THE INFLUENCE OF KIDNEY INJURY ON THE NON-INVASIVE ASSESSMENT OF HEPATIC INFLAMMATION

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Abstract: *Kidney injury plays a crucial part in the prognosis and progression of chronic hepatitis. The purpose of our study is to record the levels of serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) and to evaluate potential correlations between their level and altered renal function. Materials and methods: We ran a retrospective observational study based on information collected from 401 patient charts of the 1st Internal Medicine Clinic of the Emergency County Clinical Hospital Tirgu-Mures. The study was comprised of patients, based on informed consent, with recorded liver disease, with normal or diminished renal function. Results: Statistical significant difference was observed between serum AST and ALT levels and serum creatinine levels (p<0,0001). Conclusions: The serum aminotransferase levels tend to remain lower in patients with impaired renal function compared to the control group, thus raising the issue of underestimation of liver function in these patients and the need for different thresholds for AST and ALT or alternatives for hepatic inflammation quantification.*

INTRODUCTION

Kidney injury, whether acute or chronic, plays a crucial role in the prognosis and evolution of chronic hepatic disease, particularly in advanced stages. While a number of conditions can acutely affect both liver and kidneys, alcohol consumption and viral hepatitis cause more issues associated with cirrhosis. The most common causes of acute kidney injury are prerenal azotemia due to volume depletion, acute tubular necrosis and hepatorenal syndrome. Chronic liver disease affects the vascular reactivity, producing systemic vasodilatation and renal vasoconstriction. In its extreme form it leads to the hepatorenal syndrome. Early recognition and treatment for both conditions is important for patient survival. The accuracy of renal function assessment is usually limited due to the use of blood urea and serum creatinine only.(1,2) Creatinine level is significantly influenced by the development of cirrhosis, hyperbilirubinemia and nutritional status of the patient. Serum levels of specific enzymes, alanine aminotransferase (ALT), aspartate aminotransferase (AST) are employed to evaluate and track hepatic diseases, in terms of cellular inflammation.

Chronic kidney disease (CKD) represents a wide range of diseases associated with a progressive decrease of kidney function and modified glomerular filtration rate (GFR).(3)

It has been described that the level of serum ALT and AST commonly come in near the low normal values, in patients with CKD.(4) The exact cause of low serum ALT and AST in CKD remains disputed, accepted theories include pyridoxine deficiency or the presence of an inhibitory molecule in the uremic range. A recent study has also speculated that haemodillution could be incriminated in reducing serum ALT levels in CKD.(5,6,7)

MATERIALS AND METHODS

In order to achieve the objectives, a retrospective observational study was conducted based on information compiled from in-patient charts of the 1st Internal Medicine Clinic, County Emergency Clinical Hospital Tîrgu-Mureş in the interval of January 1st 2012 – December 31st 2013. The study enclosed, based on informed consent, 401 patients with recorded liver disease (F1to F4 fibrosis stage, of different etiology) with normal or diminished renal function. Patients with documented underlying conditions (diabetes, hypertension or obstruction) associating with renal dysfunction and those who did not give their informed consent were excluded from this study.

The following information was gathered from each chart: age, gender, transaminase level. Standard abdominal ultrasound examination and Doppler assisted ultrasound are useful for differential diagnosis with cirrhosis or space displacing lesions.

The determination of secondary or concomitant renal impairment was made using common diagnostic serological markers: urea (10-50mg/dl) and creatinine (0.7-1.2 mg/dl). Estimated GFR was calculated in each case using the Cockroft-Gault equation: CrCl, mL/min = (140 – age) × (weight, kg) × (0.85 if female) / (72 × Cr).

The statistical study of collected data was performed using the GraphPad Prism software. The information was divided as nominal or quantitative variables. Nominal variables were described by employing frequencies. Quantitative variables were subjected to testing of normality of distribution applying Kolmogorov-Smirnov test and description was made through median and percentiles (25-75%) or through mean and standard deviation (SD), where applicable.

For statistical analysis we used D'Agostino & Pearson Mann-Whitney, Chi square and Spearman tests. The confidence interval was estimated for a p value of 0,05.

RESULTS

The demographic profiles of all the subjects included in the study are shown in figures no. 1 and 2.

