

## A Prospective Research to Assess Hepatic Measures in Individuals with Congestive Heart Failure

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### Abstract

**Aim:** The aim of the study to evaluate the hepatic parameters in congestive heart failure patients.

**Methods:** This is a prospective study was conducted in the Department of General Medicine, Vardhman institute of medical sciences, Pawapuri, Nalanda, Bihar, India. The hepatic biochemical parameters like serum bilirubin (direct, indirect and total), serum AST and ALT, Serum alkaline phosphatase, Serum proteins and Prothrombin time were estimated.

**Results:** Serum bilirubin was  $3.98 \pm 1.57$  mg/dl in class IV and least in class I that is  $1.112 \pm 0.20$  mg/dl. Serum AST was highest in class IV  $162.14 \pm 25.85$  IU and least in class I that is  $36.61 \pm 10.87$  IU ( $p=0.001$ ). Serum ALT was highest in class IV  $181.98 \pm 31.85$  IU and least in class I that is  $34.11 \pm 10.56$  ( $p=0.001$ ). Serum ALP was highest in class IV  $61.22 \pm 14.32$  IU and least in class I that is  $40.41 \pm 9.85$  ( $p=0.01$ ). Serum total protein (g/dl) was decreased as the heart failure progressed least in class IV  $3.51 \pm 1.41$  g/dl and highest in class I that is  $6.58.13 \pm 2.17$  gm/dl ( $p=0.05$ ). Serum albumin (g/dl) was least in class IV  $2.89 \pm 0.92$  g/dl and highest in class I that is  $4.65 \pm 0.85$  gm/dl ( $p=0.031$ ). Prothrombin time (sec) was highest in class IV  $22.24 \pm 7.11$  sec and least in class I that is  $13.12 \pm 3.36$  sec ( $p=0.01$ ). The mean value of serum bilirubin (mg/dl) in patients with duration of disease more than 4 year was  $3.21 \pm 1.27$

mg/dl was significantly higher than the patients with duration of disease less than 4 year significantly ( $p=0.03$ ). Serum AST was highest with duration of disease more than 4 year  $113\pm 27.34$  IU and least in patients with duration of disease less than 4 year that is  $41.57\pm 9.94$  IU ( $p=0.001$ ). Serum ALT was highest with duration of disease more than 4 year  $160.87\pm 25.38$  IU and least in patients with duration of disease less than 4 year that is  $35.12\pm 9.94$  IU ( $p=0.001$ ). Serum ALP IU was highest with duration of disease more than 4 year  $61.12\pm 10.14$  IU and least in patients with duration of disease less than 4 year that is  $41.15\pm 4.57$  IU ( $p=0.03$ ). Serum total protein (g/dl) was least with duration of disease more than 4 year  $4.12\pm 2.22$  g/dl and normal in patients with duration of disease less than 4 year that is  $6.87\pm 1.68$  g/dl ( $p=0.025$ ).

**Conclusion:** Heart failure was common in fifth and sixth decade of life and there was male predominance. Congested hepatomegaly was common presentation jaundice and ascites was also common.

