BANGLADESH JOURNAL OF RADIOLOGY AND IMAGING 2023; VOL. 31(2): 95-105

Diagnostic Performance of Computed Tomography Scan in Hepatocellular Carcinoma

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Abstract:

Objectives: *To assess the diagnostic performance of Computed Tomography scan in hepatocellular carcinoma.* ***Methodology:*** *This cross-sectional study was carried out at the Department of Radiology and Imaging in Dhaka Medical College Hospital, Dhaka from July 2019 to June 2021. A total of 50 patients with suspected hepatic mass of both sexes above 20 years of age referring to the Department of Radiology and Imaging, DMCH from various departments of the same hospital for triple-phase MDCT of the abdomen were included in this study.* ***Results:*** *The mean age was found 51.5±5.3 years with a range of 25 to 79 years. The male to female ratio was 4.5:1. On triple-phase MDCT diagnosis, 84% of patients had hepatocellular carcinoma, 8% had cirrhotic nodule, 6% had metastases and 2% had hepatocellular adenoma. On histopathology, 82% had hepatocellular carcinoma, 8% had cirrhotic nodule, 8% had metastases and 2% had hepatocellular adenoma. The sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of the triple-phase MDCT in the diagnosis of hepatocellular carcinoma were 97.6%, 77.8%, 94%, 95.2%, and 87.5% respectively.* ***Conclusion:*** *Hepatocellular carcinoma is a primary liver malignancy and occurs predominantly in patients with underlying chronic liver disease and cirrhosis. CT scan is a useful non-invasive imaging modality for the evaluation of hepatocellular carcinoma.*

Keywords: *Computed tomography (CT), Hepatocellular carcinoma (HCC)*

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Introduction:

Hepatocellular carcinoma (HCC) is the most common primary liver cancer and the fourth leading cause of cancer-associated mortality worldwide.[1] The global liver cancer incidence and mortality have been increasing. There were 950,000 newly-diagnosed liver cancer cases and over 800,000 deaths in 2017, which is more than twice the numbers recorded in 1990. HBV and HCV are the major causes of liver cancer.[2] Incidence is increasing for adult liver cancers and HCC in Western countries, whereas trends are decreasing in the Asian region, although still remaining high.[3] Many causes are linked to the development of HCC, the most common of which include chronic hepatitis B (HBV) and C (HCV) viral infection, long-standing alcohol consumption, and aflatoxin-B1-contaminated food. All conditions which induce cirrhosis can cause HCC, pointing to main interactions with the host micro-environment.[4]

In the past, HCC generally presented at an advanced stage with usual presentation as right-upper-quadrant pain, weight loss, and signs of decompensated liver disease is now increasingly recognized at an earlier stage as a consequence of the routine screening of patients with known cirrhosis, using ultrasonography with or without serum alpha-fetoprotein (AFP) measurements.[5] HCCs are diagnosed by invasive methods (biopsy) and non-invasive methods, including imaging (ultrasonography, CT, and MRI) and tumor marker (serum alfa-fetoprotein). Screening with ultrasound and serum á-fetoprotein level to detect HCC in patients with chronic liver disease has become common practice.

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Received: 12 Aug 2022 **Revised:** 15 Jan 2023 **Accepted:** 29 Mar 2023 **Published:** 01 July 2023

Imaging plays a notable role in hepatocellular carcinoma (HCC) surveillance, diagnosis, and treatment response assessment. Whereas HCC surveillance among at-risk patients, including those with cirrhosis, has traditionally been ultrasound-based, there are increasing data showing that this strategy is operator-dependent and has insufficient sensitivity when used alone. Triple-phase computed tomography (CT) or contrast-enhanced magnetic resonance imaging (MRI) should be performed in patients with positive surveillance tests to confirm a diagnosis of HCC and perform cancer staging, as needed.[6]

