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Original Research Article

A Study to Correlate Liver Function Tests in Patients of Congestive Heart Failure

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Abstract

Background: The liver being a multifunctional organ with major function of various metabolisms, it is strongly dependent on hepato-cardiac vascular connection.

Objectives: To study the relationship between liver function test (LFT) and severity of congestive heart failure (CHF) and to correlate the functioning of liver with etiology of CHF patients.

Materials and Methods: This prospective observational study was conducted in General Medicine department of tertiary care teaching hospital of Udaipur, Rajasthan. All patient aged 18-65 years with CHF of any aetiology were included. Serum bilirubin, serum SGOT and SGPT, serum ALP, serum proteins and prothrombin time was measured in all the patients and these were correlated with the severity of cardiac disease.

Results: There was significant rise in mean serum ALT level, AST level, prothrombin time and bilirubin level with advancement of heart failure severity and were found highest in NYHA class IV. ($p<0.001$) The mean albumin level had decreased significantly as the severity of heart failure increased and was found lowest in NYHA class IV. ($p <0.05$) The mean serum ALP values didn't show any significant correlation with NYHA classification of heart failure. ($p>0.05$)

Conclusion: This study concluded that LFTs were significantly elevated in NYHA class IV of heart failure as compared to NYHA class I and LFTs showed significant correlation with severity of heart failure (NYHA class). Early and timely management of congestive heart failure will improve LFTs and will prevent significant liver failure.

Key words: Congestive Heart Failure, Liver Function Test, NYHA Class

Background

Heart failure is a clinical syndrome characterised by a number of clinical features that have a severe impact on every essential organ in the body. Heart failure is characterized by dysfunction of the cardiac pump that results in systemic perfusion failure due to which; the heart cannot pump enough oxygen and nutrients to meet the

body's requirement [1]. These clinical features could be the result of both systolic and diastolic dysfunction whose name has changed recently, such as reduced ejection fraction heart failure and preserved ejection fraction heart failure, respectively. Even though there have been studies on how the renal system functions in heart failure, the liver with its dual supply would bear the brunt of both types of heart failure, resulting in its dysfunction [2].

Congested lungs, fluid and water retention, dizziness, fatigue and weakness, rapid or irregular heartbeats and congested liver are the common symptoms of heart failure. HF can cause a number of liver issues, particularly in right-sided heart failure (RHF) or congestive heart failure. RHF is diagnosed using echocardiography by measuring FAC (Fractional area change) and TAPSE (Tricuspid annular plane systolic excursion) [3]. Hepatic congestion can be caused by a variety of factors that leads to right-sided heart failure; however, patients with hepatic congestion are generally asymptomatic and it can be detected by abnormal liver function tests (LFTs) only, in routine laboratory investigations. It can also show symptoms like anorexia, malaise, and easy fatigability, yellowish discoloration of sclera, nausea, vomiting, right hypochondrium pain, jaundice, decrease urine output and flapping tremors which indicates hypoperfusion of cerebrum. Here flapping tremors does not indicate hepatic encephalopathy [4].

In patients with acute heart failure, cardiac ischemic hepatitis (also known as "shock liver") can develop after a period of severe hypotension. Cardiac cirrhosis (also known as Bridging fibrosis) may result from persistent hemodynamic abnormalities, leading to impaired liver function with impaired coagulation, decreased albumin synthesis and impaired metabolism of some cardiovascular drugs, which may cause undesirable toxicity [5]. The liver being a multifunctional organ with major function of various metabolisms, it is strongly dependent on hepato-cardiac vascular connections, which provide both arterial supply for high oxygen delivery and drainage intravenously to remove catabolic waste from blood cells. Due to liver dysfunction, many biochemical changes occur in liver function tests commonly measured in hospitalized patients. The present study was planned to study liver function tests in patients of congestive heart failure (CHF).

