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RESEARCH ARTICLE

The Prevalence of Chronic Liver Disease: Implications for Renal Impairment

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Introduction. Renal disease plays an important role in the prognosis and evolution of chronic liver disease, in particular in its advanced stages. The aim of our study is to analyze the prevalence of chronic liver disease (hepatitis and cirrhosis of different etiologies) and to assess possible correlations between these and impaired renal function.
Material and methods. We conducted a retrospective observational study based on data collected from observation charts of patients admitted to the 2nd Medical Clinic, Emergency County Hospital Tirgu-Mures between January 1st 2012-December 31 2013. In this study we included, based on informed consent, 401 patients with documented liver pathology, with preserved or modified renal function.
Results. Age distribution shows that 41.1% of cases occured between 51 and 60 years of age. Sex distribution shows that 65.3% of cases were male. Toxic cirrhosis was found in 40.8% of males and viral C cirrhosis in 15.1% of women. Toxic cirrhosis associated the following complications: ascites (35.7%), encephalopathy (75%), PAH (68.6%), esophageal varices and upper GI bleed (35.7%). Analyzing the risk factors of renal failure we found that increased mean values of creatinine are associated with viral B cirrhosis (p = 0.02), portal vein diameter (OR 1.37), portal hypertension (OR 1.24), male gender (OR 1.84) and the age group 61-70 yo (OR 1.04).
Conclusions. The current study demonstrated that renal function in chronic liver disease correlates with viral etiology of liver disease, its advanced stage, presence of portal hypertension, older age and male gender.

Keywords: renal impairment, toxic cirrhosis, creatinine

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Introduction

Renal disease plays an important role in the prognosis and evolution of chronic liver disease, especially in its advanced stages [1]. For more than 30 years, Child-Pugh score was used as a prognostic score on patients with cirrhosis, using five variables: ascites, encephalopathy, serum bilirubin, serum albumin, prothrombin time. However, it has been proved to be limited, mainly because of subjectivity in the interpretation of ascites or encephalopathy [2]. Since the year of 2000, MELD score (model of end stage liver disease) proved to be simpler and more objective, using three markers chosen on the basis of statistical analyzes: total bilirubin, INR and creatinine. However, MELD score did not take into account the presence of ascites or hypoalbuminemia, which are unfavorable prognostic factors in decompensated liver cirrhosis. For this reason, the introduction of serum sodium as a forth variable for MELD score has been proposed because hiposodemia was considered a risk factor for the development of refractory ascites and hepatorenal syndrome respectively [4]. However, in Romania, the use of MELD scoring is limited to the evaluation of patient eligibility for liver transplant.

The aim of our study is to analyze the prevalence of liver disease of various etiologies and in different stages of development. We also aimed to evaluate if there are any possible correlations between these prevalences and impaired renal function.

Material and Method

We conducted a retrospective observational study based on data collected from observation charts of patients admitted to the Clinic of Internal Medicine II from the Mures County Emergency Hospital between January 1st, 2012 – December 31st, 2013. The study included 401 patients who agreed to be part of it, patients with documented liver disease, hepatitis or cirrhotic stage with preserved or modified renal function.

The examinations performed for idetifying the etiology included the determination of the viral markers (HBsAg, anti HCV), the identification of the drugs responsible for the appearance of drug-induced hepatitis, of alcohol consumption (more than 20 ml/day for men and 10ml/day for women), of metabolic causes or markers for autoimmune hepatitis (antinuclear antibodies, antimitochondrial antibodies).

Liver function test results: increased transaminase level, cholestasis enzymes (total bilirubin, gammaglutamyltranspeptidase, alkaline phosphatase), changes in serum protein electrophoresis with hypoalbuminemia and hypergammaglobulinemia, prothrombin time, INR. Standard abdominal ultrasound examination and Doppler are useful to dis-

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tinguish from cirrhosis or from space occupaying lesions. Upper endoscopy is used to confirm the signs of portal hypertension. Morphological examination is performed by percutaneous liver biopsy as the diagnosis of chronic hepatitis is done morphologically excellently.

