Section: Pathology

Original Research Article

HISTOPATHOLOGICAL EVALUATION OF LIVER TRU-CUT BIOPSIES IN DIFFERENTIATING PRIMARY HEPATIC MALIGNANCIES FROM METASTATIC LESIONS USING IMMUNOHISTOCHEMISTRY: A THREE-YEAR CROSS-SECTIONAL STUDY FROM A TERTIARY CARE CENTRE

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ABSTRACT

Background: The liver is a common site for both primary and secondary malignant tumors because of its dual blood supply and unique vascular architecture. Accurate differentiation between primary hepatic malignancies and metastatic lesions is essential for determining appropriate treatment and predicting prognosis. While radiological investigations provide valuable information, histopathological examination remains the gold standard for diagnosis. Immunohistochemistry (IHC) serves as a useful adjunct, particularly in poorly differentiated tumors and lesions with an unknown primary origin. **Aim:** To evaluate the histopathological spectrum of malignant liver lesions in tru-cut biopsy specimens and to assess the role of histopathology and immunohistochemistry in differentiating primary hepatic malignancies from metastatic lesions.

Materials and Methods: This hospital-based cross-sectional study was conducted in the Department of Pathology, Tirunelveli Medical College and Hospital, over a three-year period from January 2023 to December 2025. Thirty-seven liver tru-cut biopsy specimens diagnosed as malignant lesions were included. Clinical, radiological, histopathological, and immunohistochemical findings were analyzed. Histomorphological features including architectural pattern, cytological atypia, necrosis, desmoplastic response, and vascular invasion were evaluated. Immunohistochemical markers such as HepPar-1, Glypican-3, CK7, CK19, CK20, CDX2, ER, PR, S100, and HMB45 were utilized for definitive diagnosis.

Results: The mean age of the patients was 55.8 years, with a male predominance (male: female ratio 2.36:1). Primary hepatic malignancies constituted the majority of diagnosed tumors, with hepatocellular carcinoma (HCC) being the most common primary malignancy, followed by intrahepatic cholangiocarcinoma (ICC). Metastatic tumors represented a significant proportion of hepatic lesions. Histopathological examination alone established a diagnosis in 23 cases (62.2%), while immunohistochemistry was required in 14 cases (37.8%). IHC altered or refined the diagnosis in 6 cases (16.2%), significantly improving diagnostic accuracy and facilitating identification of the primary site in metastatic tumors.

Conclusion: Liver tru-cut biopsy is a reliable and minimally invasive diagnostic modality for the evaluation of hepatic malignancies. Histopathological examination remains the cornerstone of diagnosis, while

immunohistochemistry substantially enhances diagnostic precision in challenging cases. The combined application of morphology and immunophenotyping enables accurate differentiation between primary hepatic malignancies and metastatic lesions, thereby guiding optimal patient management and therapeutic decision-making.
Keywords: Liver tru-cut biopsy; Hepatocellular carcinoma; Intrahepatic cholangiocarcinoma; Metastatic liver tumors; Histopathology; Immunohistochemistry; Hepatic malignancies.

INTRODUCTION

The liver is frequently involved by malignant tumors owing to its extensive vascular supply and filtration function. Hepatic malignancies may be primary, arising from hepatocytes or biliary epithelium, or secondary due to metastasis from extrahepatic sites. Secondary tumors occur more commonly than primary liver cancers. [1,3,4]

Accurate classification requires adequate sampling and careful microscopic examination with ancillary techniques needed in diagnostically challenging cases.[2]

According to GLOBOCAN 2024 estimates, liver cancer remains one of the leading causes of cancer deaths globally, particularly in regions with a high prevalence of chronic hepatitis B and hepatitis C infections.[3]

Primary hepatic malignancies comprise hepatocellular carcinoma, intrahepatic cholangiocarcinoma, mixed hepatocellular-cholangiocarcinoma, hepatoblastoma, and rare mesenchymal tumors. Among these, hepatocellular carcinoma accounts for approximately 75–85% of primary liver cancers. Chronic viral hepatitis, alcohol-related liver disease, non-alcoholic fatty liver disease, and cirrhosis are recognized as major risk factors for the development of HCC. [1,4,5]