Early detection of HCC is becoming feasible due to the wide use of ultrasound for screening with high rates of ultrasound detection of small hepatic nodules. Currently ultrasonography (USG) is the recommended screening modality for periodic surveillance for HCC in at-risk patients.[7] Ultrasound has many advantages including being readily available, inexpensive, and non-invasive with a favourable safety profile.[8] A systematic review of test modalities for HCC surveillance found that ultrasound has a high sensitivity of 94% to detect HCC at any stage; however, its sensitivity to detect early-stage HCC is significantly lower at only 63%.[8] Furthermore, the wide variation in ultrasound sensitivity between studies highlights the operator-dependent nature of the examination. High ultrasound quality relies heavily on the experience of the individual performing the ultrasound examination as well as the radiologist interpreting the examination.[9] Given the limitations of ultrasound, there has been increasing interest in alternative imaging modalities, such as computed tomography (CT) or magnetic resonance imaging (MRI). CT scan has been shown to be superior in sensitivity and specificity for HCC diagnosis and staging compared to ultrasound. A small randomized trial comparing ultrasound to CT scan and result found that CT scan has better diagnostic value in the assessment of hepatocellular carcinoma.[10]

Multi-detector computed tomography (MDCT) is an advanced, improved form of computed tomography technology that permits CT scanners to acquire multiple slices or sections simultaneously and greatly increase the speed of CT image acquisition. Multi-detector CT provides potential true isotropic datasets that provide the radiologist with unparalleled capabilities for detailed analysis of normal anatomy and pathology.

Triple-phase computed tomography technique in suspected HCC patients allows imaging of the entire liver in three phases from the time of administration of contrast-arterial phase, redistribution or portal venous phase, and equilibrium or hepatic venous phase. HCC derives blood flow predominantly from the hepatic artery and enhances 10-20 seconds after beginning contrast infusion during the arterial phase. Some benign lesions such as haemangioma, focal nodular hyperplasia, and hepatocellular adenoma enhance in the arterial phase. The surrounding hepatic parenchyma obtains 75–80% of its blood flow through the portal vein and shows maximum enhancement 30-40 seconds after initiating contrast during the portal venous phase. The third phase is the hepatic venous phase or the equilibrium phase acquired 60 seconds after the scan and delayed scans can be performed 10-15 minutes after scan initiation. The delayed phase gives additional information on the vascularity of the focal hepatic lesions, which may further help to clarify the nature of the lesions.

In CT scan, classic HCC shows arterial phase enhancement followed by a washout in the portal and/or delayed phase with a pseudo capsule around the nodule. The other typical imaging features include internal mosaic pattern, presence of fat, vascular invasion, and interval growth of 50% or more on serial images obtained less than six months apart.[11] On pre-contrast images, the HCC shows the variable appearance and depends on the surrounding liver parenchyma. Most of the time, HCCs appear hypodense or isodense to the liver on unenhanced images but may show hyperdense when they develop in a background of fatty liver.[7]

Several studies have compared the accuracy of CT for the diagnosis of HCC. Compared to CT, MRI has a significantly higher sensitivity (82% vs. 66%) with similar specificity (92% vs. 91%). Conversely, MRI is associated with higher cost, greater technical complexity (including longer scan time), and less consistent imaging quality (e.g., difficulty with breath-holding, large volume ascites).[12]

Therefore, this study aimed to assess the diagnostic performance of CT scan in hepatocellular carcinoma.

Methodology:

This cross-sectional study was carried out at the Department of Radiology and Imaging in Dhaka Medical College Hospital, Dhaka from July 2019 to June 2021. A total of 50 patients with suspected hepatic mass of both sexes above 20 years of age referring to the Department of Radiology and Imaging, DMCH from various departments of the same hospital for triple-phase Following Triple phase MDCT all patients underwent USG guided core liver biopsy of the same lesion in the Department of Radiology and Imaging, DMCH, and was sent for histopathological examination. Histopathology reports were collected from the Department of Pathology, DMCH within a week and compared with the triple-phase MDCT diagnosis. Statistical analyses were carried out by the Statistical Package for Social Sciences version 22.0 for Windows.