Child Pugh staging was used in cirrhosis classification and the following were used as parameters: the presence of ascites, of encephalopathy, the values of serum albumin, of total bilirubin and INR (A = 5-6 points, B = 7-9 points, C = 10-15 points).

The determination of secondary or concomitant renal impairment was made using common diagnostic serological markers: urea (15-45mg/dl) and creatinine (0.72-1.25 mg/dl).

Patients with documented underlying renal disease (diabetic, hypertensive, obstructive nephropathy) and those who did not give their informed consent were excluded from this study.

Statistical analysis was performed using the MedCalc Software, Version 12.5.0.0. Data were considered as nominal or quantitative variables. Nominal variables were characterized using frequencies. Quantitative variables were tested for normality of distribution using Kolmogorov-Smirnov test and were characterized by median and percentiles (25-75%) or by mean and standard deviation (SD) when appropriate. A chi-square test was used in order to compare the frequencies of nominal variables. Quantitative variables were compared using t test, ANOVA. We used the Bonferroni correction in order to account for multiple comparisons. Multivariate analysis was carried out using linear regressions. We used as dependent variable the renal impairment, and we included as independent variables the data: demographic data, the etiology of liver disease, its complications. The confidence interval was estimated for a p value of 0,05.

Results

The distributions according to the etiology of liver disease, gender, groups of age and area of origin are shown in Figures 1, 2 , 3 and 4.

Analyzing the cases of cirrhosis, the following were identified:

- Toxic etiology was found on male subjects and viral C etiology on female subjects ($p < 0.0001$);
- A rate of 47.7 % of Child-Pugh Class B was found (table I);
- Toxic cirrhosis associated the following complications: ascites (35.7%), encephalopathy (75%), portal hypertension (68.6%), esophageal varices and upper gastrointestinal bleeding (35.7%).
- Presence of ascites ($p < 0.0001$), hepatic encephalopathy ($p < 0.01$) and portal hypertension ($p < 0.0001$) were identified more frequently in viral C and toxic liver cirrhosis.
- There is a 77.10 times higher risk of developing portal gastropathy because of portal hypertension presence (OR=77,10 (IC 95%: 23,7-250,3)) but no significant differences on groups of age or sex were identified.
- We have statistical significance, p - 0.001, that there is a 4.78 times higher risk of upper gastrointestinal haemorrhage on males than on females.

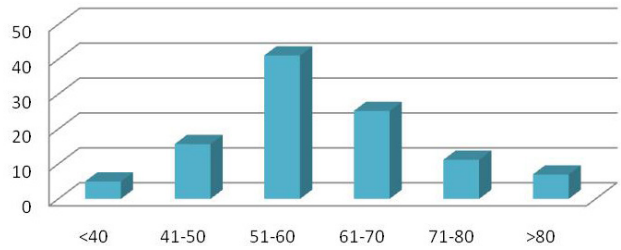


Fig. 1. Distribution of cases based on patients age

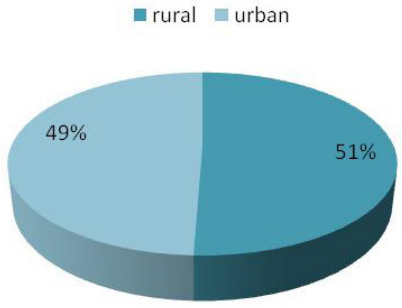


Fig. 2. Distribution of cases based on residence area

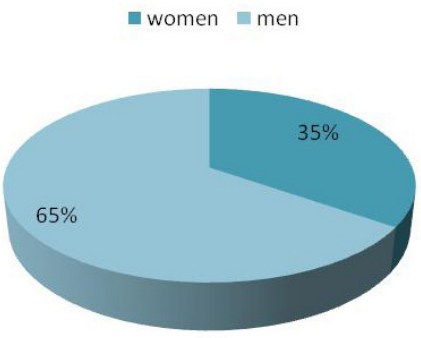
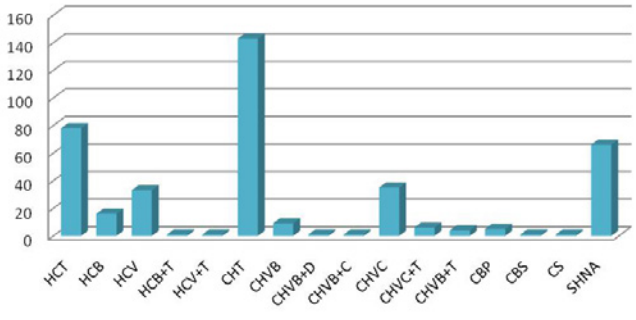


