https://doi.org/10.5272/jimab.2024304.5824

Journal of IMAB
ISSN: 1312-773X
https://www.journal-imab-bg.org

Journal of IMAB. 2024 Oct-Dec;30(4)

Original article

VALUE OF AMINOTRANSFERASES IN LIVER CIRRHOSIS

Miroslava Mihaylova[1], Strahil Strashilov[2], Pencho Tonchev[3]
1) Department of Gastroenterology, Nephrology and Hematology, Faculty of Medicine, Medical University of Pleven, University Hospital Georgi Stranski Pleven, Bulgaria.
2) Department of Plastic Restorative, Reconstructive and Aesthetic Surgery, Medical University Pleven, Bulgaria.
3) Department of Surgical Nursing Care, Faculty of Health Care, Medical University of Pleven, Bulgaria.

ABSTRACT:

Aim: To ditermine values of ASAT and ALAT and their ratio in different stages of liver cirrhosis.

Material and methods: A retrospective study was conducted, including patients with newly diagnosed liver cirrhosis from 01.01. 2017 to 31.12. 2021. Of all, 258 (71%) were men and 103 (29%) were women. The mean age of the study population was 57±11.4 years, with alcohol as the leading etiology in 262 (72.6%) of all cases. AT were measured at an upper reference limit of 40UI/ml. All were staged by Child-Pough and MELD Na score. IBM SPSS 26 and Excel statistics for data processing were used at a significant level of p< 0.05.

Results: Of all 361 individuals, normal AT were measured at 89 (24.7%), at 96 (25.76%) only with normal ASAT and at 233 (66.77%) only with normal ALAT. The mean value of ASAT increases significantly depending on the Child stage (p=.004) and is close to the significance of MELD Na (p=.036). Mean ALAT values were minimal to moderately elevated, with no significant association with them (p=.647, p=.020). 90% of individuals had an ASAT/ALAT ratio above 1, which showed substantial dependence on Child and MELD Na (p=.000, p=.000). A ratio above 2 was found at 194 (53.7%) mainly in Child C, which was associated with alcohol etiology.

Conclusion: The absolute values of ASAT and ALAT have no relationship with the severity of liver cirrhosis, unlike their ratio, which significantly increases.

Keywords:Aminotransferases, liver, Child-Pough, MELD Na,

INTRODUCTION:

The study of functional liver tests, including serum levels of ASAT and ALAT, is the most widely available and inexpensive way to detect liver dysfunction, but this does not exactly correlate with the severity and type of underlying liver damage. It is accepted that the deviation for a long time are highly suspicious for chronic liver disease, giving rise to future research [1]. A two-fold increase above the normal value is considered borderline [2], although the measured normal values of the enzymes do not exclude advanced fibrosis [3]. A rise in the ASAT/ALAT ratio is used to predict of progression to cirrhosis [4]. Based on the concept that baseline low ALAT levels can cause the ratio to rise above 1 even in healthy subjects, and higher levels in the person at risk can cause it to fall below 0.5 even in advanced fibrosis in a stage without symptoms, it has given a basis for developing new model dAAR based on these absolute values and the baseline of ALAT and age [5]**.** The same has been developed as a screening method to predict fibrosis over time. It was found that the measurement of ASAT and ALAT and subsequent APRI could identify asymptomatic cirrhotics in the general population with an incidence of 3.8‰ and gave a 59% greater chance of detection in the compensated stage as well [6].

Aim:

To determine values of ASAT and ALAT, as well their ratio in different stages in cases with liver cirrhosis.

