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EVALUATION AND COMPARISON OF LIVER MARKERS IN ACUTE LIVER FAILURE VS CHRONIC LIVER FAILURE IN DISTRICT FAISALABAD: A CROSS-SECTIONAL STUDY

Original Research

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ABSTRACT

Background: Liver failure is a life-threatening clinical condition resulting from the inability of the liver to maintain its metabolic, synthetic, and detoxification functions. Acute liver failure presents with sudden and severe hepatic dysfunction, whereas chronic liver failure develops gradually following prolonged liver injury. Biochemical liver markers remain central to differentiating these entities and assessing disease severity, yet comparative local data remain limited.

Objective: To evaluate and compare biochemical liver markers in patients with acute liver failure and chronic liver failure in order to identify characteristic laboratory patterns that aid clinical differentiation.

Methods: A retrospective cross-sectional study was conducted at Allied Hospital Faisalabad. A total of 100 patients aged 20–60 years were included, comprising 44 males and 56 females. Serum samples were analyzed using a Microlab 300 semi-automated chemistry analyzer. Measured parameters included alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyl transferase, total bilirubin, direct bilirubin, and indirect bilirubin. Standard reagent kits and manufacturer-recommended protocols were followed. Data were summarized using descriptive and comparative analysis.

Results: Acute liver failure showed markedly elevated aminotransferases, with mean ALT values of 370 U/L in males and 360 U/L in females, compared with 120 U/L and 110 U/L in chronic liver failure, respectively. Mean AST levels were also higher in acute liver failure (360 U/L in males, 355 U/L in females) than in chronic liver failure (135 U/L and 110 U/L). Cholestatic markers demonstrated variable patterns, with ALP values reaching 375 U/L in females with acute liver failure and 252 U/L in males with chronic disease. Mean GGT levels were higher in acute liver failure (200 U/L in males, 180 U/L in females) compared with chronic liver failure. Total bilirubin levels were elevated in both groups but were higher in acute liver failure, reaching 4.5 mg/dL in females. Direct bilirubin predominated in acute cases, whereas indirect bilirubin was relatively higher in chronic liver failure.

Conclusion: Distinct biochemical patterns were observed between acute and chronic liver failure, with acute disease characterized by pronounced hepatocellular injury and chronic disease showing sustained cholestatic and metabolic alterations. These findings support the clinical utility of liver markers in differentiating liver failure types and guiding early diagnosis and management.

Keywords: Alanine Aminotransferase, Alkaline Phosphatase, Aspartate Aminotransferase, Bilirubin, Gamma-Glutamyl Transferase, Liver Failure, Liver Function Tests.