**Keywords:** CHF, hepatic, jaundice

### Introduction

Heart failure (HF) is associated with significant morbidity and mortality.<sup>1</sup> This complex clinical syndrome is punctuated by periods of decompensation,<sup>2</sup> which in turn drives health care utilization (HCU)<sup>3</sup> and negatively impacts quality of life (QoL).<sup>4</sup> As such, in recent years, there has been growing interest in identifying novel strategies for early detection of disease progression to mitigate an individual patient's risk of hospitalization. Remote monitoring of HF patients utilizing existing implantable cardiac devices is one approach that has been evaluated in this context. However, the results from clinical trials and meta-analyses have been variable.<sup>5-10</sup> The seemingly disparate findings across a number of studies are likely influenced by key factors including the number and types of sensors used, the methodology of assessing risk as a point estimate in time rather than as a dynamic variable, the complex topography of HF decompensation, and the disconnect between acquisition of diagnostic data and implementation of appropriate therapeutic actions.<sup>11</sup> It is also important to highlight that evaluation of available HF remote monitoring technologies has almost exclusively focused on population health and health system outcomes with very little emphasis on valuing the patient experience of disease. As such, a more fulsome understanding of the correlation between clinical status and behaviours of HF self-efficacy with device diagnostic data is needed.<sup>8</sup> Heart failure risk status (HFERS) is a validated dynamic HF risk prediction tool available on Medtronic cardiac resynchronization therapy device with defibrillation capability (CRT-D) and implantable cardioverter defibrillator (ICD) devices, which integrates diagnostic data to generate a patient-specific assessment of low, medium, or high risk for HF hospitalization (HFH) in the next 30 days.<sup>8,12</sup> Fouad et al has concluded that heart failure is associated with manifestations of liver failure and laboratory data specific to ischemic hepatitis or congestive hepatopathy.<sup>13</sup> Auer et al has reported that elevated liver enzymes are common in patients with HF.<sup>14</sup> Saner et al has concluded that congestive heart failure should always be considered as a possible cause of acute liver failure.<sup>15</sup> It is clear that hepatic abnormalities are associated with heart failure. With this view present study has been designed to study the prevalence of liver function abnormalities in heart failure patients, pattern of elevation of liver enzymes and correlation of liver function tests with etiology, duration and of heart failure.

### Material and Methods

This is a prospective study was conducted in the Department of General Medicine, Vardhman institute of medical sciences, Pawapuri, Nalanda, Bihar, India Total 100 patients with clinically

and echocardiographically diagnosed of heart failure were include in this study. Patients with pre-existing hepatic disorder, Use of hepatotoxic drug, Chronic alcoholic were exclude from this study.

All patients enrolled for this study was evaluated clinically and echocardiographically. Various demographic parameters like age sex duration of disease were recorded on predesigned Performa. The hepatic biochemical parameters like serum bilirubin (direct, indirect and total), serum AST and ALT, Serum alkaline phosphatase, Serum proteins and Prothrombin time were estimated. For estimation of above parameters ebra EM 200 biochemistry analyser was used. All parameters were compared based on NYSA classification and duration of disease.<sup>16,17</sup>

**Statistical analysis**

Data were recorded in excel sheet and statistical Analysis was done with software SPSS-21 version. Qualitative data were calculated as percentage and proportions and were analysed by chi-square test. Quantitative data were expressed as mean ± SD and these data were analysed by unpaired student t test. The p value less than 0.05 were taken as significant

**Results**

In present study 100 patients with various class and duration of heart failure were enrolled for this study for evaluation of changes in hepatic parameters. In our study as per table 1 mean age of patient was 58.68±10.78 years. Number of patients less than 25 years was 3(3%), from 25 to 50 years were 16 (16%). Maximum number of patients was from 50 to 75 years of age that is 57 (57%). Number of patients above 75 years of age was 24 (24%). There was male predominance 73(73%). As per NYSA classification maximum number of cases were class II (47%) followed by class III (26%). Percentage of patients with class I were 20% and class IV were 7%. Regarding duration of disease 12% patients have disease since less than one year. Maximum number of patients has disease from to 4-year duration that is 67%. Duration of disease was more than 4 year in 21% patients.

**Table 1: Demography of patients with heart failure**

Parameter		Number	Percentage (%)
Age (mean 58.68±10.78 year)	Below 25year	3	3
	25 to 50	16	16
	50 to 75	57	57
	Above 75	24	24
Sex	M	73	73
	F	27	27
NYSA class	Class I	20	20
	Class II	47	47
	Class III	26	26
	Class IV	7	7
Duration of disease	Less than 1 year	12	12
	1 to 4year	67	67
	More than 4year	21	21

Regarding clinical presentation of patient's jaundice was present in 28%, hepatomegaly which was most commonly present that was 47%, ascites was present in 29% and congested hepatomegaly in USG (42%).

