Original Article

Frequency of Hepatocellular Carcinoma in Patients with Non-Cirrhotic Liver: A Cross-Sectional Study of Liver Findings on Triphasic CT Scan

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ABSTRACT

Background: Hepatocellular carcinoma (HCC) can arise in both cirrhotic and non-cirrhotic livers. In non-cirrhotic liver, diagnosis may be challenging because non-invasive imaging criteria have limitations, and histopathological confirmation may be required when guideline-based imaging criteria are not applicable. Triphasic CT provides multiphasic assessment of hepatic lesions and background liver morphology. Local data regarding HCC in patients without radiological cirrhosis are limited. This study aimed to determine the frequency of non-cirrhotic liver among patients with HCC evaluated by triphasic CT and compare selected clinical and radiological characteristics between cirrhotic and non-cirrhotic groups.

Methodology: This cross-sectional study included 116 adults aged 18–70 years referred for triphasic CT evaluation of suspicious hepatic nodule(s). Patients were consecutively enrolled during the study period September 1st 2025 to March 1st 2026, from the referral population of Chughtai Lab, Lahore. No histopathological confirmation was reported in the submitted study dataset. Cirrhosis was classified radiologically using periportal space and caudate-to-right-lobe ratio measurements. Demographic, clinical, and CT variables were recorded and analyzed using descriptive statistics and Pearson chi-square tests.

Results: Of 116 patients with HCC, 37 (31.9%) were classified as having non-cirrhotic and 79 (68.1%) as having cirrhotic liver morphology on triphasic CT. The mean age was 52.27 ± 10.50 years, and 86 (74.1%) patients were male. HCV infection was present in 52 (44.8%), HBV infection in 29 (25.0%), diabetes mellitus in 48 (41.4%), hypertension in 37 (31.9%), and smoking in 45 (38.8%). Mean lesion size was 4.94 ± 2.56 cm; 51 (44.0%) had lesions >5 cm and 82 (70.7%) had right-lobe involvement. No statistically significant associations were observed between radiological cirrhosis status and the assessed clinical or radiological variables (all p>0.05). Statistically significant differences in periportal space and caudate-to-right-lobe ratio measurements reflected the predefined radiological classification criteria for cirrhosis.

Conclusion: Consideration of HCC in patients without radiological cirrhosis and careful multiphasic CT assessment is important, particularly when conventional imaging criteria for HCC diagnosis may not be applicable. Further studies with histopathological correlation and broader populations are warranted.

Keywords: Hepatocellular carcinoma; Computed tomography; Cirrhotic; Noncirrhotic

INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common primary malignant tumour of the liver and accounts for most primary liver cancers.[1,2] Although HCC frequently different etiological and imaging characteristics from HCC develops in cirrhotic liver, a clinically important proportion arises in non-cirrhotic liver.[3,4] Non-cirrhotic HCC may have arising in cirrhosis, and diagnosis can be challenging because the background liver does not provide the same pre-test probability of HCC as cirrhosis.[4,5] Triphasic contrast-enhanced computed tomography (CT) is widely used for characterization of focal liver lesions and assessment of hepatic morphology. Arterial phase hyperenhancement with subsequent washout on portal venous or delayed phases is an important imaging pattern in HCC.[6] However, the diagnostic specificity of these imaging hallmarks is lower in some non-cirrhotic settings because benign and malignant hypervascular lesions may mimic HCC.[6,7] Current guidance therefore emphasizes careful application of non-invasive imaging criteria and, when those criteria are not applicable in a non-cirrhotic liver, pathological confirmation is mandatory.[8]

Evidence from non-cirrhotic HCC cohorts demonstrates substantial variation in tumour size, clinical presentation, underlying etiology, and imaging appearance.[4,5] Recent evidence also indicates that

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imaging-based diagnostic performance can vary according to the underlying liver disease and the population being evaluated.[10,11] These differences make it important to distinguish findings in non-cirrhotic HCC from observations derived from cirrhotic or etiology-specific cohorts. Published Pakistani data on the proportion of HCC patients without radiological cirrhosis are limited, and the available local evidence is based on selected clinical populations. The local knowledge gap is therefore the limited characterization of the frequency of radiologically non-cirrhotic liver among HCC patients undergoing triphasic CT and the associated clinical and CT findings in a referral-based Pakistani setting. This study aimed to determine the frequency of non-cirrhotic liver among patients diagnosed with HCC and to compare selected demographic, clinical, and radiological characteristics between non-cirrhotic and cirrhotic groups.

