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COLLEGE OF HEALTH SCIENCES - SCHOOL OF MEDICINE

DEPARTMENT OF PATHOLOGY

Histopathological Patterns of Neoplastic Liver Diseases and their Correlation with Imaging Findings at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, A retrospective cross-sectional analysis, 2021-2025

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A research thesis to be submitted to the Department of Pathology, College of Health Sciences, Addis Ababa University in Partial Fulfillment for the Requirement of specialty certificate in Pathology.

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Addis Ababa, Ethiopia

Declaration

I, Dr. Henock Solomon Sisay hereby declare that the research proposal entitled:

"Histopathological Patterns of Neoplastic Liver Diseases and their Correlation with Imaging Findings at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, A retrospective cross-sectional analysis, 2021-2025 " is my original work and has been prepared in accordance with the academic and ethical guidelines of Tikur Anbessa Specialized Hospital (TASH) and was fully undertaken by me under the guidance of my advisor Dr. Yonas Bekuretsion. To the best of my knowledge, this proposal has not been submitted in part or full to any other institution or for any other academic qualification.

I affirm that all sources of information, data, and ideas used in the development of this proposal have been duly acknowledged and referenced. I also confirm that ethical approval will be obtained prior to the commencement of the study, and all necessary ethical standards, including patient confidentiality and informed consent (where applicable), will be strictly adhered to.

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Abstract

Background: Liver cancer is one of the major causes of cancer-related morbidity and mortality, especially in developing countries like Ethiopia. Two of the commonest diagnosis are hepatocellular carcinoma (HCC) and metastatic carcinoma. Most cases of HCC are associated with chronic viral hepatitis (HBV & HCV), cirrhosis (commonly alcoholic), and environmental factors. Although histopathology is considered the "gold standard" diagnostic modality, imaging techniques like ultrasound, CT, and MRI are important for the initial workup, especially for pre-op evaluation of suspected patients. In a resource-constrained environment, it is vital to know the diagnostic performance and correlation of imaging techniques and histopathologic findings.

Objective: This study aimed at describing the different histopathological patterns of liver neoplastic diseases, and determining their correlation with available findings from imaging modalities at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

Methods: A review of medical records of 317 patients with histo-pathologically confirmed liver neoplasms diagnosed between the period January 2021 and December 2025 was performed. Data were obtained from pathology reports, imaging records, and clinical charts. Parameters included demographics, risk factors, imaging impressions, AFP levels, and histopathological features. The sensitivity, specificity, PPV, and NPV were used to determine concordance between the two diagnostic modalities. SPSS version 26 was employed for statistical analysis. Chi-square tests and multivariate logistic regression were applied for identifying independent predictors of malignancy and HCC.

Results: Together metastatic carcinoma and HCC were the most prevalent diagnoses, with metastatic disease being a little more frequent. A strong association was found between AFP elevation (>400 ng/mL) and the presence of cancer and specifically HCC. The first set of scans showing either HCC or micro-metastases were a separate indicator of malignant outcomes findings. The overall sensitivity of imaging for HCC was only 49.0% while the specificity was as high as 93.0%. In addition, the PPV was 76.9% and NPV was 79.4%, revealing high specificity but only modest sensitivity. Agreement between imaging impressions and histopathological diagnoses demonstrated moderate concordance (Cohen's Kappa = 0.435, $p < 0.001$). HBV and HCV status was hardly ever recorded, therefore was difficult to assess predictive value. Prognostic markers like tumor grade/differentiation, tumor necrosis, VI, and PNI were documented in a minority of cases, suggesting inconsistent use of standardized reporting.

Conclusion: Currently out of neoplastic liver conditions seen in Tikur Anbessa Specialized Hospital, metastatic carcinoma and HCC remain the most prevalent. Imaging showed high specificity but modest sensitivity. Thus, a combination of diagnostic methods using laboratory findings like AFP, imaging, and pathology is necessary. Patient clinical information alongside risk factors like Viral hepatitis status and cirrhosis along with imaging reports should be documented more appropriately and accurately. Standardized pathology templates which include tumor differentiation, necrosis, LVI, and PNI should be strictly implemented and adhered. Finally, efforts to increase access to ancillary histopathology tests should be prioritized to improve diagnostic accuracy and guide appropriate patient management.

Keywords: Hepatocellular carcinoma, Metastatic carcinoma, Imaging accuracy, Histopathology, Alpha-fetoprotein, Ethiopia, Tikur Anbessa Specialized Hospital.

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Abbreviation and acronym

Abbreviation	Full Term
WHO	World health organization
HCC	Hepatocellular carcinoma
CCA	Cholangio-carcinoma
US	Ultrasound
MRI	Magnetic resonance imaging
IHC	Immuno-histochemistry
CT	Computed tomography
PPV	Positive Predictive Value
AFP	Alpha-fetoprotein
SSA	Sub Saharan Africa
NPV	Negative predictive value
SPSS	Statistical Package for the Social Sciences
AOR	Adjusted Odds Ratio
COR	Crude odds ratio
CI	Confidence Interval
PNI	Perineural invasion
VI	Vascular invasion
TASH	Tikur Anbessa specialized hospital

1. Introduction

1.1 Background of the Study

Liver cancer constitutes a major challenge to world public health and at present it is the sixth most common type of cancer and the third main cause of death from cancer globally (1). The latest Global Cancer Statistics (GLOBOCAN 2020) report indicates that the disease causes over 900,000 new cases and nearly 8.3% of total cancer deaths annually (1). While the incidence of many other types of cancer is either stabilizing or declining in some regions, liver cancer cases are expected to increase and by 2025 it is estimated that more than one million people have been diagnosed each year (2). This worldwide trend is a matter of great concern especially in low and middle income countries where lack of screening and curative treatments results in very high mortality to incidence ratios (1, 3).

Thus, the aggressiveness of the liver cancer burden in sub, Saharan Africa (SSA) is a different story and mostly the result of local risk factors alone. The single most important cause of Hepatocellular Carcinoma (HCC) in this region has been chronic infection with the Hepatitis B virus (HBV), which has been attributed to 50-60% of HCC cases, and the presence of aflatoxin B1 from contaminated food, which further increases the risk (4). The age of onset of liver cancer in SSA patients including those of Ethiopia is 3rd to 4th decade as opposed to Western individuals where the disease is mostly found in the 6th to 7th decade (2,10). As this early manifestation affects the peak productive age of the population, the socioeconomic consequences are extremely severe. Furthermore, the clinical landscape in Africa is complicated by a high prevalence of metastatic liver disease, which can often mimic primary liver malignancies on initial clinical and radiological assessment (4,10).

Liver cancer ranks 11th in terms of incidence and 7th in mortality in Ethiopia thus pointing to a serious need for better diagnostic and management strategies in the country (7). Multicenter data from Addis Ababa show that the median survival of patients after diagnosis is just about five months, indicating that most patients present very late to the healthcare system (5,7). Besides, scarcity of specialized radiologic services and rarely available definitive histopathological confirmations in regional centers further make the diagnosis difficult. Therefore, there is a great

need to investigate the diagnostic trail-line of patients at tertiary centers such as TASH to ascertain that clinical suspicion is correctly converted into effective interventions.

