

Research Article

Cardio-Hepatic Interactions in Acute Heart Failure A Study on Liver Function Test Abnormalities

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Abstract

Background: While chronic heart failure impacts liver function, Acute heart failure's (AHF) effect remains unclear. This study investigates the prevalence and clinical significance of abnormal liver function tests (LFTs) in AHF patients.

Objective: To determine the prevalence of abnormal LFTs in patients with AHF and to examine the association between AHF severity and LFTs abnormalities' prevalence.

Methods: A cross-sectional study was conducted at the Gulab Devi Hospital Lahore, from June 26, 2023, to December 26, 2023. 100 diagnosed AHF patients were selected using a non-probability selection technique. Blood samples were processed in the Pathology lab of Gulab Devi Educational Complex. Data were analyzed using SPSS 26, with Chi-Square tests for associations and Cramer's V for significant results to measure association strength.

Results: In our study of 100 diagnosed cases of AHF, 56% were males and 44% were females. Most patients exhibited abnormal LFTs, with elevated levels of ALT, AST, ALP, and total bilirubin observed in 56%, 55%, 95%, and 37% of cases, respectively. Notably, 70% of patients had hypertension, 54% had diabetes, and 25% of patients were smokers as an additional risk factors. Our research found that these risk factors had less of an impact on abnormal LFTs, even though they seemed to be associated with an incidence of AHF.

Conclusion: A notable prevalence of abnormal LFTs was observed in AHF and those diagnosed with AHF had a higher chance of acquiring hepatic disease and hepatic dysfunction.

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Introduction

The heart, typically the size of a clenched palm, is a vital organ that supplies oxygenated blood and

nutrients to various organs in the body.¹ The heart is essential for the functioning of our circulatory system, which consists of arteries, veins, capillaries, and vessels that transport blood throughout our body. If the heart is compromised by disease or damage, organs may dysfunction from a lack of vital blood supply necessary for their proper functioning. Furthermore, changes in the hormones, neurons, or nerve impulses that control blood pressure and



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cardiac rhythm affect the pumping of blood.²

Acute decompensated heart failure (ADHF), commonly referred to as acute heart failure (AHF), is a critical medical emergency marked by a sudden decline in the cardiac output.³ This condition arises when the heart is unable to adequately provide the body with the necessary oxygen and nutrients, leading to potentially fatal consequences. Heart failure (HF) is a significant medical concern with an estimated prevalence of 64 million people globally.⁴

The liver is a vital organ that receives 25% of the cardiac output.⁵ It is situated in the upper right quadrant of the body, just below the diaphragm.⁶ Taking up four primary roles, the largest organ in the body is responsible for storing, digesting, synthesizing, eliminating, and detoxification of potentially harmful substances.⁷ It has long been recognized that the liver and heart interact extensively. Avicenna initially discovered the relationship between these organs in his well-known book "Canon" (The Law). This interaction was explained by saying that "heart warmth" prevails over "liver coldness and wetness" and that "liver dryness" was preferred to "heart wetness".⁸ Avicenna believed that an organ's disease or failure was indicated by an imbalance in the body's temperaments,⁹ The liver's role in acute heart failure has received little consideration. Subsequent investigations reveal a new angle: the cardio-hepatic syndrome, an emerging area that clarifies the delicate relationship between the liver and heart in acute heart failure patients. Patients with acute decompensated heart failure (ADHF) can develop acute ischemic hepatitis, whereas those with chronic heart failure may cause congestive hepatopathy (CH).³

Passive hepatic congestion, also known as hepatic venous congestion, occurs as a result of passive venous congestion. This usually ensues when the blood flow through the liver is decreased, leading to increased hepatic venous pressure and hypoxia.^{10,11}

Transaminase levels rapidly increase in instances of abrupt heart-related liver damage, called cardiogenic ischemic hepatitis or intense cardiogenic liver injury.¹² This occurs as a result of a severe reduction in cardiac capacity, which reduces blood supply to the

liver. This disease could develop in 20% to 30% of people with acute heart failure. Frequent causes of sudden liver injury with a cardiac origin include cardiac arrhythmia, low cardiac output, and unexpected coronary events.¹³ History of this nature implies that acute liver injury in cardiogenic shock may be triggered by both an initial reduction in blood supply to the liver and the passive venous congestion in the hepatic veins as a result of right-sided heart failure.

