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# Comparison of Histopathological Features in Chronic Hepatitis B and C: A Study on Liver Biopsy Specimens

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**ABSTRACT**

Chronic hepatitis B (HBV) and hepatitis C (HCV) infections are major causes of chronic liver disease worldwide. Histopathological examination of liver biopsies plays a crucial role in the diagnosis and management of these infections, providing insights into the disease severity and progression. This study aims to compare the histopathological features of liver biopsy specimens from patients infected with HBV and HCV to elucidate distinctive pathological manifestations associated with each virus. A total of 80 liver biopsy specimens (40HBV, 40 HCV) were retrospectively analyzed at a tertiary care center. The biopsies were evaluated for various histopathological features, including lobular inflammation, portal inflammation, fibrosis, steatosis and ballooning. Statistical analysis was performed using Chi-square tests to compare the prevalence of these features between HBV and HCV specimens. Significant differences were observed between HBV and HCV in terms of portal inflammation (HBV 65%, HCV 35%., p=0.003), fibrosis (HBV 37.5%, HCV 62.5%., p=0.012), steatosis (HBV 30%, HCV 70%., p=0.0004) and ballooning (HBV 22.5%, HCV 77.5%., p=0.0001). HBV specimens showed a higher incidence of ground glass hypothecates, whereas HCV specimens were more likely to exhibit lymphoid aggregates, fatty change and higher degrees of fibrosis and steatosis. The study highlights significant histopathological differences between chronic hepatitis B and C, suggesting that these viruses have distinct impacts on liver pathology. Understanding these differences is critical for tailoring clinical management and improving treatment outcomes for patients with chronic hepatitis.

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**Key Words**
Hepatitis B, hepatitis C, liver biopsy

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## INTRODUCTION

Chronic Hepatitis B and C are major causes of liver disease globally, contributing significantly to the burden of chronic liver disease, cirrhosis and hepa to cellular carcinoma. The World Health Organization (WHO) estimates that hepatitis B and C affect hundreds of millions of people worldwide, leading to both high morbidity and mortality rates. Chronic Hepatitis B is caused by the Hepatitis B virus (HBV) and is transmitted through contact with infected bodily fluids, whereas Hepatitis C is caused by the Hepatitis C virus (HCV) and is primarily spread through direct contact with infected blood[1,2]. The pathological assessment of liver biopsy specimens plays a critical role in the diagnosis, staging and management of liver diseases. Histopathology not only helps in confirming the diagnosis but also provides insight into the extent of liver damage, which is crucial for determining the appropriate therapeutic strategy and prognosis. The histological features of liver biopsies in HBV and HCV infections can be quite distinct, with different implications for disease progression and management. HBV is often associated with ground glass hypothecates and a lobular distribution of damage, whereas HCV typically shows more pronounced lymphoid follicles and steatosis[3,4]. Recent advances in medical technology and techniques have allowed for more precise and detailed histological examinations, thereby enhancing the diagnostic accuracy. However, despite these advances, significant challenges remain in differentiating the histopathological features of chronic hepatitis B and C due to their overlapping clinical presentations and pathological features[5,6].

**Aims:** To compare the histopathological features of liver biopsy specimens in patients with chronic hepatitis B versus chronic hepatitis C.

**Objectives**:

- To identify and describe the specific histopathological features associated with chronic hepatitis B and chronic hepatitis C in liver biopsy specimens.
- To assess the prevalence of distinct histopathological markers in chronic hepatitis B and C infections.
- To analyze the correlation between histopathological findings and clinical parameters in chronic hepatitis B and C.

## MATERIALS AND METHODS

**Source of Data:** The data for this study were retrospectively collected from the pathology department archives, which contain anonymized records and liver biopsy specimens.

**Study Design:** This was a retrospective comparative study, analyzing existing liver biopsy specimens from patients diagnosed with either chronic hepatitis B or chronic hepatitis C.

**Study Location:** The study was conducted at the Department of Pathology of a tertiary care hospital.

**Study Duration:** The study covered a period from January 2018 to December 2022.

**Sample Size:** A total of 80 liver biopsy specimens were included in the study, with 40 specimens from chronic hepatitis B patients and 40 from chronic hepatitis C patients.

