



Histopathological Spectrum of Hepatic Lesions in Liver Biopsy and Resection Specimens: A Retrospective Study

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ABSTRACT

Background and aim: Liver diseases include a broad spectrum of non-neoplastic and neoplastic conditions and remain a significant cause of morbidity and mortality worldwide. Histopathological examination is the gold standard for diagnosing many hepatic disorders and plays a crucial role in patient management. This study aimed to evaluate the demographic characteristics and histomorphological spectrum of hepatic lesions diagnosed over two years at a tertiary care centre.

Materials and methods: This retrospective descriptive study included 110 liver biopsy and resection specimens examined in the Department of Pathology at Government Stanley Medical College over 2 years. Routine histopathological evaluation was performed using Hematoxylin and Eosin staining, with immunohistochemistry applied when required. Demographic data, specimen types, and histopathological findings were analyzed.

Results: Of the 110 cases, 53 were biopsies, and 57 were resection specimens. Among biopsy specimens, 32% were non-neoplastic, and 68% were malignant. In resection specimens, 32% were non-neoplastic, 18% were benign neoplasms, and 51% were malignant. A marked male predominance was observed in both groups. Metastatic carcinoma was the most common malignant lesion in biopsy specimens, whereas hepatocellular carcinoma was the predominant malignant tumour in resection specimens. Hydatid cyst was the most frequent non-neoplastic lesion among resected specimens.

Conclusions: Hepatic lesions exhibit a wide histopathological spectrum, with malignant neoplasms comprising the majority of cases. Histopathological evaluation remains essential for accurate diagnosis, appropriate clinical management, and early detection of serious liver diseases, thereby contributing significantly to improved patient outcomes.

1. Introduction

The Liver is the largest solid visceral organ. It plays a central role in maintaining metabolic homeostasis by regulating carbohydrate, lipid, and protein metabolism; bile synthesis; detoxification; nutrient storage; and immunological regulation. Because of its unique dual blood supply and continuous exposure to dietary, metabolic, infectious, toxic, and neoplastic agents, the Liver is particularly vulnerable to a wide spectrum of pathological insults, ranging from reversible inflammatory conditions to progressive fibrosis, Cirrhosis, and malignant neoplasms.^[1] Liver diseases continue to represent a major global health burden, accounting for millions of deaths annually and imposing substantial healthcare costs worldwide. Recent epidemiological studies have demonstrated a continuous increase in the prevalence of chronic liver diseases, primarily driven by metabolic dysfunction-associated steatotic liver disease (MASLD, formerly NAFLD), alcohol-associated liver disease (ALD), chronic viral hepatitis, autoimmune

liver diseases, and hepatocellular carcinoma (HCC).^[2] Furthermore, the incidence of primary liver cancer has increased steadily over recent decades, making HCC one of the leading causes of cancer-related mortality worldwide.^[3, 4] Geographic variation in disease prevalence, environmental exposures, socioeconomic status, and lifestyle factors further influence the histopathological spectrum of hepatic lesions encountered in different populations.^[2, 5] Hepatic lesions encompass a broad and heterogeneous group of disorders that include non-neoplastic diseases such as steatosis, hepatitis, Cirrhosis, vascular disorders, parasitic infestations, and inherited metabolic diseases, as well as benign and malignant neoplasms. While hepatocellular carcinoma represents the most common primary malignant tumour of the Liver, metastatic tumour remain the most frequently encountered malignant hepatic lesions in routine pathological practice due to the Liver's rich dual vascular supply.^[1, 3] An accurate distinction between primary and secondary hepatic neoplasms is essential because their biological behavior, therapeutic