Fig. 3. Distribution of cases based on patients sex



HCT: chronic toxic hepatitis, HCB: chronic B hepatitis, HCV: chronic C hepatitis, HCB+T: chronic B and toxic hepatitis, HCV+T: chronic B and toxic hepatitis, SHNA: non alchoolic liver steatosis, CHT: toxic liver cirrhosis, CHVB: viral B liver cirrhosis, CHVC: viral C liver cirrhosis, CHVB+D: viral B&D liver cirrhosis, CHVB+C: viral B&C liver cirrhosis, CHVB+T: viral B and toxic liver cirrhosis, CHVC+T: viral C and toxic liver cirrhosis, CBP: primary biliary cirrhosis, CBS: secondary biliary cirrhosis, CS: sclerosis colangitis

Fig. 4. Etilogy of liver disease

Table I. Distribution of cirrhosis cases in Child-Pugh classes, according to etiology

	LIVER CIRRHOSIS							
CHILD CLASSES	CH TOX	CHVB	CHVB & C	CHVB &D	CHVB & TOX	CHVC	CHVC &TOX	
CHILD A	55	2	1	1	0	17	0	76 (38,2%)
CHILD B	67	6	0	0	4	14	4	95 (47,7%)
CHILD C	21	1	0	0	0	4	2	28 (14,1%)
	143 (71,9%)	9 (4,5%)	1 (0,5%)	1 (0,5%)	4 (2,0%)	35 (17,6%)	6 (3,0%)	199

Alcohol consumption was identified at 56.4% of the patients, with a frequency of 77.9 % in male gender, hoiwever with a similar distribution on different groups of age.

Analyzing the risk factors involved in renal function we found that:

- Increased creatinine value is associated with viral cirrhosis B (p = 0.02), portal hypertension (OR 1.24), 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). Instead, there were significant differences between the average values of creatinine and the stage of liver disease, Child B and C classes (p < 0.0005). (Figures 5, 6, 7)

Discussions

The accuracy of renal function assessment is usually affected by limiting the use of surveillance parameters of urea and serum creatinine [5,6]. Creatinine level is significantly influenced by the development of cirrhosis , hyperbilirubinemia and nutritional status of the patient.

Creatinine production is low in cachectic patients with liver failure, in this situation serum creatinine underestimating the severity of glomerular filtration rate decrease. Moreover,the determination of creatinine by Jaffe method is flawed in this hyperbilirubinemia. MDRD method overestimates glomerular filtration, too. Also, the levels of serum urea are often decreased on cirrhotic patients even in the presence of gastrointestinal bleeding. Also, in advanced liver failure serum levels of urea remains low (<10 mg/dl) even in the presence of gastrointestinal hemorrhage or acute renal failure [7,8].

Renal function is evaluated through a series of traditional serum biomarkers : urea , creatinine , creatinine clereance , ionogram , plasma osmolality , and urine : volume , ionogram , urinary osmolality , +/- proteinuria, microscopic hematuria. There are a number of problems that prevent correct assessment of renal function based on serum creatinine: is a specific marker but with reduced sensitivity, measurements depend on sex, age, ethnicity, nutritional status, intake of protein and very important for liver pathology associated. In chronic liver disease the low level