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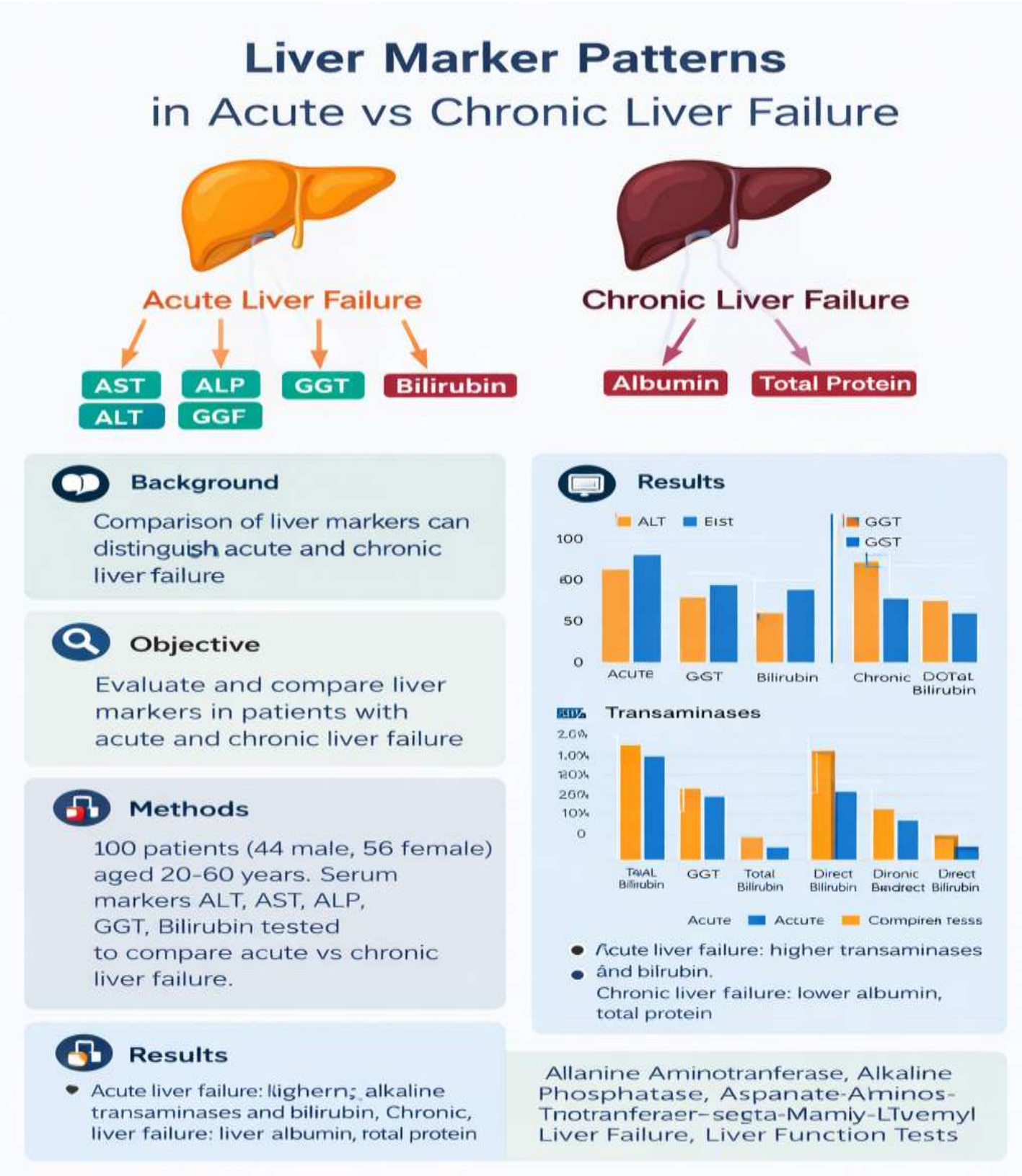

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INTRODUCTION

Liver failure represents a severe and potentially life-threatening clinical condition arising from the loss of hepatic functional capacity following acute or chronic injury. As a central metabolic organ, the liver is essential for protein synthesis, detoxification of endogenous and exogenous substances, immune regulation, bile production, and maintenance of metabolic homeostasis. Disruption of these functions results in widespread systemic consequences, often involving the nervous, renal, hematological, and cardiovascular systems, thereby explaining the high morbidity and mortality associated with liver failure. Clinically, liver failure is broadly categorized into acute liver failure (ALF) and chronic liver failure (CLF), two entities that differ markedly in etiology, tempo of progression, biochemical behavior, and prognosis (1,2). Acute liver failure is characterized by the sudden onset of hepatic dysfunction in individuals without pre-existing liver disease and typically evolves over days to weeks. It commonly presents with jaundice, coagulopathy, hepatic encephalopathy, and rapid progression to multi-organ failure. Viral hepatitis, particularly hepatitis A, B, and E, drug-induced liver injury—most notably acetaminophen toxicity—autoimmune hepatitis, ischemic injury, and toxins remain the major etiological factors. While acetaminophen overdose dominates ALF etiology in developed countries, viral hepatitis continues to be the leading cause in developing regions such as Pakistan and India (3,4). Biochemically, ALF is marked by abrupt and marked elevations in aminotransferases, profound impairment of synthetic function reflected by prolonged prothrombin time and elevated INR, and metabolic derangements that predispose to cerebral edema and death if not promptly recognized and managed (5).

In contrast, chronic liver failure develops insidiously over months or years as a consequence of sustained hepatic injury from chronic viral hepatitis B and C, alcohol-related liver disease, non-alcoholic fatty liver disease, autoimmune hepatitis, and inherited metabolic disorders such as Wilson's disease and hemochromatosis. The disease course is typically silent in early stages, with patients remaining asymptomatic until decompensation occurs. Decompensated CLF manifests clinically as ascites, variceal hemorrhage, hepatic encephalopathy, jaundice, and progressive functional decline. Globally, the burden of CLF is increasing, largely driven by the rising prevalence of obesity-related NAFLD and metabolic syndrome (6,7). Unlike ALF, CLF is pathophysiologically dominated by chronic inflammation, progressive fibrosis, and architectural distortion of hepatic parenchyma, culminating in cirrhosis. Biochemical liver markers remain central to the diagnosis, classification, monitoring, and prognostication of both acute and chronic liver failure. Conventional markers include alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyl transferase, bilirubin, albumin, and coagulation parameters such as prothrombin time and INR. Elevations in aminotransferases primarily reflect hepatocellular injury, whereas increases in alkaline phosphatase and gamma-glutamyl transferase indicate cholestasis or biliary pathology. Serum bilirubin serves as a marker of hepatic excretory function, while hypoalbuminemia and coagulopathy indicate impaired synthetic capacity (8-10). Importantly, the pattern and clinical significance of these markers differ substantially between ALF and CLF.