Intrahepatic cholangiocarcinoma (ICC) is the second most common primary liver malignancy and arises from the intrahepatic biliary epithelium. Histologically, ICC is characterized by gland-forming malignant epithelial cells associated with a prominent desmoplastic stromal response. Distinguishing ICC from metastatic adenocarcinoma can be challenging, particularly in small biopsy specimens, necessitating the use of immunohistochemical markers. [1,4,5]

Metastatic tumors are considerably more common than primary hepatic malignancies. The liver receives blood from both the portal venous and systemic circulations, making it a frequent site for hematogenous dissemination of tumors. Common primary sites include the colorectum, pancreas, stomach, breast, lung, and melanoma. The histomorphological appearance of metastatic lesions often reflects the primary tumor; however, poorly differentiated tumors may pose significant diagnostic challenges. [1,4,5]

Historically, imaging modalities such as ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI) have played a crucial role in the detection and characterization of hepatic masses. While characteristic radiological patterns may permit diagnosis of HCC in selected clinical settings, tissue diagnosis remains essential in atypical lesions, metastatic tumors, and poorly differentiated neoplasms. Core needle (tru-cut) biopsy has emerged as a safe and effective technique for obtaining adequate tissue for histopathological and ancillary studies. [4,5,7,8]

Several studies have demonstrated the diagnostic utility of liver biopsy in hepatic malignancies. Wee et al. reported that core needle biopsy provides sufficient architectural detail to distinguish hepatocellular lesions from metastatic tumors while allowing ancillary immunohistochemical investigations. Similarly, Jain et al. observed that histopathological examination remains the gold standard for establishing the diagnosis of hepatic neoplasms and guiding therapeutic decisions. [6,7]

The introduction of immunohistochemistry has significantly enhanced diagnostic accuracy in liver pathology. HepPar-1, Arginase-1, and Glypican-3 are among the most widely used markers for confirming hepatocellular differentiation. Glypican-3 has been shown to exhibit high sensitivity in moderately and poorly differentiated hepatocellular carcinomas. [1,4,5,10]

Intrahepatic cholangiocarcinomas typically express CK7 and CK19, reflecting their biliary epithelial origin. These markers are valuable in differentiating ICC from hepatocellular carcinoma, which generally lacks diffuse CK19 expression. However, overlap may occur in poorly differentiated tumors, necessitating the use of a broader immunohistochemical panel. [4,5,10]

For metastatic adenocarcinomas, organ-specific immunohistochemical markers play an important role in identifying the primary site. CK20 and CDX2 are useful indicators of colorectal origin, whereas ER, PR, and HER2 aid in confirming metastatic breast carcinoma. Melanocytic markers such as S100, HMB45, and Melan-A are highly useful in diagnosing metastatic melanoma involving the liver. [4,5,10]

Lau et al. demonstrated that a panel comprising HepPar-1, CK7, CK20, and CDX2 significantly improves the distinction between primary hepatocellular carcinoma and metastatic adenocarcinoma. Their study highlighted the importance of integrating histomorphological findings with immunohistochemical results rather than relying on a single marker.[6]

Recent advances in molecular pathology have further improved the characterization of hepatic malignancies. Molecular alterations involving TERT promoter mutations, CTNNB1 mutations, IDH1/2 mutations, and FGFR2 fusions have been identified in various hepatic tumors and may serve as diagnostic, prognostic, and therapeutic biomarkers. Nevertheless, histopathology and immunohistochemistry continue to remain the foundation of routine diagnostic practice, particularly in resource-limited settings. [1,5,8,9,10]

In summary, the available literature emphasizes that liver tru-cut biopsy provides adequate tissue for histopathological assessment and immunohistochemical characterization. The combined evaluation of morphology and immunophenotype enables accurate differentiation of primary hepatic malignancies from metastatic lesions, thereby facilitating appropriate therapeutic planning and prognostic assessment. [6,7,8,10]

Objectives

Primary objective: To differentiate primary hepatic malignancies from metastatic lesions using liver tru-cut biopsies.

Secondary objectives: To study the histopathological spectrum of malignant liver lesions, to evaluate demographic and clinicopathological characteristics, to assess the role of immunohistochemistry in establishing a definitive diagnosis.

MATERIALS AND METHODS

Study design: Hospital-based cross-sectional study.

Study setting: Department of Pathology, Tirunelveli Medical College and Hospital, a tertiary care centre in South India.

