

Original Paper

LIVER FUNCTION TESTS ANOMALIES IN PATIENTS WITH CHRONIC HEART FAILURE

Camelia C. Diaconu¹, Alice Bălăceanu², Daniela Bartoș¹

¹“Carol Davila” University of Medicine and Pharmacy, Clinical Emergency Hospital, Internal Medicine Clinic, Bucharest, Romania

²“Carol Davila” University of Medicine and Pharmacy, “Sf. Ioan” Clinical Emergency Hospital, Internal Medicine Clinic, Bucharest

REZUMAT

Anomaliile testelor funcționale hepatice la pacienții cu insuficiență cardiacă cronică

Introducere: Pacienții cu insuficiență cardiacă cronică prezintă o multitudine de anomalii ale funcțiilor hepatice, cunoscute sub numele de sindroame cardio-hepatice. Obiectivul studiului a fost de a evalua frecvența și importanța anomaliilor testelor funcționale hepatice într-un grup de pacienți cu insuficiență cardiacă cronică.

Metodă: Studiul a inclus 436 pacienți cu insuficiență cardiacă cronică internați consecutiv în Clinica de Medicină Internă a Spitalului Clinic de Urgență București pe o perioadă de 8 luni (1 ianuarie - 31 august 2012).

Rezultate: Vârsta medie a pacienților a fost de 59.2 ± 17.4 ani. Distribuția în funcție de sex: 233 (53,4%) bărbați și 203 (46,6%) femei. Anomaliile testelor funcționale hepatice au fost frecvente la pacienții cu insuficiență cardiacă cronică: hipoalbuminemie la 16.97% dintre pacienți, bilirubina totală crescută la 13.30%, fosfataza alcalină crescută la 11.92%, aspartataminotransferaza crescută la 4.12%, alanin aminotransferaza crescută la 3.66 % dintre pacienți și gamaglutamiltranspeptidaza crescută la 2.75%. Proporția pacienților cu fracție de ejeție scăzută ($\leq 40\%$) care au prezentat creșterea bilirubinei totale a fost de 15.8%, aproape dublă față de a pacienților cu fracție de ejeție păstrată ($>40\%$) (9.4%). Alte teste hepatice au fost similare la pacienții cu fracție de ejeție scăzută și păstrată. Mortalitatea intraspitalicească în întregul grup de studiu a fost de 5.9%. Anomaliile bilirubinei serice, fosfatazei alcaline și albuminei au fost frecvente la pacienții care au decedat în timpul spitalizării.

Concluzii: Anomaliile ușoare ale testelor funcționale hepatice au fost relativ frecvent întâlnite la pacienții cu insuficiență cardiacă cronică, bilirubina serică fiind mai mult crescută decât aminotransferazele. Pacienții cu fracție de ejeție scăzută au avut o frecvență mai mare a hiperbilirubinemiei decât cei cu fracția de ejeție păstrată. Bilirubina totală a fost un predictor de prognostic rezervat în timpul spitalizării.

Cuvinte cheie: teste hepatice, insuficiență cardiacă

Corresponding author:

Camelia C. Diaconu, MD, PhD, FESC, FACP, FEFIM
Medical Clinic, Emergency Clinical Hospital, Calea Floreasca 8, 014461, Bucharest, Romania
e-mail: camiluciemi@yahoo.com

ABSTRACT

Background: Patients with heart failure have a variety of liver abnormalities, known as cardio-hepatic syndromes. The aim of the study was to evaluate the frequency and the importance of liver function tests abnormalities in a group of patients with chronic heart failure.

Methods: The study included 436 patients with chronic heart failure consecutively hospitalized in the Internal Medicine Clinic of the Bucharest Clinical Emergency Hospital over an 8 month period (1st of January – August 31, 2012).

Results: The mean age of the patients was 59.2 ± 17.4 years. The distribution by gender: 233 (53,4%) men and 203 (46,6%) women. Liver function tests abnormalities were frequent in patients with chronic heart failure: low albumin in 16.97% of the patients, elevated total bilirubin in 13.30%, elevated alkaline phosphatase in 11.92%, elevated aspartate aminotransferase in 4.12%, alanine aminotransferase elevation in 3.66 % of patients and elevated gammaglutamiltranspeptidase in 2.75%. The proportion of patients with reduced ejection fraction ($\leq 40\%$) who had elevations in total bilirubin was 15.8%, almost double that of patients with preserved ejection fraction ($>40\%$) (9.4%). Other liver tests were similar in patients with reduced and preserved ejection fraction. In hospital mortality for the whole study group was 5.9%. Baseline abnormalities in bilirubin, alkaline phosphatase and albumin were more common in patients who died during hospitalization.