METHODOLOGY

This analytical cross-sectional study was conducted in the Department of Diagnostic Radiology at Chughtai Lab, Lahore, Pakistan from September 1st 2025 to March 1st 2026. Patients were referred to the study centre from its clinical/referral network for evaluation of a suspicious hepatic lesion identified on ultrasound or clinical assessment. All eligible patients presenting during the defined study period were intended to be enrolled consecutively. The study protocol received approval from the Institutional Review Board (IRB) of Chughtai Institute of Pathology Lahore [Approval number CIP/IRB/1357, dated 12-08-2025], and written informed consent was obtained from participants voluntarily with the right to withdraw from the study at any time.

Consecutive non-probability sampling was used, meaning that all eligible patients meeting the inclusion criteria during the specified study period were enrolled sequentially until the target sample was reached. The sample size was calculated using the single-proportion formula, assuming a 95% confidence level, an absolute precision of 8.5%, and an expected frequency of hepatocellular carcinoma occurring in a non-cirrhotic liver of 14% based on a Pakistani hospital-based study by Butt et al.,[9] The estimated minimum sample size was 65 participants. A total of 116 eligible participants were ultimately included in the study, thereby exceeding the minimum required sample size and providing greater precision than the prespecified margin of error.

Adults aged 18–70 years of either sex who underwent triphasic CT for evaluation of a suspicious hepatic nodule were eligible. A suspicious hepatic nodule was defined operationally as a space-occupying lesion within the liver measuring >1 cm on abdominal ultrasound. Patients with marked transaminase elevation (AST or ALT >200 IU/L), radiological evidence of metastases, or renal impairment (serum creatinine >1.3 mg/dL) were excluded. Study parameters recorded in the data-collection tool included age, sex, BMI, HBV infection, HCV infection, diabetes mellitus, hypertension, smoking status, family history of HCC, lesion size, lesion number, lesion location, periportal space (PPS), and caudate-to-right-lobe (CRL) ratio. BMI was calculated as weight in kilograms divided by height in metres squared and was included as a clinical/metabolic characteristic for comparison between the two liver-morphology groups.

Renal function was assessed before intravenous contrast administration. Triphasic CT of the abdomen was performed on a 160-slice Aquilion Lightning Ultra Helical CT scanner (Canon Inc.). Non-ionic, low osmolar Contrast iobitridol (Xenetix) in 350 mg I/1ml, concentration was used at a flow rate of 3.5 ml/sec. Weight adjusted dosage of 1ml/kg was given to each patient. The examination included a non-contrast phase, arterial phase at approximately 35 seconds after contrast injection, portal venous phase at 70 seconds, and delayed equilibrium phase at 180 seconds. Suspicious lesion was labelled HCC when it demonstrated the predefined multiphasic CT appearance used by the reporting radiologist, as in arterial phase hyperenhancement and portal venous and/or delayed phase washout, with other characteristic findings recorded where present.

Lesion location, number and maximum diameter were recorded. Background liver morphology was assessed on CT using periportal space (PPS) and the caudate-to-right-lobe (CRL) ratio. Periportal space (PPS) was measured in millimetres on axial CT images at the level of the porta hepatis, as the shortest distance between the anterior wall of the right portal vein and the adjacent hepatic parenchyma/posterior margin of the left hepatic lobe.[13] CRL was calculated as the maximal transverse diameter of the caudate lobe divided by the maximal transverse diameter of the right hepatic lobe on the same examination.[12] A PPS >10 mm and/or a CRL >0.73 was considered indicative of cirrhotic morphology on CT.[13,14] Livers demonstrating neither criterion (PPS ≤10 mm and CRL ≤0.73) were classified as having non-cirrhotic morphology. Participants meeting only one of the two criteria were classified as cirrhotic under the stated 'and/or' rule. These CT-based classifications were then used to form the cirrhotic and non-cirrhotic groups for statistical comparison. The radiological measurements were performed by the reporting radiologist using the same predefined criteria for all participants; interobserver reliability was not assessed.

Data was entered and analyzed using IBM SPSS Statistics version 27. Continuous variables (age, BMI, lesion

size, lesion number, PPS, and CRL) were summarized as mean ± standard deviation and compared using independent sample T-test. Categorical variables (sex, HBV, HCV, diabetes, hypertension, smoking, family history of HCC, lesion size category, lesion location, lesion number, and radiological cirrhosis status) were summarized as frequencies and percentages compared using chi-square test. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 116 patients were included in the study, of whom 79 (68.1%) had cirrhotic liver disease and 37 (31.9%) had non-cirrhotic liver. The mean age of the overall study population was 52.27 ± 10.50 years, with comparable mean ages in the non-cirrhotic and cirrhotic groups (52.76 ± 11.29 and 52.04 ± 10.17 years, respectively). The overall mean body mass index was 26.54 ± 4.17 kg/m². Mean lesion size was 4.94 ± 2.56 cm, while the mean number of lesions was 1.66 ± 0.82. The mean peri-portal space and caudate-to-right lobe ratio were higher among patients with cirrhosis than among those without cirrhosis (10.37 ± 2.78 vs. 7.78 ± 1.93 mm and 0.70 ± 0.14 vs. 0.58 ± 0.08, respectively).