Procedure of triple-phase MDCT scanning of the liver: Triple-phase MDCT scan was performed with a 128 slice multi-detector HITACHI SCENERIA whole body scanner (4^{th} generation) with dual head automated injector. Both pre and post contrast scan was obtained with the patient in supine position using 2.5 mm collimation, 1.5 mm pitch, 120 KV, 150 mAS, 3-5 mm slice thickness with 5 mm interval. Non-contrast scans were followed by scans with contrast. Two glasses of diluted water-soluble oral contrast medium (iodinated contrast medium, iopamidol, 15 ml in one glass) were given to drink, and after 30 minutes, the patient was taken to the CT machine where another glass of contrast medium (20 ml in one glass) was given to visualize the stomach. 1mg/kg body weight of non-ionic water-soluble contrast medium (Iopamiro) 370 mg/ml strength was injected in the antecubital vein by an automated injector and post-contrast images were obtained. The arterial phase of scanning began 10 secs after the start of the bolus, the second phase (portal venous phase or redistribution phase) 25 secs after the start of the bolus, and the last phase (hepatic venous) began at 60 secs. 3-5 mm contiguous slices were obtained through the upper abdomen in a craniocaudal direction during a single breath-hold.

Image interpretation: On pre-contrast images, the size of liver along with the size, number, and location of the lesion was seen. Density of the lesion was noticed in pre-contrast images (hypo/iso/hyperdense relative to the surrounding liver parenchyma). On each phase of post-contrast scan, each lesion was judged to be of homogeneous or heterogeneous attenuation. On arterial and portal venous phase images, heterogeneous lesion was judged as having a predominantly ring, peripheral nodular, or mosaic pattern of enhancement. A mosaic pattern was present when the enhancement pattern was heterogeneous and did not meet the other definitions. On hepatic arterial phase images, the presence or absence of hypervascular components within the lesion was recorded. A hypervascular component was defined as an area of enhancement greater than the surrounding liver parenchyma. Each lesion was evaluated for the presence or absence of contrast material washout on the portal venous phase images. The wall of lesions was carefully observed either ill or well defined. The presence of vascular invasion and abdominal lymphadenopathy was noted if any.

Comparison with histopathology: Histopathology reports were collected from the Department of Pathology, DMCH. Then collected reports were compared with the triple-phase multi-detector computed tomography findings. Statistical analyses of the results were obtained by using window-based computer software device with Statistical Packages for Social Sciences (SPSS-22). The results were presented in tables, figures, diagrams. For the validity of study outcome, sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of triple-phase multi-detector computed tomography in the diagnosis of hepatocellular carcinoma was calculated.

Results & Observations:

Table I

Distribution of the study patients by age (N=50)

Age group (years)	Frequency	Percentage
25-30	02	04
31-40	10	20
41-50	11	22
51-60	15	30
61-70	07	14
71-79	05	10
Total	50	100
Mean ± SD (Range)	51.5±5.3	
Range (min-max)	(25-79)	

Table I shows the distribution of age group of the study patients. It was observed that majority 15 (30%) patients belonged to age 51-60 years followed by 11 (22%) had 41-50 years. The mean age was found 51.5±5.3 years with a range of 25 to 79 years.

Among the study subjects 41(82%) were male patients and 09(18%) female with a male female ratio of 4.56:1.

Table II

Distribution of the study patients by pre-contrast findings of triple- phase MDCT (N=50)

CT findings	Number of patients	Percentage
Size of liver		
Normal	13	26
Enlarged	33	66
Small & irregular	04	08
No. of focal lesion		
Single	26	52
Multiple	19	38
Diffuse	05	10
Location of lesion		
Right lobe	24	48
Left lobe	06	12
Both lobe	20	40
Size of lesion (cm)		
≤ 2 cm	21	42
>2 cm	29	58
Density of lesion		
Isodense	12	24
Hypodense	26	52
Hyperdense	02	04
Mixed density	10	20

Table II shows findings of pre-contrast scans of triple-phase MDCT of abdomen. It was observed that normal size liver was found 13(26%) cases, enlarged liver 33(66%) cases, small & irregular liver 4(8%) cases. More than half (52%) patients had single focal lesion. Almost half (48%) patients had right lobe lesion. 58% patients had lesions > 2 cm of size and 42% had ≤2cm size. Isodense lesions were found in 12(24%) casess, hypodense lesions in 26(52%) cases, hyperdense lesions in 02(4%) cases and mixed density lesions in 10(20%) cases.