While the association between liver function tests and chronic heart failure is well established, the prevalence and clinical implications of abnormal liver function tests in patients with acute heart failure. About 26% of patients are readmitted to the hospitals after getting the treatment for acute heart failure and these readmissions are due to non-cardiovascular diseases¹⁴. By establishing the association between abnormal liver function tests and acute heart failure, we can identify liver injury during acute heart failure and the patient may get treatment for the liver so the readmission and mortality rate can be reduced leading to better patient care. So in this study, we aimed to examine the levels of ALT, AST, ALP, and total bilirubin to determine the association between acute heart failure and abnormal Liver function tests and the extent of damage to the liver.

Methods

It was a descriptive cross-sectional study. The research spanned from June 26, 2023, to December 26, 2023, a period of six months. The study was conducted at the Chemical Pathology Laboratory of the Gulab Devi Educational Complex. The IRB approval was taken from the Gulab Devi Educational Complex. 100 patients diagnosed with acute heart failure who had been admitted to the cardiology ward of Gulab Devi Teaching Hospital were selected after obtaining ethical approval and informed consent from all participants.

This cross-sectional study included blood samples from 100 people.

$$\text{Formula: sample size} = n = \frac{Z^2 \alpha / 2pq}{\rho^2}$$

Where n=sample size, P=prevalence, Z = confidence

interval, $q = 1-p$, ρ =margin of error. Using $P=65\%$, the margin of error is i.e., $\rho=5\%$ at a 95% confidence interval.

As the duration of the study was six months and during this timeframe, the informed consent, ethical approval, and data were taken from the patients, the limited availability of patients meeting the inclusion/exclusion criteria as well as limited resources and limited timeframe led to the sample size of 100. Despite these limitations, strict methodological protocols were adhered to ensuring the reliability and validity of the study while minimizing the potential bias.

A non-probability (purposive) sampling technique was used. A 3 cc clotted blood sample of acute heart failure patients was collected from the cardiac ward of Gulab Devi Hospital and processed in the pathology lab of the Gulab Devi Educational Complex.

Inclusion criteria for participant selection were patients aged above 18 years, both male as well as female patients included, and patients with acute heart diseases such as acute coronary syndrome, myocardial Infarction, and right bundle branch block. Exclusion criteria were patients below the age of 18 as this study was conducted on the adult population, patients with alcoholism, chronic liver disease, jaundice, and with positive viral markers as their transaminase levels would be already deranged.

3cc Clotted blood samples of 100 diagnosed acute heart failure patients were collected and processed in the Pathology lab of Gulab Devi Educational Complex. These blood samples are treated to extract serum and perform tests to rule out abnormality. It is carried out using MicroLab 400 instrument working at the principle of a spectrophotometer. A spectrophotometer is an instrument used to measure the amount of photons absorbed after it passes through a sample solution. Spectrophotometry is the quantitative measurement of the reflection or transmission properties of a material as a function of wavelength. Spectrophotometers determine enzyme activities, protein concentrations, enzymatic kinetic constants, and ligand binding reactions.

Beer's Law, also known as Beer-Lambert Law, is a

mathematical relationship that describes the absorption of light by a material. It states that the absorbance (A) of light is directly proportional to the concentration (c) of the absorbing substance and the path length (l) of the light through the material.¹⁵

$A = \epsilon Bc$ Where: A is the absorbance (unit less) ϵ is the molar absorptivity (L/mol/cm) B is the path length (cm) c is the concentration (mol/L). This law is commonly used in spectroscopy to determine the concentration of a substance in a solution and is a fundamental principle in many scientific and industrial applications.

Qualitative data were analyzed by tables and charts. Descriptive statistics like mean and standard deviation were applied for the quantitative data. A chi-square test was performed to find the association and degree of relationship between cardiac diseases and liver function tests and cramer's v was used to measure the strength of association where significant results were observed. Data were statistically analyzed by using SPSS 26. Quantitative data have been presented in the form of tables. Qualitative data have been presented in a form of chart.