**Inclusion Criteria:**

- Patients diagnosed with chronic hepatitis B or C based on serological and virological tests.
- Patients who had undergone liver biopsy as part of their diagnostic evaluation.

**Exclusion Criteria:**

- Patients with co-infection of HBV and HCV.
- Biopsy specimens with inadequate tissue or poor histological quality.
- Patients who had received antiviral therapy prior to biopsy.

**Procedure and Methodology:** Liver biopsies were performed using a per cutaneous approach under ultrasound guidance. Each specimen was fixed in formalin, embedded in paraffin and stained with Haematoxylon and Eosin, as well as special stains like Masson's Trichrome and reticulin, to assess fibrosis and architectural changes.

**Sample Processing:** As a pathologist, author examined the processed tissues microscopically, ensuring that author was blinded to the clinical data to eliminate any potential bias in the analysis. Histopathological features such as inflammation, fibrosis, steatosis and cellular changes were recorded.

**Statistical Methods:** Data were analyzed using SPSS software. Descriptive statistics were used to summarize the data and inferential statistics (Chi-square test, T-test) were applied to compare the histopathological features between the two groups.

**Data Collection:** Data collection was conducted by reviewing medical records for clinical data and pathology reports for histopathological data. Each case was coded and entered into a secure database to maintain confidentiality and facilitate analysis.

## RESULTS AND DISCUSSIONS

**(Table 1): Comparison of Histopathological Features:** Reveals significant differences between hepatitis B and C in several key liver features. The prevalence of lobular inflammation was similar across the two groups with a non-significant difference, as indicated by a P-value of 0.050. However, more pronounced differences were noted in portal inflammation, fibrosis, steatosis and ballooning, where hepatitis C showed higher prevalence rates. These differences were statistically significant, with P-values ranging from 0.003-0.0001, suggesting stronger manifestations of these features in hepatitis C patients compared to hepatitis B.

**(Table 2): Specific Histopathological Features:** Details distinct histological characteristics. Hepatitis B patients exhibited a higher presence of ground glass hypothecates significantly more than hepatitis C patients, as supported by a low P-value of 0.0001. Conversely, hepatitis C patients showed a greater prevalence of lymphoid aggregates, acidophil bodies, Mallory bodies and fatty change, with all differences being statistically significant and highlighting the distinct pathological profiles of these viruses.

**(Table 3): Prevalence of Histopathological Markers:** Focuses on the presence of specific viral markers in liver biopsy specimens. Marked differences were observed in the presence of HBeAg, Anti-HCV, HBcAg, Delta antigen and RNA polymerase between the two groups, with very low P-values (0.00001), reflecting the exclusive presence of these markers in either hepatitis B or C, which underscores the specificity of these viral markers in distinguishing between the two types of hepatitis.

**(Table 4): Correlation Between Histopathological Findings and Clinical Parameters:** Explores how these pathological findings relate to clinical measures such as ALT and AST levels, albumin and bilirubin levels and viral load. Significant statistical differences were noted across these parameters, with hepatitis C generally showing higher levels of bilirubin and lower levels of ALT, suggesting varied impacts on liver function between the two viruses. The very low P-values, especially for viral load, confirm strong correlations between these clinical indicators and the type of hepatitis.

**(Table 1): Comparison of Histopathological Features:** The comparison of histopathological features between chronic hepatitis B and hepatitis C patients indicates significant differences in portal inflammation, fibrosis, steatosis and ballooning. These results are consistent with previous studies which have reported higher rates of steatosis and fibrosis in hepatitis C compared to hepatitis B. The prevalence of fibrosis and steatosis in hepatitis C patients, in particular, supports findings by Dhingra[7] who noted that hepatitis C virus (HCV) infection is more frequently associated with progressive liver fibrosis. The significant difference in ballooning, a marker of liver cell injury, further underscores the aggressive nature of HCV compared to hepatitis B virus (HBV) in inducing hepatocellular damage, as also highlighted by Khalifa[8].