Table III

Distribution of the study patients by post-contrast findings of triple-phase MDCT (N=50)

Post contrast findings	Number of patients (n)	Percentage (%)
Appearance of lesion in arterial phase		
Hyperdense	37	74
Isodense	09	18
Hypodense	04	08
Portal venous phase		
Hypodense	32	64
Isodense	15	30
Hypodense with enhancing rim	03	06
Hepatic venous phase		
Hypodense	42	84
Isodense	08	16
Hypervascular component in arterial phase		
Present	37	74
Absent	13	26
Intralesional washout in portal venous phase		
Present	42	84
Absent	08	16
Vascular invasion	18	36
Abdominal lymphadenopathy	04	08

Table III shows post-contrast findings of triple-phase MDCT in study patients. It was observed that in the arterial phase, the hyperdense lesion was found in 37(74%) cases, isodense was 09(18%) cases and hypodense was 04(8%) cases. In portal venous phase, hypodense was 32(64%) cases, isodense was 15(30%), hypodense with enhancing rim was 03(6%) cases. In the hepatic venous phase, hypodense was 42(84%) cases and isodense was 8(16%) cases. The hypervascular component in the arterial phase was found in 37(74%) cases. Intralesional contrast washout in the portal venous phase was found in 42(84%) cases. Vascular invasion was noted in 18(36%). Abdominal lymphadenopathy was seen in only 04(8%).

Results showed that in most of the cases wall of the lesions were ill defined (n-39,78%) and only in 11 cases (22%) the lesion wall were well defined.

It was also observed that heterogeneous contrast enhancement was seen in 44 cases (88%), homogeneous enhancement in 04 cases(08%) and only rim enhancement in 04 (08%) cases.

Table IV

Distribution of the study patients by triple-phase MDCT diagnosis (N=50)

Findings	Frequency	Percentage
Hepatocellular carcinoma	42	84
Cirrhotic nodule	04	08
Metastases	03	06
Hepatic adenoma	01	02
Total	50	100

Triple-phase MDCT diagnosis was patients having HCC 42 (84%), cirrhotic nodule 04 (8%), metastases 03 (6%) and hepatic adenoma 01 (2%).

Table V

Distribution of the study patients by histopathology report (N=50)

Findings	Frequency	Percentage
Hepatocellular carcinoma	41	82
Cirrhotic nodule	04	08
Metastases	04	08
Hepatic adenoma	01	02
Total	50	100

According to histopathology report, patients having HCC 41 (82%), cirrhotic nodule 04 (8%), metastases 04 (8%) and hepatic adenoma 01 (2%).

Table VI shows the distribution of CT diagnosis by histopathological diagnosis. Out of all cases 42 were diagnosed as hepatocellular carcinoma by CT and among them 40 were confirmed by histopathological evaluation. They were true positive. Two cases were diagnosed as having HCC by CT but not confirmed by histopathological findings. They were false positive. Out of 8 cases of non-HCC which were confirmed by CT, 7 were confirmed as non-HCC and 1 was HCC by histopathological findings. They were true negative and false negative respectively. The result was statistically significant ($p<0.05$).

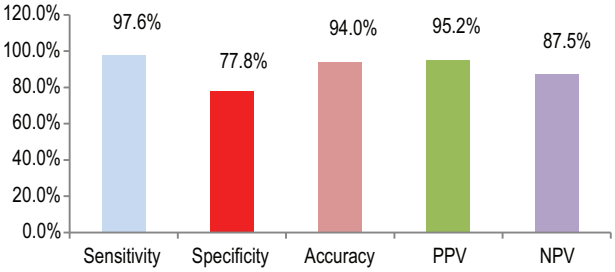

Fig.-1: *Bar diagram showing validity test of triple-phase MDCT for HCC*

Table VI

Comparison between histopathology and triple-phase MDCT diagnosis of HCC (N=50).