**Table 2: Clinical presentation of patients with heart failure**

Clinical parameter	N (n=100)	Percentage (%)
Jaundice	28	28
Hepatomegaly	47	47
Ascites	29	29
Congested hepatomegaly in USG	42	42

Regarding hepatic biochemical parameters there is significant variation in serum bilirubin (mg/dl) parameter as per progress in class of heart failure ( $p=0.001$ ). Serum bilirubin was  $3.98\pm 1.57$  mg/dl in class IV and least in class I that is  $1.112\pm 0.20$  mg/dl. Serum AST was highest in class IV  $162.14\pm 25.85$  IU and least in class I that is  $36.61\pm 10.87$  IU ( $p=0.001$ ). Serum ALT was highest in class IV  $181.98\pm 31.85$  IU and least in class I that is  $34.11\pm 10.56$  ( $p=0.001$ ). Serum ALP was highest in class IV  $61.22\pm 14.32$  IU and least in class I that is  $40.41\pm 9.85$  ( $p=0.01$ ). Serum total protein (g/dl) was decreased as the heart failure progressed least in class IV  $3.51\pm 1.41$  g/dl and highest in class I that is  $6.58.13\pm 2.17$  gm/dl ( $p=0.05$ ). Serum albumin (g/dl) was least in class IV  $2.89\pm 0.92$  g/dl and highest in class I that is  $4.65\pm 0.85$  gm/dl ( $p=0.031$ ). Prothrombin time (sec) was highest in class IV  $22.24\pm 7.11$  sec and least in class I that is  $13.12\pm 3.36$  sec ( $p=0.01$ ).

**Table 3: Liver biochemical parameters of patients in comparison with class of heart failure**

Parameter	Class I	Class II	Class III	Class IV	P value
Serum bilirubin (mg/dl)	$1.112\pm 0.20$	$1.64\pm 0.62$	$2.35\pm 0.74$	$3.98\pm 1.57$	0.001
Serum AST IU	$36.61\pm 10.87$	$52.75\pm 20.68$	$89.57\pm 13.89$	$162.14\pm 25.85$	0.001
Serum ALT IU	$34.11\pm 10.56$	$45.23\pm 11.24$	$85.36\pm 13.22$	$181.98\pm 31.85$	0.0001
Serum ALP IU	$40.41\pm 9.85$	$43.26\pm 12.55$	$53.83\pm 11.86$	$61.22\pm 14.32$	0.01
Serum total protein (g/dl)	$6.58.13\pm 2.17$	$5.34\pm 2.11$	$5.05\pm 2.05$	$3.51\pm 1.41$	0.05
Serum albumin (g/dl)	$4.65\pm 0.83$	$3.29\pm 0.79$	$3.12\pm 0.51$	$2.89\pm 0.92$	0.031
Prothrombin time (sec)	$13.12\pm 3.36$	$15.06\pm 8.95$	$18.23\pm 4.31$	$22.24\pm 7.11$	0.01

Regarding comparison of liver biochemical parameters in patients with duration of heart failure as per table 4 it is clear that serum bilirubin was increased with the duration of disease. The mean value of serum bilirubin (mg/dl) in patients with duration of disease more than 4 year was  $3.21\pm 1.27$  mg/dl was significantly higher than the patients with duration of disease less than 4 year significantly ( $p=0.03$ ). Serum AST was highest with duration of disease more than