1.2 Statement of the Problem

Patients with liver tumors seen at TASH are mostly first, diagnosed with very advanced stages of the diseases, which are clinically manifested with huge tumor size, portal vein invasion and multifocality of the tumors (5). This late presentation was further aggravated by the fact that there was no organized national surveillance program to identify early those at high risk such as patients with chronic HBV or cirrhosis (20). Hence, for many patients their point of first contact with the health system is when they are symptomatic and at that time curative options like surgical resection or liver transplantation are no longer possible. The difficulty is not only in the early detection but also in differential diagnosis as the distinction between primary HCC, CCA, and metastatic deposits is becoming increasingly challenging at diagnostic level (8).

In both local and international context, there exists a considerable diagnostic gap in the performance of imaging modalities for liver malignancies (4,6,27). On the one hand, the international guidelines by the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver permit the diagnosis of HCC based on the demonstration of certain key features on imaging; however, the question remains if these criteria are reliable enough in the Ethiopian set, up where there is a scarcity of resources (8,9,27). The local data depict that the TASH imaging department has a high specificity but a moderate sensitivity for differentiating HCC cases, which means that significant number of pathologically confirmed cases are negative by the initial radiological impression (27). This discrepancy in sensitivity is unfortunate as it not only prolongs the time to diagnosis but also increases the possibilities of mismanagement of a considerable number of patients (4,5).

Often times lesions seen as primary HCC on Computed Tomography (CT) scans, when subjected to biopsy, have been often revealed to be metastatic carcinoma or biliary malignancies. This kind of discordance represents a pitfall in healthcare as it not only risks the patient to an erroneous treatment but is also a misallocation of very limited expensive therapeutic resources such as chemotherapy or palliative agents. Knowledge of local histopathological profiles and their

concordance with imaging is an essential prerequisite for increasing outcome of liver oncology in Ethiopia, hence showing the need to eliminate this diagnostic 'blind spot' (5, 27).

1.3 Significance of the Study

The study will provide vital information on the spectrum, risk factors and characteristics of neoplastic liver disease in Ethiopia. It will generate data on common histopathological types/subtypes of the liver tumors, which in turn will help in creating a structured diagnostic pathways for the clinician so as to improve patient management. Example of this will be aiding in narrowing down the primary extrahepatic sites in the patients with liver masses of unknown origin.

This study will also represent a significant clinical and strategic milestone by presenting the first complete assessment of imaging and pathology correlation in context of liver neoplasms at the largest referral hospital in Ethiopia. This will be helpful in estimating relative diagnostic accuracy of local imaging tools, and the study would also equip the treating physicians with evidence that will aid in formulation of diagnostic algorithms. Hence, we expect this to increase awareness on avoiding over-reliance on potentially misleading radiological impressions (13,27).

In fact, the results will become a reference point for the rewrite of the national guidelines that highlight the synergetic use of serological markers, sophisticated imaging, and compulsory histopathology for cases of doubt, thus leading to the overall improvement of care of liver cancer patient in Ethiopia.

2: Literature Review

2.1 Global Epidemiology of Liver Neoplasms

Primary liver cancer is still one of the leading oncological problems in the world today. It is the third most common cause of cancer death globally, with around 830,000 deaths reported annually (1, 11). The geographic distribution of liver cancer is very different, as more than 70% of the cases are in Asia, mainly in China (1). Nevertheless, the incidence of liver cancer in sub, Saharan Africa is increasing rapidly due to the combined effect of chronic viral hepatitis and other environmental factors (4). Hepatocellular carcinoma (HCC) is the dominant organ malignancy of the liver, accounting for 75, 85% of the cases, whereas intrahepatic cholangiocarcinoma (iCCA) comprises 10- 15% of the cases (1).

2.2 Liver Cancer Trends in Ethiopia

Historically, in Ethiopia, liver cancer has been associated with late-stage presentation & high mortality. HCC remains the dominant primary malignancy although recent studies have demonstrated the presence of a shift in the epidemiology of liver tumors (3,7). According to earlier the data from TASH metastatic malignancies and HCC are among the confirmed neoplastic lesions of the liver (26,28). Thus, evidences supporting the fact that liver is becoming more and more a site of revelation for other hidden malignancies, especially those of gastrointestinal and breast origin are being discovered in literature (10,28).

2.3 Etiological Drivers and Risk Factors

The causes of liver malignancy in Ethiopia are different from their Western counterparts; Chronic Hepatitis B (HBV) remains a major cause, with a high HBsAg prevalence in the general population (23).

- Viral Hepatitis: A recent multicenter study in Ethiopia revealed that 46.5% of patients with HCC had viral hepatitis as their base pathology besides those on antiviral therapy achieved significantly improved survival (104 vs. 469 days) (5).
- Aflatoxin exposure: Ethiopia's climate and grains storage practices for teff and corn have become a great risk to Aflatoxin B1 exposure, a very strong carcinogen, that HBV and it act in synergy (5).

- NASH and Alcohol: Along with alcoholic liver disease, Non-Alcoholic Steatohepatitis (NASH) has become an emerging risk factor among the residents of urban centers such as Addis Ababa reflecting the changes in the diet and the sedentary lifestyle (13).

2.4 Diagnostic Imaging Performance

The diagnosis of liver lesions is primarily determined by imaging; however, the accuracy of these diagnostic tools differs depending on the modality and institutional capability.

- Ultrasound (US): As the first, line screening method in Ethiopia, US is reported to have a sensitivity as low as 30-47% for detecting early-stage HCC, thus it is not a sufficiently accurate modality to make a definitive diagnosis in high-risk patients (5,18,21).
- Computed Tomography (CT): It is the preferred modality with relatively higher accuracy in detecting large tumors, but its detection rate drastically decreases for smaller lesions (<2cm) or atypical lesions, especially compared to MRI (68% vs. 80%) (13,21,27).
- MRI: Especially with the use of hepatobiliary contrast agents, is nowadays worldwide accepted as the gold standard for non-invasive diagnosis especially for non-HCC tumors. However, few local data exist due to its limited availability in Ethiopia (5, 21).

2.5 The LI-RADS Reporting System

The Liver Imaging Reporting and Data System (LIRADS) was created to facilitate the uniformity of the reports of liver imaging in high, risk patients. It assigns a category to the lesions from LR-1 (definitely benign) to LR-5 (definitely malignant/HCC) (15). Recent assessments of LIRADS indicate that there is a strong agreement between histopathology and LIRADS for LR-5 lesions (almost 100% predictive value); nevertheless, the categories such as LR-3 (intermediate probability) and LR-M (malignant but not specific) still require biopsy for confirmation (15,21). Furthermore, the absence of standardized LIRADS reporting in SSA and Ethiopia may be one of the factors for radiology vs pathology correlation issues noted (21,27)

2.6 Histopathology: The Gold Standard

Even if the non-invasive diagnostic methods are preferred initially, histopathology is still considered the "gold standard " diagnostic modality; especially in when imaging is doubtful or metastatic disease is suspected (8,9). But additional ancillary tests like immunohistochemistry

(IHC) are very important in reaching definite final diagnosis. Core needle biopsy (CNB) is the method of choice globally and at TASH, especially for preoperative diagnosis and confirmation of metastasis, as it gives insight into tissue architecture (compared to fine needle aspiration (FNA)); But resection specimen is required for definitive diagnosis, sub-typing and staging (8,9).