Materials and Methods

Study Design: Prospective observational study**.**

Study Place: General Medicine department of tertiary care teaching hospital of Udaipur, Rajasthan

Study Duration: January 2020 to June 2021

Sampling Technique: Purposive Sampling

Sample size

The formula used for calculation of sample size was $n= \underline{(Z\alpha + Z_{1-\beta})^2 P(1 - P)/E^2} = 89$

$Z\alpha = 1.96$ at 95% confidence level, $Z_{1-\beta} = 0.8413$ at 80 % power of study, E = 10% absolute error, P = prevalence of CHD in India 13%; thus, the minimum sample size required was 89, but we enrolled 100 patients for ease of calculations.

Inclusion criteria: All patient aged 18-65yrs with congestive heart failure of any aetiology admitted in General medicine department were included.

Exclusion criteria: Patients of history of chronic alcoholism, past history of jaundice, recent intake of hepatotoxic and cholestatic drugs**,** presence of HBs Antigen and Anti HCV Antibodies**,** pregnancy women and patients who refused to give written consent were excluded out.

Procedure

After taking approval from the institutional ethics committee the present study was conducted in all patients aged 18-65 years

with congestive heart failure of any aetiology admitted in General medicine department. Informed consent was taken from all the patients. Data was collected through a structured proforma which includes demographic profile history and thorough physical examination along with detailed clinical examination was done. Relevant blood investigations CBC, ESR, FBS, PBF, URINE RM, KFT, LFT, PT, HIV, HBsAg, HCV, TROPI, BNP and other necessary investigations was performed. Radiological investigations ECG, CHEST X-RAY (PA), USG WHOLE ABDOMEN, 2DEcho. Other investigation as needed was performed. Family history, general and systemic examination, diagnostic data and treatment details were also collected. Liver profile of all patients was recorded viz; serum bilirubin, serum SGOT and SGPT, serum ALP, serum proteins and prothrombin time was measured in all the patients.

Statistical analysis

The data was entered in MS Excel software version 17 and analysed using statistical packages for social sciences (SSPS). For descriptive analysis, number and proportion with percentages was used. The quantitative data was analysed using Chi-square test. P value less than 0.05 was considered as significant.

Results

Out of total 100 subjects, 56 were males (56%) and 44 were females (44%). The male: female ratio was 1.27:1. There were 47 patients in the age group >55 years. Out of 100 patients, 28 were classified as NYHA class I, 40 as NYHA class II, 18 as NYHA class III and 14 as NYHA class IV. (Table 1)

Table 1: Demographic details of all the patients (n=100)

	No. of patients	Percentage
Sex		
Male	56	56%
Female	44	44%
Age group (Years)		
18-24	2	2%
25-29	3	3%
30-34	6	6%
35-39	7	7%
40-44	7	7%
45-49	12	12%
50-54	16	16%
55-59	25	25%
60-64	22	22%
NYHA Class		
Class I	28	28%
Class II	40	40%
Class III	18	18%
Class IV	14	14%

On clinical examination, jaundice was present in 31% cases, ascites in 25% cases and hepatomegaly was observed in 65%. Congestive liver disease/hepatomegaly was detected in 74% of the patients. 82% patients had abnormal LFT's at the time of admission. (Table 2)

Table 2: Characteristics related to liver dysfunction at the time of admission on clinical examination (n=100)

	No. of Patients	Percentage
Jaundice		
Present	31	31%
Absent	69	69%
Ascites		
Present	25	25%
Absent	75	75%
Hepatomegaly		
Present	65	65%
Absent	35	35%
Congestive hepatomegaly on USG		
Present	74	74%
Absent	26	26%
Liver function tests		
Abnormal	82	82%
Normal	18	18%

There was significant rise in mean serum ALT level, AST level, prothrombin time and bilirubin level with advancement of heart failure severity and were found highest in NYHA class IV. ($p<0.001$) The mean albumin level had decreased significantly as the severity of heart failure increased and was found lowest in NYHA class IV. ($p <0.05$) The mean serum ALP values didn't show any significant correlation with NYHA classification of heart failure. ($p>0.05$) (Table 3) Liver function tests showed significant improvement after management of heart failure. (Figure 1 a,b,c,d)

Table 3: Distribution according to NYHA class of heart failure and liver parameters

