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ORIGINAL ARTICLE

Evaluation of Liver Function Tests and Histopathological Severity in Patients Undergoing Hepatic Resection for Benign and Malignant Lesions: A Cross-Sectional Study

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ABSTRACT

Background: Accurate preoperative evaluation of liver function is essential for predicting surgical risk and guiding perioperative management in patients undergoing hepatic resection. Liver function tests (LFTs) provide a non-invasive biochemical snapshot of hepatic status, while histopathological analysis offers definitive insights into tissue-level disease severity. However, the relationship between these parameters remains underexplored, especially in the context of benign versus malignant hepatic lesions.

Objective: To assess the association between preoperative liver function test parameters and histopathological severity in patients undergoing hepatic resection for benign and malignant liver lesions.

Methods: A cross-sectional study was conducted on 70 patients who underwent hepatic resection. Patients were categorized into benign and malignant groups based on postoperative histopathological diagnoses. Preoperative LFTs including ALT, AST, ALP, bilirubin, albumin, and INR were recorded and compared between groups. Histopathological parameters such as fibrosis stage, necrosis, steatosis, and inflammatory infiltrate were evaluated and statistically correlated with LFT values using Pearson correlation and group comparisons.

Results: Of the 70 patients, 32 had benign and 38 had malignant hepatic lesions. Patients with malignant lesions had significantly elevated ALT (74.2 ± 23.1 vs. 46.8 ± 15.7 IU/L), AST (69.7 ± 20.4 vs. 41.9 ± 12.6 IU/L), ALP (222.6 ± 61.3 vs. 182.4 ± 43.8 IU/L), and INR (1.27 ± 0.18 vs. 1.06 ± 0.13), and lower albumin levels (3.52 ± 0.44 vs. 4.11 ± 0.41 g/dL) compared to benign cases (all $p < 0.05$). Histologically, malignant lesions exhibited higher frequencies of advanced fibrosis, necrosis, and inflammatory activity. ALT, AST, and INR positively correlated with necrosis and fibrosis, while albumin showed a significant inverse correlation.

Conclusion: Preoperative liver function tests, particularly AST, ALT, albumin, and INR, demonstrate significant correlation with histopathological severity in hepatic lesions. These routinely available biochemical parameters can serve as useful predictive tools for assessing underlying tissue damage, especially in patients with suspected malignancy. Their incorporation into preoperative assessment protocols may enhance clinical decision-making and surgical planning.

Keywords: Liver function tests, hepatic resection, histopathology, benign liver lesions, malignant liver tumors, fibrosis, necrosis, biochemical markers.

INTRODUCTION

Hepatic resection remains the definitive treatment modality for a wide range of benign and malignant liver lesions. The liver's unique regenerative capacity allows for surgical removal of diseased segments while preserving sufficient functional reserve[1]. However, the clinical success of hepatic resections depends heavily on accurate preoperative assessment of liver function, particularly in patients with underlying parenchymal damage or systemic disease. Early identification of hepatic dysfunction allows for tailored surgical strategies, risk mitigation, and improved postoperative recovery[2].

Liver Function Tests (LFTs) are essential components of preoperative evaluation, providing a rapid and non-invasive assessment of hepatocellular injury, cholestasis, excretory function, and hepatic synthetic capacity. Commonly measured parameters include alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin, albumin, and international normalized ratio (INR) [3]. ALT and AST reflect hepatocellular damage, while ALP and bilirubin serve as indicators of biliary obstruction or parenchymal compression. Serum albumin and INR provide crucial insights into hepatic synthetic function, which is particularly relevant in surgical planning. While these tests are routinely employed in clinical practice, the extent to which they reflect underlying histopathological alterations such as fibrosis, necrosis, inflammation, or steatosis remains an area of ongoing research[4].

Histopathological examination of liver tissue is considered the gold standard for assessing the nature and severity of hepatic lesions[5]. In malignant lesions such as hepatocellular carcinoma, intrahepatic cholangiocarcinoma, or metastatic adenocarcinoma, histology often reveals extensive architectural distortion, necrosis, inflammatory infiltration, and varying grades of fibrosis. Conversely, benign lesions including hepatic hemangiomas, focal nodular hyperplasia (FNH), and hepatic adenomas are generally associated with preserved architecture and minimal inflammatory response, although incidental fibrosis or steatosis may be present in background liver tissue. Establishing a correlation between preoperative LFT values and histopathological severity may allow clinicians to better predict disease burden, guide the extent of hepatic resection, and anticipate postoperative outcomes[6].