Immunohistochemistry (IHC): Identification of HCC from metastatic adenocarcinoma has been greatly facilitated by the use of markers such as Glypican 3, HepPar, Arginase, Albumin ISH and the other IHC for the suspected primary tumor site (20). Once again, the lack of availability of most of these markers in most Ethiopian labs is a huge hinderance in clinical practice (5,28).

2.7 Imaging-Pathology Correlation Studies

Across Africa, among the very few studies done on the topic, the literatures show a recurrent theme of diagnostic inconsistency. A study conducted in Nigeria revealed that although imaging was strongly indicative of malignancy, histopathology was the only way to establish the correct diagnosis in 24% of cases (18). Another study revealed that numerous patients are being wrongly classified when using imaging alone especially in earlier stage lesions (21). This is especially the case with metastatic lesions, which may show hyper-vascular patterns like HCC, thereby causing significant diagnostic confusion (6,21).

2.8 The Role of Alpha-fetoprotein (AFP)

AFP continues to be a useful supplement in settings with limited resources. Although its sensitivity is only moderate (40-60%), really high levels (>400 ng/mL) are very much associated with HCC (12). In fact, elevated AFP has been identified as a very strong independent predictor of HCC (AOR = 2.8) in Ethiopia, and using AFP together with CT scan leads to a significant diagnostic specificity improvement (5).

2.9 Survival and Management Challenges

The prognosis for liver cancer in Ethiopia is among the most dismal worldwide. According to multicentric data, 87% of patients present with tumors larger than 5 cm with majority of patients belonging in the palliative stage of the Barcelona Clinic Liver Cancer (BCLC) system (5, 19).

Palliative treatments such as Transarterial Chemoembolization (TACE) have been available recently at MCM Hospital at Addis Ababa, with the median survival after it being around 12.7 months, which is a clear indication of the huge demand for early diagnosis (19).

3. OBJECTIVES

3.1 General Objective

To describe the histopathological patterns of neoplastic liver diseases and evaluate their correlation with imaging findings at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia (2021–2025).

3.2 Specific Objectives

1. To determine the frequency and distribution of histopathologically confirmed neoplastic liver lesions, including hepatocellular carcinoma (HCC), cholangiocarcinoma, metastatic tumors, benign tumors, and other or unclassified lesions.

2. To describe the sociodemographic and clinical characteristics of patients with liver neoplasms, including age, sex, and selected clinical and laboratory findings (HBV status, HCV status, cirrhosis, alcohol use, non-alcoholic steatohepatitis, and serum alpha-fetoprotein levels).

3. To describe the imaging modalities used and the primary radiologic impressions in the evaluation of liver neoplasms.

4. To assess the concordance between imaging impressions and histopathological diagnoses, and evaluate the diagnostic accuracy of imaging for hepatocellular carcinoma and identify clinical and imaging factors associated with malignant liver tumors and HCC.

5. To evaluate prognostic features from both histo-pathology (grade, VI, PNI, necrosis) and imaging findings

Expected outcome: This research will generate updated local evidence on liver tumor histopathology, demographics, risk factors, and imaging correlation—improving diagnostic accuracy and aid in updating clinical follow up and management protocols.

4. METHODS

4.1 Study Area and Study Period

The study was conducted at Tikur Anbessa Specialized Hospital (TASH), Addis Ababa, Ethiopia. TASH is the largest referral and teaching hospital in the country, with a pathology department established in 1965. Data collection was carried out between November and December 2025, covering all liver neoplasm cases diagnosed histopathologically between January 2021 and December 2025.

4.2 Study Design

This was a retrospective, consecutive, single-center chart review.

4.3 Sources of Population

4.3.1 Target Population

All patients with histologically confirmed liver neoplasms at TASH.

4.3.2 Study Population

All eligible cases diagnosed during the study period that fulfilled the inclusion criteria.

4.4 Inclusion and Exclusion Criteria

4.4.1 Inclusion Criteria

- Histologically confirmed cases of liver neoplasms.
- All age groups.

4.4.2 Exclusion Criteria

- Incomplete records.
- Cases of patients with recurrent tumors and repeat biopsies.

4.5 Sample Size Determination

All eligible cases diagnosed between January 2021 and December 2025 were included. No formal sample size calculation was required, as consecutive sampling was employed.

4.6 Sampling Technique

A consecutive sampling technique was used, hence every case fulfilling the inclusion/exclusion criteria was reviewed without random selection.

4.7. Operational definitions

- Imaging diagnosis = radiologist's primary impression.
- Histopathology diagnosis = final diagnosis

4.8 Variables

4.8.1 Dependent Variables

- Histopathological diagnosis.
- Histopathological grade/differentiation.
- Specific histomorphological features such as tumor grade, necrosis, VI, PNI.

4.8.2 Independent Variables

- Age and sex.
- Underlying liver disease (HBV, HCV, cirrhosis, alcohol-related liver disease, aflatoxin exposure, NASH).
- Laboratory and serological findings (AFP, liver enzymes).
- Imaging characteristics (ultrasound, CT, MRI).

4.9 Data Collection Instruments

A structured abstraction and collection tool was developed for this study by incorporating validated instruments from the literature.

4.10 Data Collection Methods

Patient records including laboratory tests findings and imaging reports combined with histopathology reports were the main sources from which data were obtained. The abstraction instrument was pilot tested for its practicality to cull data and subsequently adjusted according to the feedback. Data abstraction was done by trained personnel & the principal investigator supervised and checked the completeness before analysis.

4.11 Data Quality Control

Prior to data entry into SPSS, all collected data was examined for its completeness and in cases where entries were unclear or missing, crosschecks were done with the source documents.

4.12 Data Processing and Analysis

The data was systematically arranged, then necessary codes were assigned and then fed into SPSS version 26. Demographic and clinical characteristics were described using descriptive statistics. The relationship between categorical variables was gauged by chi-square or Fishers exact tests. Variables with $p < 0.25$ in the univariate analysis were used to build a multivariate logistic regression model to adjust for confounders. A p-value less than 0.05 was considered statistically significant.

4.13 Ethical Consideration

Ethical clearance was secured from the Institutional Review Board of Addis Ababa University, College of Health Sciences. Department of Pathology at TASH granted the permission.

Patient confidentiality was ensured through anonymization of patient records, and the dataset contained no personal identifiers.

4.14 Dissemination of Findings

The outcome of this work will be submitted to a public defense at the Department of Pathology, College of Health Sciences, Addis Ababa University. The feedback from the examiners and the advisors will be used to revise the final thesis document.

Following the approval, the results will be shared with the relevant parties such as the Department of Pathology and the clinical teams of Tikur Anbessa Specialized Hospital.

Besides this, the report is being finalized as a manuscript for a peer-reviewed scientific journal with the aim of adding to the global understanding of liver neoplasms in Ethiopia.

5. Results

5.1. Socio-demographic Characteristics

A total of 317 patients were included in this study. The majority of study participants were in the 40 – 59 years (40.4%) and ⩾60 years (40.1%) age groups, which together accounted for 80.5% of the study population. Only 3.2% of participants were younger than 18 years, while 16.4% were aged 18–39 years.

Regarding sex distribution, 53.3% of participants were male and 46.7% were female. Overall, the study population was predominantly composed of middle-aged and older adults, with a slight predominance of male participants (Figure 1&2).