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approaches, and prognostic outcomes differ substantially.^[6] Although remarkable advances in radiological imaging, molecular pathology, and serum biomarkers have significantly improved the diagnostic evaluation of liver diseases, histopathological examination remains the gold standard for establishing a definitive diagnosis in many hepatic disorders. Liver biopsy provides invaluable information on disease etiology, tumour classification, grading, staging, fibrosis assessment, and therapeutic decision-making.^[3] In addition, immunohistochemistry has become an indispensable adjunct in surgical pathology, facilitating the differentiation of hepatocellular carcinoma from cholangiocarcinoma and metastatic malignancies, particularly in poorly differentiated tumour or unusual histological variants.^[3, 7] Several studies have investigated the histopathological spectrum of hepatic lesions in tertiary care institutions; however, most have focused exclusively on liver biopsies or specific disease entities rather than evaluating the entire spectrum of biopsy and resection specimens.^[3-8] Comprehensive institutional data describing the relative frequencies of non-neoplastic, benign, and malignant hepatic lesions remain limited, particularly in developing countries where disease patterns may differ considerably from those reported in Western populations. Such information is valuable not only for understanding regional epidemiology but also for improving diagnostic accuracy, optimizing pathological reporting, and supporting clinical decision-making. Therefore, the present study was undertaken to evaluate the demographic characteristics and histomorphological spectrum of hepatic lesions diagnosed in liver biopsy and resection specimens received at a tertiary care centre over two years. The study further aimed to describe the relative distribution of non-neoplastic, benign, and malignant lesions and to highlight the pathological diversity encountered in routine diagnostic practice.

2. Material and methods

Study design and setting

This retrospective descriptive study was conducted in the Department of Pathology, Government Stanley Medical College and Hospital, Chennai, India. The study included all liver biopsy and liver resection specimens received over two years, from January 2022 to December 2023. The study was approved by the Institutional Ethics Committee prior to data collection.

Study population

A total of 110 consecutive liver specimens were included in the study, comprising both core needle biopsy specimens and surgically resected liver specimens. Cases with inadequate tissue for histopathological evaluation, severely autolyzed specimens, or incomplete clinicopathological records were excluded from the analysis.

Data collection

Demographic and clinicopathological data, including patient age, sex, specimen type, and final histopathological diagnosis, were retrieved from the departmental pathology archives and histopathology request forms. Clinical information in the medical records was reviewed as needed to facilitate pathological interpretation.

Histopathological evaluation

All specimens were fixed in 10% neutral buffered formalin, processed routinely, embedded in paraffin wax, sectioned at 3–5 µm thickness, and stained with Hematoxylin and Eosin (H&E). Each case was reviewed independently by experienced pathologists, and the final diagnosis was established based on characteristic histomorphological features. Whenever indicated, immunohistochemistry (IHC) was performed using an appropriate

panel of antibodies to differentiate primary hepatic neoplasms from metastatic malignancies and to confirm the diagnosis of uncommon hepatic tumours. Histopathological diagnoses were rendered in accordance with the current WHO Classification of Tumours of the Digestive System (5th Edition).

Study variables

The hepatic lesions were categorized as:

- Non-neoplastic lesions
- Benign neoplasms
- Malignant neoplasms

Malignant lesions were further classified as primary hepatic malignancies or metastatic tumours, as applicable. Demographic distribution and frequency of each pathological entity were recorded.

Statistical analysis

Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics software (Version XX.0; IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean ± standard deviation (SD) or median (interquartile range), as appropriate, whereas categorical variables were expressed as frequencies and percentages. Because the primary objective of the study was to describe the histomorphological spectrum of hepatic lesions, the analysis was predominantly descriptive. Where appropriate, comparisons between categorical variables were performed using the Chi-square test or Fisher's exact test. A p-value <0.05 was considered statistically significant.

3. Results

Clinicopathological characteristics

A total of 110 liver specimens were included in the present study, comprising 53 liver biopsy specimens (48.2%) and 57 liver resection specimens (51.8%). Among the biopsy specimens, 17 cases (32.1%) were diagnosed as non-neoplastic lesions, whereas 36 cases (67.9%) were malignant lesions. No benign neoplastic lesion was identified in biopsy specimens. In contrast, among the resection specimens, 18 cases (31.6%) were non-neoplastic lesions, 10 cases (17.5%) were benign neoplasms, and 29 cases (50.9%) were malignant neoplasms.