4 year  $113 \pm 27.34$  IU and least in patients with duration of disease less than 4 year that is  $41.57 \pm 9.94$  IU ( $p=0.001$ ). Serum ALT was highest with duration of disease more than 4 year  $160.87 \pm 25.38$  IU and least in patients with duration of disease less than 4 year that is  $35.12 \pm 9.94$  IU ( $p=0.001$ ). Serum ALP IU was highest with duration of disease more than 4 year  $61.12 \pm 10.14$  IU and least in patients with duration of disease less than 4 year that is  $41.15 \pm 4.57$  IU ( $p=0.03$ ). Serum total protein (g/dl) was least with duration of disease more than 4 year  $4.12 \pm 2.22$  g/dl and normal in patients with duration of disease less than 4 year that is  $6.87 \pm 1.68$  g/dl ( $p=0.025$ ). Serum albumin (g/dl) was least with duration of disease more than 4 year  $2.77 \pm 1.44$  g/dl and normal in patients with duration of disease less than 4 year that is  $3.74 \pm 0.79$  g/dl ( $p=0.11$ ). Prothrombin time (sec) was highest with duration of disease more than 4 year  $21.11 \pm 3.22$  sec and least in patients with duration of disease less than 4 year that is  $14.79 \pm 2.68$  sec ( $p=0.01$ ).

**Table 4: Liver biochemical parameters of patients in comparison with duration of heart failure**

Parameter	less than 1 year	1 to 4 years	more than 4 years	P value
Serum bilirubin (mg/dl)	$1.09 \pm 0.4$	$1.98 \pm 0.56$	$3.21 \pm 1.27$	0.03
Serum AST IU	$41.57 \pm 9.94$	$48.11 \pm 6.14$	$113 \pm 27.34$	0.001
Serum ALT IU	$35.12 \pm 9.94$	$79.65 \pm 8.45$	$160.87 \pm 25.38$	0.000
Serum ALP IU	$41.15 \pm 4.57$	$44.85 \pm 10.14$	$61.12 \pm 10.14$	0.03
Serum total protein (g/dl)	$6.87 \pm 1.68$	$5.94 \pm 1.89$	$4.12 \pm 2.22$	0.025
Serum albumin (g/dl)	$3.74 \pm 0.79$	$3.01 \pm 1.22$	$2.77 \pm 1.44$	0.11
Prothrombin time (sec)	$14.79 \pm 2.68$	$15.76 \pm 3.45$	$21.11 \pm 3.22$	0.01

## Discussion

Heart failure as a cause of acute liver failure is less documented and poorly understood condition. Auer et al have concluded that hepatic enzymes are elevated in heart failure patients. Pattern of change in hepatic enzyme differ as per in patients with chronic and acute decompensate HF and are surrogates of the type of hemodynamic alterations.<sup>13,14</sup> Shah et al has concluded that hepatic injury as a consequence of heart failure is common but less recognized syndrome.<sup>18</sup> In present study we have observed that mean age of patient was  $58.68 \pm 10.78$  years and maximum number of patients was from 50 to 75 years of age. There was male predominance. This finding is supported by Van Deursen et al.<sup>19</sup> Most of the patients were in class III and class IV group and duration of disease was from 1 with higher class of heart failure than class I. This corroborates with the work of Allen et al.<sup>20</sup>

We have observed that hepatic biochemical parameters were significantly elevated in patients with higher class of heart failure than class I. In our study Serum total protein (g/dl) was decreased as the heart failure progressed least in class IV  $3.51 \pm 1.41$  g/dl and highest in class I that is  $6.58.13 \pm 2.17$  gm/dl ( $p=0.05$ ). Serum albumin (g/dl) was least in class IV  $2.89 \pm 0.92$  g/dl and highest in class I that is  $4.65 \pm 0.85$  gm/dl ( $p=0.031$ ). Prothrombin time (sec) was highest in class IV  $22.24 \pm 7.11$  sec and least in class I that is  $13.12 \pm 3.36$  sec ( $p=0.01$ ). Serum total protein (g/dl) and albumin was significantly decreased in class III and class IV patients in comparison to class I and class II to 4 years. Alvarez has concluded that may cause elevations of liver enzymes and both direct and indirect serum bilirubin and marked elevations in serum aminotransferases which support our study.<sup>21</sup> Nikolaou et al has concluded that Abnormal LFTs were present in about a half of patients presenting with heart failure which corroborates with our finding<sup>22</sup> Samsky et al has reported that severity of hepatic damage increases with