Triple phase MDCT diagnosis	Histopathological findings Positive	Total Negative	p-value 0.001
HCC positive	40(True positive)	02(False positive)	42
HCC negative	01(False negative)	07(True negative)	08
Total	41	09	50

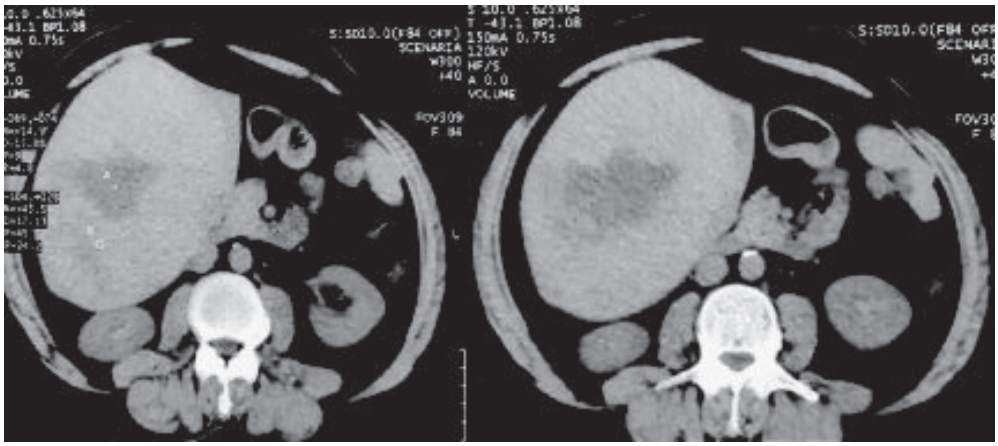

Fig.-2: *Axial non-contrast CT scan of the abdomen in a 52-year-old male with HCC showing an irregular hypo dense area in the right lobe of the liver (Case 19)*

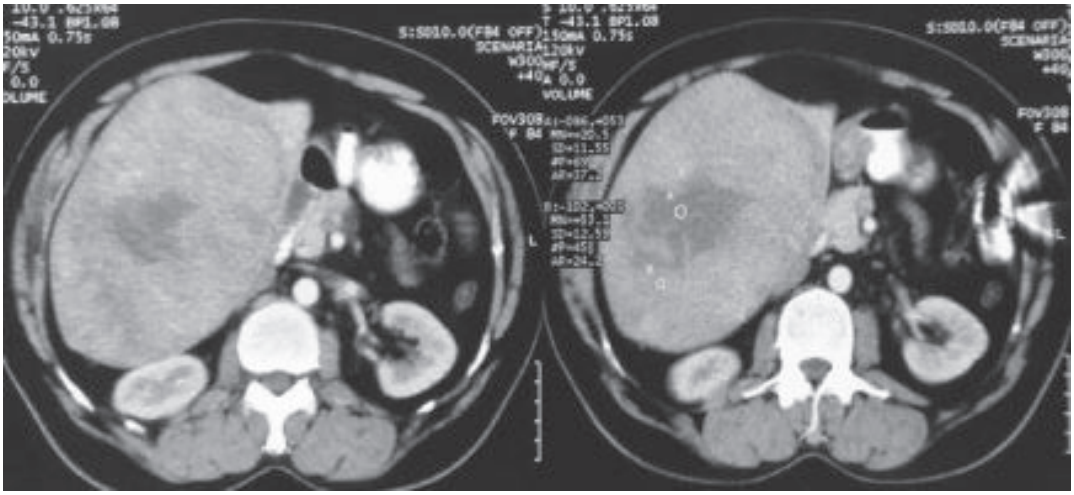

Fig 3: *Axial arterial phase image of the same patient shows heterogeneous enhancement of the lesion (Case 19)*