Demographic profile

The patients' ages ranged from 3 to 77 years, with the majority of cases occurring in the fifth and sixth decades of life. Overall, a marked male predominance was observed. Of the 53 biopsy specimens, 42 patients (79.2%) were males, and 11 (20.8%) were females. Similarly, among the 57 resection specimens, 39 patients (68.4%) were males and 18 (31.6%) were females, yielding an overall male-to-female ratio of approximately 2.7:1. (Tables 1 and 2)

Table 1. Gender wise distribution of lesions in biopsy.

Biopsy	Non-neoplastic	Malignant	Benign	Total
Male	11	31	0	42
Female	6	5	0	11
Total	17	36	0	53

Table 2. Gender-wise distribution of lesions in resected specimens.

Resection	Non- neoplastic	Malignant	Benign	Total
Male	12	24	3	39
Female	6	5	7	18
Total	18	29	10	57

Spectrum of Non-neoplastic Lesions

A total of 35 non-neoplastic lesions were identified during the study period. Among biopsy specimens, cirrhosis represented the most frequent diagnosis, followed by steatosis, chronic hepatitis, and other inflammatory conditions. In resection specimens, hydatid cyst was the predominant non-neoplastic lesion, while less common entities included Wilson disease, liver abscess, and other benign inflammatory or cystic lesions (Tables 3 and 4).

Table 3. Incidence of non-neoplastic lesions in biopsy.

Steatosis	7
Wilson's	1
Cirrhosis	3
Chronic hepatitis	1
Acute hepatitis	2
Autoimmune hepatitis	1
Budd-chiari syndrome	1
Extramedullary hematopoiesis	1

Table 4. Incidence of non-neoplastic lesions in resected specimen.

Resection-Non-neoplastic lesions	
Hydatid cyst	5
Cirrhosis	4
Steatosis	4
Caroli's disease	1
Hepatoolithiasis	2
Chronic hepatitis	2

Benign hepatic neoplasms

Benign hepatic neoplasms were identified exclusively in resection specimens. The most common benign tumour was cavernous haemangioma, followed by hepatocellular adenoma, focal nodular hyperplasia, and mesenchymal hamartoma. These lesions collectively accounted for 10 cases (17.5% of all resection specimens).

Malignant hepatic lesions

Malignant neoplasms constituted the largest pathological category in the present study. Among biopsy specimens, metastatic carcinoma was the most

common malignant diagnosis, followed by hepatocellular carcinoma (HCC) and cholangiocarcinoma. In contrast, hepatocellular carcinoma was the predominant malignant tumour in resection specimens, followed by cholangiocarcinoma, while relatively uncommon tumours such as hepatic angiosarcoma and primary neuroendocrine tumour were encountered in a small number of cases (Tables 5, 6 and 7).

Table 5. Incidence of malignant lesions in biopsy.

Malignant lesions in biopsy	
Metastasis	17
Hepatocellular carcinoma	9
Cholangiocarcinoma	7
Neuroendocrine carcinoma of the liver	1
Angiosarcoma	2

Table 6. Incidence of malignant lesions in resected specimen.

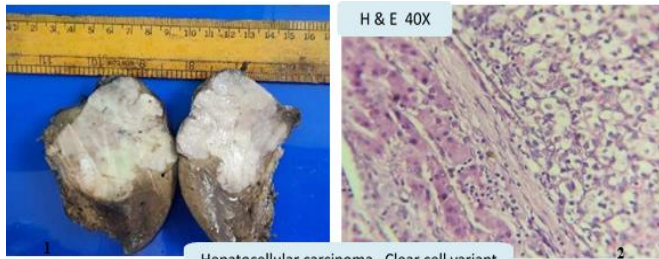
Resection-malignant neoplasms	
Hepatocellular carcinoma	13
Cholangiocarcinoma	10
Metastasis	6

Table 7. Site-wise metastatic lesions that spread to the liver.