Study duration: January 2023 to December 2025 (3 years).

Study population: All liver biopsy specimens received during the study period.

Sample size: Thirty seven cases.

Inclusion Criteria

1. All liver biopsy specimens diagnosed with neoplastic lesions (tumors).
2. Biopsy specimens with adequate tissue for histopathological evaluation and immunohistochemical studies.
3. Ultrasound-guided liver biopsies.
4. Intraoperative liver biopsy specimens.

Exclusion Criteria

1. Non-neoplastic liver biopsy specimens.
2. Inadequate or insufficient biopsy samples for histopathological evaluation.

Data collection

The following parameters were retrieved from pathology records:

- Age
- Sex
- Clinical presentation
- Radiological findings
- Type of biopsy (ultrasound-guided/Intraoperative)
- Histopathological diagnosis
- Immunohistochemical profile
- Final diagnosis

Histopathological evaluation

All specimens were fixed in 10% neutral buffered formalin and processed routinely. Hematoxylin and eosin-stained sections were examined for architectural pattern, cytological atypia, tumor differentiation, bile production, necrosis, desmoplastic response and vascular invasion.

Immunohistochemistry: Immunohistochemistry was performed in cases requiring further characterization.

Hepatocellular markers: HepPar-1 and Glypican-3

Biliary markers: CK 7 and CK 19

Markers for metastatic lesions: CK 20, CDX2, S100, ER, PR, Her2neu and HMB45

Outcome measures

Primary outcomes:

Differentiation of primary hepatic malignancies from metastatic lesions.

Secondary outcomes:

1. Histopathological spectrum of hepatic malignancies.
2. Frequency of primary versus metastatic tumors.
3. Diagnostic utility of immunohistochemistry.
4. Distribution of metastatic primary sites.

Statistical analysis

Data were entered into Microsoft Excel and analysed using SPSS version 26

- Continuous variables: Mean ± standard deviation.
- Categorical variables: Frequency and percentages.
- Association between variables: Chi-square test or Fisher's exact test.
- A p-value <0.05 was considered statistically significant

RESULTS

Table 1: Demographic profile

Variable	Findings
Number of cases	37
Mean age	55.8
Age range	18 – 79
Male	26
Female	11

Table 2: Type of biopsy

Biopsy type	Number (%)
Ultrasound-guided 32	
Intraoperative 5	

Table 3: Histopathological categorization

Parameter	Number of Cases
Total liver biopsies received	37
Primary liver neoplasms	20
– Hepatocellular carcinoma	14
– Intrahepatic cholangiocarcinoma	6
Metastatic liver tumors (secondaries)	17

Table 4: Diagnostic utility of IHC

Parameter	Number (%)
Cases diagnosed by morphology alone	23
Cases requiring IHC	14
Cases where IHC altered diagnosis	6

