. ALAT and ASPT are largely employed in clinical investigations as sensible, although not specific indices of the acute hepatic lesions, independently on any etiological consideration. The literature of the field evidences that, out of the two aminotransferases, the ALAT activity is much more specific to the liver, comparatively with that of ASPT (Negură, 2008).

Determination of the plasmatic activity of γ -GT represents a sensible marker of hepatobiliary pathology, even if such an analysis makes no differentiation between cholestatic and hepatocellular pathologies.

The present paper aims at determining the activity of certain enzymes, playing a major part in the evaluation of liver physiological condition, such as alanine- and aspartate-aminotransferase, γ -glutamyl-transferase and sanguine alkaline phosphatase, in patients suffering from alcoholic and non-alcoholic hepatic steatosis with ages between 31 and 77 years.

MATERIALS AND METHOD

The activity of some enzymes with special importance in liver pathology (alkaline phosphatase, alanine- and aspartate-aminotransferase, γ -glutamyl-transferase) has been determined in patients of various ages, suffering from alcoholic and non-alcoholic hepatic steatosis, hospitalized at the “Mavromati” County Hospital of Botoșani. Colorimetric methods have been applied, the determinations being made on a Hitachi 912 ISE biochemical analyzer.

For assuring the reliability of the obtained data, the experimental results obtained have been statistically processed, a series of statistical indices - such as standard error, coefficient of average value variation and probability - being calculated (Varvara *et al.*, 2001; Zamfirescu and Zamfirescu, 2008).

RESULTS AND DISCUSSION

Study on the activity of seric enzymes in patients of feminine sex affected by non-alcoholic hepatic steatosis evidences, for all categories of age under study, higher values of aminotransferases, comparatively with the values of the normal interval. Thus, the 31-40 year category of age recorded an average ALAT value of 64.975 U/L, while - in the same group - the average value of the ASPT enzyme was of 63.425 U/L. For patients of feminine sex belonging to the 41-50 years category, the average value of ALAT was of 58.7 U/L, and that of ASPT - of

54.05 U/L. The last category of age (61-71 years) showed an average value of ALAT of 41.74 U/L and an ASPT average value of 38.86 U/L, respectively (Table I).

According to literature data, in non-alcoholic hepatic steatosis, the plasmatic concentrations of aminotransferases may be 2-3 times higher than the normal concentrations, the ASPT /ALAT ratio recorded being ≤ 1 (Negură, 2008). The results of the present study show double average values of ALAT, comparatively with the superior limit of the normal values for the 31-40 and 51-60 year categories of age.

Table I. Activity of some enzymes with diagnosis value in female persons with non-alcoholic hepatic steatosis

Biochemical parameters	Normal values	Statistical indices	Group of age			
			31-40 years	41-50 years	51-60 years	61-71 years
AF	50-250 U/L	n	8	8	6	5
		X (%)	96.93	100	71.08	81.27
		± SE	1.13592	0.86602	2.28643	2.92574
		VC %	1.16	0.86	2.78	2.83
		t	-	6.046	28.865	14.166
		p	-	p<0.001	p<0.001	p<0.001
ALAT	Under 31 U/L	n	8	8	6	5
		X (%)	79.01	72.46	100	51.53
		± SE	0.42542	0.38591	0.59986	0.59632
		VC %	1.85	1.85	1.8	3.19
		t	-	10.924	22.402	31.719
		p	-	p<0.001	p<0.001	p<0.001
ASPT	Under 31 U/L	n	8	8	6	5
		X (%)	81.3	69.29	100	49.82
		± SE	0.34576	0.36253	0.5808	0.45563
		VC %	1.54	1.89	1.81	2.62
		t	-	18.713	22.302	42.947
		p	-	p<0.001	p<0.001	p<0.001
γ-GT	12-48 U/L	n	8	8	6	5
		X (%)	63.23	85.46	98.88	100
		± SE	0.81913	0.48011	1.39628	2.583
		VC %	2.56	1.11	2.41	4.01
		t	-	33.479	31.499	19.711
		p	-	p<0.001	p<0.001	p<0.001

AF = alkaline phosphatase; ALAT = alanine-aminotransferase; ASPT = aspartate-aminotransferase;

γ-GT = γ-glutamyl-transferase; n = count; X = average value; SE = average standard error;

VC = average variation coefficient; t = Student test; p = probability

As to the activity of cholestasis enzymes, AF recorded normal average values for the 51-60 year and 61-70 year categories of age, of 201.166 U/L and 230.4 U/L, respectively, higher values being recorded for the other groups of age, while γ-GT registered higher average values in all four categories of age under investigation.

