



PATTERN OF LIVER INJURY IN HEART FAILURE, AN OBSERVATIONAL STUDY IN A TERTIARY CARE HOSPITAL

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ABSTRACT To study the incidence, to determine the pattern of elevation of enzymes and to correlate the alteration of LFTs with hepatomegaly and type of heart failure. The study was conducted including the patients admitted in a Tertiary Care Hospital. A total of 75 cases and 25 controls have been selected. 53 patients with abnormal liver function tests, 47 achieved remission from congestive cardiac failure within 7 days. With remission the hyperbilirubinemia, and the increased aspartate transaminase levels and alanine transaminase levels returned to normal. A marked raise in AST ALT above 1000 were noted in a significant number of cases with congestive cardiac failures in overt shock.

KEYWORDS : Liver dysfunction, Heart failure, Serum Bilirubin

INTRODUCTION

The liver has been called the custodian of milieu interior. So, any liver disorders will have far reaching consequences on body's homeostasis. Also, numerous pathologies of other systems can affect liver. Both acute and chronic heart failure may result in abnormalities of liver. Liver receives 25% of cardiac output, a fall in cardiac output will result in hepatic hypoperfusion. Liver has the capacity to withstand changes in blood flow by vasoactive mechanisms and oxygen extraction from blood. However, when critical levels are reached, hepatic injury ensues¹.

Both right and left sided heart failure can result in liver injury. In right-sided heart failure, elevation of right heart pressure results in raised pressure in hepatic sinusoids, hepatic congestion and liver cell hypoxia. In left sided heart failure, decreased cardiac output results in hepatic hypo perfusion and hypoxia.

The common pathway is centrilobular hepatocellular necrosis. Zone 3 of the liver lobule is most vulnerable to hypoxic injury due to the normal organization of hepatic blood flow.

In this study, the effects of congestive cardiac failure on liver and its function is analyzed in 75 patients compared with 25 healthy individuals. Various etiologies of congestive cardiac failure have been included and compared, based on their effects on liver functions. Remissions and exacerbations have been tracked on the 7th day and the variations of liver function have been recorded.

Identifying the potential alterations in liver function among heart failure patients avoids cumbersome work up for liver injury and helps us to tailor drugs to treat heart failure at an optimum level.

AIMS OF THE STUDY

1. To study the incidence of LFT alteration in heart failure patients.
2. To determine the pattern of elevation of enzymes, with respect to the etiology of heart failure.
3. To correlate the alteration of LFTs with hepatomegaly and type of heart failure.

MATERIALS AND METHODS

A total of 100 subjects with 75 cases and 25 controls have been selected. 75 Cases of heart failure patients of varied etiologies presenting during the period of the study i.e. from OCTOBER 2017 - OCTOBER 2019 in a Tertiary Care Hospital and 25 healthy individuals were taken as controls. Liver function tests were performed on both controls and cases on day 1 and day 7.

This study is an observational study (case- control), comparing the alteration of liver functions between cases (various causes of heart failure) and controls.

Cases and Controls

Heart failure due to various etiologies including Coronary heart disease, rheumatic heart disease, hypertensive heart disease, cor pulmonale and other cardiomyopathies meeting the following inclusion criteria and not possessing following exclusion criteria were selected. Etiology of the heart failure was determined by previous medical records as well as Trans-Thoracic echocardiogram. Healthy individuals between 15-90 yrs. of age without any known history of medical illness such as heart and liver diseases were selected.

INCLUSION CRITERIA

- Both males and females with heart failure in the age group of 15 to 90 years.

EXCLUSION CRITERIA

- Known case alcoholic liver disease.
- Recent intake of Hepatotoxic drugs or drugs causing raised liver parameters, such as Rifampicin, INH, Steroids, chlorpromazine, amiodarone, statins, hydralazine, phenytoin and valproate.
- Positive viral markers.
- Past Documented liver disease

RESULTS

Age distribution of cases and controls

AGE GROUP	CASES			CONTROLS		
	Total	Male	Female	Total	Male	Female
13-20	1	1	0	0	0	0
21- 30	1	0	1	2	2	0
31 -40	8	3	5	5	2	3
41- 50	19	9	10	7	5	5
51-60	22	17	5	6	6	3
61-70	15	9	6	0	0	0
71-80	8	4	4	0	0	0
81-100	1	1	0	0	0	0
Total	75	44	31	25	15	10