COLOUR PLATES

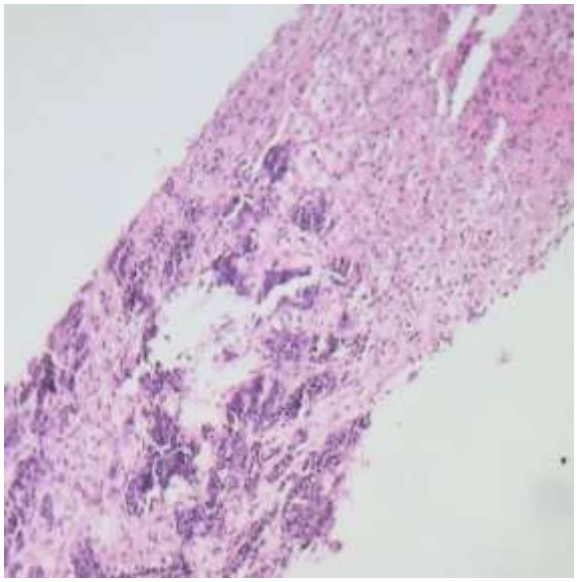

Figure 1: CNB – HCC, H&E stain, 10x

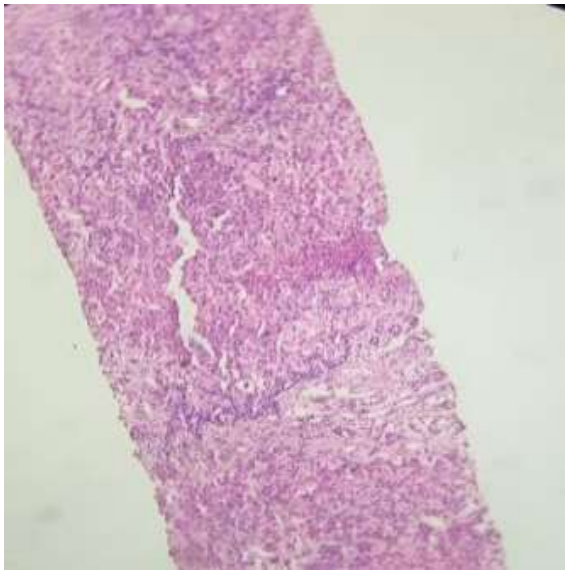

Figure 2: CNB – HCC, H&E stain

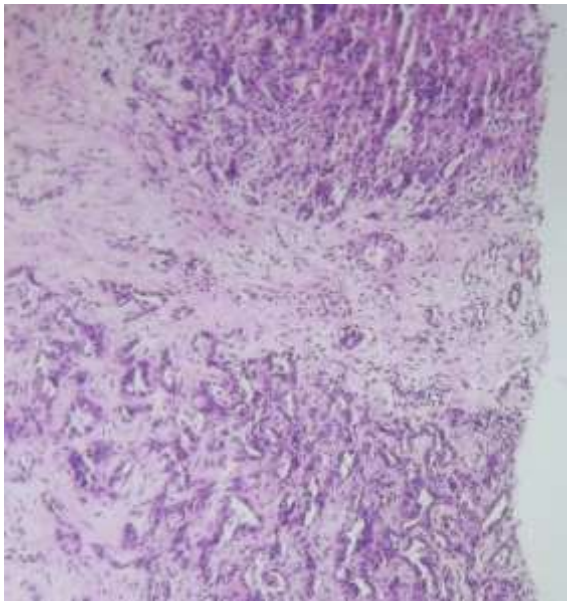

Figure 3: CNB – HCC, H&E stain, 10x

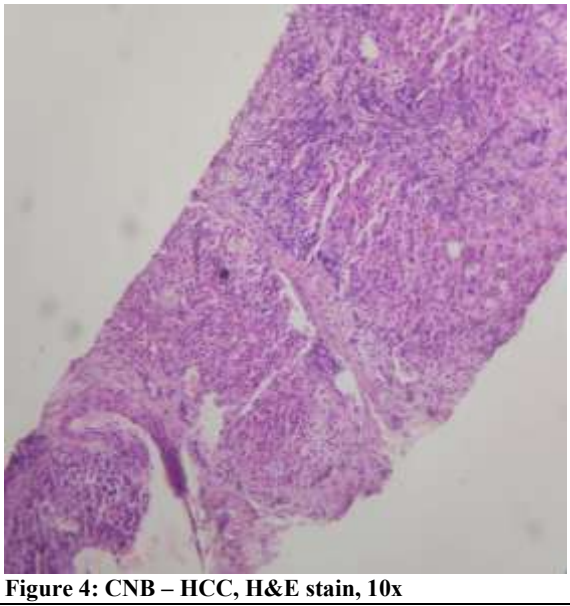

Figure 4: CNB – HCC, H&E stain, 10x

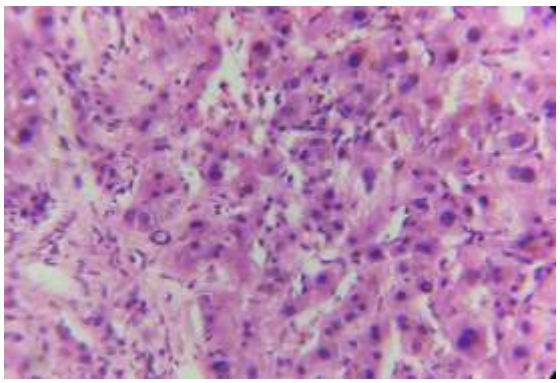

Figure 5: CNB – HCC, H&E stain, 40x

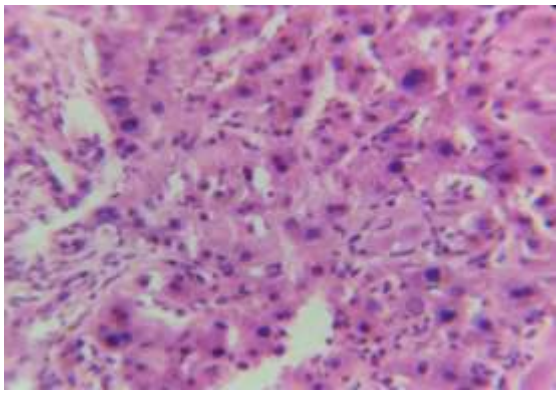

Figure 6: CNB – HCC, H&E stain, 40x

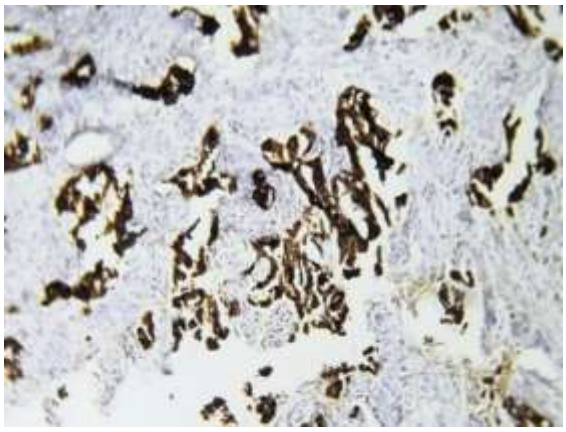