MATERIAL AND METHODS:

The study was conducted retrospectively on cases with newly diagnosed liver cirrhosis in compliance with the ethical norms of the Helsinki Declaration. All included persons are over 18 years of age, admitted for treatment at the Gastroenterology Clinic and undiagnosed to date. Three hundred sixsty-one persons were included for the period from 01. 01. 2017 to 31. 12 2021. Of those examined, 258 (71%) were men and 103 (29%) were women. The mean age of the study population was 57±11.4 years, with alcohol as the leading etiology in 262 (72.6%) of cases. A panel of standard laboratory tests, as well as serological screening for Hepatitis B and C, abdominal ultrasound diagnostics to detect as-

cites, and upper gastrointestinal endoscopy to detect esophageal varices were made. All were graded by Child-Pough score system [https://www.mdcalc.com/calc/340/child-pugh-score-cirrhosis-mortality] and MELD Na [https://www.mdcalc.com/calc/10437 model-end-stage-liver-disease-meld?] was calculated. ASAT and ALAT values at an upper reference limit of 40 UI/ml were determined, as well as the ASAT/ALAT ratio. The analysis of the obtained results were established manly with Crosstabulation, Pearson Chi-Square tests, ANOVA and non-parametric test of Kruskal-Wallis, at a certain level of statistical dependence and p-value < 0.05. IBM SPSS 26 and Excel statistics for data processing were used.

RESULTS:

The measurement of ASAT in the three stages shows a progressive increase in its mean value and a measurement range that is significantly dependent on the Child stage and close to a significant MELD Na score. The level of ALAT shows that in all three stages, there are no significant defferences in the mean value, wich is slighty elevated above the reference limit, and the smallest variations are found in Child A. There is no significant relationship with the severity of liver disease. The ASAT/ALAT ratio increased with each stage, showing absolute significance in the direction of both scores (table 1, table 2).

Table 1. Values of measured indicators:

Child-Pough	MELD Na mean±sd	ASAT UI/ml mean±sd	ALAT UI/ml mean±sd	ASAT/ALAT ratio mean±sd
Child A (n=98)	9±2.75 (6 -19)	75.47± 88.80 (12.90 - 679.0)	53.15±46.47 (7.68- 222)	1.5±0.68 (0.47-3.78)
Child B (n=144)	13.6±4.88 (6-30)	105.42±150.86 (17.10-1134)	60±149.7 (6.50-1286)	2.32±1.12 (0.17-7.60)
Child C (n=121)	22.3±9 (6.5-40)	152.62±233.15 (21.70-1922)	68.12±119.66 (6.40- 812)	2.85±1.54 (0.62-8.60)

Table 2. ANOVA statistics shows significant difrences between measurments and score systems:

Dependence:	df	F	p-value
ASAT / Child-Pough	2	5.74	0.004
ALAT / Child-Pough	2	0.435	0.647
ASAT /ALAT ratio / Child-Pough	2	35.484	0
ASAT / MELD Na	32	1.533	0.035
ALAT / MELD Na	32	1.623	0.02
ASAT/ALAT ratio /MELD Na	32	321.439	0

Of the 361 examined, 223 (61.77%) had ALAT values in normal range, regardless of their stage according to Child, with the majority in all three groups showing normal ALAT values, without statistically significant difference between them (fig. 1). Out of all individuals, 96 (25.76%) had normal ASAT values. Across all three stages, based on the Child score, the number of cases with normal value is smaller, which is most pronounced for those in Child C (fig. 2). Additionally, 89 (24.7%), of those examined the measured values of both AT are normal. As the stage progresses, the number of cases with normal AT decreases, particularly in Child C (fig. 3). In terms of the ASAT/ALAT ratio, only 36 (9.97%) of the studied cirrhotic population had a ratio below 1, with Child A comprising the largest proportion at 21 (58.3%). A ratio above 1 was found in 131 (36.28%) individuals and above 2 in 194 (53.7%), with the ratio increasing significantly as the disease worsening. Statistically significant differences were noted in the Child-Pough and MELD Na scores for cases with ASAT/ALAT ratio above 1 and above 2. (Table 3).

Fig. 1. Distribution of cases with normal and elevated ALAT.