	NYHA Class I	NYHA Class II	NYHA Class III	NYHA Class IV	P value
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
Serum Albumin (g/dl)	3.39±0.38	3.27±0.33	3.16±0.40	3.09±0.36	<0.05*
Serum ALT (IU/L)	31.04±18.63	73.45±17.25	104.61±24.05	279.86±204.24	<0.001*
Serum AST (IU/L)	36.82±21.38	96.40±16.81	159.78±32.90	443.50±294.43	<0.001*
Serum Bilirubin (mg/dl)	0.58±0.28	0.86±0.55	1.46±0.75	3.21±1.35	<0.001*
Serum ALP (IU/L)	125.43±47.91	129.13±46.75	138.28±40.50	140.29±43.70	0.68
Prothrombin Time (sec)	13.54±0.27	14.41±2.17	18.27±1.06	20.59±1.01	<0.01*

*Significant

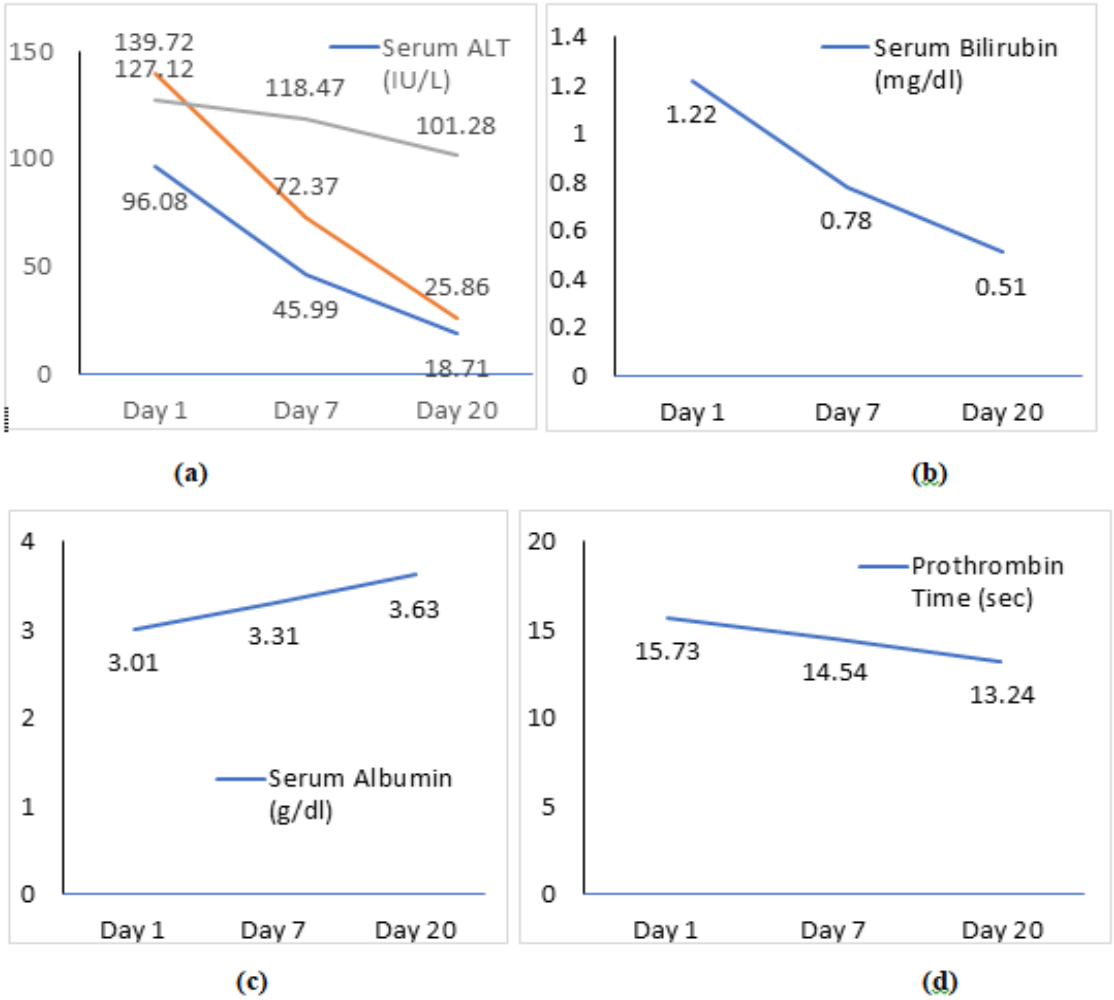

Figure 1: Liver parameters on day of admission, day 7 and day 20; (a) Serum ALT, AST and ALP, (b) Serum bilirubin, (c) Serum albumin (d) Prothrombin time

Among the various etiologies, coronary artery disease accounted for maximum number of cases i.e., 32% followed by cor pulmonale comprising 19%, rheumatic heart disease (RHD) accounted for 15%, cardiomyopathy and hypertensive heart disease accounted for 12% each. In present study hyperbilirubinemia was found in all patients of myocarditis, pulmonary embolism and right ventricular (RV) outflow obstruction and in 73.68% cases of cor pulmonale and 68.67% cases of coronary artery disease. (Table 4)

Table 4: Correlation of abnormal serum bilirubin level with different etiology of CHF (at admission)

	Abnormal Serum bilirubin N(%)
Cardiomyopathy (n=12)	7(58.33%)
Cor pulmonale (n=19)	14(73.68%)
Coronary artery disease (n=32)	22(68.75%)
Hypertensive heart disease (n=12)	8(66.67%)
Myocarditis (n=3)	3(100%)
Pericardial tamponade (n=5)	2(40%)
Pulmonary embolism (n=1)	1(100%)
RHD (n=15)	9(60%)
RV outflow obstruction (n=1)	1(100%)

On admission, mean SGPT level was found to be more elevated in patients with cardiomyopathy (181.33±200.22 IU/L) and it was found least in pulmonary embolism patient. (Table 5)

Table 5: Mean serum SGPT level in different etiology of CHF (at admission)

	Serum SGPT level (IU/L) Mean±SD
Cardiomyopathy	181.33±200.22
RHD	168.27±221.60
Pericardial tamponade	159.20±46.29
Hypertensive heart disease	143.92±155.47
Coronary artery disease	136.88±197.88
Cor pulmonale	108.00±84.71
Myocarditis	86.33±53.72
RV outflow obstruction	39.00
Pulmonary embolism	19.00

Discussion

