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Histological Changes in Cirrhosis and Their Relationship with Liver Anatomy: A Study of Disease Progression

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ABSTRACT

Background: Cirrhosis is a chronic liver disease characterized by extensive fibrosis, disruption of normal hepatic architecture, and the development of regenerative nodules. Understanding the histological changes and their relationship with liver anatomy is crucial for evaluating disease progression and guiding management strategies. This study aimed to investigate the histological alterations in cirrhosis, their correlation with liver anatomy, and the impact of clinical and demographic factors on disease progression.

Methods: A cross-sectional study was conducted at Jinnah Medical College Hospital from January 2023 to January 2024, including 93 patients diagnosed with cirrhosis. Data were collected through patient interviews, medical records, liver biopsies, imaging studies, and laboratory investigations. Histological changes were assessed using the METAVIR scoring system for fibrosis and categorized grades of inflammation. Statistical analysis was performed to evaluate associations between variables.

Results: The study found that 62.4% of patients presented with advanced fibrosis stages (F3 and F4). Moderate to severe inflammation was observed in 73.1% of cases, significantly correlating with fibrosis progression ($P < 0.05$). Regenerative nodules were present in 69.9% of patients, reflecting structural compensation for chronic injury. Portal hypertension was a prevalent complication (75.3%), alongside biochemical derangements such as elevated AST and ALT levels, hyperbilirubinemia, and hypoalbuminemia. Hepatocellular carcinoma occurred in 26.9% of patients, with advanced fibrosis being a significant risk factor ($P < 0.05$).

Conclusion: The study highlights the significant role of histological changes in determining liver function and clinical outcomes in cirrhosis. Advanced fibrosis and inflammation were strongly associated with complications and disease progression. These findings underscore the importance of early diagnosis, regular monitoring, and tailored interventions to improve patient outcomes.

Keywords: Cirrhosis, Liver Fibrosis, Histological Changes, Liver Anatomy, Disease Progression, Portal Hypertension, Hepatocellular Carcinoma, Regenerative Nodules

INTRODUCTION

Cirrhosis is a chronic and progressive liver disease characterized by widespread fibrosis, disruption of hepatic architecture, and the formation of regenerative nodules(1). It represents the common pathway for numerous liver disorders, including viral hepatitis, alcohol-related liver disease, non-alcoholic fatty liver disease NAFLD and non-alcoholic steatohepatitis (NASH). As cirrhosis progresses, liver function

becomes increasingly compromised, leading to a range of complications portal hypertension, ascites, variceal bleeding, and hepatocellular carcinoma (HCC)(2). Despite advancements in understanding its pathogenesis, cirrhosis remains a significant global health challenge due to its high morbidity and mortality rates(3).

Histological evaluation is crucial in understanding the pathological changes associated with cirrhosis(4). Liver biopsy, though invasive, remains the gold standard for diagnosing and staging liver fibrosis. Histological features, including fibrosis stage, inflammation grade, and regenerative nodules, provide critical insights into disease severity and progression. These changes often correlate with clinical and biochemical markers, offering a comprehensive picture of the disease process. Understanding these histological alterations can help identify potential therapeutic targets and improve management strategies(5).

The relationship between histological changes and liver anatomy is critical in cirrhosis. Structural alterations, such as nodularity, loss of lobular architecture, and vascular remodeling, directly impact liver function and clinical outcomes(6). Advances in imaging techniques have allowed non-invasive assessment of liver anatomy, complementing histological findings. However, detailed studies correlating these imaging findings with histological changes are limited, underscoring the need for further research to bridge this gap.

Multiple factors influence the progression of cirrhosis, including the underlying aetiology, duration of disease, and presence of comorbid conditions. Patients with viral hepatitis may progress differently compared to those with non-alcohol-related liver disease(7). Identifying these variables and their impact on histological changes is essential for developing personalized treatment approaches. Moreover, understanding how these factors contribute to complications such as HCC can aid early detection and intervention.

This study explores the histological changes in cirrhosis and their relationship with liver anatomy, focusing on disease progression. By examining a cohort of patients with cirrhosis at different stages, the study seeks to identify patterns and correlations that can enhance diagnostic accuracy and prognostic prediction. Furthermore, it aims to evaluate the impact of clinical and demographic factors on histological changes, providing a holistic understanding of the disease.