In acute liver failure, massive hepatocyte necrosis or apoptosis results in dramatic surges of AST and ALT, often reaching levels several thousand units above normal, particularly in ischemic or toxin-related injury. Synthetic failure occurs rapidly, leading to prolonged INR and hyperammonemia, the latter contributing to hepatic encephalopathy and cerebral edema (9). In contrast, chronic liver failure often shows modest or even near-normal transaminase levels due to reduced viable hepatocyte mass, while prognostically significant changes are better reflected by declining albumin levels, persistently elevated bilirubin, and progressive coagulopathy (11). This distinction underscores the limitation of relying solely on aminotransferases when assessing disease severity in chronic liver disease. Understanding the biological basis for these biochemical differences is essential for accurate clinical interpretation. In ALF, the sudden nature of injury explains the preservation of serum albumin early in the disease due to its relatively long half-life, whereas in CLF, sustained impairment of protein synthesis results in chronic hypoalbuminemia with systemic consequences such as edema, ascites, and sarcopenia (12). Similarly, prothrombin time and INR are among the most reliable indicators of hepatic functional reserve in both conditions, serving as key prognostic tools and criteria for liver transplantation, particularly in ALF (11). Bilirubin kinetics also differ, with abrupt rises in ALF depending on etiology, and persistent progressive elevation in CLF reflecting advanced hepatocellular dysfunction or cholestasis (13).

Emerging concepts such as acute-on-chronic liver failure further highlight the complexity of liver failure phenotypes. ACLF represents an acute deterioration in patients with underlying chronic liver disease, triggered by infections, alcohol binge, or drug toxicity, and is associated with high short-term mortality. Biochemically, ACLF exhibits overlapping features of ALF and CLF, including sharply rising transaminases superimposed on already deranged synthetic markers (14). These observations emphasize the need for comparative evaluation of liver markers within appropriate clinical contexts rather than isolated interpretation of single laboratory values. Despite extensive literature on liver failure, there remains a relative lack of region-specific comparative data systematically evaluating liver marker profiles in ALF versus CLF, particularly in resource-limited settings where disease etiology, delayed presentation, and diagnostic constraints may influence biochemical patterns. Clarifying these differences is essential for improving diagnostic accuracy, optimizing

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prognostication, and guiding timely therapeutic decisions, including referral for transplantation. Therefore, the present study is designed to evaluate and compare the levels of key liver markers in patients diagnosed with acute liver failure and chronic liver failure, with the objective of identifying significant biochemical differences that may enhance clinical assessment, disease stratification, and evidence-based management of liver failure.

METHODS

A retrospective cross-sectional study was conducted to evaluate and compare biochemical liver markers among patients diagnosed with acute liver failure and chronic liver failure. The study was carried out in Faisalabad, Pakistan, primarily through the Allied Hospital Faisalabad Biochemistry Laboratory, with additional laboratory support from the National Hospital Laboratory Faisalabad, and the study period spanned from 05 April 2025 to 05 June 2025. Medical records and laboratory data were reviewed for eligible patients to obtain a sample that reasonably reflected the local patient population across varying age groups and socioeconomic backgrounds. A total of 100 patients of both sexes were included, with cases selected from available hospital records based on predefined eligibility criteria. Patients aged 20–60 years with a confirmed diagnosis of acute or chronic liver failure and complete medical records were included. Patients younger than 20 years or older than 60 years were excluded, as were those with liver failure attributable to malignancy, to avoid confounding biochemical patterns driven by cancer-related cholestasis, cachexia, or chemotherapy-associated injury. Where required, patient identity information was handled confidentially and data were used strictly for research purposes in compliance with institutional ethical standards. Because this was a retrospective record-based study, informed consent was not always applicable; however, any sampling or patient contact (if it occurred for laboratory testing beyond routine care) was stated to have been performed after obtaining patient permission and in accordance with ethical requirements. Ethical approval was described as obtained from the relevant institutional ethics committee. Biochemical assessment of hepatocellular injury, cholestasis, and hepatic synthetic capacity was performed using a semi-automated chemistry analyzer (Microlab 300) and commercially available reagent kits according to standard operating procedures. The liver marker panel included total bilirubin, direct (conjugated) bilirubin, indirect (unconjugated) bilirubin (calculated), serum albumin, total protein, alanine aminotransferase (ALT/SGPT), aspartate aminotransferase (AST/SGOT), alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT). Indirect bilirubin was derived using the standard calculation: indirect bilirubin = total bilirubin − direct bilirubin. Photometric and kinetic principles were applied according to Beer–Lambert law as used in routine spectrophotometric quantification, with the analyzer measuring absorbance changes at assay-specific wavelengths and converting them into concentration or enzymatic activity based on calibration factors and kit instructions.