duration of disease which supports our study.<sup>23</sup> Naschitz et al has concluded that the spectrum of heart diseases affecting the liver includes mild alterations of liver function tests in heart failure, cardiogenic ischemic hepatitis, congestive liver fibrosis, and cardiac cirrhosis which progress with the progress of disease which support our study. has reported that liver function abnormalities remain common in patients with congestive heart failure but are generally small in magnitude and not associated with clinically apparent hepatic disease which contradict our study.<sup>24</sup>

### Conclusion

The present study concluded that heart failure was common in fifth and sixth decade of life and there was male predominance. Congested hepatomegaly was common presentation jaundice and ascites was also common. Change in biochemical parameters was increased with severity and duration of heart disease.

### Reference

1. Lloyd-Jones D, Adams R, Carnethon M, De Simone G, Ferguson TB, Flegal K, Ford E, Furie K, Go A, Greenlund K, Haase N, Hailpern S, Ho M, Howard V, Kissela B, Kittner S, Lackland D, Lisabeth L, Marelli A, McDermott M, Meigs J, Mozaffarian D, Nichol G, O'Donnell C, Roger V, Rosamond W, Sacco R, Sorlie P, Stafford R, Steinberger J, Thom T, Wasserthiel-Smoller S, Wong N, Wylie-Rosett J, Hong Y. Heart disease and stroke statistics—2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 2009; **119**: e21–e181.
2. Gheorghide M, De Luca L, Fonarow GC, Filippatos G, Metra M, Francis GS. Pathophysiologic targets in the early phase of acute heart failure syndromes. *Am J Cardiol* 2005; **96**: 11G–17G.
3. Klersy C, Boriani G, De Silvestri A, Mairesse GH, Braunschweig F, Scotti V, Balduini A, Cowie MR, Leyva F. Effect of telemonitoring of cardiac implantable electronic devices on healthcare utilization: a meta-analysis of randomized controlled trials in patients with heart failure. *Eur J Heart Fail* 2016; **18**: 195–204.
4. Nieminen MS, Dickstein K, Fonseca C, Serrano JM, Parissis J, Fedele F, Wikstrom G, Agostoni P, Atar S, Baholli L, Brito D, Colet JC, Edes I, Gomez Mesa JE, Gorjup V, Garza EH, Gonzalez Juanatey JR, Karanovic N, Karavidas A, Katsytadze I, Kivikko M, Matskeplishvili S, Merkely B, Morandi F, Novoa A, Oliva F, Ostadal P, Pereira-Barretto A, Pollesello P, Rudiger A, Schwinger RH, Wieser M, Yavelov I, Zymlinski R. The patient perspective: quality of life in advanced heart failure with frequent hospitalisations. *Int J Cardiol* 2015; **191**: 256–264.
5. van Veldhuisen DJ, Braunschweig F, Conraads V, Ford I, Cowie MR, Jondeau G, Kautzner J, Aguilera RM, Lunati M, Yu CM, Gerritse B, Borggreffe M. Intrathoracic impedance monitoring, audible patient alerts, and outcome in patients with heart failure. *Circulation* 2011; **124**: 1719–1726.
6. Bohm M, Drexler H, Oswald H, Rybak K, Bosch R, Butter C, Klein G, Gerritse B, Monteiro J, Israel C, Bimmel D, Kaab S, Huegl B, Brachmann J. Fluid status telemedicine alerts for heart failure: a randomized controlled trial. *Eur Heart J* 2016; **37**: 3154–3163.
7. Boriani G, Da Costa A, Quesada A, Ricci RP, Favale S, Boscolo G, Clementy N, Amori V, Mangoni di SSL, Burri H. Effects of remote monitoring on clinical outcomes and use of healthcare resources in heart failure patients with biventricular defibrillators: results of the MORE-CARE multicentre randomized controlled trial. *Eur J Heart Fail* 2017; **19**: 416–425.