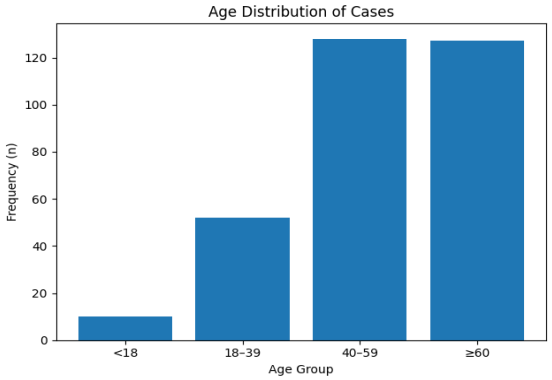


Figure 1 Socio-demographic Characteristics (Age distribution)

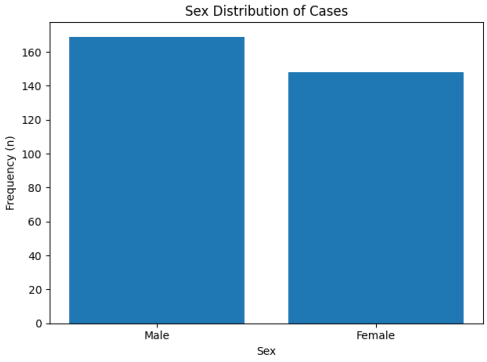


Figure 2 Sociodemographic characteristics Sex distribution

5.2 Clinical Risk Factors and Laboratory Findings

The clinical documentation for the 317 study participants showed a notable absence of viral hepatitis data, as positive HBV and HCV results were only identified in 6% and 1.6% of the cohort. Records were largely incomplete. Although documented inconsistently, cirrhosis was identified in 7.9% of patients, 11.7% were reported as having increased alcohol consumption and NASH was identified in 5.0% of study population. This exists alongside laboratory findings for Alpha-fetoprotein (AFP), which provided further nuance to the clinical profiles, showing that testing/data documentation remained inconsistent for many. 27.8% of patients had normal AFP levels, while 18.6% exhibited mild elevations between 20 and 400 ng/mL. Markedly elevated AFP levels (>400 ng/mL) were observed in 10.4% of patients, whereas AFP testing was not performed in 43.2% of cases (most of which were from the confirmed secondary liver neoplasm group). Overall, viral hepatitis markers were uncommon in the study population largely due to lack of proper documentation, while a proportion of patients demonstrated elevated AFP levels and other clinical risk factors (Table 1).

Table 1 Clinical Risk Factors and Laboratory Findings (Full cohort, n = 317)

Variable	Category	Frequency (n)	Percentage (%)
HBV status	Positive	19	6.0
	Negative	9	2.8
	Unmentioned	289	91.2
HCV status	Positive	5	1.6
	Negative	14	4.4
	Unmentioned	298	94
Cirrhosis	Present	25	7.9
	Absent/Unknown	292	92.1
Alcohol use	Yes	37	11.7

	No/Unknown	280	88.3
NASH	Present	16	5.0
	Unmentioned	301	95.0
AFP	Normal (<20)	88	27.8
	Mildly elevated (20–400)	59	18.6
	Elevated (>400)	33	10.4
	Not Done	137	43.2

Note: "Documented" refers to the presence of any recorded viral hepatitis status (positive or negative). Due to substantial missing clinical records, this does not reflect true prevalence of HBV or HCV in the study population.

5.3 Imaging Modalities and Primary Impressions

CT scan was the most frequently used imaging modality, which accounted for 46.4% of cases, followed by ultrasound (30.9%). Magnetic resonance imaging (MRI) was used in only 0.9% of cases, while 21.8% of records did not specify the imaging modality. When evaluating primary imaging impressions, metastasis was the most commonly reported finding (21.1%). It was followed closely by hepatocellular carcinoma (HCC) (20.5%). Cholangiocarcinoma (CCA) was suggested in 14.8% of cases, while benign lesions such as hemangioma accounted for 4.7%. A substantial proportion of cases (24.9%) were reported as having indeterminate/nonspecific findings and the rest of the uncommon diagnosis accounted 9.5%. These findings indicate that CT was the predominant imaging modality used in the evaluation of liver lesions especially when malignant lesion was suspected. But still a considerable proportion of imaging results labeled as indeterminate was noted in this cohort (Table 2).

Table 2 Imaging Modalities and Primary Impressions

Variable	Category	Frequency (n)	Percentage (%)
Imaging modality	CT	147	46.4
	MRI	3	0.9
	Ultrasound	98	30.9
	None	8	2.5
	Unspecified	69	21.8
Imaging impression	Suggestive of HCC	65	20.5
	Suggestive of CCA	47	14.8
	Suggestive of Metastasis	67	21.1
	Suggestive of Benign (Hemangioma/FNH)	15	4.7
	Indeterminate/Mixed	79	24.9
	Other/Non-specific	30	9.5

- Specimen Types and Diagnostic Yield

Core needle biopsy was the predominant method specimen was acquired (67.5%), followed by resection (31.9%). Only 0.6% were categorized as "unspecified/other". Thus, CNB was the main diagnostic approach identified in this cohort (Table 3).

Table 3 Specimen Type and Diagnostic Yield

Specimen type	Frequency (n)	Percentage (%)
Resection	101	31.9
Core needle biopsy	214	67.5
Other	2	0.6

5.4 Final Histopathologic Diagnoses

Metastatic carcinoma was the most frequent diagnosis in this study consisting of 33.8% of the total cases. Primary liver malignancies like hepatocellular carcinoma (including 3 cases subtyped as fibrolamellar) (32.2%) and cholangiocarcinoma (9.5%) were the second and third prevalent diagnoses, while smaller clusters of benign neoplasms like Focal nodular hyperplasia and hemangioma also appear in the data. But nearly one in five patients remains stuck in an "unclassified" category. The remaining findings are demonstrated in the pie chart below. (Figure-3). This relatively high rate of ambiguity points towards a gap in definitely diagnosing both primary and secondary liver neoplasms. And especially for the suspected primary tumors there is a significant inconsistency in documented patient data as well as laboratory test results like AFP and Viral markers. This inconsistency in documentation extends into VI, PI, tumor necrosis and tumor differentiation, of which for the later only 21.2% of primary liver neoplasm group had a recorded grade. Hence, we have clear evidence that synoptic reporting was not the standard of operation for most of the cases in the study period.