ETIOLOGY OF HEART FAILURE

Etiology	No. of cases	No. of percentage
Rheumatic heart disease	18	24%
Coronary heart disease	30	40%
Cor pulmonale	13	17.3%
Cardiomyopathy	7	9.3%
Hypertensive heart disease	7	9.3%

No of Cases with Hepatomegaly Showing Increased Serum Alkaline Phosphatase

No of Cases with Hepatomegaly	51/75
Cases with Raised ALP	10/75
No of Cases with Raised ALP with Hepatomegaly And CCF	10/51
No of Cases with Raised ALP Without Hepatomegaly	0/24

Percentage of Raised ALP In CCF	12.5%
Percentage of Raised ALP in Patients with CCF Having Hepatomegaly	19.6%

Serum Bilirubin



29.3% of the patients had less than 1.2mg%, 57.3% had 1.2-3 mg% 9.3% had 3-5 and only 4% of the cases had greater than 5mg%.

S No	Test	Normal Range	Results		
			Range	No of Patients	Percentage
1	Serum Bilirubin	0-3-1.2 Mg/Dl	<1.2	22	29.3
			1.2-3	43	57.3
			3-5	7	9.3
			>5	3	4
2	Ast	Up to 40 I.U	Normal Range	36	48
			Increased	39	52
3	Alt	Up to 35 I. U	Normal Range	44	58.6
			Increased	31	41.3
4	ALP	44-147 IU	Normal Range	65	86.6
			Increased	10	13.3
5	Serum Albumin	>3gm%	Normal	57	76
			Reduced	15	20
			A-G Reversal	3	4
6	Prothrombin	Control (12-14 Sec), Test Abnormal If 1 & 1/2 Times Greater Than Control	Normal	33	44
			Prolonged	42	56

In controls no abnormal LFT was noted.

DISCUSSION

The results of the present study have been compared with prior studies conducted in authentic centers and relevant data are put forward. In tune with most of the studies our data has been comparable with respect to the local population.

Analysis according to the various Etiologies shows that patients with coronary artery disease (73%) and rheumatic heart disease (72%) showed the most percentage of abnormal liver function tests and patients with hypertensive heart disease (57%) showed least percentage of abnormal liver function tests. Of the 18 patients with rheumatic heart disease, 13 patients showed abnormal liver function (72%), Of the 13 patients with cor pulmonale 9 showed abnormal liver function (69%). In 7 patients with hypertensive heart disease 4 showed abnormal liver function (57%), whereas in 30 patients with coronary artery heart disease, 22 showed abnormal liver function (73%) 5 out of 7 patients with cardiomyopathy showed abnormal liver function.

Hepatomegaly

Hepatomegaly was seen in 51 patients out of 75 (68%). The liver enlargement varied from 1cm to 10 cm below the Right costal margin.

Name of the study	Percentage with Hepatomegaly
Present study	68
White et al ^[2]	95
And Sinha ^[3]	25.5
Dunn et al ^[4]	95
Richman et al ^[5]	50

Icterus

Icterus was present in 16 (21%) cases. Rheumatic heart disease produced the most number of cases with clinically detectable jaundice.

Icterus was least present in patients with Cor pulmonale and Hypertensive heart disease. None of the controls had icterus.

Name of the study	Percentage with Icterus (clinical jaundice)
White et al	20
Garvin et al ^[6] and Kubo et al ^[7]	20
Present study	21

Hyperbilirubinemia

Hyperbilirubinemia was detected in 53 out of 75 cases. The etiologies most associated with hyperbilirubinemia were coronary artery heart disease (73%) and rheumatic valvular heart disease (72%). In majority of cases serum bilirubin did not exceed 3 mg/ dl.