Statistically, the values recorded by the seric enzymes here analyzed for all categories of age are highly significant ($p < 0.001$).

In some situations, steatosis evolves towards steatohepatitis and fibrosis, involving deterioration of the hepatic functions and, finally, even cirrhosis. The cause of such an evolution is not known, but it may be related to an increased oxidative stress (Negură, 2008).

Another objective of the present study was to determine the activity of the same enzymes in male patients affected by alcoholic hepatic steatosis (Table II), the average values of amino-transferases being moderately increased, comparatively with the normal interval, for all categories of age under study.

Table II. Activity of some enzymes with diagnosis value in male persons with alcoholic hepatic steatosis

Biochemical parameters	Normal values	Statistical indices	Group of age			
			31-40 years	41-50 years	51-60 years	61-71 years
AF	100-290 U/L	n	5	5	10	6
		X (%)	100	96.18	87.21	77.51
		± SE	0.5099	0.86023	0.9	2.171
		VC %	0.28	0.5	0.81	1.72
		t	-	15.6	49.593	40.298
		p	-	p<0.001	p<0.001	p<0.001
ALAT	Under 40 U/L	n	5	5	10	6
		X (%)	56.86	100	35.8	37.54
		± SE	0.46	3.096	1.218	0.75483
		VC %	2.51	9.58	14.94	6.83
		t	-	9.991	11.639	15.732
		p	-	p<0.001	p<0.001	p<0.001
ASPT	Under 40 U/L	n	5	5	10	6
		X (%)	55.48	100	38.87	38.84
		± SE	0.4565	4.675	1.605	1.977
		VC %	1.21	6.89	8.65	8.25
		t	-	14.436	15.022	12.373
		p	-	p<0.001	p<0.001	p<0.001
γ-GT	12-48 U/L	n	5	5	10	6
		X (%)	41.83	78.97	100	77.83
		± SE	0.86023	20.068	0.38873	0.47726
		VC %	1.56	19.32	0.41	0.51
		t	-	5.426	181.782	107.377
		p	-	p<0.001	p<0.001	p<0.001

AF = alkaline phosphatase; ALAT = alanine-aminotransferase; ASPT = aspartate-aminotransferase; γ-GT = γ-glutamyl-transferase; n = count; X = average value; SE = average standard error; VC = average variation coefficient; t = Student test; p = probability

The activity of AF recorded average values outside the limits of the reference interval, namely a slight increase in all groups of age, the observation being made that, in male patients suffering from alcoholic hepatic steatosis, the enzyme attained its highest value in the 31-40 year category of age, and the lowest one - in the 61-77 year category. According to literature data, AF increases moderately in alcoholic hepatic steatosis, as well as γ-GT, a γ-GT/AF ratio > 5 between the two enzymes being evidenced in 50% of the cases (Gherasim, 2000).

As to the γ-GT activity, in all groups of age, higher average values of this cholestasis - indicative enzyme were recorded, comparatively with the superior limit of the normal interval, as follows: 123.2 U/L in the 31-40 year group, 232.2 U/L in the 41-50 year group, 294.8 in the 51-60 year group and 228.8 U/L, respectively, in the last group (61-77 year). The average values γ-GT activity in the group patient with ages between 31 and 40 years are two times higher than the superior limit of the reference interval while, in the 41-50 year and 61-77 year groups, they are 4.5 times higher than the superior limit of the normal extreme limit (Table II).

A comparative graphical representation (Fig.1) of the alkaline phosphatase activity in women and men of various ages, affected by non-alcoholic and alcoholic hepatic steatosis evidences considerably higher values in men, for all groups of age under investigation (31-77 years).