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Figure no. 1. Patient distribution by age

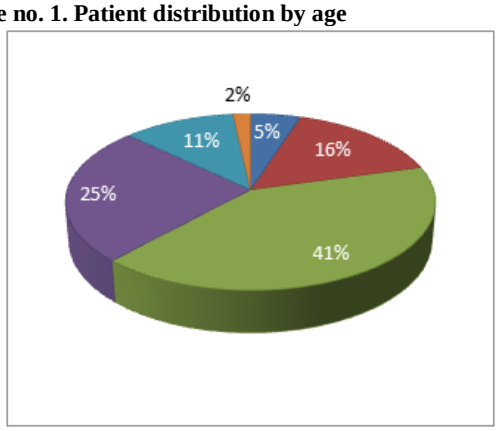
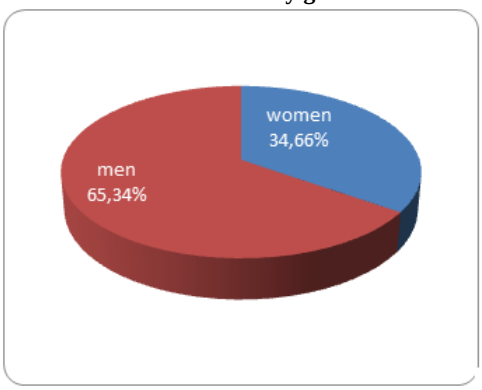


Figure no. 2. Patient distribution by gender



There was statistical significant difference (p-0.0004) between age of the patients and serum creatinine levels. Increased creatinine value is associated with male gender (OR 1.84) and group of age 61-70 years (OR 1,04).

No statistically significant differences were found between the average values of creatinine and etiology of liver disease (p = 0.47).

Mean ALT value in the study group was 99.20±61.47 U/L, while mean AST was 102.5±61.52 U/L, mean serum creatinine was 0.8495±0.3462 mg/dl, mean creatinine clearance was 109.6±37.64 ml/min.

We found a statistically significant difference between AST and ALT median values when comparing the control group to the kidney injury group.(p<0,05)

Table no. 1. The mean of AST, ALT, creatinine and creatinine clearance values of the renal impaired and non-impaired groups

	With renal impairment	Without renal impairment	P value
ALT (U/L)	53.37±18.79 (54.00)	120.9±62.75 (113.0)	<0.0001
AST (U/L)	55.11±16.85 (55.00)	125.0±62.24 (114.6)	<0.0001
Creatinine (mg/dl)	1.188±0.3947 (1.090)	0.6889±0.1516 (0.6600)	<0.0001
Clereance creatinine (ml/min)	69.08±15.31 (70.00)	128.9±28.73 (124.0)	<0.0001

A statistically significant difference was noticed between AST and ALT levels and serum creatinine levels and creatinine clearence (p<0,0001)

DISCUSSIONS

Chronic kidney disease patients represent an important group, presenting chronic comorbidities, requiring regular laboratory investigations, accurate enough to precisely evaluate current status and to predict future evolution. Inside this group, compelling differences of biochemical patterns of patients was observed, hinging on the different stages of CKD. Hepatitis B and hepatitis C, as comorbidities, but also alcohol, are recurrent among patients with CKD.(3,4,5) In this outline, liver activity monitoring, particularly through serum liver enzymes, portrays an important aspect of diagnosis and monitoring of liver damage in this particular group.

Various recent studies have also concluded that ALT levels are decreased in patients with CKD in comparison to individuals with preserved renal function.(8,9,10,11,15,16) Furthermore, a study conducted in Italy exposed lower AST and ALT levels amidst dialysis patients compared to pre-dialysis patients with CKD, in extension to decreased levels of aminotransferases in CKD correlated to healthy individuals.(4) Our findings are predominantly similar to the results of the aforementioned studies.(12,13) At the same time, only few studies have observed both AST and ALT levels in the same patients. As a result, the current study is the first of this type done in our geographical area and illustrates a similar lowering of aminotransferases in CKD patients associating hepatitis compared those with normal kidney function.

The pathophysiological structure for this decrease of aminotransferase levels in patients with CKD remains in debate. The potential mechanisms cover the reduction in pyridoxal-5-phosphate (coenzyme of aminotransferase), the existence of ultraviolet absorbing material and elevated levels of uremic compounds. Other options include deteriorated synthesis and interference of release of AST and ALT from hepatocytes or increased clearance.(4,5,6,7,16) A low aminotransferase level could also be attributed to water retention and haemodillution in patients of CKD.(15)

Discerning the scale of kidney disease in the context of liver inflammation allows for treatment to be discriminated to individual patients and also offers understanding on the reversibility of renal disease with ramifications on liver function. Furthermore, our results come to underline the need for different ranges for AST and ALT values in CKD patients as well as the need of evaluating alternative methods of liver inflammation assessment, independent of biochemical alteration induced by chronic kidney disease.