Passive blockage due to elevated filling pressures or decreased cardiac output and subsequent hypoperfusion is the most common etiology associated with liver dysfunction. High central venous pressure (CVP) can cause passive hepatic congestion, resulting in increased serum direct and indirect bilirubin and liver enzymes [5]. Acute hepatocellular necrosis with significantly increase in liver enzymes may be coupled with systemic hypoperfusion caused by a rapid decrease in cardiac output [6].

In present study male: female ratio was 1.27:1. Thus males have a higher prevalence of cardiac disease and failure. In present study most of the patients were above 55 years of age. Previous studies had also shown similar results [7-9]. This shows that cardiac disease and progression to cardiac failure is more common in the elderly age group. Euroheart Survey in the United States studied demographic and clinical characteristics of patients admitted with heart failure and they found that heart failure was more common in the older age group and among men [10]. In most recent research, the median age at first presentation was in the mid-70s, with men having a higher frequency than women of all ages.

In present study, among the various etiologies coronary artery disease was found to be the most common cause of heart failure i.e. 32% followed by cor pulmonale comprising 19%. Similarly in a study by Jayganesh *et al*, 38.3% cases had coronary artery disease [9]. This demonstrates that coronary artery disease is becoming the leading cause of congestive heart failure. In contrast to present study Jeraud *et al* reported rheumatic heart disease in the maximum number of cases as 40% [7]. The prevalence of RHD as the leading cause of congestive heart failure has decreased, indicating a change in the etiology of congestive heart failure. Study done by Cowie *et al* found that coronary heart disease is the single most frequent cause of congestive heart failure in the developed world [11]. In present study majority of the patients were in NYHA class I and II. Jayganesh *et al* in their study also reported similar results [9]. This higher number of patients in NYHA class I and II in present study and other studies indicate presentation of congestive heart failure patients to hospital is in early stages of heart failure which is most likely due to more awareness regarding health, health related diseases and easy availability of primary health facility.