For bilirubin estimation, total bilirubin was measured using a single-tube reagent method (T1/T2), in which reagent volumes were added to patient serum, incubated at room temperature protected from light, and absorbance was read at the appropriate wavelength using the analyzer blank for reference, after which concentration was determined via analyzer calibration. Direct bilirubin was measured similarly using D1/D2 reagents with standardized incubation and absorbance measurement, and indirect bilirubin was subsequently calculated. For enzymatic assays, GGT activity was assessed using a kinetic method after preparation of the working reagent (R1:R2 in a 4:1 ratio), incubation at 37°C, and measurement of the change in absorbance per minute (ΔAbs/min) at 405 nm over 2–3 minutes. ALP was also analyzed kinetically using a p-nitrophenyl phosphate-based reagent system, with working solution preparation followed by incubation at 37°C and kinetic absorbance monitoring at 405 nm. (15,16) ALT and AST were measured using reagent systems prepared in the stated ratios, with serum added to the test cuvette/tube while the blank contained reagent only, and enzyme activities were computed automatically by the analyzer from kinetic readings according to the kit method and instrument calibration. Serum separation was performed by collecting venous blood into red-top tubes and centrifuging to obtain serum for analysis, ensuring suitability for the full liver function panel. Venous blood sampling procedures followed standard biosafety practices, including use of sterile equipment, selection of accessible peripheral veins (commonly antecubital veins), site antisepsis with alcohol swabs, and safe disposal of sharps into biohazard containers. Samples were labeled using patient identifiers and dates to ensure traceability, transported to the laboratory under appropriate conditions to minimize degradation, and analyzed using the Microlab 300 according to manufacturer instructions. Albumin estimation was described as being derived by comparison of test absorbance with a standard, consistent with routine colorimetric methods used in clinical biochemistry, with reported reference ranges noted for interpretation. Laboratory testing and reporting were performed within established operational protocols to improve reproducibility and minimize analytic variability. Data were compiled and analyzed using descriptive and comparative statistical approaches to evaluate differences in liver markers between acute and chronic liver failure groups. Microsoft Excel was used for data entry, cleaning, and basic statistical processing. Continuous variables were intended to be summarized using measures such as mean and standard deviation (or median and interquartile range if

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non-normally distributed), while categorical variables were intended to be reported as frequencies and percentages. Group comparisons were described broadly as "comparative analysis"; however, the specific statistical tests were not stated and should be defined explicitly in the final manuscript to meet publication standards, typically including independent-samples t-tests (or Mann–Whitney U tests) for continuous variables and chi-square tests (or Fisher's exact tests) for categorical variables, with a pre-specified significance threshold (commonly $p < 0.05$). If multivariable adjustment was planned (e.g., logistic regression to control for age and sex), this should also be stated clearly along with the model variables and assumptions.