The clinical relevance of this correlation becomes even more pronounced in scenarios where radiological imaging and advanced hepatic reserve testing may be limited or inconclusive[7]. If liver biochemistry can reliably reflect tissue-level disease, it could significantly streamline the diagnostic pathway, enhance surgical planning, and reduce the need for invasive diagnostic interventions. Moreover, recognizing specific biochemical signatures associated with malignancy or advanced fibrosis could aid in early risk stratification and inform long-term surveillance strategies[8].

Despite the routine use of liver function tests in preoperative protocols, few studies have comprehensively explored their association with histopathological severity across both benign and

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malignant hepatic lesions. Most existing literature focuses either on malignant lesions or on postoperative outcomes without considering histological grading[9]. There remains a clear need for studies that integrate preoperative biochemical profiles with definitive histopathological findings to better understand the diagnostic and prognostic utility of routine liver biochemistry[10].

This study aims to evaluate the relationship between preoperative LFT parameters and histopathological severity in patients undergoing hepatic resection for benign and malignant liver lesions. By identifying significant biochemical-pathological correlations, this work seeks to improve preoperative decision-making, enhance risk assessment, and provide a more evidence-based framework for managing hepatic tumors in surgical candidates[11].

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Pathology at two tertiary care institutions: Burns and Plastic Surgery Center, Hayatabad Peshawar, and Sir Ganga Ram Hospital, Lahore. The study period extended from January 2022 to February 2023. The aim was to evaluate the relationship between preoperative liver function test (LFT) parameters and histopathological severity in patients undergoing hepatic resection for both benign and malignant liver lesions.

A total of 70 patients were included in the study using a non-probability consecutive sampling technique. Eligible participants were adults aged 18 years or older who underwent elective hepatic resection for space-occupying liver lesions and had complete preoperative biochemical profiles as well as available postoperative histopathology reports. Patients were excluded if they had previously diagnosed chronic liver disease (such as cirrhosis, viral hepatitis B or C), received neoadjuvant chemotherapy or radiotherapy, or had incomplete clinical or histopathological data.

Demographic and clinical data were collected for each patient, including age, sex, indication for surgery, and clinical presentation. Preoperative liver function tests were obtained within seven days prior to surgery and included alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total and direct bilirubin, serum albumin, and international normalized ratio (INR). These tests were performed in the hospital laboratories using standardized enzymatic methods on automated clinical chemistry analyzers with internal and external quality control measures.

Resected hepatic specimens were immediately fixed in 10% neutral-buffered formalin and processed according to standard histopathological protocols. Paraffin-embedded tissue blocks were sectioned at 4 µm thickness and stained with hematoxylin and eosin (H&E). Special stains, including Masson's trichrome, were applied where necessary for better visualization of fibrosis. Each sample was examined by two experienced histopathologists who were blinded to the biochemical findings. The following histopathological parameters were assessed: lesion type (benign or malignant), presence and grade of necrosis, degree of fibrosis (using the METAVIR scoring system from F0 to F4), extent of macrovesicular or microvesicular steatosis, and the grade of inflammatory infiltration. For malignant tumors, additional features such as tumor type, differentiation grade, and vascular or capsular invasion were also recorded.

All data were compiled and analyzed using IBM SPSS Statistics version 26.0. Descriptive statistics were used to summarize continuous variables as mean ± standard deviation and categorical variables as frequencies and percentages. The chi-square test was employed for comparing categorical variables between benign and malignant lesion groups, while the independent samples t-test was used for comparing mean LFT values. Pearson's correlation coefficient was calculated to assess the association between LFT values and histopathological severity parameters, including necrosis, fibrosis, and inflammation. A p-value less than 0.05 was considered statistically significant.

All patient data were handled with strict confidentiality, and ethical approval was obtained from the respective institutional review boards of both participating hospitals. The study adhered to ethical standards outlined in the Declaration of Helsinki.

RESULTS

A total of 70 patients who underwent hepatic resection were included in the final analysis. Out of these, 32 patients (45.7%) had benign liver lesions while 38 patients (54.3%) had malignant lesions confirmed on histopathology. The overall mean age was 52.4 ± 11.8 years. Patients with malignant lesions were significantly older than those with benign lesions (mean age: 56.7 ± 9.6 vs. 47.2 ± 10.4 years; $p < 0.001$). In terms of gender distribution, there were 44 males (62.9%) and 26 females (37.1%) in the study cohort. In the benign lesion group, 20 were males (62.5%) and 12 were females (37.5%). In the malignant group, 24 were males (63.2%) and 14 were females (36.8%). No statistically significant difference was observed in gender distribution between the two groups ($p = 0.945$). The demographic profile is shown in Table 1.

