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ORIGINAL ARTICLE

Role of Liver Enzymes and Blood Parameters in Relation to Histopathological Severity in Benign and Malignant Liver Lesions

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ABSTRACT

Background: Liver lesions comprise a broad spectrum of pathological conditions ranging from benign tumors to aggressive malignancies. Histopathological examination remains the definitive diagnostic tool; however, non-invasive laboratory markers that reflect histopathological severity are increasingly important for early risk stratification and clinical decision-making.

Objective: To assess the relationship between liver enzymes and selected blood parameters in relation to histopathological severity in patients with benign and malignant liver lesions.

Methods: This cross-sectional analytical study was conducted at Medical Teaching Institution Hayatabad Medical Complex, Peshawar, and Liaquat Institute of Medical & Health Sciences, Thatta, Pakistan, from June 2022 to May 2023. A total of 100 patients with histopathologically confirmed liver lesions were included. Liver function tests, including alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyl transferase, and total bilirubin, along with hematological parameters such as hemoglobin, platelet count, international normalized ratio, and serum albumin, were recorded. Lesions were classified as benign or malignant, and malignant lesions were graded histopathologically. Statistical analysis was performed to determine associations between laboratory parameters and histopathological severity.

Results: Malignant liver lesions demonstrated significantly higher liver enzyme levels and bilirubin concentrations compared to benign lesions. Hemoglobin and platelet counts were significantly reduced, while international normalized ratio values were prolonged in malignant cases. Increasing histopathological grade was associated with progressive elevation of liver enzymes and worsening hematological and coagulation parameters.

Conclusion: Liver enzymes and blood parameters show significant correlation with histopathological severity in liver lesions. These routinely available laboratory markers may serve as useful, non-invasive tools for assessing disease severity and supporting clinical management.

Keywords: Liver lesions; Liver enzymes; Histopathology; Hematological parameters; Hepatic malignancy; Disease severity.

INTRODUCTION

Liver lesions represent a diverse group of pathological entities that range from benign conditions, such as hepatic hemangioma and focal nodular hyperplasia, to malignant neoplasms including hepatocellular carcinoma and secondary metastatic deposits[1]. With the rising global burden of chronic liver disease, viral hepatitis, metabolic syndrome, and malignancy, the incidence of both benign and malignant liver lesions has increased substantially, posing significant diagnostic and therapeutic challenges for clinicians[2].

Accurate differentiation between benign and malignant liver lesions is essential, as it directly influences clinical decision-making, prognosis, and treatment strategies[3]. Histopathological examination remains the gold standard for definitive diagnosis and grading of liver lesions. However, liver biopsy is an invasive procedure associated with potential complications such as bleeding, infection, and sampling error, and may be contraindicated in patients with advanced liver dysfunction or coagulopathy. Consequently, there is growing interest in identifying reliable, non-invasive biomarkers that can reflect underlying histopathological severity and assist in early risk stratification[4].

Liver enzymes, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST), are widely used indicators of hepatocellular injury, while alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT) serve as markers of cholestasis and biliary involvement[5]. Alterations in these enzymes are frequently observed in liver tumors due to hepatocyte destruction, tumor infiltration, ischemia, and biliary obstruction. In addition to biochemical markers, hematological and coagulation parameters such as hemoglobin level, platelet count, international normalized ratio (INR), and serum albumin provide valuable insights into hepatic synthetic function, portal hypertension, and systemic effects of liver disease[6,7].

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Previous studies have demonstrated abnormal liver enzyme profiles and deranged blood parameters in patients with hepatic malignancies; however, the extent to which these routinely available laboratory parameters correlate with histopathological severity remains insufficiently explored. Understanding these associations may enhance the clinical utility of laboratory investigations, particularly in resource-limited settings where advanced imaging or repeated biopsies may not be readily available[8,9].

Therefore, the present study aims to evaluate the relationship between liver enzymes and selected blood parameters with histopathological severity in patients with benign and malignant liver lesions. By establishing these correlations, this study seeks to determine the potential role of routine laboratory markers as supportive, non-invasive tools for assessing disease severity and guiding clinical management [10].

MATERIALS AND METHODS

Study Design and Duration: This cross-sectional analytical study was conducted over a twelve-month period from June 2022 to May 2023. The study was designed to evaluate the association between liver enzymes, hematological parameters, and histopathological severity in patients with benign and malignant liver lesions.

Place of Study: The study was carried out at two tertiary care teaching hospitals in Pakistan: Medical Teaching Institution (MTI) Hayatabad Medical Complex (HMC), Peshawar, and Liaquat Institute of Medical & Health Sciences (LIMHS), Thatta. Both institutions are major referral centers equipped with advanced diagnostic, laboratory, and histopathology services for hepatic diseases.