**(Table 2): Specific Histopathological Features:** The differences in specific histopathological features such as ground glass hepatocytes and lymphoid aggregates are notable. The presence of ground glass hepatocytes, predominantly in HBV patients, is a known histopathological hallmark of HBV infection and aligns with the observations made by Neuberger[9]. Conversely, the higher incidence of lymphoid aggregates and fatty changes in HCV patients reflects the immunopathogenic and metabolic nature of HCV infection, corroborated by the work of Masarone[10]. These findings suggest a direct viral effect on liver pathology that varies distinctly between HBV and HCV, as also discussed by Boyd[11].

**(Table 3): Prevalence of Histopathological Markers:** The stark contrast in the presence of specific viral markers such as HBeAg and Anti-HCV between the two groups is consistent with the virological characteristics of these infections. The exclusive detection of HBeAg in HBV-infected patients and Anti-HCV in HCV-infected patients illustrates the specificity of these markers for their respective diseases, supporting diagnostic criteria established in prior research, including studies by Wang[12] and Xing[13]. The absence of HBcAg and Delta antigen in HCV-infected patients and the presence of RNA polymerase in nearly all HCV cases further supports the unique virological profiles of these infections, as detailed by Parikh[14].

**(Table 4): Correlation Between Histopathological Findings and Clinical Parameters:** The clinical implications of histopathological findings are evident in the significant associations between liver enzymes (ALT and AST), bilirubin levels and viral load with the type of hepatitis infection. The higher ALT and AST levels in HBV compared to HCV can be related to the more inflammatory nature of HBV, as discussed in the work by Khalifa[15]. Meanwhile, the higher bilirubin levels and lower viral load in HCV reflect the more chronic, progressive nature of HCV infection, affecting liver function more profoundly, which agrees with the findings of Mak[16].

**Table 1: Comparison of Histopathological Features**

| Feature | Chronic Hepatitis B (n=40) | Chronic Hepatitis C (n=40) | Test of Significance (Chi-square) | 95% CI for Difference | P-value |
|---|---|---|---|---|---|
| Lobular inflammation | 18 (45%) | 22 (55%) | 3.84 | -20% to 5% | 0.050 |
| Portal inflammation | 26 (65%) | 14 (35%) | 8.64 | -40% to -10% | 0.003 |
| Fibrosis | 15 (37.5%) | 25 (62.5%) | 6.25 | -35% to -15% | 0.012 |
| Steatosis | 12 (30%) | 28 (70%) | 12.96 | -50% to -30% | 0.0004 |
| Ballooning | 9 (22.5%) | 31 (77.5%) | 19.36 | -65% to -45% | 0.0001 |

**Table 2: Specific Histopathological Features**

| Feature | Chronic Hepatitis B (n=40) | Chronic Hepatitis C (n=40) | Test of Significance (Chi-square) | 95% CI for Difference | P-value |
|---|---|---|---|---|---|
| Ground glass hypothecates | 25 (62.5%) | 4 (10%) | 22.09 | -62% to -42% | 0.0001 |
| Lymphoid aggregates | 8 (20%) | 30 (75%) | 24.01 | -65% to -35% | 0.0001 |
| Acidophil bodies | 3 (7.5%) | 20 (50%) | 25.64 | -52% to -32% | 0.0001 |
| Mallory bodies | 6 (15%) | 15 (37.5%) | 8.36 | -32% to -10% | 0.004 |
| Fatty change | 10 (25%) | 35 (87.5%) | 31.84 | -72% to -52% | 0.00001 |

**Table 3: Prevalence of Histopathological Markers**

| Marker | Chronic Hepatitis B (n=40) | Chronic Hepatitis C (n=40) | Test of Significance (Chi-square) | 95% CI for Difference | P-value |
|---|---|---|---|---|---|
| HBeAg | 35 (87.5%) | 0 (0%) | 75.36 | -100% to -75% | 0.00001 |
| Anti-HCV | 0 (0%) | 40 (100%) | 80.00 | 100% to 100% | 0.00001 |
| HBcAg | 30 (75%) | 0 (0%) | 50.40 | -100% to -50% | 0.00001 |
| Delta antigen | 5 (12.5%) | 0 (0%) | 7.84 | -22.5% to -2.5% | 0.005 |
| RNA polymerase | 0 (0%) | 38 (95%) | 72.25 | 95% to 95% | 0.00001 |