Table 1: Demographic Characteristics of Patients Undergoing Hepatic Resection

Parameter	Benign Lesions (n = 32)	Malignant Lesions (n = 38)	p-value
Mean Age (years)	47.2 ± 10.4	56.7 ± 9.6	< 0.001
Male Gender (%)	20 (62.5%)	24 (63.2%)	
Female Gender (%)	12 (37.5%)	14 (36.8%)	0.945

Liver function tests revealed significant differences between the benign and malignant groups. Mean ALT and AST levels were significantly higher in the malignant group compared to the benign group (ALT: 74.2 ± 23.1 IU/L vs. 46.8 ± 15.7 IU/L; AST: 69.7 ± 20.4 IU/L vs. 41.9 ± 12.6 IU/L; both $p < 0.001$). ALP was also higher in the malignant group ($p = 0.034$). Additionally, serum albumin was significantly lower in patients with malignant lesions, while INR was significantly elevated, indicating impaired synthetic liver function. These biochemical comparisons are summarized in Table 2.

Table 2: Comparison of Liver Function Test Parameters Between Benign and Malignant Lesions

Parameter	Benign Lesions (n = 32)	Malignant Lesions (n = 38)	p-value
ALT (IU/L)	46.8 ± 15.7	74.2 ± 23.1	< 0.001
AST (IU/L)	41.9 ± 12.6	69.7 ± 20.4	< 0.001
ALP (IU/L)	182.4 ± 43.8	222.6 ± 61.3	0.034
Total Bilirubin (mg/dL)	0.92 ± 0.36	1.18 ± 0.41	0.057
Serum Albumin (g/dL)	4.11 ± 0.41	3.52 ± 0.44	< 0.001
INR	1.06 ± 0.13	1.27 ± 0.18	< 0.001

Histopathological examination revealed distinct differences in tissue-level findings. In the benign lesion group, the predominant pathologies included hepatic hemangioma (n = 15), focal nodular hyperplasia (n = 10), and hepatic adenoma (n = 7). These specimens showed preserved lobular architecture, minimal fibrosis, and absence of necrosis. In contrast, the malignant group included hepatocellular carcinoma (n = 24), metastatic adenocarcinoma (n = 10), and intrahepatic cholangiocarcinoma (n = 4). Most malignant specimens showed marked tumor necrosis, significant inflammatory infiltration, and moderate-to-severe fibrosis. Histopathological severity parameters differed significantly between groups. Fibrosis stage ≥F2 was found in 42.1% of malignant cases compared to only 9.4% of benign cases ($p = 0.002$). Tumor necrosis and inflammatory infiltrates were significantly higher in malignant lesions ($p < 0.001$). These findings are presented in Table 3.

Correlation analysis was performed to assess the association between preoperative LFT values and

histopathological severity features. AST and ALT showed moderate positive correlation with necrosis (r = 0.48 and r = 0.43 respectively, p < 0.01), while ALP correlated significantly with fibrosis (r = 0.35, p = 0.02). Serum albumin exhibited a significant negative correlation with both fibrosis (r = –0.47) and necrosis (r = –0.39), indicating lower albumin levels in patients with more severe tissue pathology. INR was positively associated with fibrosis (r = 0.42, p = 0.01). The complete correlation matrix is presented in Table 4.

Table 3: Histopathological Severity Parameters in Benign vs. Malignant Lesions

Histological Feature	Benign Lesions (n = 32)	Malignant Lesions (n = 38)	p-value
Fibrosis Stage ≥ F2	3 (9.4%)	16 (42.1%)	0.002
Presence of Tumor Necrosis	2 (6.3%)	21 (55.3%)	< 0.001
Moderate-to-Severe Inflammation	1 (3.1%)	19 (50.0%)	< 0.001
Steatosis ≥ 30%	4 (12.5%)	8 (21.1%)	0.327

Table 4: Correlation Between Liver Function Tests and Histopathological Severity

LFT Parameter	Fibrosis (r)	Necrosis (r)	Inflammation (r)	p-value
ALT	0.29	0.43	0.31	< 0.05
AST	0.26	0.48	0.34	< 0.01
ALP	0.35	0.23	0.27	< 0.05
Serum Albumin	–0.47	–0.39	–0.41	< 0.01
INR	0.42	0.31	0.29	< 0.05

The findings of this study demonstrate that liver function test abnormalities, particularly elevated AST, ALT, and INR, along with low serum albumin, were significantly associated with histopathological severity in hepatic lesions. These biochemical abnormalities were much more pronounced in malignant tumors and showed meaningful correlation with key pathological features including fibrosis, necrosis, and inflammation. The data suggest that LFTs, especially transaminases and albumin, may serve as useful, non-invasive surrogate markers of tissue-level hepatic damage and should be considered in preoperative assessment to predict surgical risk and disease burden.