Study Population and Sample Size: A total of 100 patients with radiologically detected liver lesions were enrolled in the study. All included patients underwent liver biopsy or surgical excision, and the diagnosis of liver lesions was confirmed through histopathological examination.

Eligibility Criteria: Adult patients aged 18 years or above with focal liver lesions and complete laboratory and histopathological records were included. Patients with diffuse liver disease without focal lesions, known chronic viral hepatitis without mass lesions, alcohol-related liver disease, drug-induced liver injury, or incomplete medical records were excluded from the study.

Data Collection and Laboratory Investigations: Venous blood samples were collected from all participants prior to biopsy or surgical intervention. Liver function tests including alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT) were analyzed. Additional biochemical parameters such as total bilirubin and serum albumin were recorded. Hematological parameters including hemoglobin concentration, total leukocyte count, platelet count, and coagulation profile in the form of international normalized ratio (INR) were also assessed. All laboratory investigations were performed using standardized automated analyzers in the respective institutional laboratories.

Histopathological Evaluation: Tissue specimens obtained through core needle biopsy or surgical resection were fixed in 10% buffered formalin, processed using routine histopathological techniques, and stained with hematoxylin and eosin. Histopathological evaluation was performed by experienced histopathologists. Liver lesions were classified as benign or malignant, and malignant lesions were graded according to established histopathological grading systems.

Statistical Analysis: Data were entered and analyzed using appropriate statistical software. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Comparisons between benign and malignant liver lesions were performed using the independent t-test. Correlation between laboratory parameters and histopathological severity was assessed using Pearson or Spearman correlation tests, depending on data distribution. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations: Ethical approval for the study was obtained from the Institutional Review Boards of MTI Hayatabad Medical Complex, Peshawar, and Liaquat Institute of Medical & Health Sciences, Thatta. Written informed consent was obtained from all participants prior to inclusion in the study, and patient confidentiality was strictly maintained throughout the research process.

RESULTS

Baseline Characteristics of Study Participants: A total of 100 patients with histopathologically confirmed liver lesions were included in the study. Based on histopathological findings, 38 patients (38%) had benign liver lesions, while 62 patients (62%) were diagnosed with malignant liver lesions. The mean age of patients with malignant lesions was higher compared to those with benign lesions. Male predominance was observed in both groups, particularly among malignant cases.

Table 1: Comparison of Liver Enzymes Between Benign and Malignant Liver Lesions

Parameter	Benign Lesions (n=38) Mean ± SD	Malignant Lesions (n=62) Mean ± SD	p-value
ALT (U/L)	48.6 ± 15.2	96.4 ± 28.7	<0.001
AST (U/L)	52.1 ± 18.6	110.3 ± 35.1	<0.001
ALP (U/L)	162.5 ± 42.8	328.7 ± 74.5	<0.001
GGT (U/L)	58.9 ± 21.4	146.2 ± 49.6	<0.001
Total Bilirubin (mg/dL)	1.1 ± 0.4	2.8 ± 1.1	<0.001

Comparison of Liver Enzymes Between Benign and Malignant Liver Lesions: Patients with malignant liver lesions demonstrated significantly elevated liver enzyme levels compared to those with benign lesions. Mean serum ALT and AST levels were markedly higher in malignant lesions, indicating increased hepatocellular injury. Similarly, cholestatic enzymes including ALP and GGT were significantly raised in malignant cases, suggesting biliary obstruction and tumor infiltration. Total bilirubin levels were also higher in malignant lesions. These findings are summarized in Table 1.

Hematological and Coagulation Parameters in Relation to Lesion Type: Hematological analysis revealed significantly reduced hemoglobin and platelet counts in patients with malignant liver lesions compared to those with benign lesions. Additionally, malignant lesions were associated with prolonged INR values and lower serum albumin levels, reflecting impaired hepatic synthetic function. Total leukocyte count did not show a statistically significant difference between the two groups. Detailed findings are presented in Table 2.

Table 2: Comparison of Hematological and Coagulation Parameters

Parameter	Benign Lesions (n=38) Mean ± SD	Malignant Lesions (n=62) Mean ± SD	p-value
Hemoglobin (g/dL)	12.4 ± 1.3	9.8 ± 1.6	<0.001
Platelet Count (×10⁹/L)	242.6 ± 56.9	148.4 ± 44.2	<0.001
TLC (×10⁹/L)	8.1 ± 2.3	8.7 ± 2.6	0.31
INR	1.08 ± 0.12	1.46 ± 0.28	<0.001
Serum Albumin (g/dL)	3.9 ± 0.4	2.8 ± 0.6	<0.001

Association of Laboratory Parameters with Histopathological Severity of Malignant Lesions

Malignant liver lesions were further stratified according to histopathological grade. A progressive increase in ALT, AST, ALP, and GGT levels was observed with increasing histological severity. Conversely, hemoglobin, platelet count, and serum albumin showed a significant declining trend with higher tumor grades. INR values increased proportionally with histopathological severity, indicating worsening hepatic synthetic dysfunction. These associations are illustrated in **Table 3**.