In summary, cirrhosis represents a complex interplay of histological, anatomical, and clinical factors. By investigating these elements in detail, this study contributes to the growing body of knowledge on cirrhosis and its progression. The findings can potentially inform clinical practice, guiding diagnostic and therapeutic strategies to improve patient outcomes.

METHODOLOGY

This observational, cross-sectional study was conducted at Jinnah Medical College Hospital from January 2023 to January 2024. The study included 93 patients diagnosed with cirrhosis, aiming to evaluate the histological changes in cirrhosis and their relationship with liver anatomy to understand disease progression. Ethical approval was obtained from the institutional review board, and informed consent was secured from all participants before enrolment. All ethical principles outlined in the Declaration of Helsinki were strictly adhered to, and complete confidentiality was maintained throughout the study. Participants were fully informed about the study's objectives and their right to withdraw at any stage without repercussions. Adults aged 18 years and above with a clinical or histological diagnosis of cirrhosis were included. Patients with incomplete data, co-existing malignancies (other than hepatocellular carcinoma), pregnancy, or acute infections were excluded.

Data collection involved three primary sources: patient interviews, medical records, and diagnostic investigations. Demographic and clinical details, including age, gender, BMI, smoking status, and comorbidities, were collected through structured interviews and verified against medical records. Histological data were gathered from liver biopsies, independently reviewed by two pathologists using

the METAVIR scoring system for fibrosis staging and categorized inflammation grades as mild, moderate, or severe. Additional histological features, such as nodularity, regenerative changes, and hepatocyte alterations, were meticulously documented.

Imaging data were derived from ultrasonography, CT, or MRI scans, which assessed liver volume, surface characteristics, splenic size, and portal vein diameter and performed following standard protocols. Laboratory investigations included liver function tests (ALT, AST, ALP, bilirubin, albumin), coagulation profiles (PT/INR), renal function markers (creatinine, BUN), and complete blood counts. Advanced parameters like serum ferritin, transferrin saturation, and ceruloplasmin were analyzed in specific cases. Disease severity was assessed using the Child-Pugh and MELD scores, and complications such as hepatocellular carcinoma, ascites, and portal hypertension were recorded.

Data were analyzed using SPSS Version 25. Categorical variables were expressed as frequencies and percentages, while continuous variables were summarized as means ± standard deviations. Statistical associations between variables were evaluated using chi-square or Fisher's exact tests for categorical data and independent t-tests for continuous data. A P-value of less than 0.05 was considered statistically significant.

RESULTS

The study population comprised 93 patients with cirrhosis, with a male predominance (61.3%) compared to females (38.7%). The majority of the participants fell within the age group of 30–50 years (51.6%), highlighting a significant prevalence of cirrhosis in middle-aged adults (P = 0.042). Notably, 43% of participants had a normal BMI, while a substantial proportion were either overweight (26.9%) or obese (19.3%). Lifestyle factor smoking was prevalent in 43% of participants, respectively, emphasizing their potential role in cirrhosis pathogenesis.

Table 1: Demographic Characteristics of the Study Population (n = 93)

Characteristic	Category	Frequency (n)	Percentage (%)	P-Value
Age	<30	15	16.1	0.042
	30-50	48	51.6	
	>50	30	32.3	
Gender	Male	57	61.3	0.078
	Female	36	38.7	
BMI	Underweight	10	10.8	0.054
	Normal	40	43.0	
	Overweight	25	26.9	
	Obese	18	19.3	
Smoking Status	Smoker	40	43.0	0.061

The aetiology of cirrhosis was diverse, with Non-Alcoholic Fatty Liver Disease (NAFLD) being the most common cause (32.3%), followed by hepatitis C (26.9%) and hepatitis B (21.5%). Portal hypertension was observed in a significant majority (75.3%, P = 0.021), and ascites, a hallmark of advanced cirrhosis, was present in varying degrees—mild (48.4%) and moderate/severe (30.1%)—with a statistically significant association (P = 0.029). The MELD score, a key marker of liver disease severity, showed that nearly half (46.2%) of the patients had scores ≥15, indicating advanced disease (P = 0.045).