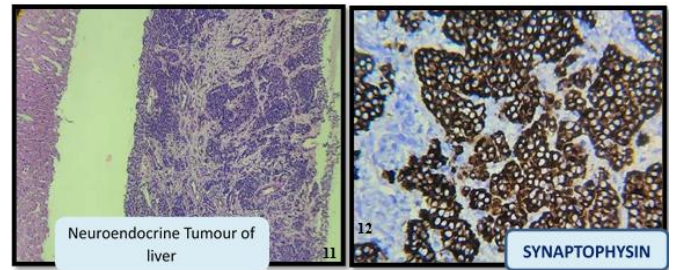
Metastasis	GIT	Pancreas	Others	Total
Biopsy	9	4	4	17
Resection	5	1	0	6
Total	14	5	4	23

Histopathological findings

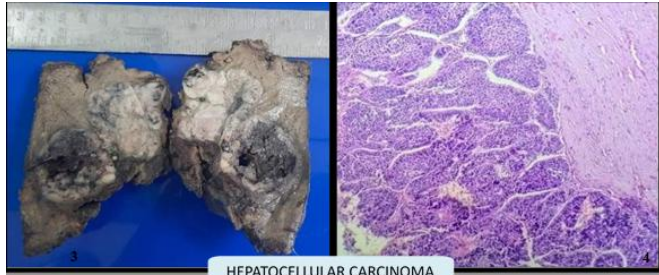
Microscopically, hepatocellular carcinoma demonstrated malignant hepatocytes arranged predominantly in trabecular architecture with varying degrees of cytological atypia. Cholangiocarcinoma exhibited infiltrating malignant glands embedded within a desmoplastic stroma. Metastatic adenocarcinomas showed histomorphological features consistent with their respective primary sites. Rare tumours, including hepatic angiosarcoma and a primary neuroendocrine tumour, displayed characteristic microscopic features confirmed by immunohistochemistry. Hydatid cysts demonstrated laminated cyst walls with surrounding granulomatous inflammatory reaction. Representative gross and histopathological features of the major hepatic lesions are illustrated in Figs. 1–12.



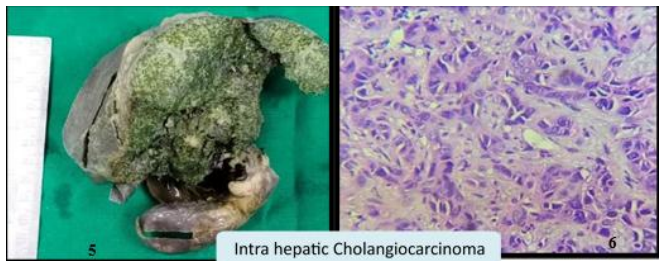
Figs. 1 and 2. Gross and Microscopic picture of Hepatocellular carcinoma clear cell variant.



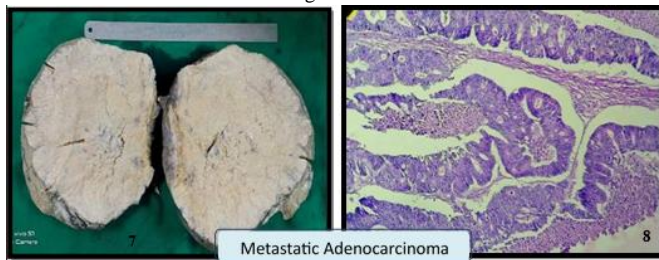
Figs. 11 and 12. Microscopic picture of Neuroendocrine Tumour and IHC image showing Synaptophysin.



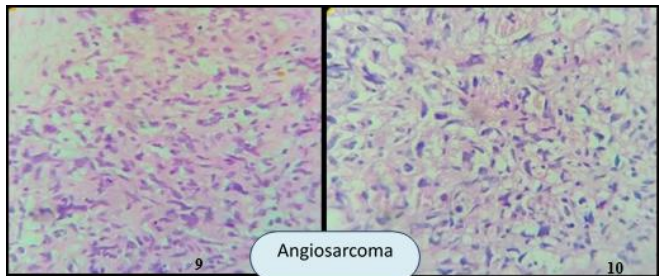
Figs. 3 and 4. Gross and Microscopic pictures of Hepatocellular carcinoma.