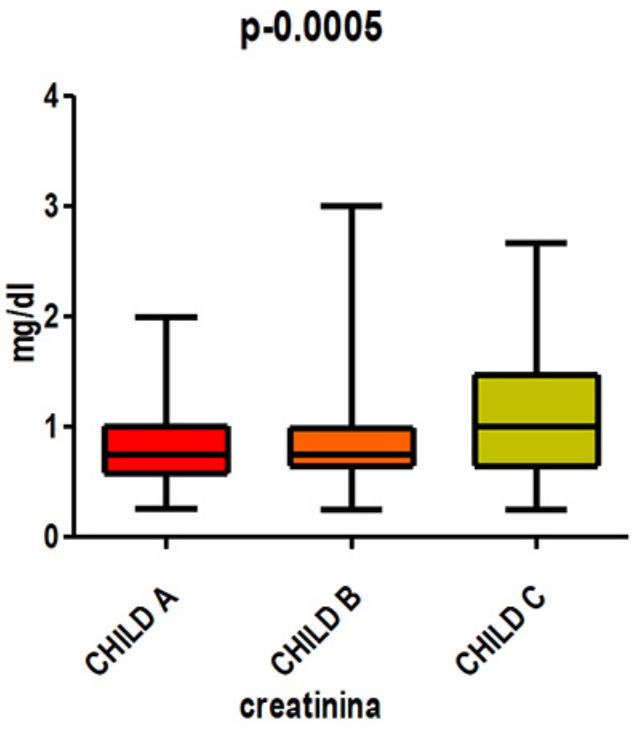


Fig. 5. The average values of serum creatinine based on Child Pugh score

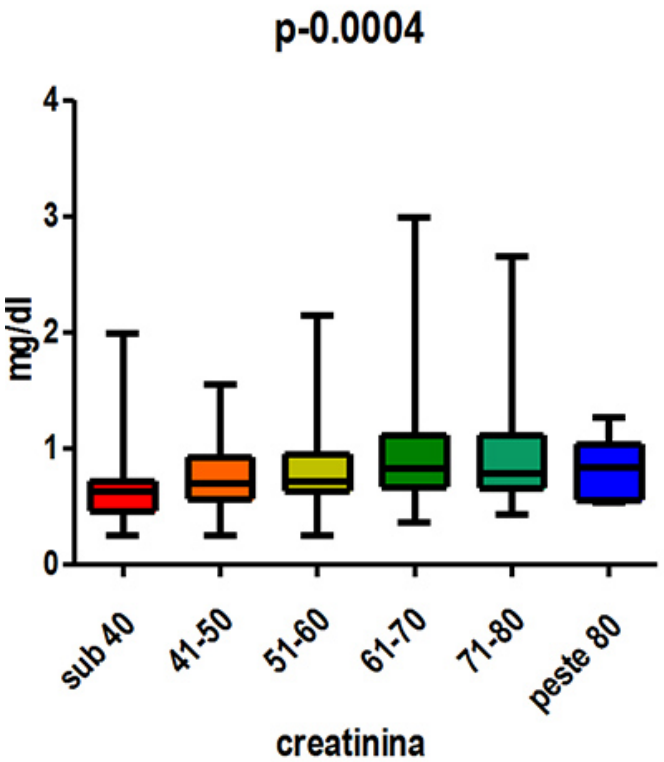


Fig. 6. The average values of serum creatinine based on group of age

of serum creatinine is due to the reduction of up to 50% of its production according to the stage liver disease [5]. Thus, from the research made so far it was observed that serum levels of creatinine can not demonstrate the appearance of renal dysfunction unless in advanced stages of liver disease [9-12].

Conclusions

Liver pathology seems to be more prevalent in males, especially due to alcohol consumption. Toxic alcohol etiology and viral etiology with hepatitis virus C also prevailedC, with significant differences between the two genders. Analyzing the cases in the advanced stage of the disease, we demonstrated that complications were more frequent in alcoholic cirrhosis and in viral etiology C. Although the risk of development of portal gastropathy was increased in patients with signs of portal hypertension, no significant differences were found between sexes or different groups of age. Instead, the risk of upper gastrointestinal bleeding was significantly increased in male patients.

The current study demonstrated that renal function in chronic liver disease correlates well with viral etiology of liver disease, its late stage, the presence of portal hypertension, advanced age and male gender.

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