Figure 7: CNB – Liver, IHC-HepPar1,

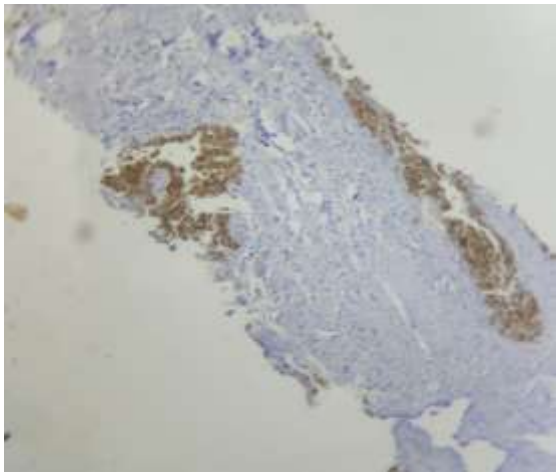

Figure 8: CNB – Liver, IHC- Glypican3, 10x

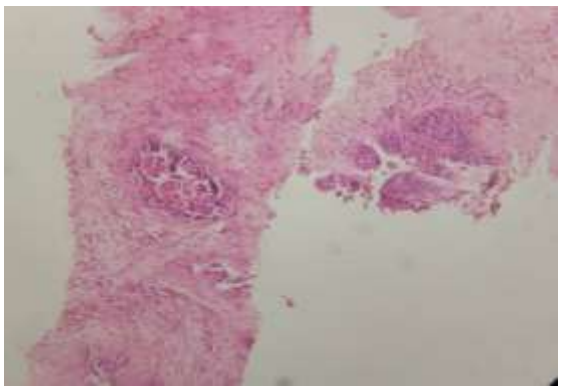

Figure 9: CNB – ICC, 10x

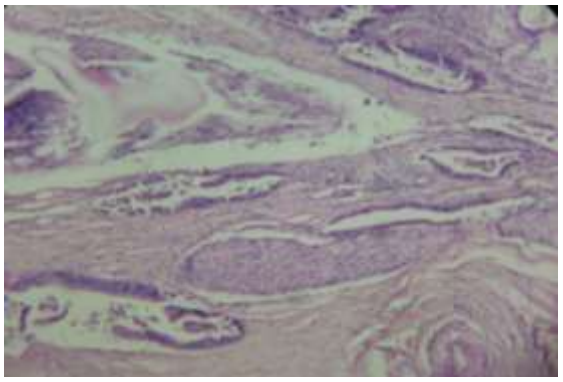

Figure 10: CNB – ICC, 10x

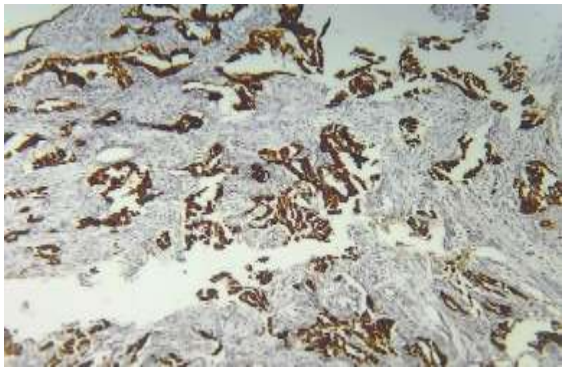

Figure 11: CNB – Liver, IHC-CK19, 10x

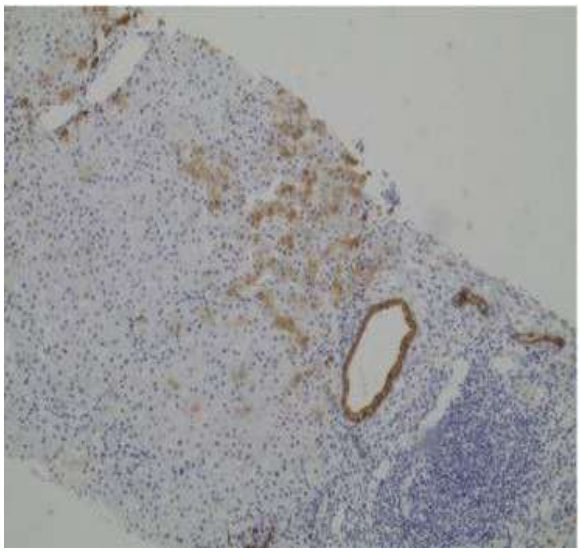

Figure 12: CNB – Liver, IHC- CK7, 10x

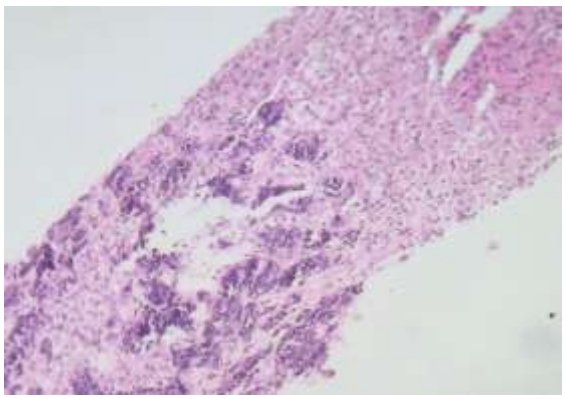