CONCLUSIONS

In this manner, our study bolsters the evidence that the serum aminotransferases tend to persist lower in CKD patients in comparison to normal population. subsequently, a n aminotransferase level occurring within the current normal range does not exclude hepato-biliary pathology in CKD patients. Our research, although retrospective, enrolling a small sample size underlines the critical demand of larger, well outlined studies for the completion of a separate normal reference spectrum of serum aminotransferases differentiated through the different stages of CKD.

REFERENCES

1. McWilliam A, Macnab R. Laboratory tests of renal function- Anaestheasia and intensive care; 2009. p. 296-299.
2. Slocum JL, Heung M, Pennathur S. Makin renal injury-can we move beyond serum creatinine? Translational Research. 2012;159(4):277-289.
3. Bargman JM, Skorecki K. Chronic kidney disease. In: Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, et al. editors. Harrison's Principles of Internal Medicine. 17 th ed. New York, NY: McGraw Hill Medical; 2008. p. 1761-71.

4. Fabrizi F, Lunghi G, Finazzi S, Colucci P, Pagano A, Ponticelli C, et al. Decreased serum aminotransferase activity in patients with chronic renal failure: Impact on the detection of viral hepatitis. Am J Kidney Dis 2001;38:1009-15.National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. Am J Kidney Dis. 2002;39:S1-266.
5. Cohen GA, Goffinet JA, Donabedian RK, Conn HO. Observations on decreased serum glutamic oxalacetic transaminase (SGOT) activity in azotemic patients. Ann Intern Med. 1976;84:275-80.
6. Wolf PL, Williams D, Coplon N, Coulson AS. Low aspartate transaminase activity in serum of patients undergoing chronic hemodialysis. Clin Chem. 1972;18:567-8.
7. Rej R, Fasce CF Jr, Vanderlinde RE. Increased aspartate aminotransferase activity of serum after in vitro supplementation with pyridoxal phosphate. Clin Chem 1973;19:92-8.
8. Al-Wakeel J, Malik GH, al-Mohaya S, Mitwalli A, Baroudi F, el Gamal H, et al. Liver disease in dialysis patients with antibodies to hepatitis C virus. Nephrol Dial Transplant 1996;11:2265-8.
9. Yuki N, Ishida H, Inoue T, Tabata T, Matsushita Y, Kishimoto H, et al. Reappraisal of biochemical hepatitis C activity in hemodialysis patients. J Clin Gastroenterol 2000;30:187-94.
10. Mustafa LA, Al-Abachi SB, Khalaf DS. Some biochemical changes in serum of hemodialysis patients. Natl J Chem 2008;32:695-700.
11. Levey AS, Coresh J, Greene T, Stevens LA, Zhang YL, Hendriksen S, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. Ann Intern Med. 2006;145:247-54.
12. Lopes EP, Sette LH, Sette JB, Luna CF, Andrade AM, Moraes M, et al. Serum alanine aminotransferase levels, hematocrit rate and body weight correlations before and after hemodialysis session. Clinics (Sao Paulo) 2009;64:941-5.
13. Trevizoli JE, de Paula Menezes R, Ribeiro Velasco LF, Amorim R, de Carvalho MB, Mendes LS, et al. Hepatitis C is less aggressive in hemodialysis patients than in nonuremic patients. Clin J Am Soc Nephrol. 2008;3:1385-90.
14. Cotler SJ, Diaz G, Gundlapalli S, Jakate S, Chawla A, Mital D, et al. Characteristics of hepatitis C in renal transplant candidates. J Clin Gastroenterol. 2002;35:191-5.
15. Yasuda K, Okuda K, Endo N, Ishiwatari Y, Ikeda R, Hayashi H, et al. Hypoaminotransferasemia in patients undergoing long-term hemodialysis: Clinical and biochemical appraisal. Gastroenterology. 1995;109:1295-300.
16. Ono K, Ono T, Matsumata T. The pathogenesis of decreased aspartate aminotransferase and alanine aminotransferase activity in the plasma of hemodialysis patients: The role of vitamin B6 deficiency. Clin Nephrol 1995;43:405-8.