Results

Out of 100 diagnosed acute heart failure cases 56 (56%) were males and 44 (44%) were females. The variable involved in this study had a mean \pm SD age of 55.83 ± 16.267 . Liver function tests were done. AST, ALT, and ALP (The mean and standard deviation of AST was 102.41 ± 148.66 . The mean and standard deviation of ALT and ALP were 91.23 ± 146.99 and 309.06 ± 172.244 respectively), exhibited abnormalities in the majority of cases. Our research revealed that, out of 100 patients, almost 56% had elevated ALT levels, 55% aberrant AST levels, 95% aberrant ALP levels, and 37% abnormal bilirubin levels at presentation (Table 1)

A closer examination of potential risk factors contributing to acute heart failure yielded fascinating discoveries. Smoking, a known correlate with heart disease, was prevalent in 25% of the patient cohort. Additionally, diabetes was present in 54% of patients, and hypertension was discovered in 70% of cases, emerging as an additional risk factor associating

Table 1: Liver Function Tests

Sr. No.	Test	Normal Range	Results		
			Range	No. of Patients	Percentage (%)
1	Total Bilirubin	0.1-1.2 mg/dl	Normal Range	63	63%
			Increased	37	37%
2	AST	08-40 IU/L	Normal range	45	45%
			Increased	55	55%
3	ALT	08-40 IU/L	Normal range	44	44%
			Increased	56	56%
4	ALP	44-147 IU/L	Normal range	5	5%
			Increased	95	95%

AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase

cardiovascular health with liver diseases. This revelation broadens our knowledge of the relationship between cardiovascular health and liver function while generating new queries regarding the complicated interplay between the two. The p-value in reported symptoms among the Cardiac Diseases and liver function tests was less than 0.05, but in the case of Bilirubin it was greater than 0.05, so we

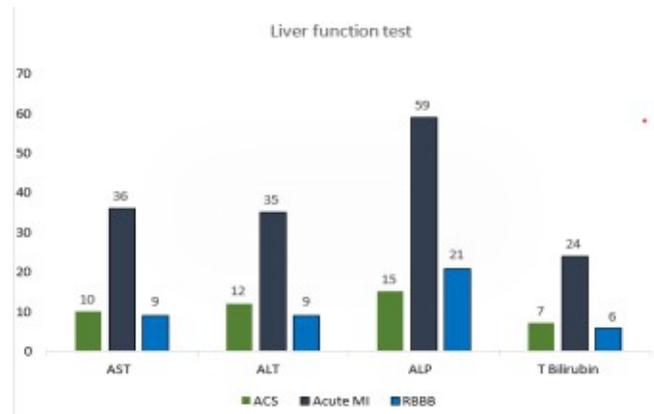
Table 2: Chi-Square Test

PARAMETERS	Values	Cardiac Disease			chi-square (X ²) test	P VALUE	Cramer's V
		ACS	Acute MI	RBBB			
AST	Normal	15 -15%	20 -20%	10 -10%	6.111	0.047*	0.175
	High	10 -10%	36 -36%	9 (9%)			
ALT	Normal	16 -16%	15 -15%	13 -13%	5.801	0.05*	0.2409
	High	12 -12%	35 -35%	9 (9%)			
ALP	Normal	2 (2%)	2 (2%)	1 (1%)	6.784	0.034*	0.2605
	High	15 -15%	59 -59%	21 -21%			
Total Bilirubin	Normal	17 -17%	36 -36%	10 -10%	0.865	0.649	
	High	7 (7%)	24 -24%	6 (6%)			

ACS: Acute coronary syndrome; MI: Myocardial Infarction; RBBB: Right bundle branch block; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase
 p < 0.05 ***Cramer's V: Indicates the strength of association for statistically significant results (p < 0.05)***. ****For Total Bilirubin, no statistically significant association was found (p > 0.05), and therefore, Cramer's V was not interpreted****

concluded that there is an association between Cardiac Disease and liver function tests (Table 2).

The Figure 1 shows the abnormal level of liver function tests in Cardiac Disease. In this study, the majority of acute myocardial infarction patients had elevated liver function tests.

**Figure-1: Bar Chart of Prevalence of abnormal Liver function tests with Cardiac Diseases.**

Our study provided knowledge on the relationship between the function of the heart and liver by indicating a strong association between abnormal liver function tests and the considerable prevalence of acute heart failure.

Discussion

The heart, a marvel of physiological engineering, orchestrates the circulation of about 2,000 gallons of blood daily, ensuring that every cell receives its life-sustaining amount of oxygen.¹⁶ Simultaneously, the liver which is regarded to be the largest organ normally gets 25% of the blood pumped by the heart, or 1500 mL/min, featuring its fundamental functioning in the body's general physiology.^{17,18} Their shared blood supply serves as more evidence of the heart and liver's dependency, a relationship that becomes more crucial when considering the repercussions of heart failure. Heart failure is a medical condition that is characterized by the impaired ability of the heart to pump blood as well as increased intra-cardiac pressures.¹⁹ It has a major impact on both the heart and the liver. The recent focus on the relationship between the heart and the liver emphasizes how heart failure impairs the liver's normal physiological activities, which in turn

impacts the heart's capacity to work. Inspired by this complicated relationship, we set out to clarify the association between acute heart failure and liver disease.