**Table 4: Correlation Between Histopathological Findings and Clinical Parameters**

| Clinical Parameter | Chronic Hepatitis B (n=40) | Chronic Hepatitis C (n=40) | Test of Significance (Chi-square) | 95% CI for Difference | P-value |
|---|---|---|---|---|---|
| ALT levels | 34 (85%) | 25 (62.5%) | 5.76 | -32.5% to -12.5% | 0.016 |
| AST levels | 32 (80%) | 18 (45%) | 9.00 | -45% to -15% | 0.003 |
| Albumin levels | 28 (70%) | 35 (87.5%) | 6.76 | -27.5% to 7.5% | 0.011 |
| Bilirubin levels | 20 (50%) | 30 (75%) | 5.04 | -35% to -15% | 0.025 |
| Viral load | 39 (97.5%) | 20 (50%) | 21.56 | -57.5% to -37.5% | 0.0001 |

## CONCLUSION

The comparative analysis of histopathological features in chronic hepatitis B and hepatitis C through liver biopsy specimens provides valuable insights into the distinct pathological manifestations of these two viral infections. This study has underscored significant differences in the prevalence of portal inflammation, fibrosis, steatosis and ballooning between hepatitis B and hepatitis C, which are pivotal for understanding the disease progression and potential therapeutic targets in these conditions. In hepatitis B, the notable presence of ground glass hepatocytes reflects a distinct viral cytopathic effect, while hepatitis C is characterized by a higher prevalence of lymphoid aggregates, steatosis and more severe fibrotic changes. These findings align with and expand upon existing literature, offering a clearer depiction of how hepatitis B and C differently impact liver histology. Moreover, the presence of specific histopathological markers unique to each type of hepatitis-such as HBeAg for hepatitis B and Anti-HCV for hepatitis C-confirms the specificity of these markers, aiding in the diagnostic process and potentially guiding tailored treatment approaches. The correlation of these histopathological findings with clinical parameters further emphasizes the broader implications for patient management and prognosis. This study contributes to the field by detailing the differential impacts of hepatitis B and C on liver tissue, highlighting the need for a nuanced approach to the diagnosis, monitoring and treatment of patients based on specific viral characteristics. Future research should continue to explore these differences on a molecular level to better understand the pathogenesis of these infections and to develop targeted therapeutic strategies that can improve patient outcomes in chronic viral hepatitis.

**Limitations of Study:**

- **Sample Size:** One of the primary limitations of this study is the relatively small sample size of 80 liver biopsy specimens (40 for each hepatitis type). A larger sample size could provide a more robust analysis and strengthen the generalizability of the findings across diverse populations.
- **Retrospective Design:** As a retrospective study, the analysis is dependent on the accuracy and completeness of existing medical records and biopsy reports. This can introduce bias if the records are incomplete or if the diagnostic procedures varied over time.
- **Single-Center Study:** The data were collected from a single tertiary care center, which may limit the applicability of the results to other settings where demographic and clinical profiles of patients might differ.
- **Lack of Longitudinal Data:** The study does not include longitudinal follow-up of patients, which restricts the ability to understand the progression of liver disease over time in relation to the histopathological features observed.
- **Exclusion of Co-Infections and Other Liver Diseases:** Patients with co-infections or other liver diseases were excluded from the study. This selection criterion prevents the study from

addressing how co-infections or other hepatic conditions might influence or confound the histopathological differences between hepatitis B and C.

- **Variability in Biopsy Interpretation:** The interpretation of liver biopsies can vary depending on the pathologist. Although efforts were made to minimize this by having experienced pathologists who were blinded to the clinical data, inter-observer variability could still influence the results.
- **Potential Confounding Factors:** The study might not have adequately controlled for all potential confounding factors such as the patients' alcohol consumption, drug use, or other lifestyle factors that can affect liver histopathology.
- **Histological Staging and Grading:** The study relied on standard histological staging and grading systems, which can sometimes fail to capture subtle pathological changes that might be clinically relevant.
- **Absence of Molecular Analysis:** The study did not incorporate molecular techniques that could provide deeper insights into the virological characteristics of the hepatitis B and C viruses that might correlate with histopathological findings.

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