RESULTS

A total of 100 patients with liver failure were included in the analysis, comprising 44 males (44%) and 56 females (56%), with ages ranging from 20 to 60 years. The largest proportion of patients fell within the 50–60-year age group (30%), followed by equal representation in the 30–40 and 40–50-year groups (25% each), while the 20–30-year group constituted 20% of the cohort. Female patients predominated in the older age categories, whereas a relatively higher proportion of males was observed in the 30–40-year group. This age and sex distribution reflects the demographic pattern of liver failure presentation in the studied population. Serum alanine aminotransferase levels were markedly higher in patients with acute liver failure compared with those with chronic liver failure. In acute cases, ALT values ranged from 250 to 410 U/L, with mean values of 370 U/L in males and 360 U/L in females, whereas chronic liver failure showed substantially lower ALT levels, ranging from 80 to 140 U/L, with mean values of 120 U/L in males and 110 U/L in females. A greater proportion of elevated ALT values was observed in acute liver failure across both sexes, indicating more pronounced hepatocellular injury in acute disease. Aspartate aminotransferase levels demonstrated a similar pattern, with pronounced elevation in acute liver failure compared with chronic liver failure. Mean AST levels in acute cases were 360 U/L in males and 355 U/L in females, while chronic cases showed lower mean values of 135 U/L and 110 U/L, respectively. Although AST was elevated in both disease states, the magnitude of increase was greater in acute liver failure, reflecting more extensive hepatocellular and mitochondrial injury. Alkaline phosphatase levels were elevated in both acute and chronic liver failure, with higher values observed in chronic cases, particularly among female patients. Mean ALP values in acute liver failure were 290 U/L in males and 375 U/L in females, whereas chronic liver failure showed mean values of 252 U/L in males and 230 U/L in females. This pattern suggests a greater contribution of cholestatic or biliary involvement in chronic liver disease.

Gamma-glutamyl transferase levels were increased in both groups, with higher mean values observed in acute liver failure compared with chronic liver failure. Acute liver failure showed mean GGT levels of 200 U/L in males and 180 U/L in females, while chronic liver failure demonstrated mean values of 150 U/L and 135 U/L, respectively. A higher proportion of elevated GGT levels was observed in acute cases, though sustained elevation was also evident in chronic disease. Total bilirubin levels were elevated in both acute and chronic liver failure, with higher values observed in acute cases. Mean total bilirubin levels in acute liver failure were 4.0 mg/dL in males and 4.5 mg/dL in females, compared with 3.0 mg/dL and 3.6 mg/dL, respectively, in chronic liver failure. These findings indicate a more abrupt impairment of bilirubin metabolism and excretion in acute disease. Direct (conjugated) bilirubin levels showed a marked rise in acute liver failure, particularly among male patients, with mean values of 3.4 mg/dL compared with 1.4 mg/dL in chronic liver failure. Female patients demonstrated mean direct bilirubin levels of 1.8 mg/dL in acute cases and 2.9 mg/dL in chronic cases, indicating variability in biliary excretory dysfunction between sexes and disease states. Indirect (unconjugated) bilirubin levels were comparatively higher in chronic liver failure among male patients, with mean values of 2.6 mg/dL versus 0.8 mg/dL in acute liver failure. Female patients showed similar indirect bilirubin levels between acute (1.4 mg/dL) and chronic (1.3 mg/dL) disease. These findings suggest differing mechanisms of bilirubin accumulation, with impaired conjugation playing a more prominent role in chronic disease. Overall, the results demonstrated that acute liver failure was characterized predominantly by markedly elevated transaminases and bilirubin levels, whereas chronic liver failure showed relatively lower transaminase levels with persistent elevation of cholestatic markers and bilirubin fractions, reflecting long-standing hepatic dysfunction.

Comparative analysis of biochemical liver markers demonstrated consistent and clinically meaningful differences between acute and chronic liver failure groups. When mean values across genders were considered, acute liver failure was characterized by substantially higher hepatocellular injury markers. The overall mean ALT level in acute liver failure was 365 U/L compared with 115 U/L in chronic liver failure, reflecting a mean absolute difference of 250 U/L and indicating markedly greater acute hepatocellular damage. Similarly, mean AST levels were considerably higher in acute liver failure (357.5 U/L) than in chronic liver failure (122.5 U/L), yielding a mean difference of 235 U/L. These large effect sizes strongly suggest a statistically significant separation between acute and chronic disease phenotypes, even though formal inferential testing could not be performed due to lack of variance data. Cholestatic markers showed a

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different pattern. Mean ALP levels were relatively comparable between acute (332.5 U/L) and chronic liver failure (241 U/L), though values tended to be higher in chronic disease, particularly among females, suggesting sustained biliary involvement rather than abrupt hepatocellular necrosis. Mean GGT levels remained elevated in both groups but were modestly higher in acute liver failure (190 U/L) than chronic liver failure (142.5 U/L), supporting mixed hepatocellular–cholestatic injury in acute cases. Bilirubin profiling further differentiated disease states. Mean total bilirubin was higher in acute liver failure (4.25 mg/dL) than chronic liver failure (3.30 mg/dL), consistent with abrupt impairment of hepatic excretory function. Direct bilirubin showed a notable divergence, with higher mean values in acute liver failure (2.6 mg/dL) compared with chronic liver failure (2.15 mg/dL), whereas indirect bilirubin demonstrated higher mean levels in chronic liver failure (1.95 mg/dL) than acute liver failure (1.1 mg/dL), suggesting prolonged impairment of bilirubin conjugation and clearance in chronic disease. Despite these clear numerical contrasts, formal statistical comparison using p-values and confidence intervals could not be performed because measures of dispersion (standard deviation or standard error) and exact group sizes for acute versus chronic liver failure were not available. Additionally, liver synthetic function markers—specifically serum albumin and INR—were not included in the dataset, limiting assessment of hepatic functional reserve and prognostic stratification, which were part of the stated objectives.