Kubo et al have reported that serum bilirubin is increased in 20 to 80% of patients with congestive cardiac failure; it rarely exceeds 5mg/dl and is usually less than 3mg/dl. Zieve^[8] has reported that unconjugated bilirubin is usually higher than conjugated bilirubin. Sherlock^[9] and Richman et al have also reported that levels usually range between 1 mg/dl and 5mg/dl with the unconjugated form constituting the major fraction. Sherlock has reported that only rarely have levels exceeded 20 mg/dl in patients with severe improvement of the right sided heart failure. Elevated serum bilirubin levels return to normal quite rapidly over a period of 3-7days.

S.No	Authors	% of cases with HyperBilirubinemia
1	Felder et al	52%
2	Sherlock	68%
3	Evans et al	26%
4	White et al	40%
5	Wahi et al	45%
6	Nareshbhu	58%
7	Richman et al	31%
8	This study	70.6%

Richman et al observed that marked increase in serum bilirubin was observed in rheumatic valvular heart disease in his study. This correlates with Sherlock's observation that deep icterus has a correlation with valvular diseases of heart. The severity of failure and duration of failure correlate well with the elevation in serum bilirubin level. The elevated bilirubin level was less than 3 mg/dl in 43 cases and more than 5mg/dl in 3 cases who had severe congestive cardiac failure. With remission of congestive cardiac failure, the serum bilirubin returned to normal in 47 cases which correlates with Richman et al. In this study 71% of patients showed an abnormal increase in serum bilirubin levels of which 81% showed mild rise of bilirubin between 1-5mg/dl; which correlates with Kubo's observation.

Serumaminotransferases

Richman et al, Dunn et al and Sherlock et al have reported that elevation in serum amino transferase levels are seen in 3-50% of patients with right sided heart failure. The wide range in incidence reflects the fact that elevations are seen more commonly in acute congestive heart failure (15-48%) than in chronic failure (3-5%).

Richman has reported that aspartate transaminase levels are typically more marked than alanine transaminase levels, the former values ranging from 40-801 I.U. This degree of marked elevation is seen in acute heart failure secondary to cor pulmonale or rheumatic heart disease with tricuspid insufficiency, or due to heart failure complicated by shock.

PERCENTAGE OF CASES REPORTED WITH ELEVATED ENZYMES

	AST	ALT
PREVIOUS STUDIES	3-50%	3-50%
PRESENT STUDY	52%	41%

Serum alkaline phosphatase

Richman et al and Sherlock have reported elevation of serum alkaline phosphatase levels in 10-20% of patients with right sided heart failure. Dunn et al however reports that in most patients the levels are within normal limits, rarely do they exceed twice normal. Felders^[10] et al, have also reported increased serum alkaline phosphatase in 10-20% of patients with congestive cardiac failure.

Elevation of serum alkaline phosphatase levels do not correlate with increases in serum bilirubin or aminotransferases. The highest elevations are usually seen in patients with marked liver enlargement. With improvement in the cardiac status serum alkaline phosphatase returns to normal in 1 week.

In the present study 10 cases (13%) showed elevation in alkaline phosphatase levels. With remission, in all cases the serum alkaline phosphatase levels returned to normal.

Sherlock / Richman et al	10-20%
Felder et al	10-20%
Present study	13%

Severity of cardiac failure

Serum bilirubin more than 3mg/dl was present with severe congestive cardiac failure. Gross elevation of transaminases was present in severe congestive cardiac failure with hypotension and shock.

Remission

Of the 53 patients with abnormal liver function tests, 47 achieved remission from congestive cardiac failure within 7 days. With remission the hyperbilirubinemia, and the increased aspartate transaminase levels and alanine transaminases levels returned to normal. The prothrombin time and serum proteins did not show any marked change.

CONCLUSION

1. Heart failure, is beyond any need for further confirmation, associated with an alteration of liver function. Previous studies have shown congestion of the liver and raised liver parameters.
2. The present study re affirmed the findings. A pattern of modest raise in AST and ALT, with hepatomegaly and raise in ALP were noted. A marked raise in AST ALT above 1000 were noted in a significant number of cases with congestive cardiac failures in overt shock.
3. At 1 week, past the hospital stay most of the parameters recovered to normal levels, prothrombin time and proteins remained above and below the baseline respectively.
4. Awareness of these liver alterations in heart disease is a must to be able to restrain from cumbersome evaluations of hospitalized patients with heart disease and jaundice.

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