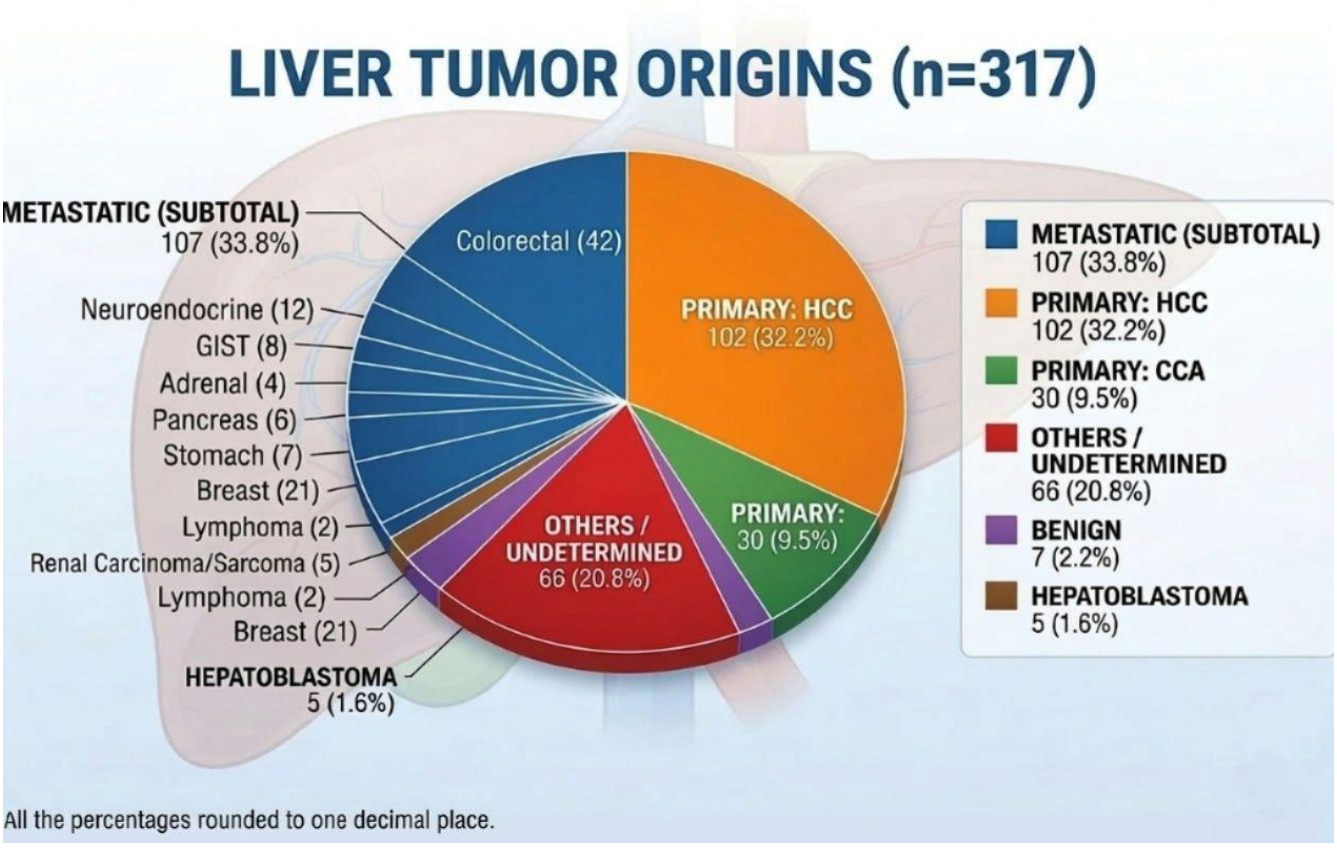


Figure 3 Final Histopathologic Diagnoses

Table 4 Prognostic Parameters in Primary Liver Tumors (HCC + CCA, n=132)

Variable	Category	Frequency (n)	Percentage (%)
AFP	Normal (<20)	41	31.1
	Mildly elevated (20–400)	42	31.8
	Elevated (>400)	27	20.5
	Not Done	22	16.7
Hepatitis B/C	Positive - HBV	19	14.4
	Positive - HCV	5	3.8
	Negative for both	14	10.6
	Unknown	94	71.2
Cirrhosis	Present	18	13.6
	Absent/Unknown	114	86.4
Differentiation	Well differentiated	13	9.8
	Moderately differentiated	10	7.6
	Poorly differentiated	5	3.8
	Unknown	104	78.8
Vascular invasion	Present	24	18.2
	Absent	10	7.6
	Not Documented	98	74.2
Tumor Necrosis	Present	38	28.8
	Absent	8	6.1
	Not Documented	86	65.1

Perineural invasion	Present	2	1.5
	Absent	8	6.1
	Not Documented	122	92.4

5.5. Imaging–Pathology Concordance

Diagnostic relation/correlation between initial radiology impression and histopathologic diagnosis was evaluated using 125 confirmed cases with defined reports from both CT scan and histopathology. This evaluation produced a Cohen's Kappa coefficient of 0.435 ($p < 0.001$), a result that marks moderate agreement between the two methods. Hence it suggests that the imaging impressions, especially from the mentioned modality, can play a vital role in deciding the management of patients, even in setups where histopathology might be initially inaccessible. Radiologists reported features of HCC in 53 specific instances. Of these 53 suspected cases, 50 were confirmed by the histopathologic findings, thus showing that imaging's (CT scan) relatively high reliability for this specific liver cancer. However, this reliability does not extend to other types of malignancies with discrepancies appearing more frequently when trying to separate cholangiocarcinoma from metastatic tumors. These specific errors stem from overlapping radiologic traits, hence showing need for correlation with clinical and laboratory findings.

A Pearson chi-square test was used to measure the overall strength of the data ($\chi^2 \approx 38.372$, $p < 0.001$). Therefore, there is a statistically significant association between the variables, even with the "mismatches" noted in some of the types of tumors. Using these imaging benchmarks allows for a structured approach to the initial evaluation of the cohort. (Table 5)

Table 5 Imaging–Pathology Concordance (Definitive pairs, n=125)

Imaging Diagnosis → / Pathology Diagnosis ↓	**HCC**	**CCA**	**Metastasis**	**Benign**	**Total**
Imaging: HCC	50	2	0	1	53
Imaging: CCA	4	3	0	1	8
Imaging: Metastasis	8	12	0	0	20
Imaging: Indeterminate/non specific	33	8	2	1	44

Total	95	25	2	3	125

Cohen's Kappa = 0.435, $p < 0.001$

Pearson Chi-Square = 38.372, $p < 0.001$

5.6. Diagnostic Accuracy of Imaging for HCC

The overall diagnostic performance of imaging for detecting HCC showed moderate sensitivity and high specificity. Imaging demonstrated a sensitivity of 49.0% and specificity of 93.0%. The positive predictive value (PPV) was 76.9%, while the negative predictive value (NPV) was 79.4%. These findings indicate that while imaging was highly specific for identifying HCC, nearly half of true HCC cases were not detected by imaging, resulting in a relatively low sensitivity (Table 6).

Table 6 Diagnostic Accuracy of Imaging for HCC (Overall)

Modality	TP	FP	FN	TN	Sensitivity %	Specificity %	PPV %	NPV %
Overall	50	15	52	200	49.0	93.0	76.9	79.4

*TP = True Positive; FP = False Positive; FN = False Negative; TN = True Negative; PPV = Positive Predictive Value; NPV = Negative Predictive Value.

5.7. Metastatic Origins

Of 317 cases, 107 were confirmed/suggestive of metastatic tumor. Colorectal carcinoma, Breast carcinoma, Neuroendocrine tumors and Gastrointestinal stromal tumors/GIST were the most frequent identifiable origins. However, 20.8% were classified as "other/undetermined," emphasizing the difficulty of confirming/tracing primary sites (Table 7).