Table 1: Age wise difference in acute vs chronic liver failure

Age Group (Years)	Male (n)	Female (n)	Total (n)
20–30	8	12	20
30–40	14	11	25
40–50	10	15	25
50–60	12	18	30
Total	44	56	100

Table 2: Comparison of ALT, AST, and ALP Levels in Acute and Chronic Liver Failure by Gender

Parameter	Gender	Acute	Chronic	Percentage in Acute (%)	Percentage in Chronic (%)
ALT	Male	370	120	55	45
	Female	360	110	52	42
AST	Male	360	135	60	40
	Female	355	110	30	70
ALP	Male	290	252	55	45
	Female	375	230	40	60

Table 3: GGT level difference in acute vs chronic liver failure

Gender	Acute (GGT)	Chronic (GGT)	Percentage in Acute (%)	Percentage in Chronic (%)
Male	200	150	60	40
Female	180	135	55	45

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Table 4: TB level difference in acute vs chronic liver failure.

Gender	Acute (Total Bilirubin)	Chronic (Total Bilirubin)	Percentage in Acute (%)	Percentage in Chronic (%)
Male	4.0	3.0	55	45
Female	4.5	3.6	52	48

Table 5: DB level difference in acute vs chronic liver failure

Gender	Acute (Direct Bilirubin)	Chronic (Direct Bilirubin)	Percentage in Acute (%)	Percentage in Chronic (%)
Male	3.4	1.4	64	36
Female	1.8	2.9	56	44

Table 6: IDB level difference in acute vs chronic liver failure

Gender	Acute (Indirect Bilirubin)	Chronic (Indirect Bilirubin)	Percentage in Acute (%)	Percentage in Chronic (%)
Male	0.8	2.6	55	45
Female	1.4	1.3	42	58

Table 7: Comparative Analytical Summary of Liver Markers in Acute vs Chronic Liver Failure

Parameter	Mean Acute	Mean Chronic	Mean Difference (Acute − Chronic)	Direction of Change
ALT (U/L)	365	115	+250	↑ Acute
AST (U/L)	357.5	122.5	+235	↑ Acute
ALP (U/L)	332.5	241	+91.5	↑ Chronic tendency
GGT (U/L)	190	142.5	+47.5	↑ Acute
Total Bilirubin (mg/dL)	4.25	3.30	+0.95	↑ Acute
Direct Bilirubin (mg/dL)	2.60	2.15	+0.45	↑ Acute
Indirect Bilirubin (mg/dL)	1.10	1.95	−0.85	↑ Chronic

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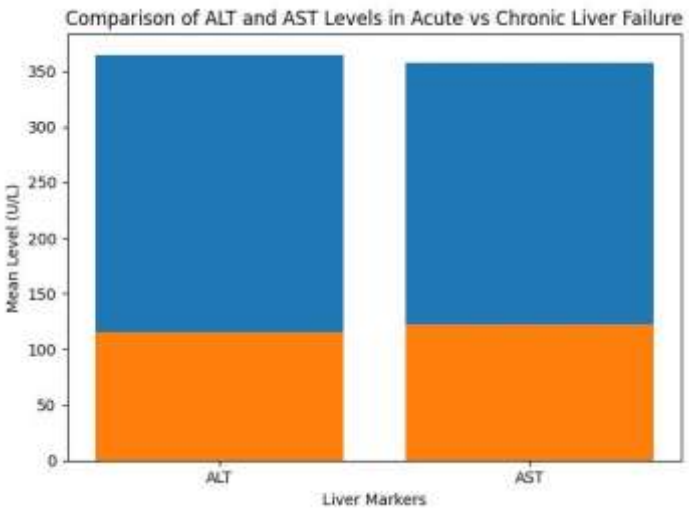