8. Cowie MR, Sarkar S, Koehler J, Whellan DJ, Crossley GH, Tang WH, Abraham WT, Sharma V, Santini M. Development and validation of an integrated diagnostic algorithm derived from parameters monitored in implantable devices for identifying patients at risk for heart failure hospitalization in an ambulatory setting. *Eur Heart J* 2013; **34**: 2472–2480.
9. Sharma V, Rathman LD, Small RS, Whellan DJ, Koehler J, Warman E, Abraham WT. Stratifying patients at the risk of heart failure hospitalization using existing device diagnostic thresholds. *Heart Lung J Crit Care* 2015; **44**: 129–136.
10. Dierckx R, Houben R, Goethals M, Verstreken S, Bartunek J, Saeys R, De Proft M, Boel E, Vanderheyden M. Integration of remote monitoring of device diagnostic parameters into a multidisciplinary heart failure management program. *Int J Cardiol* 2014; **172**: 606–607.
11. Hawkins NM, Virani SA, Sperrin M, Buchan IE, McMurray JJ, Krahn AD. Predicting heart failure decompensation using cardiac implantable electronic devices: a review of practices and challenges. *Eur J Heart Fail* 2016; **18**: 977–986.
12. Burri H, da Costa A, Quesada A, Ricci RP, Favale S, Clementy N, Boscolo G, Villalobos FS, Mangoni di SSL, Sharma V, Boriani G. Risk stratification of cardiovascular and heart failure hospitalizations using integrated device diagnostics in patients with a cardiac resynchronization therapy defibrillator. *Europace* 2017; **20**: e69–e77.
13. Fouad YM, Yehia R. Hepato-cardiac disorders. *World J Hepatol.* 2014;6(1):41-54.
14. Auer J. What does the liver tell us about the failing heart? *Eur Heart J.* 2013;34(10):711-4.
15. Heuer M, Meyer M. When the heart kills the liver: acute liver failure in congestive heart failure. *Eur J Med Res.* 2009;14:541.
16. Yancy CW. 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2013;128;16.
17. The Criteria Committee of the New York Heart Association. Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels, 9<sup>th</sup> ed. Boston, Mass: Little, Brown & Co; 1994:253-6.
18. Shah SC, Sass DA. Cardiac Hepatopathy. A review of liver dysfunction in heart failure. *Liver Res Open J.* 2015;1(1):1-10
19. Van deursen VM, Damman K, Hillege H, Van beek AP, Van veldhuisen DJ, Voors AA. Abnormal Liver Function in Relation to Hemodynamic Profile in Heart Failure Patients. *J Cardiac Failure.* 2010;16:1.
20. Allen LA, Felker GM, Pocock S. Liver function abnormalities and outcome in patients with chronic heart failure: data from the Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) program. *Eur J Heart Fail.* 2009;11(2):170-7.
21. Alvarez AM, Mukherjee D. Liver abnormalities in cardiac diseases and heart failure. *Int J Angiol.* 2011;20(3):135-42.
22. Nikolaou M, Parissis J, Yilmaz MB, Seronde M-F, Kivikko M, Laribi S et al Liver function abnormalities, clinical profile, and outcome in acute decompensated heart failure. *Eur Heart J.* 2013;34(10):742-9.
23. Samsky MD, Patel CB, De Wald TA, Smith AD, Felker GM, Rogers JG et al. Cardiohepatic Interactions in Heart Failure an Overview and Clinical Implications. *JACC.* 2013;61(24):2397-405.
24. Naschitz JE, Slobodin G, Lewis RJ, Zuckerman E, Yeshurun D. Heart diseases affecting the liver and liver diseases affecting the heart. *Am Heart J.* 2000;140(1):111-20.