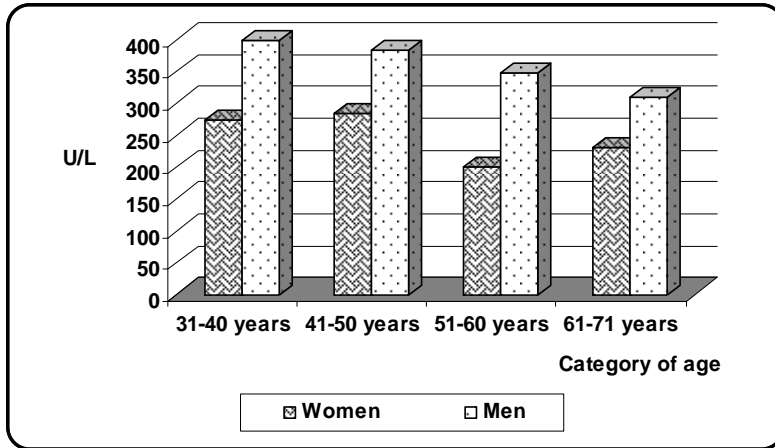


Fig.1. Alkaline phosphatase activity in patients with alcoholic and non-alcoholic hepatic steatosis

As to the activity of aminotransferases (Figs. 2-3), differences have been recorded, on one hand, as a function of sex and, on the other, as a function of the specific substrate of each enzyme in part, but also as a function of age category.

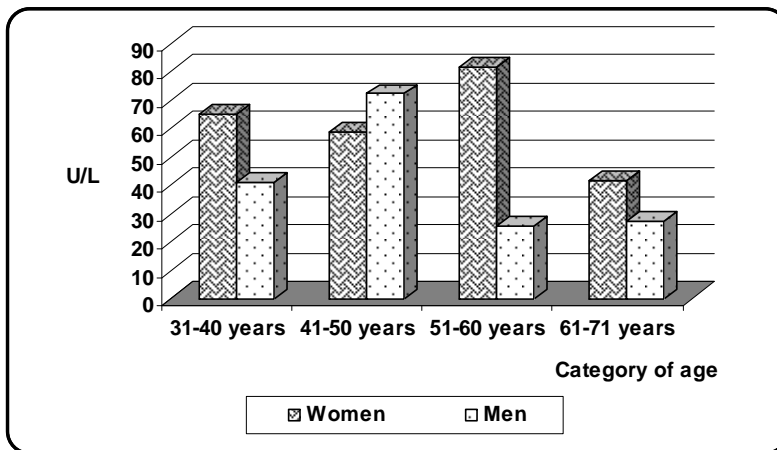


Fig.2. Alanine-aminotransferase activity in patients with alcoholic and non-alcoholic hepatic steatosis

Mention should be made of the fact that, in the case of alanine-aminotransferase, women evidence higher values in the activity of this enzyme, with the exception of the 41-50 year group

of age, while the aspartate-aminotransferase is higher in men than in women, with the only exception of the patients from the 51-60 year group of age. At the same time, the ALAT activity represents, on the average, half of the value registered for ASPT.

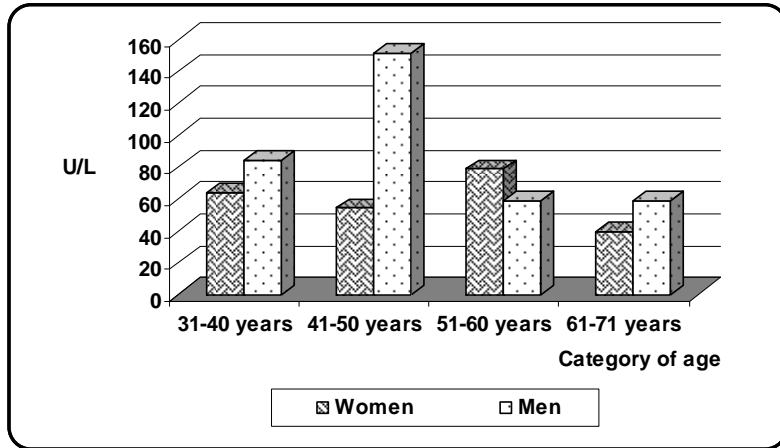


Fig.3. Aspartate-aminotransferase activity in patients with alcoholic and non-alcoholic hepatic steatosis

γ -Glutamyl-transferase shows higher values in the case of men, comparatively with women, quite ample oscillations being observed from one category of age to another, the highest levels being attained in patients with alcoholic hepatic steatosis with ages between 51 and 60 years (Fig.4).