Figure 13: CNB, Invasive Breast Carcinoma deposits- H&E stain, 10x

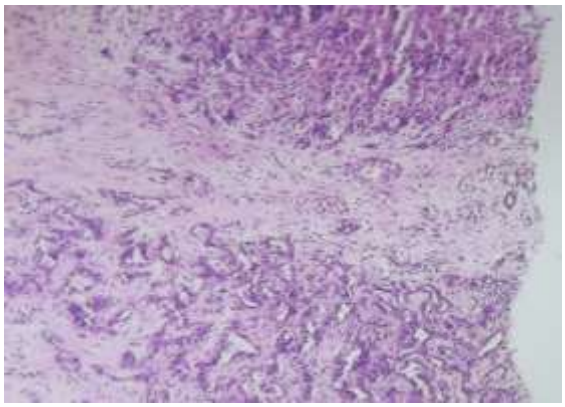

Figure 14: CNB, IBC deposits- H&E stain, 10x

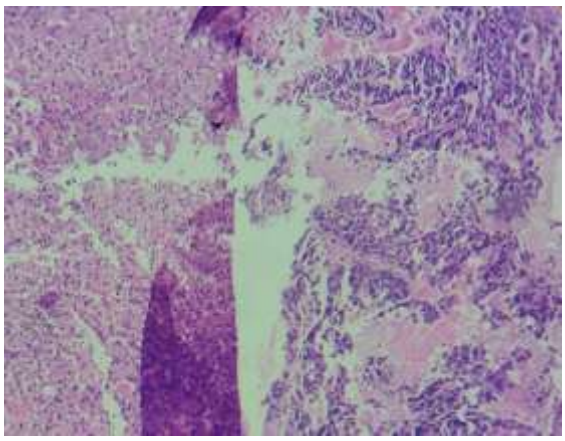

Figure 15: CNB, Adenocarcinomatous deposits

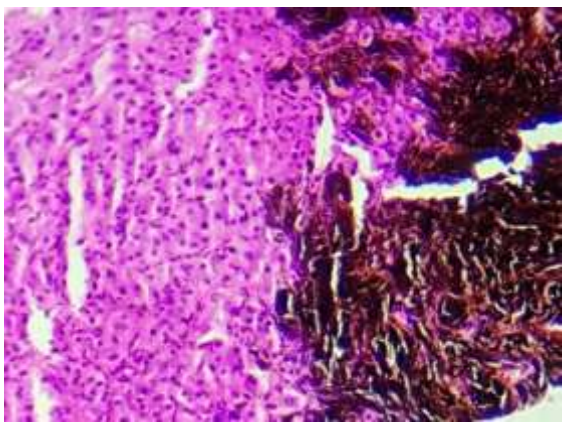

Figure 16: CNB, Melanoma deposits- H&E, 10x

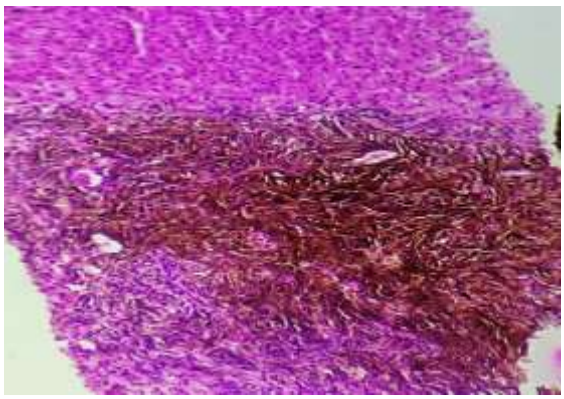

Figure 17: CNB, Melanoma deposits- H&E, 10x

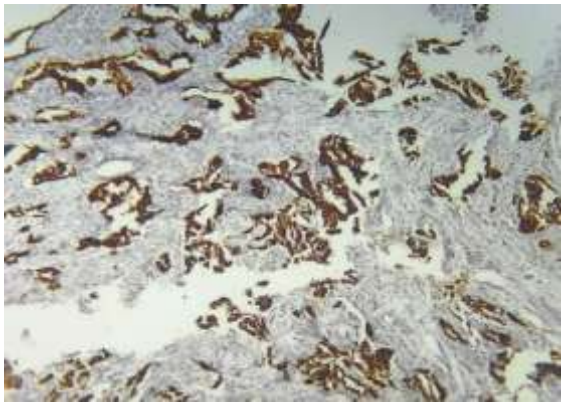

Figure 18: CNB, CK 7 positivity- IHC, 10x

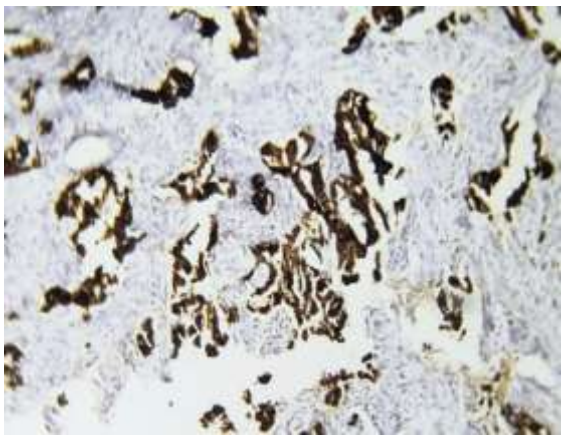