Males constituted the majority of the study population (74.1%). The proportion of males was higher in the cirrhotic group than in the non-cirrhotic group (79.7% vs. 62.2%), although the difference did not reach statistical significance (p = 0.074). HBV infection was present in 25.0% of participants and was more frequent among patients with cirrhosis than among those without cirrhosis (29.1% vs. 16.2%; p = 0.206). HCV infection was observed in 44.8% of the overall cohort, with no significant difference between the cirrhotic and non-cirrhotic groups (46.8% vs. 40.5%; p = 0.663). Diabetes mellitus was present in 41.4% of patients and hypertension in 31.9%. Neither condition differed significantly according to cirrhosis status (p = 0.630 and p = 1.000, respectively). Similarly, smoking was reported by 38.8% of participants and a family history of hepatocellular carcinoma by 17.2%, with no significant differences between the two groups (p = 0.952 and p = 0.949, respectively). The baseline demographic and clinical characteristics of the study participants according to liver cirrhosis status are summarized in Table 1. Categorical-variable p-values are those reported in the original analysis. Continuous-variable p-values of peri-portal space (PPS) and Caudate-to-right lobe ratio (CRL ratio) were statistically significant (p value < 0.05).

Triphasic CT findings showed that, overall, 44.0% of patients had lesions larger than 5 cm, while 30.2% had lesions measuring 3–5 cm and 25.9% had lesions smaller than 3 cm. Lesions larger than 5 cm were relatively more common in the cirrhotic group than in the non-cirrhotic group (46.8% vs. 37.8%); however, the overall distribution of lesion size did not differ significantly between the groups (p = 0.647). The right hepatic lobe was the most frequent lesion location, accounting for 70.7% of cases, followed by the left lobe in 19.0% and involvement of both lobes in 10.3%. Lesion location was comparable between cirrhotic and non-cirrhotic patients (p = 0.859). A single lesion was identified in 54.3% of the study population, whereas 45.7% had multiple lesions. The frequency of single and multiple lesions was also similar between the two groups (p = 0.871). The distribution of triphasic CT findings according to liver cirrhosis status is presented in Table 2.

Table 1: Baseline characteristics of the study participants according to liver cirrhosis status

Characteristics	Overall (n = 116)	Non-cirrhotic (n = 37)	Cirrhotic (n = 79)	p-value
Continuous variables, mean ± SD				
Age, years	52.27 ± 10.50	52.76 ± 11.29	52.04 ± 10.17	0.733
Body mass index, kg/m²	26.54 ± 4.17	26.09 ± 4.09	26.75 ± 4.21	0.433
Lesion size, cm	4.94 ± 2.56	4.76 ± 2.67	5.02 ± 2.52	0.609
Number of lesions	1.66 ± 0.82	1.62 ± 0.80	1.67 ± 0.84	0.766
Periportal space, mm	9.55 ± 2.81	7.78 ± 1.93	10.37 ± 2.78	<0.001
Caudate-to-right lobe ratio	0.66 ± 0.13	0.58 ± 0.08	0.70 ± 0.14	<0.001
Categorical variables, n (%)				
Male gender	86 (74.1)	23 (62.2)	63 (79.7)	0.074
HBV infection	29 (25.0)	6 (16.2)	23 (29.1)	0.206
HCV infection	52 (44.8)	15 (40.5)	37 (46.8)	0.663
Diabetes mellitus	48 (41.4)	17 (45.9)	31 (39.2)	0.630
Hypertension	37 (31.9)	12 (32.4)	25 (31.6)	1.000
Smoking status	45 (38.8)	15 (40.5)	30 (38.0)	0.952
Family history of HCC	20 (17.2)	7 (18.9)	13 (16.5)	0.949

Abbreviations: HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; SD, standard deviation.

Table 2: Triphasic CT findings according to liver cirrhosis status

CT finding	Overall (n = 116), n (%)	Non-cirrhotic (n = 37), n (%)	Cirrhotic (n = 79), n (%)	p-value*
Lesion size				0.647
<3 cm	30 (25.9)	11 (29.7)	19 (24.1)	
3–5 cm	35 (30.2)	12 (32.4)	23 (29.1)	
>5 cm	51 (44.0)	14 (37.8)	37 (46.8)	
Lesion location				0.859
Right lobe	82 (70.7)	27 (73.0)	55 (69.6)	
Left lobe	22 (19.0)	7 (18.9)	15 (19.0)	
Both lobes	12 (10.3)	3 (8.1)	9 (11.4)	
Number of lesions				0.871
Single (n = 1)	63 (54.3)	21 (56.8)	42 (53.2)	
Multiple (≥2)	53 (45.7)	16 (43.2)	37 (46.8)	

*The p-values were calculated using the Pearson chi-square test. A p-value <0.05 was considered statistically significant.