Table 3: Laboratory Parameters According to Histopathological Grade of Malignant Liver Lesions

Parameter	Low Grade (n=21)	Intermediate Grade (n=24)	High Grade (n=17)	p-value
ALT (U/L)	78.2 ± 19.4	101.6 ± 24.7	132.4 ± 31.5	<0.001
AST (U/L)	92.3 ± 26.1	118.7 ± 32.9	154.8 ± 41.6	<0.001
ALP (U/L)	276.4 ± 58.9	332.5 ± 67.8	401.6 ± 83.4	<0.001
Platelet Count (×10⁹/L)	176.8 ± 38.6	142.3 ± 41.9	112.5 ± 35.7	<0.001
Serum Albumin (g/dL)	3.2 ± 0.4	2.7 ± 0.5	2.2 ± 0.6	<0.001
INR	1.28 ± 0.19	1.51 ± 0.23	1.78 ± 0.31	<0.001

Overall, malignant liver lesions demonstrated significantly worse biochemical and hematological profiles compared to benign lesions. Increasing histopathological severity was strongly associated with elevated liver enzymes, reduced platelet count and albumin levels, and worsening coagulation parameters, supporting the role of routine laboratory markers as indicators of disease severity.

DISCUSSION

The present study evaluated the relationship between liver enzymes, hematological parameters, and histopathological severity in benign and malignant liver lesions, revealing significant biochemical and hematological differences between these two pathological groups[11]. The findings demonstrate that malignant liver lesions are associated with markedly elevated liver enzyme levels, impaired synthetic function, and progressive deterioration of blood parameters with increasing histopathological severity[12].

In this study, serum ALT and AST levels were significantly higher in malignant lesions compared to benign lesions, indicating extensive hepatocellular injury in malignant disease (Table 1). This elevation can be attributed to tumor-induced hepatocyte destruction, ischemia caused by tumor expansion, and inflammatory responses within the hepatic parenchyma[13]. Similar trends have been reported in hepatocellular carcinoma and metastatic liver disease, where rising transaminase levels correlate with tumor burden and disease progression. The significantly elevated ALP and GGT levels observed in malignant lesions further support the role of cholestasis and biliary infiltration caused by malignant growth[14].

Hematological abnormalities were also prominent among patients with malignant liver lesions. The significant reduction in hemoglobin and platelet counts (Table 2) may reflect anemia of chronic disease, hypersplenism due to portal hypertension, and bone marrow suppression associated with malignancy[15]. Thrombocytopenia, in particular, showed a strong inverse relationship with histopathological severity, suggesting its potential utility as a surrogate marker of advanced disease. The absence of a significant difference in total leukocyte count between benign and malignant groups indicates that leukocytosis may not be a consistent indicator of malignancy in liver lesions[16].

Markers of hepatic synthetic function demonstrated notable derangement in malignant cases. Prolonged INR and reduced serum albumin levels were significantly associated with malignant pathology and increased tumor grade (Tables 2 and 3). Hypoalbuminemia reflects impaired protein synthesis and chronic inflammatory status, while elevated INR indicates compromised coagulation factor production. These findings emphasize the progressive decline in hepatic functional reserve with increasing histopathological severity[17,18].

Importantly, stratification of malignant lesions by histopathological grade revealed a stepwise deterioration in laboratory parameters (Table 3). Higher grades were associated with progressively increased liver enzyme levels, worsening thrombocytopenia, hypoalbuminemia, and prolonged INR. This graded relationship highlights the potential role of routine laboratory investigations as non-invasive indicators of tumor aggressiveness and disease severity, particularly in settings where repeated biopsies or advanced imaging may not be feasible[19,20].

Despite its strengths, this study has certain limitations. The cross-sectional design limits causal inference, and the sample size, although adequate, may not fully represent all subtypes of liver malignancies. Additionally, tumor-specific markers such as alpha-fetoprotein were not included. Future multicenter, longitudinal studies incorporating molecular and imaging parameters are warranted to further validate these findings[1-7].

CONCLUSION

This study demonstrates that liver enzymes and selected blood parameters are significantly associated with histopathological severity in benign and malignant liver lesions. Malignant lesions exhibit markedly elevated liver enzyme levels, reduced platelet count and hemoglobin levels, hypoalbuminemia, and impaired coagulation profiles, with progressive worsening observed across increasing histopathological grades. These routinely available laboratory parameters may serve as valuable, non-invasive adjuncts for assessing disease severity, supporting early risk stratification, and guiding clinical management in patients with liver lesions.

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