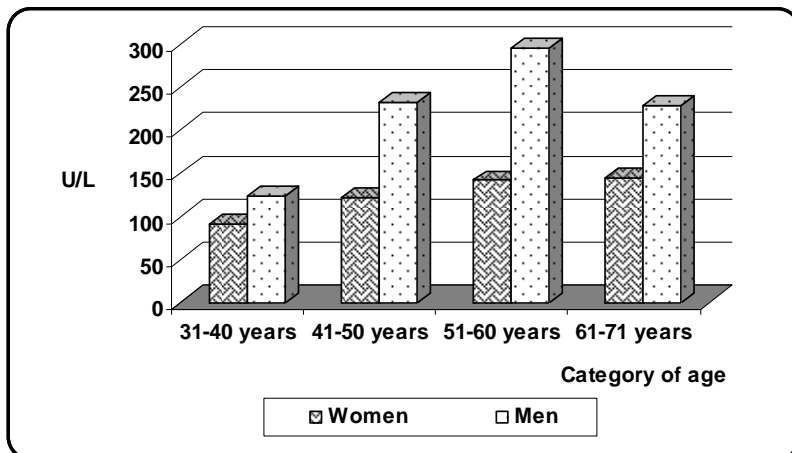


Fig.4. γ -Glutamyl-transferase activity in patients with alcoholic and non-alcoholic hepatic steatosis

CONCLUSIONS

Out of the enzymes here under investigation, alkaline phosphatase and γ -glutamyl-transferase record significantly higher activities in men, comparatively with women, for all groups of age under study, while the alanine-aminotransferase activity is more intense in women, with the exception of the 40-50 year category of age, and that of aspartate-aminotransferase is higher in men, with the exception of the 51-60 year category of age.

REFERENCES

- Abdelmack, M., Ludwig, J., Lindor, K.D., 1995. *Two cases from the spectrum of nonalcoholic steatohepatitis*, J. Clin. Gastroenterol., **20**: 127-130.
- Angulo, P., 2002. *Medical progress: nonalcoholic fatty liver disease*, N. Engl. J. Med., **346**: 1221-1231.
- Cojocaru, D.C., 1997. *Enzimologie*, Ed. Gama, Iași, 186-187.
- Cojocaru, D. C., Olteanu, Zenovia, Ciornea, Elena, Oprică, Lăcrămioara, Cojocaru, Sabina Ioana, 2007. *Enzimologie generală*, Ed. Tehnopress, Iași, 34-35.
- Gherasim, L., 2000 (sub red.). *Medicina internă- Bolile digestive hepatice și pancreatice*, vol. III, Ed. Medicală, București, 725-726.
- Negură, Anca-Mihaela, 2008. *Introducere în biochimia clinică*, Ed. Tehnopress, Iași, 240-245.
- Pâslaru, L., 2004. *Biochimie clinică*, Ed. Universității „Carol Davila”, București, 33-68.
- Varvara, M., Zamfirescu, Șt., Neacșu, P., 2001. *Lucrări practice de ecologie*, Ed. Univ. „Alexandru Ioan Cuza” Iași, 13-17.
- Zamfirescu, ȘT., Zamfirescu, Oana, 2008. *Elemente de statistică aplicate în ecologie*, Ed. Univ. „Alexandru Ioan Cuza” Iași, 85-88.

¹ Department of Biochemistry and Experimental Biology, Faculty of Biology, „Alexandru Ioan Cuza” University, Bd. Carol I, Nr. 20 A, 700506, Iași, Romania.

* ciornea@uaic.ro