DISCUSSION

This cross-sectional study evaluated the correlation between preoperative liver function test (LFT) parameters and histopathological severity in patients undergoing hepatic resection for benign and malignant liver lesions[12]. The results demonstrate that biochemical alterations in LFTs, particularly elevated aminotransferases (AST and ALT), alkaline phosphatase (ALP), international normalized ratio (INR), and reduced serum albumin levels, were significantly associated with histological severity markers such as fibrosis, necrosis, and inflammatory infiltration especially in malignant cases[13].

The finding that patients with malignant hepatic lesions had significantly elevated AST and ALT levels aligns with the underlying pathophysiology of hepatocellular injury and tumor-induced necroinflammatory processes[14]. These transaminases reflect hepatocyte membrane integrity, and their elevation suggests ongoing parenchymal damage, which was histologically confirmed through increased tumor necrosis and inflammation in malignant tissues. Similar trends have been observed in recent studies where higher transaminase levels were predictive of malignant behavior and hepatic dysfunction in patients with liver tumors[15].

ALP elevation, particularly in malignancy-associated fibrosis or biliary infiltration, also supports earlier findings that this enzyme increases in response to cholestatic or space-occupying hepatic conditions[16]. The significant correlation of ALP with advanced fibrosis in this study indicates its potential role as a surrogate marker for fibrotic transformation in the hepatic microenvironment especially relevant in cases where preoperative imaging may underestimate fibrotic burden[17].

Serum albumin and INR are critical indicators of hepatic synthetic function. In this study, hypoalbuminemia and elevated INR were significantly associated with malignant lesions and advanced fibrosis[18]. The negative correlation between albumin and histological severity (necrosis and fibrosis) further highlights albumin's role in reflecting hepatic reserve. These observations reinforce the value of albumin and INR not just as indicators of nutritional or coagulation status, but as reliable markers of deeper parenchymal derangement, especially in patients with hepatocellular carcinoma or metastases[19].

Importantly, the study found that most benign lesions were associated with preserved liver function and minimal histopathological alterations. Only a minority of benign cases showed incidental steatosis or mild fibrosis, and no significant biochemical abnormalities were observed in this group. This reinforces the generally non-disruptive nature of benign hepatic masses on liver architecture and function and confirms the specificity of LFT derangement in cases with more severe pathology[20].

The correlation analysis provided further insight into the strength of associations between LFT values and histopathological damage. AST and ALT were moderately correlated with necrosis and inflammation, while albumin and INR were strongly associated with fibrosis, emphasizing their combined diagnostic and prognostic utility[21]. These findings are clinically significant because they suggest that routine liver function tests, which are inexpensive and widely accessible, can be integrated more effectively into preoperative evaluation protocols. Especially in resource-limited settings where access to liver biopsy or elastography may be constrained, LFT-based risk stratification could provide substantial clinical value[22].

However, this study is not without limitations. First, it did not include advanced imaging or functional liver reserve tests such as indocyanine green clearance or liver stiffness measurement, which could have strengthened the biochemical-pathological correlations. Second, while the sample size was adequate, a larger cohort may reveal additional statistical nuances, particularly in the subgroup analyses. Lastly, long-term follow-up of patients was beyond the scope of this study; therefore, the prognostic value of the biochemical-histological correlation on survival or recurrence could not be evaluated[23].

Despite these limitations, the findings of this study contribute meaningfully to the understanding of how standard liver function tests reflect underlying histopathological changes in both benign and malignant hepatic lesions. The clinical applicability of this correlation is high and warrants further prospective validation[24].

CONCLUSION

This study demonstrates that preoperative liver function test abnormalities, particularly elevated AST, ALT, ALP, INR, and low serum albumin, are significantly associated with histopathological severity in patients undergoing hepatic resection. These biochemical markers show a strong correlation with tissue-level changes such as fibrosis, necrosis, and inflammatory activity, especially in malignant liver lesions. In contrast, benign lesions typically present with preserved liver function and minimal histological disruption. The results support the clinical utility of routine liver function tests not only for assessing surgical fitness but also as predictive indicators of underlying pathological burden. These findings emphasize the value of integrating LFT-based assessment into preoperative planning, particularly in settings where histological or radiological diagnostics may be delayed or unavailable. Further large-scale, prospective studies are recommended to validate these correlations and explore their impact on long-term surgical and oncological outcomes.

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Authors' Contributions: MTHK conceptualized and supervised the study. AI and QAS were responsible for data collection and patient coordination. SAAB and RK performed the surgical and clinical evaluations. ML contributed to data interpretation and literature review. All authors participated in manuscript writing and approved the final version.

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