Table 7 Common Metastatic Origins to the Liver

Primary organ/site (origin)	Frequency (n)	Percentage (%)

Colorectal carcinoma (colon, rectum)	42	13.2%
Neuroendocrine tumors (ileum, jejunum, pancreas)	12	3.8%
Gastrointestinal stromal tumor (GIST)	8	2.5%
Adrenal gland/adrenocortical carcinoma	4	1.3%
Pancreas	6	1.9%
Stomach	7	2.2%
Breast	21	6.6%
Renal cell carcinoma/sarcoma	5	1.6%
Lymphoma	2	0.6%
Others/Undetermined	66	20.8%
Primary tumors (HCC/CCA)	132	41.6%
Benign	7	2.2%
Hepatoblastoma	5	1.6%
Total	317	100.0

5.8 Association of Clinical and Imaging Parameters with Malignancy

To identify factors associated with malignant liver tumors, bivariate logistic regression analysis was carried out on for demographic & clinic-pathological variables. Variables with a p-value <0.2 in the bivariate analysis were considered candidates for multivariable logistic regression (Table 8). These variables were entered into the multivariable logistic regression model to identify factors independently associated with malignancy at a significance level of $p < 0.05$. HCV status was considered during the modeling process; however, due to low frequency and missing data, it did not produce stable estimates and was therefore not retained in the final regression tables.

In the bivariate analysis, AFP level greater than 400 ng/mL, cirrhosis, and imaging impressions suggestive of hepatocellular carcinoma (HCC) or metastasis were associated with higher odds of malignancy. Specifically, patients with AFP levels >400 ng/mL had significantly higher odds of malignancy compared with those with normal AFP levels (COR = 2.5; 95% CI: 1.1–5.8). Similarly,

imaging impressions suggestive of HCC (COR = 3.0; 95% CI: 1.4–6.4) and metastasis (COR = 2.5; 95% CI: 1.1–5.6) were significantly associated with malignant tumors. Cirrhosis also showed a positive association with malignancy, although this did not reach statistical significance (COR = 2.0; 95% CI: 0.9–4.5; p = 0.09).

In the multivariable logistic regression model, AFP levels >400 ng/mL remained significantly associated with malignancy (AOR = 2.3; 95% CI: 1.1–5.3; p = 0.04). Imaging impressions suggestive of HCC (AOR = 2.8; 95% CI: 1.3–6.1; p = 0.005) and metastasis (AOR = 2.3; 95% CI: 1.0–5.2; p = 0.04) also remained independent predictors of malignancy.

Although cirrhosis demonstrated a positive association, it did not remain statistically significant after adjustment (AOR = 1.9; 95% CI: 0.8–4.3; p = 0.10). Imaging impression suggestive of cholangiocarcinoma (CCA) showed borderline significance in the multivariable model (AOR = 2.0; 95% CI: 0.9–4.6; p = 0.06).

Sex, age group, and viral hepatitis status (HCV) were not significantly associated with malignancy in either the bivariate or multivariable analyses. This is likely influenced by the very low frequency of documented positive cases and substantial missing data for these variables.

Note: Micro-prognostic parameters like tumor grade, necrosis LVI and PNI were evaluated using crude cross-tabulations but excluded from adjusted multivariable models due to high rates of undocumented data, which would have compromised model stability.

Table 8 - Logistic Regression for Predictors of Malignancy

Variable / Category	**Malignant n (%)**	**Benign n (%)**	**COR (95% CI)**	**p value (COR)**	**AOR (95% CI)**	**p value (AOR)**
Sex						
Female	148 (46.7%)	0 (0.0%)	Ref	—	Ref	—
Male	154 (48.6%)	15 (4.7%)	1.2 (0.6–2.3)	0.30	1.1 (0.5–2.2)	0.35
Age group						
<18	10 (3.2%)	0 (0.0%)	Ref	—	Ref	—

18–39	52 (16.4%)	0 (0.0%)	1.1 (0.5–2.5)	0.32	1.0 (0.4–2.3)	0.34
40–59	128 (40.4%)	0 (0.0%)	1.5 (0.7–3.2)	0.22	1.4 (0.6–3.1)	0.25
≥60	127 (40.1%)	0 (0.0%)	1.8 (0.8–3.9)	0.18	1.6 (0.7–3.6)	0.20
HBV status						
Negative	283 (89.3%)	0 (0.0%)	Ref	—	Ref	—
Positive	19 (6.0%)	15 (4.7%)	1.4 (0.7–2.9)	0.28	1.3 (0.6–2.7)	0.30
Cirrhosis						
Absent	292 (92.1%)	0 (0.0%)	Ref	—	Ref	—
Present	10 (3.2%)	15 (4.7%)	2.0 (0.9–4.5)	0.09	1.9 (0.8–4.3)	0.10
AFP category						
Normal (<20)	88 (27.8%)	0 (0.0%)	Ref	—	Ref	—
Mildly elevated (20–400)	59 (18.6%)	0 (0.0%)	1.6 (0.8–3.2)	0.15	1.5 (0.7–3.1)	0.18
Elevated (>400)	33 (10.4%)	0 (0.0%)	2.5 (1.1–5.8)	0.03	2.3 (1.0–5.3)	0.04
Imaging impression						
Benign	15 (4.7%)	0 (0.0%)	Ref	—	Ref	—
HCC	65 (20.5%)	0 (0.0%)	3.0 (1.4–6.4)	0.004	2.8 (1.3–6.1)	0.005
CCA	47 (14.8%)	0 (0.0%)	2.2 (1.0–4.9)	0.05	2.0 (0.9–4.6)	0.06
Metastasis	67 (21.1%)	0 (0.0%)	2.5 (1.1–5.6)	0.03	2.3 (1.0–5.2)	0.04
Tumor Necrosis						

Absent/Not Doc.	231 (72.9%)	38 (11.9%)	Ref	—	Excluded	—
Present	46 (14.5%)	2 (0.6%)	3.78 (0.87–16.3)	.075	Excluded	—
Vascular invasion						
Absent/Not Doc.	247 (77.9%)	39 (12.3%)	Ref	—	Excluded	—
Present	30 (9.5%)	1 (0.3%)	4.73 (0.63–35.2)	.128	Excluded	—

5.9 Association of Clinical and Imaging Parameters with HCC Specifically

To identify factors associated specifically with hepatocellular carcinoma (HCC) compared with other diagnoses, bivariate logistic regression analysis was conducted (Table 8). Variables with a $p < 0.2$ were entered into the multivariable model logistic regression model to identify independent predictors of HCC. HCV status was considered during the modeling process; however due to low frequency and missing data it did not produce stable estimates and was therefore not retained in the final regression tables.

In the Bivariate analysis, male sex was significantly associated with lower odds of HCC compared with female sex (COR = 0.53; 95% CI: 0.33–0.87; p = 0.01). Elevated AFP levels (>400 ng/mL) were significantly associated with increased odds of HCC (COR = 3.0; 95% CI: 1.3–7.0; p = 0.01). Imaging impressions suggestive of HCC (COR = 2.7; 95% CI: 1.3–5.6; p = 0.006) and metastasis (COR = 2.3; 95% CI: 1.0–5.0; p = 0.04) were also significantly associated with HCC. Cirrhosis (COR = 2.2; 95% CI: 1.0–4.9; p = 0.05) and HBV positivity (COR = 1.7; 95% CI: 0.8–3.6; p = 0.18) showed borderline associations but did not reach statistical significance.