Conclusions: Mild abnormalities of LFT are relatively frequent in patients with chronic heart failure, with a greater elevation of bilirubin than aminotransferases. Patients with reduced ejection fraction had a higher prevalence of increased bilirubin than those with preserved ejection fraction. Total bilirubin was a predictor of poor prognosis during hospitalization.

Key words: liver tests, heart failure

INTRODUCTION

Chronic heart failure is a major public health problem, with increasing prevalence due to population aging and increased survival of cardiovascular patients. Chronic heart failure is a clinical syndrome characterized by a variety of effects on other organs and systems. Occasionally, patients with chronic heart failure may present with signs and symptoms of a noncardiac disorder, such as hepatic dysfunction. The main pathophysiologic mechanism involved in hepatic dysfunction of patients with heart failure is either passive congestion due to increased filling pressures or low cardiac output and the consequences of impaired perfusion. Passive hepatic congestion may lead to increase of liver enzymes and total bilirubin. Right ventricular dysfunction can be associated with severe hepatic congestion, which can be asymptomatic and revealed only by abnormal liver function tests. When hemodynamic abnormalities are prolonged, the hepatic function is further altered, with impaired coagulation tests and decreased albumin synthesis. Morphologically, the liver becomes fibrotic and ultimately cardiac cirrhosis appears. Decreased perfusion from low cardiac output may be associated with hepatocellular necrosis

and increased serum aminotransferases. Acute cardiogenic liver injury appears in severe systemic hypotension due to exacerbation of heart failure; the level of aminotransferases increases, as well as lactic dehydrogenase and prothrombin time.

The aim of our study was to evaluate the frequency and the importance of liver function tests abnormalities in a group of patients with chronic heart failure, as well as the prognostic value of these liver tests.

METHODS

The retrospective study included 436 patients with chronic heart failure consecutively hospitalized in the Internal Medicine Clinic of the Clinical Emergency Hospital of Bucharest over a period of 8 months (1st of January – August 31, 2012). We analyzed data from the hospital record database. In each patient clinical examination, laboratory tests, 2-D echocardiography were performed.

RESULTS

The patients mean age was 59.2 ± 17.4 years. The distribution by gender: 233 (53,4%) men and 203

(46,6%) women (**Fig. 1**). Liver function tests abnormalities were frequent in patients with chronic heart failure: low albumin in 16.97% of the patients, elevated total bilirubin in 13.30%, elevated alkaline phosphatase in 11.92%, elevated aspartate aminotransferase in 4.12%, alanine aminotransferase elevation in 3.66 % of patients and elevated gammaglutamyltranspeptidase in 2.75% (**Fig. 2**). The proportion of patients with reduced ejection fraction ($\leq 40\%$) who had elevations in total bilirubin was

15.8% (**Fig. 3**), as compared to 9.4% in patients with preserved ejection fraction ($>40\%$) (**Fig. 4**). Other liver tests were similar in patients with reduced and preserved ejection fraction. In hospital mortality rate for the whole study group was 5.9% (26 patients). The median hospitalization period was 7 days. Baseline abnormalities in bilirubin, alkaline phosphatase and albumin were more common in patients who died during hospitalization. In the group of 26 patients who died during hospitalization: 17 patients

Figure 1. The distribution by sex in the group of study.

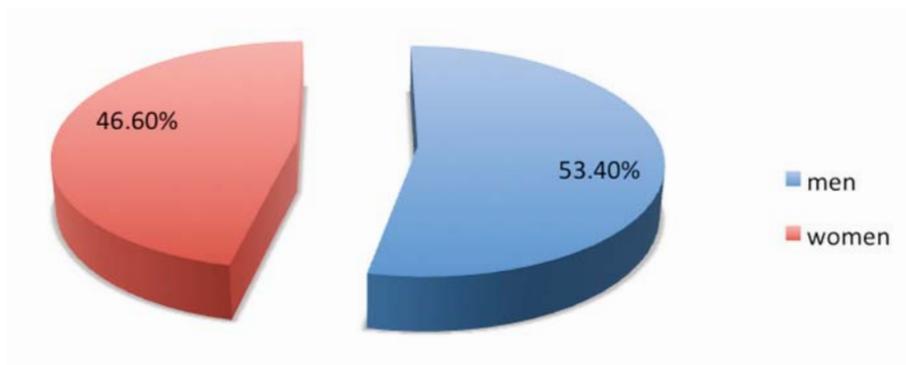


Figure 2. Liver function tests anomalies in patients with chronic heart failure.