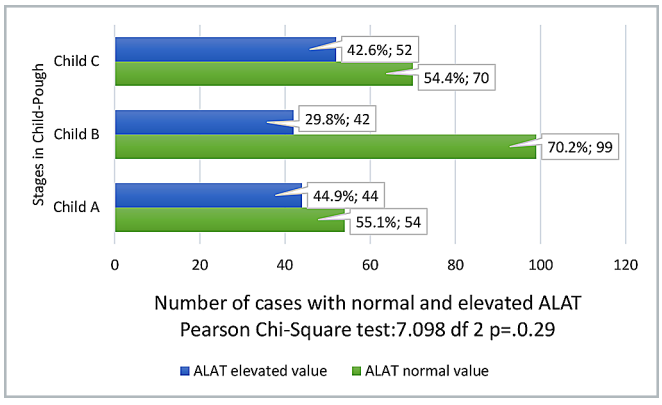

Fig. 2. Distribution of cases with normal and elevated ASAT.

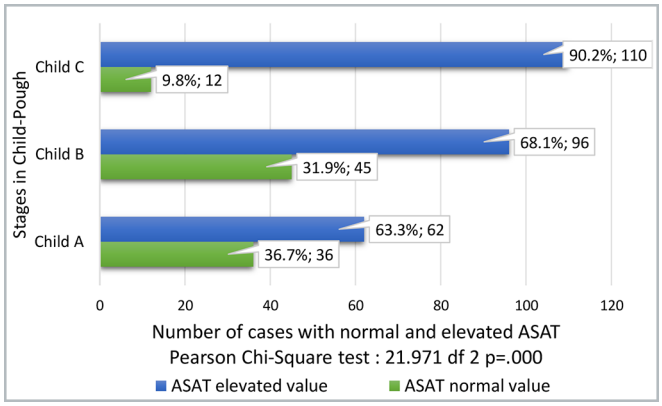

Fig. 3. Number of cases with normal Aminotransferases in the cirrhotic population.

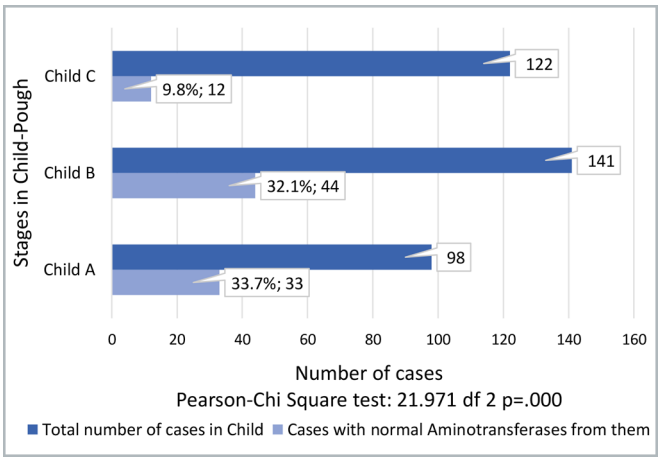

Table 3. Change in Child-Pough points and MELD Na when ASAT/ALAT increase:

ASAT/ALAT ratio	Child-Pough score	Kruskal-Wallis H test
<1 (n=36; 9.97%)	6.92±1.87	57.011 df 1 p=.000
>1 (n=131; 36.28%)	7.31±2.32	
>2 (n=194; 53.7%)	9.38±2.22	
ASAT/ALAT ratio	MELD Na score	Kruskal-Wallis H test
<1 (n=36; 9.97%)	12.22±5.1	15.857 df 1 p=.000
>1 (n=131; 36.28%)	13.92±6.6	
>2 (n=194; 53.7%)	17.05±7.57	

DISCUSSION:

The measurement of the value of aminotransferases is a simple, easy and accessible method to detect liver function deviation. Our findings suggest that abnormal liver enzyme levels can signal a serious underlying liver disease, and normal values do not rule out such. Elevated enzyme levels alongside other lab parameters, like low albumin and high bilirubin, indicate progression to fibrosis and cirrhosis in a review of cases with chronic hepatitis [7]. In studies with CHC and CHB cohorts, those transitioning to cirrhosis had higher values than healthy test controls [8]**.** Another study found, higher AT levels in CHB and cirrhosis, compared to those with pure CHB [9]**.** Our study group is heterogeneous, with a predominance of alcohol etiology. It was found that there was no significant difference in AT values between the different etiologies of liver cirrhosis [10]. Results showed ASAT values increased with the stage of Child and MELD Na score despite large variations. Only 25.76% of individuals had ASAT values within norm, and only 9.8% of them in Child C. Increased ASAT, rather than its absolute value, better indicated chronic liver disease presence. Chronic CHB cases with persistent elevated ASAT and normal or near-normal ALAT could indicate severe inflammation and progression to cirrhosis [11]. Histology showed higher ASAT in advanced fibrosis cases (grades 3 and 4) compared to grade 0 [12]. Mean ALAT levels were similar across the disease stages, with minimal to moderate elevations. Of all individuals 61.77% had normal values, independent of Child and MELD Na scores. These results show the ALAT test does not correlate with liver cirrhosis severity. Histology indicated ALAT values do not align with fibrosis severity, as normal and near-normal values can occur advanced liver disease [12]. An ALAT threshold value below 20 UI/ml can rule out serious underlying disease [13], but higher ones, even within the normal range, cannot ditermine diseases severity in HHC [13] and HHÂ studies [14]. On the other hand, higher enzyme values near or above the normal range in cirrhosis-free cases is more common in men, obesity and diabetes mellitus, and are linked to higher cardiovascular risk and alcohol liver damage, even with low-risk consumption [15,16]. Normal enzymes were found in 24.7% of the individuals with more cases with normal ALAT, regardless of the ASAT value in a leading alcohol etiology. ASAT and ALAT values have low specificity and sensitivity, for

identifying liver cirrhosis, and ALAT can be normal even in advanced disease, consistent with other studies [17]. A study of alcoholic cirrhosis found no correlation between AT values, complications, and mortality of patients having normal or near-normal AT [18]**.** Our results indicate that 90% of the individuals had an ASAT/ALAT ratio above 1, regardless of absolute AT values, significantly linked to Child score and MELD Na. Monitoring the ASAT/ALAT ratio can predict progression to liver cirrhosis, even with near-normal enzyme values that may mask it [19, 20]. In our group, 53.7% had a ratio above 2, and 75.4% of them in Child C, confirming its increase relates to liver disease severity [21]. High ratio were associated with the leading alcoholic etiology in our population and clinical decompensation, as supported by other studies [21, 22, 23, 24]. Its complex measurement with MELD predicts survival in severe liver dysfunction [23].

CONCLUSION:

Liver enzyme values by themselves are not informative about the severity of liver cirrhosis. The ASAT/ALAT ratio, however increases with the progression of liver disease and its decompensation. Its comprehensive assessment and other laboratory predictors may be better used to predict the severity of liver dysfunction. Despite its limited diagnostic value, measuring enzyme levels remains a simple and cost-effective method for detecting liver problems in the general population.

Abbreviations:

ALAT - Alanine aminotransferase
APRI - ASAT to Plated count ratio
ASAT - Aspartate aminotransferase
AT - Aminotransferases
CH - Chronic hepatitis
CHB - Chronic hepatitis B
CHC - Chronic hepatitis C
d AAR - dynamic ASAT/ALAT ratio
MELD Na - The Model for End-Stage Liver Disease

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Please cite this article as: Mihaylova M, Strashilov S, Tonchev P. Value of Aminotransferases in Liver cirrhosis. *J of IMAB*. 2024 Oct-Dec;30(4):5824-5828. [Crossref - https://doi.org/10.5272/jimab.2024304.5824]

Received: 20/05/2024; Published online: 22/10/2024

Adress for correspondence:
Miroslava Ivanova Mihaylova
Department of Gastroenterology, Nephrology and Hematology, Faculty of Medicine, Medical University of Pleven, University Hospital Georgi Stranski, Pleven;
8A, Georgi Kochev Blvd., Pleven 5800, Bulgaria.
E-mail: mihailova75.md@gmail.com,