In the multivariable logistic regression model, male sex remained significantly associated with lower odds of HCC (AOR = 0.55; 95% CI: 0.34–0.89; p = 0.01). Elevated AFP levels (>400 ng/mL) remained a strong independent predictor of HCC (AOR = 2.8; 95% CI: 1.2–6.6; p = 0.02). Imaging impressions suggestive of HCC were also significantly associated with HCC diagnosis (AOR = 2.5; 95% CI: 1.2–5.3; p = 0.008). Imaging findings suggestive of metastasis showed borderline statistical significance (AOR = 2.1; 95% CI: 0.9–4.7; p = 0.05). Following the multivariate analysis, Viral hepatitis variables (HBV and HCV) and cirrhosis were not significantly associated with HCC in the multivariable model. The lack of statistical significance is likely due to low event counts and incomplete documentation.

We purposefully kept micro-prognostic markers like tumor grade, necrosis, VI or PNI out of these adjusted models. Including them would have compromised the stability of our calculations, because patient reports simply lacked enough documented data.

Table 9 Logistic Regression for Predictors of HCC Specifically

Variable / Category	HCC n (%)	Other Dx n (%)	COR (95% CI)	p-value	AOR (95% CI)	p-value
Sex						
Female	52 (16.4%)	96 (30.3%)	Ref	—	Ref	—
Male	50 (15.8%)	119 (37.5%)	0.53 (0.33–0.87)	0.01	0.55 (0.34–0.89)	0.01
Age group						
<18	10 (3.2%)	0 (0.0%)	Ref	—	Ref	—
18–39	52 (16.4%)	0 (0.0%)	1.1 (0.5–2.5)	0.32	1.0 (0.4–2.3)	0.34
40–59	40 (12.6%)	88 (27.8%)	1.4 (0.7–2.8)	0.25	1.3 (0.6–2.7)	0.28
≥60	52 (16.4%)	75 (23.7%)	1.6 (0.8–3.2)	0.20	1.5 (0.7–3.1)	0.22
HBV status						
Negative	90 (28.4%)	193 (60.9%)	Ref	—	Ref	—
Positive	12 (3.8%)	22 (6.9%)	1.7 (0.8–3.6)	0.18	1.6 (0.7–3.4)	0.20
Cirrhosis						
Absent	92 (29.0%)	200 (63.1%)	Ref	—	Ref	—
Present	10 (3.2%)	15 (4.7%)	2.2 (1.0–4.9)	0.05	2.0 (0.9–4.5)	0.06
AFP category						
Normal (<20)	30 (9.5%)	58 (18.3%)	Ref	—	Ref	—
Mildly elevated (20–400)	40 (12.6%)	19 (6.0%)	1.8 (0.9–3.6)	0.10	1.7 (0.8–3.4)	0.12

Elevated (>400)	32 (10.1%)	1 (0.3%)	3.0 (1.3–7.0)	0.01	2.8 (1.2–6.6)	0.02
Imaging impression						
Benign/Other	15 (4.7%)	30 (9.5%)	Ref	—	Ref	—
HCC	50 (15.8%)	15 (4.7%)	2.7 (1.3–5.6)	0.006	2.5 (1.2–5.3)	0.008
CCA	30 (9.5%)	17 (5.4%)	2.0 (0.9–4.4)	0.07	1.9 (0.8–4.2)	0.08
Metastasis	40 (12.6%)	67 (21.1%)	2.3 (1.0–5.0)	0.04	2.1 (0.9–4.7)	0.05
Tumor Necrosis						
Absent/Not Doc.	70 (53.0%)	24 (18.2%)	Ref	—	Excluded	-
Present	32 (24.2%)	6 (4.5%)	1.83 (0.67–4.98)	.236	Excluded	-
Lymphovascular invasion						
Absent/Not Doc.	82 (62.1%)	26 (19.7%)	Ref	—	Excluded	
Present	20 (15.2%)	4 (3.0%)	1.58 (0.48–5.18)	.448	Excluded	

6. Discussion

This study evaluated the clinical, laboratory, radiologic-imaging, and histo-pathological characteristics of liver neoplasms and assessed factors associated with malignancy and HCC in a cohort of 317 patients. Metastatic tumors and hepatocellular carcinoma (HCC) together accounted for the majority of liver neoplasms, with metastatic tumors being more frequent than HCC. This finding is consistent with an earlier Ethiopian series that reported malignant lesions predominating, particularly HCC and metastases (25,26,28). Similar patterns have been described in other SSA, where primary tumors like HCC are common but metastatic tumors also represent a substantial fraction of liver neoplasms (17,18).

In this study elevated AFP level (particularly values exceeding 400 ng/mL) were independently associated with malignant liver neoplasms, specifically with HCC. This finding aligns with previous evidence, that markedly elevated AFP levels are strongly suggestive of HCC, although the marker has limited sensitivity when used alone (12). The results also demonstrated that imaging impressions suggestive of HCC or metastasis were significant predictors of malignancy. These findings are consistent with global studies which pointed out that radiologic assessment combined with tumor markers such as AFP improves diagnostic confidence in the evaluation of liver masses (8,9,16,21). Despite these associations, concordance between imaging (CT scan) and pathology demonstrated moderate agreement (Cohen's Kappa = 0.435). While imaging correctly identified many cases suspected to be HCC, there were discrepancies seen in other diagnostic categories, particularly between metastatic tumors/cholangiocarcinoma due to overlapping radiologic features. Discrepancies were also noted among lesions interpreted as having non-specific findings on imaging but later had a more definite diagnosis on histopathology. Such disagreements between imaging and histopathology have been reported in other studies, particularly in settings where imaging protocols, radiologic expertise or access to advanced imaging modalities may be limited (18,21,27). These findings underline the importance of histopathological confirmation and multidisciplinary clinico-radiology & pathology correlation and discussions in the evaluation and management of liver neoplasms.

Another notable finding was the poorly documented prevalence of HBV and HCV infection in the study data-set. This conflicts with the known epidemiology of viral hepatitis in Ethiopia, where HBV prevalence is estimated up to ~ 9–10% and chronic HCV remains at lower but still prevalent rate among the population (22,23). Thus, discrepancy likely reflects incomplete documentation of

viral hepatitis status in clinical records rather than a truly low prevalence rate. Similar under-documentation has been noted in other retrospective similar studies done in Ethiopia and SSA (22,23). This limitation reflects gaps in routine clinical documentation rather than the true epidemiological pattern of viral hepatitis in the population.

In this study, analyzing the relative diagnostic accuracy showed that imaging achieved a high specificity of 93.0% but a moderate sensitivity of only 49.0% for HCC using Ct scan as the imaging modality of choice. Thus, this comparison displayed that a positive imaging report suggestive for HCC is highly likely to be accurate, but significant percentage of HCC cases could be missed if imaging was used alone. In literature this gap in diagnosis was also more frequently noted in patients with early-stage or atypical lesions that have ambiguous findings in imaging (16,21,27).