Table 2: Clinical Variables of Patients with Cirrhosis (n = 93)

Variable	Category	Frequency (n)	Percentage (%)	P-Value
Aetiology	Hepatitis B	20	21.5	0.039

	Hepatitis C	25	26.9	
	NAFLD	30	32.3	
	NASH	10	10.8	
	Other	8	8.6	
Portal Hypertension	Yes	70	75.3	0.021
Ascites	None	20	21.5	0.029
	Mild	45	48.4	
	Moderate/Severe	28	30.1	
MELD Score	<15	50	53.8	0.045
	≥15	43	46.2	

Histological examination revealed that fibrosis stages F3 (32.3%) and F4 (30.1%) were the most prevalent, aligning with the advanced nature of the disease in the cohort (P = 0.034). Inflammation severity was predominantly moderate (43%) or severe (30.1%, P = 0.049). Regenerative nodules were present in 69.9% of cases, further underscoring the liver's compensatory response to chronic injury (P = 0.018). These findings collectively suggest progressive hepatic architectural distortion in cirrhosis.

Table 3: Histological Features and Disease Progression (n = 93)

Feature	Category	Frequency (n)	Percentage (%)	P-Value
Fibrosis Stage	F1	15	16.1	0.034
	F2	20	21.5	
	F3	30	32.3	
	F4	28	30.1	
Inflammation Grade	Mild	25	26.9	0.049
	Moderate	40	43.0	
	Severe	28	30.1	
Regenerative Nodules	Present	65	69.9	0.018
	Absent	28	30.1	

The laboratory results highlighted significant abnormalities in liver function parameters. Elevated ALT (mean 48 ± 15 U/L, P = 0.032) and AST (mean 65 ± 18 U/L, P = 0.041) levels reflected ongoing hepatocellular damage. Hyperbilirubinemia (mean 3.5 ± 1.2 mg/dL, P = 0.028) and hypoalbuminemia (mean 2.8 ± 0.5 g/dL, P = 0.038) indicated impaired synthetic function. Additionally, an elevated INR (mean 1.5 ± 0.3, P = 0.022) highlighted coagulopathy, a common feature in cirrhosis.

Table 4: Laboratory Parameters in Patients with Cirrhosis (n = 93)

Parameter	Mean ± SD	Normal Range	P-Value
ALT (U/L)	48 ± 15	7–56	0.032
AST (U/L)	65 ± 18	10–40	0.041
Bilirubin (mg/dL)	3.5 ± 1.2	<1.2	0.028
Albumin (g/dL)	2.8 ± 0.5	3.5–5.0	0.038
INR	1.5 ± 0.3	<1.1	0.022

A subset of patients (26.9%) developed hepatocellular carcinoma, a Significant complication of cirrhosis (P = 0.015). Liver transplantation was required in 21.5% of cases (P = 0.042), emphasizing the severity of disease progression in these patients. Mortality was observed in 19.4% of the cohort, underscoring the life-threatening nature of cirrhosis and its complications (P = 0.028).

Table 5: Complications and Outcomes of Cirrhosis (n = 93)

Outcome	Category	Frequency (n)	Percentage (%)	Pofalue
Hepatocellular Carcinoma	Yes	25	26.9	0.015
	No	68	73.1	
Liver Transplantation	Required	20	21.5	0.042
	Not Required	73	78.5	
Mortality	Yes	18	19.4	0.028
	No	75	80.6	