Figure 19: CNB, ER positivity-IHC, 10x

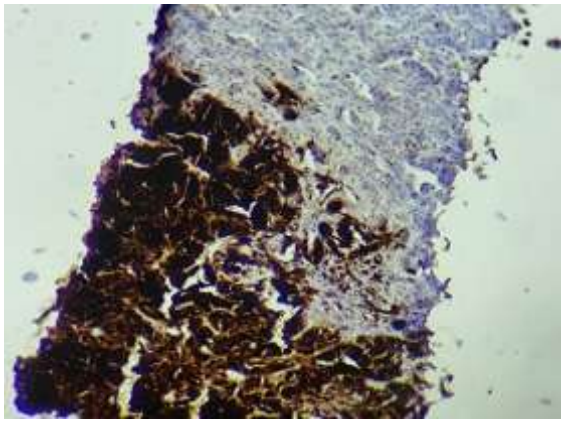

Figure 20: CNB, HMB-45 positivity-IHC, 10x

DISCUSSION

The present study evaluated the utility of liver tru-cut biopsy in differentiating primary hepatic malignancies from metastatic lesions in a tertiary care centre over a three-year period. Histopathological examination remains the cornerstone of diagnosis, while immunohistochemistry serves as an indispensable adjunct in lesions with ambiguous morphology.