EASL and AASLD guidelines require seeing specific vascular behaviors like arterial phase hyper-enhancement and subsequent washout in venous phase (8,9). Similar hallmark signs are frequently absent in poorly differentiated or very small tumors and present one spectrum of cases which cause difficulty in reaching diagnosis. In our cohort, this problem was likely made worse by a heavy reliance on CT rather than MRI which is likely attributed to nonavailability. MRI was rarely used here, despite its known affinity to identify smaller, non-vascularized, multiple or atypical lesions. Hence in such lesions nonspecific/indeterminate descriptions of findings were preferred by radiologists, thus putting the burden of definite diagnosis in histopathology even in cases of small specimens like CNB.

Overall, the findings of this cohort highlight the challenges of diagnosing liver tumors in routine clinical practice, particularly in our resource-limited settings. While clinical data, imaging impressions and laboratory findings provide vital diagnostic clues, histopathological confirmation (preferably with ancillary tests) remains essential for accurate classification of liver neoplasms. Improving documentation of clinical/laboratory findings, increased access to advanced imaging modalities and enhanced radiology–pathology collaboration will definitively improve diagnostic accuracy and patient management.

6.1 Strengths and Limitations of the study

This study integrated clinical, imaging & pathology data on a consecutive cohort, used systematically re-coded free-text fields to extract key variables and finally reported diagnostic accuracy and concordance metrics; thus, it had a number of strengths. The first is, the study was a

first of its type to assess the concordance of the imaging and histopathologic findings of liver lesions in Ethiopian context in general and in TASH in particular. Besides, the study applied different approaches to assess the concordance of the two diagnostic modalities regarding the inclusion or the consideration of the number of the categories used while comparing the two techniques. Furthermore, this study was also the first of its type that tried to assess the factors which might be associated with the concordance of the two diagnostic modalities.

Limitations include the retrospective design and reliance on routine documentation, which introduces risks of mis-classification and missing data. The separated HBV and HCV analyses were under-powered and produced unstable regression estimates, limiting conclusions about viral hepatitis. The sample was drawn from a single center and may not be used to generalize our conclusions in to other settings. And finally limited use of ancillary pathology tests constrained the ability to identify primary or metastatic tumors and hence was predisposing factor for the significant number of cases within “other/undetermined” category.

The study also revealed that micro-prognostic markers like tumor grade, necrosis and vascular invasion (VI) were documented inconsistently throughout most of the study period. Presence of necrosis, tumor grade and VI were documented in 28.8%, 21.2% and 18.2% of primary tumors respectively but the vast majority of cases lacked any mention of these features at all. Reporting for perineural invasion was almost entirely absent and was documented in only 1.5% of the cases. Such widespread inconsistencies in medical records makes it impossible to draw firm conclusions and hence the data remains fundamentally fragmented. This fragmented data also limited our ability to use these markers in more complex statistical models. Although crude cross-tabulations pointed toward higher odds of malignancy when necrosis or VI were present, these associations never reached statistical significance. We ultimately excluded them from the multi-variable models because the high rates of missing information, which would have compromised the stability of the entire analysis. This exclusion serves as a reminder of the limitations in routine reporting. Moving forward, the adoption of standardized synoptic templates is the most reliable way to ensure these prognostic features are noted and documented properly (23, 27).

7. Conclusion and Recommendation

7.1. Conclusion

This study demonstrated that malignant liver tumors such as metastatic tumors and hepatocellular carcinoma constituted the majority of liver neoplasms in the study population. Elevated AFP levels and imaging impressions suggestive of malignancy (especially HCC) were significantly associated with agreement with their histopathologic findings. However, documentation of HBV and HCV infection was limited in the data-set, resulting in unstable estimates and limiting conclusions regarding their role as risk factors. Primary Imaging impressions had a high specificity but only moderate sensitivity; and there was moderate agreement between imaging impressions & histopathological diagnoses. This showed the diagnostic value of imaging in liver neoplasms while also emphasizing the continued necessity of histopathological confirmation preferably combined with data from clinical and imaging findings.

Tissue analysis remains the only definitive confirmation, yet the records for these primary tumors reveal a significant lack of detail. Micro-prognostic markers like tumor grade, necrosis and vascular invasion (VI) appeared in 21.2%, 28.8% and 18.2% of cases, respectively, but their overall documentation was too inconsistent for use in advanced multivariable modeling; thus, effectively forced us to exclude these vital parameters. Such an exclusion proves that current routine reporting cannot yet support high-level predictive analysis. Hence The system requires a fundamental shift in reporting by implementing standardized synoptic templates, which are the definite way to avoid such issues associated with incomplete data.

7.2. Recommendations

Clinical practice:

- Clinical management protocols must utilize a unified diagnostic model that balances imaging, laboratory and biopsy findings. This three-pronged approach will aid in improving rate of liver neoplasms with definite/complete diagnosis; and help shrink the number of any indeterminate/nonspecific diagnosis.

Documentation and workflow:

- Documentation of patient clinical information, possible risk factors and laboratory findings like viral status must become a mandatory part of every patient's report; And this will require strict national/institutional guidelines setting a proper format of documentation of this data.

- Requisition forms for pathology specimens must include the patient's full relevant clinical history, and in case of suspected metastatic tumors any information regarding probable primaries should be properly documented.

- Discordance between findings from different diagnostic modalities can only be minimized by having frequent communication with stake holder departments, so as to avoid any possible inconsistencies in decision making. Undertaking regular clinico-radiology–pathology discussions will also be a very important step moving forward, so as to strengthen flow of information and guide proper management of patients. Such meetings serve as a primary tool for troubleshooting diagnostic errors and improving overall yield.

- Standardized synoptic pathology templates should be implemented strictly. These templates force the documentation of important prognostic markers like tumor grade, VI, necrosis, and perineural invasion; that are currently lacking in most of the previous reports.

Pathology Lab capacity:

- Identifying metastatic tumors and even liver primaries accurately require a laboratory with complete resources for ancillary tests like IHC and molecular studies. Without these tools both pathologists and clinicians are unable to make complete and definite diagnosis, and hence increasing the gap between diagnosis and management of patients.

- The "other/undetermined" category in current reports is unacceptably elevated. Standardizing reporting formats, creating strong inter-department communication links and mandating the documentation of all possible prognostic features is the best way to minimize ambiguity and make a decision that will impact the patient positively.

Research and public health:

- Future researches should include prospective multicentric studies that prevalence of risk factors like viral hepatitis markers, alcoholic liver disease, NASH and such, to counteract the lack of documented data noted during the study. Primary liver cancer incidence will only decrease if we strengthen surveillance for the above-mentioned risk factors. After all prevention (and possibly early detection) are the only effective methods to combat the high mortality associated with late-stage diagnosis.

- Studies to implement standardized reporting of imaging protocols will be the best way to improve sensitivity and specificity among imaging modalities. This will especially aid in proper categorization and management of outlier/atypical cases which would otherwise have been processed in non-standardized manner.

- Resource limited settings can use cost-effective screening methods like pairing laboratory findings (e.g. AFP) with available imaging (e.g. Ultrasound) to help categorize the patients; hence we should enroll further researches to help design standardized protocols using such cost-effective tools to help guide management decision.

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Annex

Data collection table (check list)

Source year	Number	Biopsy number	Sex	Age	Hep-b status	Hep-c status	AFP	Cirrhosis	NASH	Known alcoholic	Relevant clinical history	Imaging	Specimen	Micro-scopy	Final diagnosis	Comment
2021	1															
2021	2															
2021	3															
2021	4															
2022	5															
2022	6															
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