Figs. 5 and 6. Gross and Microscopic pictures of Intrahepatic Cholangiocarcinoma.



Figs. 7 and 8. Gross and Microscopic pictures of Metastatic adenocarcinoma.



Figs. 9 and 10. Microscopic pictures of Angiosarcoma of the liver.

4. Discussion

Liver lesions comprise a heterogeneous group of pathological entities ranging from inflammatory and metabolic disorders to primary and metastatic malignancies. In the present study, malignant lesions were the predominant pathological category, with metastatic carcinoma the most frequent diagnosis in liver biopsy specimens. In contrast, hepatocellular carcinoma was the most common malignant tumour in resection specimens. These findings provide an overview of the histomorphological spectrum of hepatic lesions encountered in routine pathology practice at a tertiary care referral centre and emphasize the continuing importance of tissue-based diagnosis despite significant advances in imaging technologies and molecular diagnostics.^[2, 3, 13-16] Recent reviews continue to recognize liver biopsy as the diagnostic reference standard whenever imaging findings are inconclusive or accurate tumour classification is required. In recent years, the diagnostic approach to liver diseases has evolved considerably with the introduction of advanced imaging techniques, digital pathology, artificial intelligence, and molecular diagnostics. Nevertheless, none of these modalities can completely replace conventional histopathological examination in the assessment of many focal and diffuse hepatic lesions. Histopathology remains indispensable for tumour typing, grading, assessment of fibrosis, and evaluation of inflammatory activity, particularly when clinicoradiological findings are equivocal or therapeutic decisions depend on tissue diagnosis.^[13-16] The predominance of malignant lesions observed in our study is consistent with previous studies demonstrating that malignant hepatic lesions constitute the majority of pathological diagnoses in tertiary referral centres.^[3-8] This pattern most likely reflects institutional referral bias, as patients with radiologically suspicious liver masses are more frequently referred for biopsy or surgical resection. Similar observations have recently been reported in large contemporary liver biopsy cohorts, confirming that neoplastic lesions continue to represent a substantial proportion of pathological specimens in specialized hepatobiliary centres. Metastatic carcinoma was the most common malignant diagnosis among biopsy specimens, whereas hepatocellular carcinoma predominated in surgically resected specimens. This observation is biologically plausible because the liver is one of the most common sites of hematogenous tumour dissemination, owing to its dual blood supply via the portal vein and hepatic artery. Conversely, patients with resectable hepatocellular carcinoma are more likely to undergo hepatic resection, resulting in a greater representation of primary hepatic malignancies in surgical specimens. Recent pathological reviews have highlighted that integrating histomorphology with immunohistochemistry remains essential for distinguishing primary liver tumours from metastatic malignancies, particularly in poorly differentiated neoplasms.^[12-16] The predominance of hepatocellular carcinoma among resection specimens observed in the present study is also consistent with current surgical practice, as patients with localized HCC are increasingly managed by curative liver resection or transplantation whenever feasible.

Conversely, metastatic tumours are more frequently diagnosed by image-guided core needle biopsy because surgical resection is often not indicated in disseminated disease. This difference in clinical management largely explains the distinct distribution of malignant lesions observed between biopsy and resection specimens.^[13,15]