The majority of patients in the present study were males, with a mean age of 55.8 years. This demographic profile is comparable to previously published studies, which have demonstrated a male predominance among patients with hepatic malignancies, particularly hepatocellular carcinoma (HCC), owing to the higher prevalence of chronic liver disease and viral hepatitis among men.

Among primary hepatic malignancies, HCC was the most common diagnosis. Histologically, HCC demonstrated characteristic trabecular architecture, hepatocellular differentiation, bile production and sinusoidal vascular patterns. Immunohistochemical markers such as HepPar-1 and Glypican-3 proved useful in confirming hepatocellular differentiation, especially in poorly differentiated tumors. These findings are in agreement with the studies of International Agency for Research on Cancer (IARC) and WHO classifications that identify HCC as the predominant primary liver cancer worldwide. .[1,4,5]

Metastatic lesions constituted a significant proportion of liver tumors. The liver is a common site for metastasis because of its dual blood supply and fenestrated sinusoidal system. Metastatic adenocarcinoma represented the most frequent secondary malignancy encountered. In several cases, morphology alone was insufficient to identify the primary site, necessitating immunohistochemical evaluation using CK7, CK20, CDX2, ER, PR, S100 and HMB45. The use of lineage-specific markers substantially improved diagnostic precision and aided in identifying the probable primary tumor origin. [1,4,5]

In the present study, immunohistochemistry was required in approximately one-third of cases and altered or refined the diagnosis in a considerable proportion of patients. This observation highlights the complementary role of IHC in routine liver biopsy practice. Similar findings have been reported by Lau et al. and Wee et al., who demonstrated that immunohistochemical panels significantly increase diagnostic confidence in poorly differentiated hepatic tumors and metastatic lesions of unknown primary origin. [6,7]

The study further emphasizes the value of core needle biopsy as a minimally invasive procedure capable of providing adequate tissue for both histopathological assessment and ancillary testing. The preservation of tissue architecture in tru-cut biopsies facilitates evaluation of growth patterns, stromal response and vascular invasion, all of which contribute to accurate classification. [7,8,9]

The major limitations of the present study include the relatively small sample size, single-centre design and absence of long-term follow-up data. Future multicentric studies with larger cohorts and incorporation of molecular diagnostic techniques may further enhance diagnostic accuracy and prognostic stratification. .[8,9,10]

Overall, the findings reaffirm that the integration of morphology and immunohistochemistry remains the gold standard approach for differentiating primary hepatic malignancies from metastatic liver tumors and plays a critical role in guiding clinical management. [1,4,5,6,7,10]

CONCLUSION

Liver tru-cut biopsy is a highly effective diagnostic modality for evaluating hepatic malignancies. Histopathological examination, supplemented by immunohistochemistry, remains indispensable for differentiating primary hepatic malignancies from metastatic lesions and directly influences therapeutic decisions. [6,7,8,10]

The study further emphasizes the value of core needle biopsy as a minimally invasive procedure capable of providing adequate tissue for both histopathological assessment and ancillary testing. The preservation of tissue architecture in tru-cut biopsies facilitates evaluation of growth patterns, stromal response and vascular invasion, all of which contribute to accurate classification. [7-9]

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Overall, the findings reaffirm that the integration of morphology and immunohistochemistry remains the gold standard approach for differentiating primary hepatic malignancies from metastatic liver tumors and plays a critical role in guiding clinical management. [1,4-7,10]

Limitations

1. Small sample size.
2. Single-centre study.
3. Lack of long-term follow-up.
4. Limited molecular studies.

Declarations

Funding: Nil

Conflict of interest: None

Ethical approval: Obtained from Institutional Ethics Committee

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