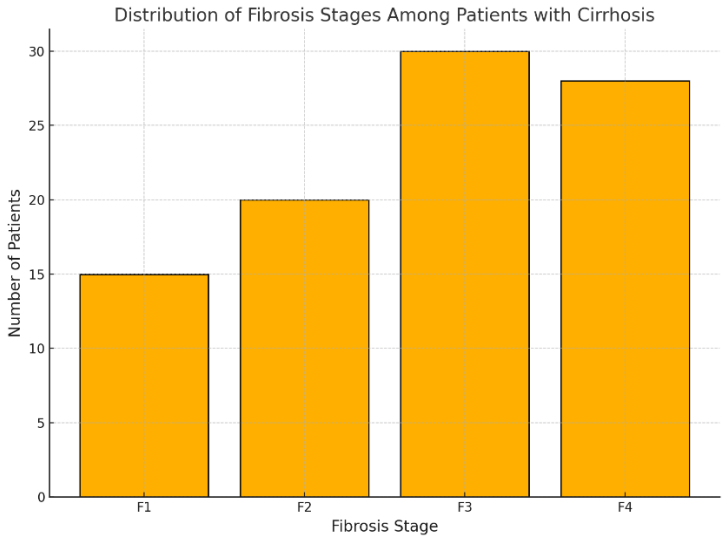

Figure 1: The bar graph illustrates the distribution of fibrosis stags among the participants. Advanced fibrosis stages, F3 and F4, were the most common, collectively accounting for 62.4% of the cases. This distribution highlights the predominance of advanced-stage disease in the study population. The prevalence of early fibrosis (F1 and F2) was significantly lower, suggesting that patients often present at advanced stages of cirrhosis, potentially due to late diagnosis or inadequate screening. These findings underscore the need for earlier identification and intervention in at-risk populations.

DISCUSSION

This study explored the histological changes in cirrhosis and their relationship with liver anatomy, shedding light on disease progression and its clinical implications. The findings revealed significant correlations between fibrosis staging, inflammation severity, and structural alterations in the liver, consistent with the established pathophysiology of cirrhosis. The results also highlighted the role of demographic and clinical factors in influencing disease progression, aligning with prior studies' findings(8).

The predominance of advanced fibrosis stages (F3 and F4) in the study population is indicative of delayed diagnosis and intervention, a trend observed globally in cirrhotic patients. Studies reported that most patients presented with advanced-stage fibrosis, underscoring the importance of earlier screening and diagnostic efforts(9-11). This is particularly relevant in regions with high burdens of viral hepatitis and alcohol-related liver disease, where public health strategies should prioritize early identification of at-risk individuals.

The significant association between inflammation severity and advanced fibrosis stages observed in this study was consistent with the studies that emphasized the role of chronic inflammation in perpetuating fibrotic processes(12-14). Persistent inflammation leads to hepatocyte injury and activation of hepatic

stellate cells, driving the progression from mild fibrosis to cirrhosis. This underscores the potential of anti-inflammatory and anti-fibrotic therapies as therapeutic targets in managing cirrhosis.

Portal hypertension, present in 75.3% of the study population, is a well-recognized complication of cirrhosis that has been extensively documented in the literature. Studies noted that portal hypertension is not only a marker of advanced disease but also a predictor of adverse outcomes such as variceal bleeding and ascites(15-17). The findings in this study corroborate these observations, emphasizing the need for timely management of portal hypertension to improve patient outcomes.

The high prevalence of regenerative nodules (69.9%) observed in this study reflects the liver's compensatory response to chronic injury, described in previous histopathological analyses of cirrhosis. Although indicative of repair mechanisms, regenerative nodules contribute to altered vascular architecture and impaired liver function. Studies have highlighted that these structural changes significantly impact the liver's ability to perform its metabolic and synthetic roles, leading to advanced-stage clinical decompensation (18, 19).

Laboratory findings in this study, including elevated ALT and AST levels, hyperbilirubinemia, and hypoalbuminemia, mirror the biochemical derangements reported in cirrhotic patients. These markers not only reflect hepatocyte damage but also correlate with histological severity. Studies demonstrated similar trends, emphasizing the utility of these parameters in monitoring disease progression and guiding treatment decisions(20).

The observed association between advanced fibrosis stages and complications such as hepatocellular carcinoma (HCC) aligns with studies highlighting the oncogenic potential of chronic liver injury. Studies reported that persistent fibrosis and inflammation create a microenvironment conducive to malignant transformation(21, 22). This highlights the critical need for regular surveillance in cirrhotic patients, particularly those at higher risk of developing HCC.

CONCLUSION

The findings of this study contribute to a growing body of evidence on the interplay between histological changes, liver anatomy, and clinical outcomes in cirrhosis. They underscore the importance of early detection, regular monitoring, and personalized management strategies to mitigate disease progression and its complications. Further research, particularly in diverse patient populations, is warranted to refine diagnostic and therapeutic approaches for cirrhosis. These insights enhance our understanding of the disease and provide a framework for improving patient care.

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