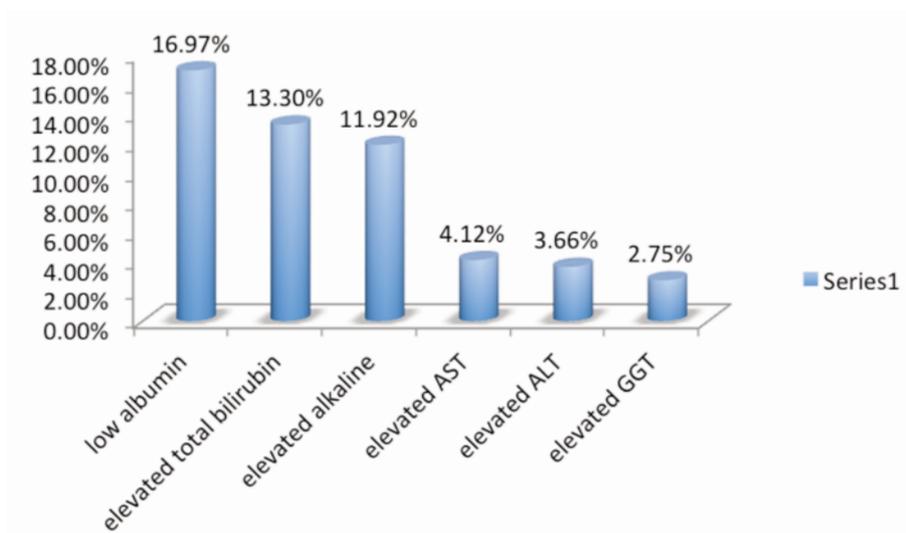


Figure 3. The proportion of patients with reduced ejection fraction ($\leq 40\%$) who had elevations in total bilirubin

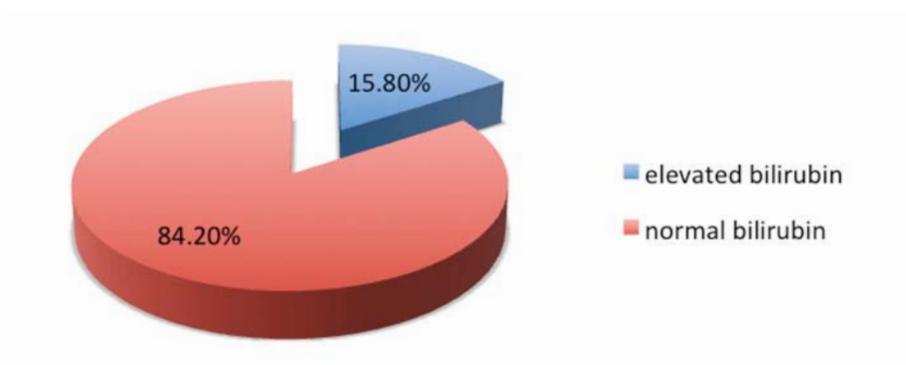


Figure 4. The proportion of patients with preserved ejection fraction (> 40%) who had elevations in total bilirubin

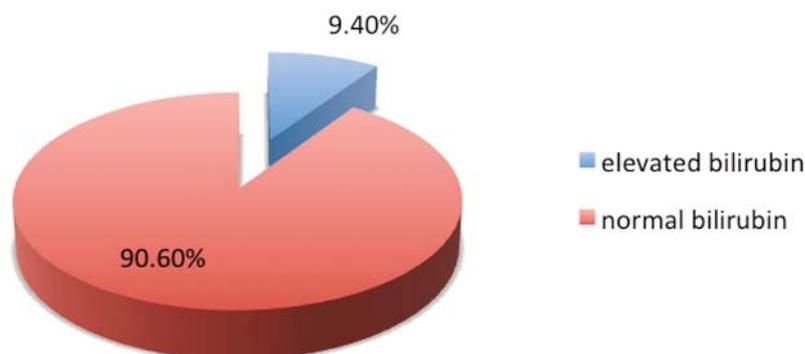
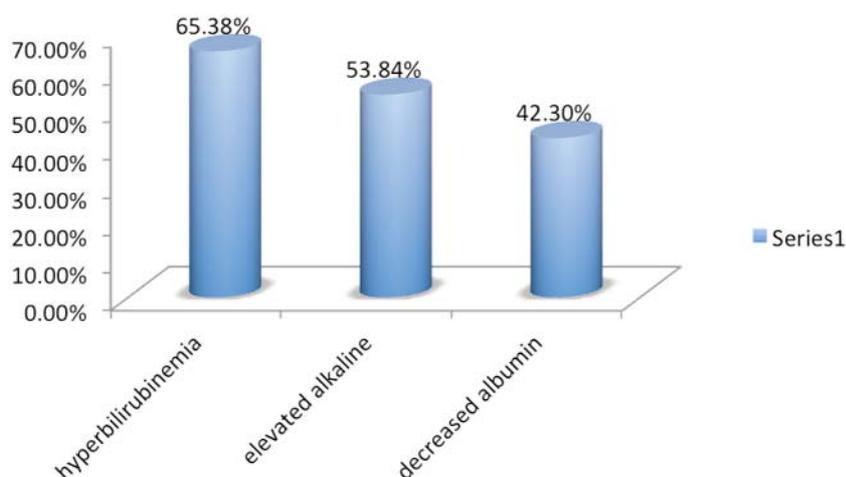