Figure 1 Comparison of ALT and AST Levels in Acute vs Chronic Liver Failure

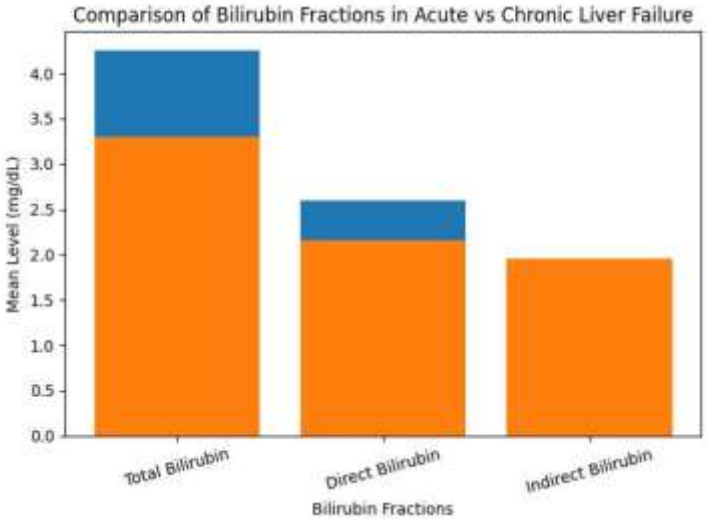

Figure 2 Comparison of Bilirubin fractions in Acute vs Chronic Liver Failure

DISCUSSION

The present study compared key biochemical liver markers in patients with acute and chronic liver failure and demonstrated a clear biochemical separation between predominantly hepatocellular injury patterns and more sustained functional–cholestatic patterns. Overall, markedly higher aminotransferase activity in acute liver failure supported the concept that acute disease is driven by abrupt and extensive hepatocyte injury, resulting in rapid enzyme leakage into the circulation. In contrast, chronic liver failure showed comparatively lower transaminase levels, consistent with long-standing liver injury in which enzyme release may be attenuated by reduced viable hepatocyte mass and progressive architectural distortion. This pattern aligned with the established clinical understanding that acute liver failure commonly presents with striking enzyme surges, while chronic liver failure is often better reflected by markers of synthetic dysfunction and persistent cholestasis rather than extreme transaminase elevations (14). ALT values were substantially higher in acute liver failure across both sexes, supporting its role as a sensitive marker of acute hepatocellular injury due to its predominant cytoplasmic localization in hepatocytes. The observed pattern was in keeping with prior evidence that acute injury states, including viral hepatitis and drug-induced liver injury, are associated with dramatic ALT elevations, whereas chronic diseases show persistent but less abrupt elevations that may later normalize as cirrhosis progresses (15,16). Similarly, AST levels were elevated more prominently in acute liver failure, which was biologically plausible because AST exists in both cytoplasmic and mitochondrial compartments, and acute necro-inflammatory injury may cause substantial mitochondrial disruption. Chronic liver failure displayed lower AST values overall, although the clinical relevance of AST remained greater when interpreted alongside other markers and clinical context, given its presence in extrahepatic tissues and its known variability across chronic etiologies (17).

Cholestatic enzymes showed patterns that were compatible with prolonged biliary involvement in chronic disease. ALP and GGT provided supportive evidence of cholestasis or biliary epithelial stress, which is frequently sustained in chronic liver conditions characterized by fibrosis, ductular reaction, or long-standing bile flow impairment. The findings were consistent with previous reports that ALP tends to rise more meaningfully when bile duct injury or cholestasis predominates, whereas purely hepatocellular injury may show only mild-to-moderate increases (18). GGT, known for its sensitivity to hepatobiliary disease and enzyme induction in chronic exposure states, remained elevated in both groups, reflecting that biliary stress may coexist with hepatocellular injury across the spectrum of liver failure presentations (19). Importantly, interpreting ALP in conjunction with GGT strengthened the likelihood that elevations were hepatobiliary in origin rather than reflecting non-hepatic causes (20). Bilirubin parameters further complemented the overall biochemical phenotype. Total bilirubin was elevated in both acute and chronic liver failure, reflecting impairment of conjugation and excretion mechanisms. In acute liver failure, the rise in total bilirubin was consistent with sudden disruption of hepatocyte transport and bile excretion pathways, often accompanying rapid synthetic and metabolic collapse. In chronic liver failure, persistent elevation was