Similar to previously published studies, a clear male predominance was observed in the present study.^[3-8] This finding is consistent with the well-established epidemiology of chronic liver disease and hepatocellular carcinoma, which demonstrates higher incidence among males because of differences in viral hepatitis prevalence, alcohol consumption, metabolic syndrome, and sex hormone-mediated mechanisms of hepatocarcinogenesis. Contemporary international guidelines continue to identify male sex as an important epidemiological determinant for primary liver cancer.^[13,14] Among the non-neoplastic lesions, hydatid cyst represented the most frequent lesion in resection specimens, whereas Cirrhosis and chronic inflammatory liver diseases predominated in biopsy specimens. The relatively higher frequency of hydatid disease probably reflects regional epidemiological characteristics, as parasitic infections remain endemic in several developing countries. The coexistence of metabolic, inflammatory, infectious, and inherited disorders in the present series further illustrates the broad pathological spectrum encountered in routine liver pathology practice.^[2,9-11] One of the strengths of the present study is the inclusion of both biopsy and resection specimens, allowing comprehensive assessment of the complete histopathological spectrum of hepatic lesions.

Furthermore, immunohistochemistry proved particularly valuable in confirming uncommon hepatic neoplasms, including Angiosarcoma and primary neuroendocrine tumours. Recent reviews have emphasized that immunohistochemistry is no longer considered merely an ancillary investigation but an integral component of contemporary hepatopathology, substantially improving diagnostic accuracy when interpreted alongside routine histomorphology.^[12-16] Another noteworthy observation in the present study was the identification of uncommon hepatic neoplasms, including primary Angiosarcoma and neuroendocrine tumour. Although these entities are rare, they pose significant diagnostic challenges because of overlapping morphological features with metastatic malignancies. Recent studies have highlighted that an appropriate immunohistochemical panel substantially improves diagnostic confidence and minimizes diagnostic pitfalls in these uncommon hepatic tumours.^[11-16] The findings of the present study have important clinical implications. Knowledge of the local distribution of hepatic lesions may facilitate more accurate clinicopathological correlation, improve diagnostic algorithms, and assist multidisciplinary teams in selecting appropriate therapeutic strategies. Institution-based pathological data also provide valuable epidemiological information that may support regional healthcare planning and future hepatobiliary research. The present study has several strengths. It included both liver biopsy and resection specimens, thereby providing a comprehensive overview of the histopathological spectrum of hepatic lesions encountered in routine diagnostic practice. Furthermore, the inclusion of both common and rare hepatic lesions, along with selective immunohistochemistry, enhances the study's diagnostic relevance. The findings also provide useful regional epidemiological data that may serve as a reference for future clinicopathological studies from similar healthcare settings.

Limitations of the study

The present study has several limitations. First, its retrospective single-centre design may limit the generalizability of the findings to other institutions and geographical regions. Second, the relatively small sample

size, particularly for uncommon hepatic neoplasms, restricted detailed subgroup analyses. Third, comprehensive clinicoradiological correlation, treatment information, and long-term follow-up data were unavailable for all patients, precluding survival analysis and prognostic assessment. Finally, molecular characterization of hepatic tumours was beyond the scope of the present study. Future multicentre prospective studies incorporating larger patient cohorts, molecular profiling, and long-term clinical outcomes are warranted to validate and expand these findings.

5. Conclusion

The present study highlights the wide histopathological diversity of hepatic lesions encountered in routine diagnostic practice and reinforces the pivotal role of histopathological examination in the evaluation of liver diseases. Although advances in imaging, molecular pathology, and precision medicine have significantly improved the diagnostic approach to hepatic disorders, tissue diagnosis remains indispensable for accurate classification, prognostic assessment, and therapeutic decision-making. The predominance of malignant lesions, together with the broad spectrum of non-neoplastic and benign hepatic diseases observed in this study, underscores the importance of a systematic histopathological approach complemented by immunohistochemistry whenever appropriate. In addition to providing clinically relevant diagnostic information, the present study offers valuable regional epidemiological data that may help improve pathological reporting, multidisciplinary patient management, and future hepatobiliary research. Further multicentre prospective studies integrating histopathological findings with clinicoradiological features, molecular biomarkers, and long-term patient outcomes are recommended to define disease patterns better and optimize personalized management strategies for patients with hepatic lesions.

Conflict of Interest

The authors declared that there is no conflict of interest.

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