DISCUSSION

This cross-sectional study found that 37 of 116 patients (31.9%) with HCC were classified as having non-cirrhotic liver on the predefined CT criteria. The finding demonstrates that a substantial proportion of patients evaluated for HCC in this referral-based cohort did not show radiological evidence of cirrhosis. However, the estimate should not be interpreted as a population prevalence because the study was conducted in a single referral-based diagnostic setting and used a selected HCC study population. Direct comparison with previous studies is challenging because the definitions of non-cirrhotic HCC, study populations, referral pathways, etiological composition, and diagnostic confirmation differ. However, a study by Butt et al., 1998 carried out in Shaikh Zayed Postgraduate Medical Institute, Lahore consisted of a clinical HCC cohort where the investigators enrolled 76 consecutive patients with HCC admitted between September 1994 and November 1996, out of which 86% had underlying cirrhosis and 14% were non-cirrhotic.[9] The paper explicitly states that cirrhosis was determined using clinical features and ultrasound findings. It also states that only 14% had a normal ultrasound appearance of the liver.

Triphasic CT remains important for multiphasic characterization of focal liver lesions and assessment of background liver morphology. The arterial hyperenhancement and portal venous/delayed washout pattern is characteristic of HCC, but current guidance emphasizes that non-invasive imaging criteria are not universally applicable to non-cirrhotic patients. The updated EASL guidance and recent diagnostic studies underscore the need to apply imaging criteria according to the patient's risk category and to use pathological confirmation when imaging criteria are not sufficient.[8,10] Recent evidence in non-cirrhotic chronic hepatitis C also demonstrates that LI-RADS-based imaging can have high diagnostic performance in selected populations, reinforcing that diagnostic accuracy depends on the underlying clinical setting and the criteria used.[7]

In the present cohort, 51 (44.0%) patients had lesions >5 cm and 82 (70.7%) had right-lobe involvement. These are overall-cohort findings. Desai and coworkers have highlighted that non-cirrhotic HCC often presents at a more advanced stage due to the absence of structured hepatic surveillance programs in this subgroup.[4] The lack of routine screening in non-cirrhotic patients may explain the larger mean lesion size of 4.94 ± 2.56 cm observed in our cohort. These results show the necessity for increased awareness among healthcare professionals to enable timely detection and effective management of HCC in patients who do not present with underlying cirrhosis.

No statistically significant association was detected between radiological non-cirrhotic status and the prespecified demographic, clinical, or CT variables. The possible explanation can be limited statistical power in the relatively small (n = 37) non-cirrhotic subgroup to detect modest associations.

First, the cross-sectional design limits causal inference and does not establish incidence or causation. Second, the diagnosis of HCC in the submitted study was based on triphasic CT without a documented histo-pathological confirmation procedure. This is an important limitation because current guidance recommends pathological confirmation in non-cirrhotic patients when applicable non-invasive imaging criteria are not sufficient. Third, radiological classification of cirrhosis using PPS and CRL may result in misclassification because these measurements do not encompass all clinical, laboratory, and morphological features of chronic liver disease. Fourth, exclusion based on AST/ALT >200 IU/L may have introduced selection bias by excluding patients with active hepatic inflammation. Fifth, the study was conducted in a single referral-based diagnostic setting, and the referring population was not fully characterized; therefore, external validity is limited and referral/selection bias is possible. Finally, the non-cirrhotic subgroup contained only 37 patients, limiting statistical power. Future multicentre studies should use clearly defined referral populations, standardized imaging criteria, and appropriate

pathological confirmation where required by current guidelines.

CONCLUSION

In this single-centre, referral-based cross-sectional cohort of 116 patients evaluated for HCC, 37 (31.9%) had no radiological evidence of cirrhosis according to the predefined CT criteria. This finding indicates that HCC may be encountered in patients without radiological cirrhosis and supports careful multiphasic CT assessment of both the lesion and background liver.

Author Contributions

GT: Conception and design, analysis and interpretation of data, drafting the article, critical revision for important intellectual content, final approval. FA: Conception and design, analysis and interpretation of data. MMUH: Analysis and interpretation of data, proofreading. MI: Conception and design, analysis

AI Disclosure

The authors declared that no generative AI or AI-assisted technologies were used in the preparation of this manuscript

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