Building on the findings from other investigations (one study found liver function test abnormalities in 76% of patients), our investigation of 100 individuals diagnosed with acute heart failure unveiled significant trends.

Notably, liver function tests, including AST, ALT, and ALP exhibited abnormalities in a majority of cases. These results led to a more thorough investigation of possible risk factors that could be causing acute heart failure. About 25% of our patients were smokers, which is linked to heart diseases.²⁰ Hypertension was observed in 70% of instances and diabetes in 54% of patients, respectively, and was considered an additional factor linking liver impairment to cardiovascular health. It's interesting to note that although these risk variables seemed to influence the incidence of acute heart failure, in our investigation, they had less of an effect on deranged liver function tests.

Upon conducting a comprehensive analysis of our data in conjunction with existing literature, we observed a relatively high prevalence of liver function test abnormalities in our study, aligning with similar findings in patients with acute heart failure. Regarding Total Bilirubin (T-BIL), Shinagawa et al. reported a much higher prevalence of abnormal serum levels (64%) compared to the work of Lau et al. (19%) and our study (37%). It's worth noting that Shinigava's study did not include de novo acute heart failure, which may explain the higher prevalence of Total bilirubin abnormalities, primarily associated with chronic (predominantly right-sided) cardiac failure. Transaminase abnormalities (AST and ALT) were much greater in our research (55% and 56%, respectively) than in the studies of Nikolau et al. (33% and 25%) and Lau et al. (4% and 7%). The distinction might be made sense to some extent by the way to the inclusion of individuals with acute syndromes which includes acute coronary syndrome and acute myocardial infarction.²¹

The dominance of abnormal ALT, AST, and ALP

levels in our study, which delves deeper into the nuances of liver enzymes, supports the conclusion that acute heart failure has a significant impact on liver function (The liver contains more AST than ALT, which is restricted to the cytoplasm while AST is restricted to the mitochondria).²² Consequently, any increase in these values indicates liver disease. Since ALP is an enzyme found in the liver, kidney, and bones, any abnormality in ALP along with abnormal ALT and AST suggests that the cause is in the liver.

The collective aberration in liver enzymes in our study implies a tangible impact of acute heart failure on the liver, overshadowing the relatively normal bilirubin levels, which, albeit predominantly within the normal range, may not truly reflect the extent of parenchymal hepatic disease given the liver's larger excretory capacity.

This modern interpretation of the heart-liver link is consistent with the historical awareness expressed by Avicenna in his well-known work, the Canon.²³ Avicenna's remarks show a timeless recognition of the complex interrelationships among these essential organs, underscoring the significance of comprehending these relationships for comprehensive patient care.

This study has certain limitations. Firstly, the study duration was six months during which the informed consent, ethical approval, and data were collected, the limited availability of patients, coupled with resource constraints and the limited timeframe, restricted the sample size to 100 and this study was conducted at a single center which may affect the overall generalizability of the findings. Secondly, a non-random sampling technique was used which may introduce some bias in the study and the reliance on medical records for certain data points such as smoking or comorbidities, etc. may produce some misleading or incomplete information. Despite these limitations, strict adherence to methodological protocols and inclusion/exclusion criteria minimized potential biases, ensuring the reliability of the findings. This study provides a strong foundation for future research with larger cohorts and extended timelines.

Conclusion

Our study reveals a solid and noteworthy association between acute heart failure and abnormal liver function tests. The discoveries give us valuable data on the complicated relationship between acute heart failure and liver function, including the value of a careful understanding of these relationships for the treatment and visualization of acute heart failure.

Ethical Approval: The Institutional Review Board of Gulab Devi Educational Complex, Lahore approved this study vide letter GPMI/AHS/IRB-15623.

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Author Contribution

ARK: Conception & design, acquisition of data, drafting of article, analysis & interpretation, final approval.

FJ: Conception & design, analysis & interpretation, critical revision of the article, final approval of the version to be published.

SA: Conception & design, acquisition of data, drafting of article, final approval.

AC: Conception & design, acquisition of data, drafting of article, final approval.

SI: Conception & design, final approval.

HKS: Conception & design, drafting of article, final approval.

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