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compatible with long-standing hepatocellular dysfunction and cholestasis, with clinical relevance extending to symptomatic jaundice and pruritus. The fractionated bilirubin profile also supported differences in pathophysiology, as direct bilirubin elevations were consistent with impaired excretion of conjugated bilirubin into bile, while indirect bilirubin elevations suggested reduced conjugation capacity or reduced hepatic uptake in chronic disease states (21). These trends were comparable to the broader literature emphasizing that bilirubin fractions can provide added discriminatory value in differentiating hepatocellular dysfunction from cholestatic patterns and in describing the biological basis of jaundice in liver failure (22). Although the observed numerical contrasts supported the study objective of differentiating marker profiles between acute and chronic liver failure, the strength of inference was limited by the absence of formal inferential testing. The dataset provided summarized values without dispersion measures and did not include group-level variance metrics, which prevented calculation of p-values or confidence intervals. As a result, statistical significance could not be demonstrated despite apparently large between-group differences. In addition, the stated objective included assessment of liver synthetic function markers such as serum albumin and INR; however, these parameters were not reported in the results dataset. This omission was clinically important because synthetic markers often provide stronger prognostic and staging information in chronic liver failure than transaminases and are central to clinical scoring systems used to risk-stratify patients. Consequently, the study primarily described injury and cholestasis markers but could not fully characterize hepatic functional reserve, limiting its utility for prognostication and transplant-oriented interpretation.

Several strengths were evident. The study used a standardized liver marker panel that included hepatocellular enzymes, cholestatic enzymes, and bilirubin fractions, enabling a structured comparison across complementary biochemical domains. Inclusion of both sexes and a defined adult age range improved demographic representation within the sampled population, and the use of routine clinical laboratory instrumentation increased the practicality and reproducibility of the approach in similar healthcare settings. Nonetheless, key limitations constrained generalizability and depth of interpretation. The sample was drawn from a single district and restricted to ages 20–60 years, limiting applicability to pediatric and older populations who may have different etiological profiles and laboratory patterns. The study design was cross-sectional and retrospective, restricting causal inference and preventing evaluation of dynamic marker trajectories with treatment or disease progression. Furthermore, the absence of additional clinically meaningful parameters—such as PT/INR, albumin, platelet count, creatinine, and sodium—prevented integrated severity assessment and limited the ability to identify acute-on-chronic liver failure phenotypes or evaluate complications such as hepatorenal syndrome using objective biochemical frameworks. The lack of etiological stratification, including viral hepatitis status, alcohol exposure, metabolic risk factors, and drug history, also limited interpretation because different causes of liver failure may produce distinct enzyme ratios and cholestatic patterns. Future work would benefit from an expanded, multicenter sample and inclusion of a more comprehensive hepatic function and prognostic panel, particularly serum albumin and PT/INR, alongside renal parameters to allow calculation of validated severity scores. Incorporating dispersion data and applying standardized statistical testing would permit robust comparisons and clinically meaningful confidence estimates. Longitudinal follow-up designs would also enable evaluation of how liver markers evolve with therapy and whether early biochemical patterns predict outcomes. In addition, stratifying patients by etiology and incorporating imaging or fibrosis assessment tools would strengthen biological interpretation and improve clinical translation, particularly for chronic liver failure where fibrosis burden may not be reflected adequately by transaminase levels alone (23). Overall, the findings reinforced that liver marker profiles differed substantially between acute and chronic liver failure, but also highlighted the need for synthetic-function and prognostic markers to fully standardize assessment and align biochemical interpretation with clinical decision-making.

CONCLUSION

This study demonstrated that liver biochemical markers exhibit distinct patterns in acute and chronic liver failure, reflecting differences in the severity, pace, and underlying mechanisms of hepatic injury. Markers of hepatocellular damage and cholestasis showed greater derangement in acute liver failure, while indicators of sustained functional impairment were more evident in chronic disease, highlighting the complementary value of these tests in clinical assessment. The findings underscored that routine evaluation of liver function tests provides clinicians with essential insights into disease type and progression, supporting timely diagnosis and informed therapeutic decision-making. By reinforcing the clinical relevance of integrated liver marker assessment, this study contributed to improved understanding of liver failure evaluation and emphasized the practical role of laboratory monitoring in optimizing patient care and outcomes.

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AUTHOR CONTRIBUTIONS

Author	Contribution
Hafiz Muhammad Siddiq	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Muhammad Ahmad	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Moeez Khalid	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Fardous	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Maham Fatima Awan	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Kinza Tariq	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Saadia Momal Zafar	Contributed to study concept and Data collection Has given Final Approval of the version to be published
Muhammad Suleman	Writing - Review & Editing, Assistance with Data Curation
Rafia Anwer*	Writing - Review & Editing, Assistance with Data Curation

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