In present study, on clinical examination Jaundice was found in 31% cases which were similar to other studies [7,8,12]. Ascites was detected 25% cases. Such analysis was not noted in other studies. Hepatomegaly was present in 65% of patients. Our findings were similar to those of Rajee *et al* who reported liver enlargement in 64% of patients [8]. In a study done by Jayganesh *et al* hepatomegaly was identified in 41.7% [9]. Dunn *et al* found liver enlargement in more than 90% of the cases [13]. In nearly half of the cases, Richman *et al* found liver enlargement. On USG abdomen, 74% of patients were diagnosed with congestive liver/ hepatomegaly [14]. Jayganesh *et al* also performed USG abdomen in all cases in their study and 38.3% of them revealed variations in abdominal ultrasound due to congestive hepatomegaly [9].

In present study there was significant rise in mean serum ALT level, AST level, prothrombin time and bilirubin level with advancement of heart failure severity and were found highest in NHYA class IV. The mean albumin level had decreased significantly as the severity of heart failure increased and was found lowest in NHYA class IV. Richman *et al* also observed that controlling ventricular failure resulted in serum bilirubin levels returning to baseline in less than a week, which is consistent with present findings [14]. These findings imply that higher class of heart failure are associated to a greater degree of liver impairment. Lefkowitch *et al* and Kubo *et al* also made this claim in their research [15,16]. Similar results were also shown by Rajee *et al* study [8].

Mean ALP levels did not show much change in CHF patients. Richman *et al* have reported elevation of serum alkaline phosphatase levels in 10-20% of patients with right sided heart failure [14]. Dunn *et al* reported that in most patients the levels are within normal limits, rarely do they exceed twice normal [13]. This shows patients belonging to NYHA class 4 patients had marked liver function abnormality. However, our findings were in contrast to those of Jeraud *et al* who reported significant correlation with NYHA classes and serum ALP values [7].

In present study liver function test parameters also improved over period of few weeks to months along with improvement of underlying cardiac pathology after management. Similar results were reported by other studies [8,9,13,14].

Hyperbilirubinemia was found in all cases of myocarditis, pulmonary embolism and RV outflow obstruction, in 73.68% cases of cor pulmonale, in 68.75% cases of coronary artery disease, in 66.67% cases of hypertensive heart disease, in 60% cases of RHD, in 58.33% cases of cardiomyopathy and in 40% cases of pericardial tamponade. Rajee *et al* study also showed most common etiology associated with hyperbilirubinemia were coronary artery heart disease (73%) and rheumatic valvular heart disease (72%) [8].

On admission, mean SGPT/ALT levels were found to be more elevated in patients with cardiomyopathy (181.33±200.22 IU/L) in comparison to RHD (168.27 ± 221.60 IU/L). It was also elevated in pericardial tamponade (159.20±46.29 IU/L), hypertensive heart disease (143.92±155.47 IU/L), coronary artery disease (136.88±197.88 IU/L) and myocarditis (86.33±53.72 IU/L). As ALT is more liver specific than AST, we had compared SGPT in various etiologies of congestive heart failure. Such comparison was not studied in any previous studied.

Limitations: Due to multiple etiology of congestive heart failure and different treatment approach in each etiology, treatment modalities were not compared.

Conclusion

This study concluded that LFTs were significantly elevated in NYHA class IV of heart failure as compared to NYHA class I

and LFTs showed significant correlation with severity of heart failure (NYHA class). Early and timely management of congestive heart failure will improve LFTs and will prevent significant liver failure. More attention is needed, not only for the management of heart failure and its accompanying consequences, but also for the influence of heart failure on hepatic functioning and the cardio hepatic interactions that occur in the complete spectrum of heart failure.

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