Figure 5. The proportion of patients with hyperbilirubinemia, increased alkaline phosphatase and decreased albumin in the group of 26 patients who died during hospitalization



had hyperbilirubinemia (65.38%), 14 patients had increased alkaline phosphatase (53.84%), 11 patients had decreased albumin (42.30%) (Fig. 5).

Limitations of the study

Excepting the liver function tests, we do not have other information about liver pathology, such as hepatitis serology or histological information. Also, we could not exclude the fact that in some patients altered hepatic tests could be due to drug toxicity.

DISCUSSION

The liver's complex vascular supply and high metabolic activity rate make it vulnerable to circulatory disturbances. Any cause of right-sided heart failure can result in hepatic congestion. Congestive hepatopathy is often associated with altered hepatic functions. The indicators of these impaired hepatic functions consist in serum aminotransferases, lactic

dehydrogenase, gamma-glutamyl transpeptidase and alkaline phosphatase. Increased total bilirubin, secondary to the increase in both direct and indirect bilirubin, is another indicator. The most common liver biochemical abnormality in patients with chronic heart failure is a mild elevation in the serum bilirubin level, which occurs in up to 70% of patients (1). The total serum bilirubin is usually less than 3 mg/dL (1). In some cases, severe acute right-sided heart failure can present with very high values of total bilirubin (2). In one study, the total serum bilirubin level was predictor of mortality and morbidity in heart failure patients (3). Serum aminotransferases levels are elevated in approximately 1/3 of the patients, two to three times the upper limit of normal (4,5). Serum albumin levels are rarely less than 2.5 g/dL, most probably due to malnutrition and protein-losing gastroenteropathy (6). One study described a cholestatic pattern of liver function tests in patients with stable heart failure and showed a

positive correlation between elevations in cholestatic liver function tests and disease severity as assessed by the New York Heart Association (NYHA) functional classification (7). The liver function tests can be used as prognostic markers in patients with heart failure. Some studies have described higher death rates and heart failure re-hospitalizations in patients with increased plasma bilirubin (7,8). Hypoalbuminemia has been shown to be an independent death predictor in both acute and chronic heart failure. Hypoalbuminemia was associated with significantly increased 1 and 5 year all-cause mortality, progressive heart failure death and increased risk of urgent cardiac transplantation in a cohort of patients with NYHA class III/IV symptoms (9). Low albumin levels have also been found to have prognostic value in patients with acute decompensate heart failure after adjustment for multiple prognostic variables, including N-terminal pro-B-type natriuretic peptide (10,11).

The liver plays a major role in the absorption, distribution and clearance of the majority of drugs, which are transformed by enzymatic conversion into active, inactive or even toxic metabolites. This can have major implications for the treatment of patients with chronic heart failure and hepatic dysfunction. Hepatic alterations can alter the pharmacokinetics of cardiovascular drugs, leading to toxicity. Dosage adjustments are necessary for some cardiovascular drugs.

CONCLUSIONS

The aim of our study was to evaluate the frequency and the importance of liver function tests abnormalities in a group of patients with chronic heart failure consecutively admitted in the Internal Medicine Clinic of the Clinical Emergency Hospital of Bucharest, as well as the prognostic value of these

liver tests. We found that mild abnormalities of liver function tests are relatively frequent in patients with chronic heart failure, with a greater elevation of bilirubin than aminotransferases. Patients with reduced ejection fraction had a higher prevalence of increased bilirubin than those with preserved ejection fraction. Total bilirubin was a predictor of adverse prognosis during hospitalization. A better understanding of the complex relationship between heart and liver in patients with chronic heart failure may be useful for a successful management of these patients

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