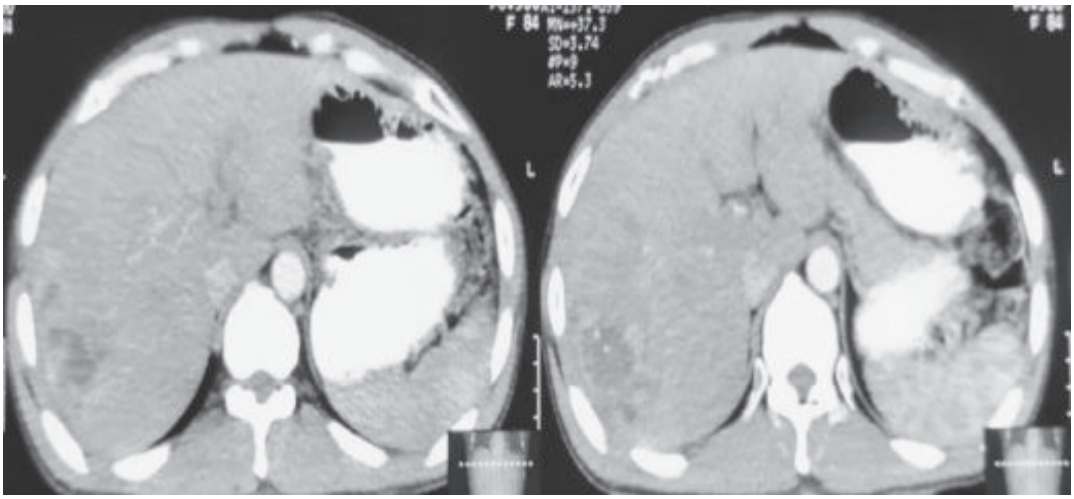

Fig 4: *Axial post-contrast image in a 53-year-old male patient shows early arterial enhancement of the lesion consistent with HCC (Case 36)*

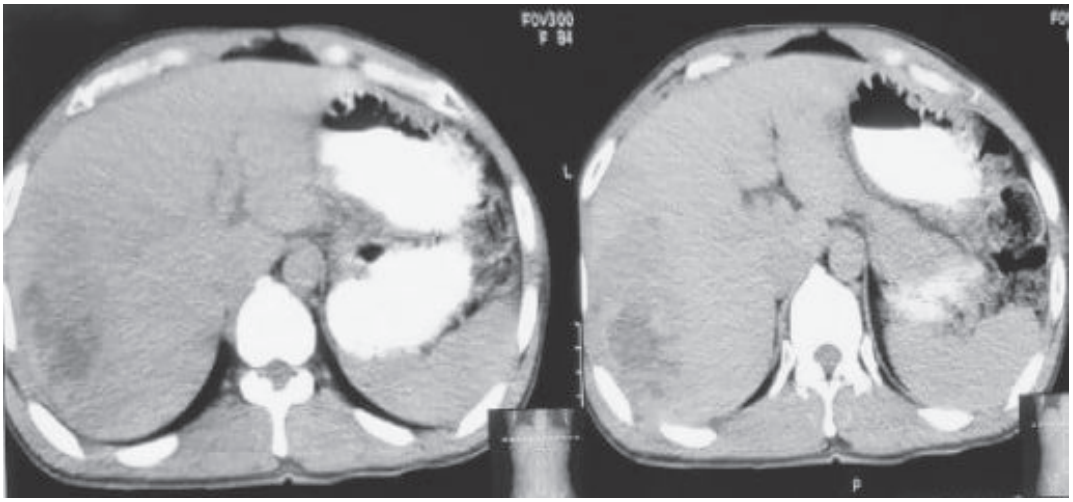

Fig 5: *Axial post-contrast CT scan image of the abdomen of the above case with HCC shows wash out of a contrast in portal venous phase (Case 36)*

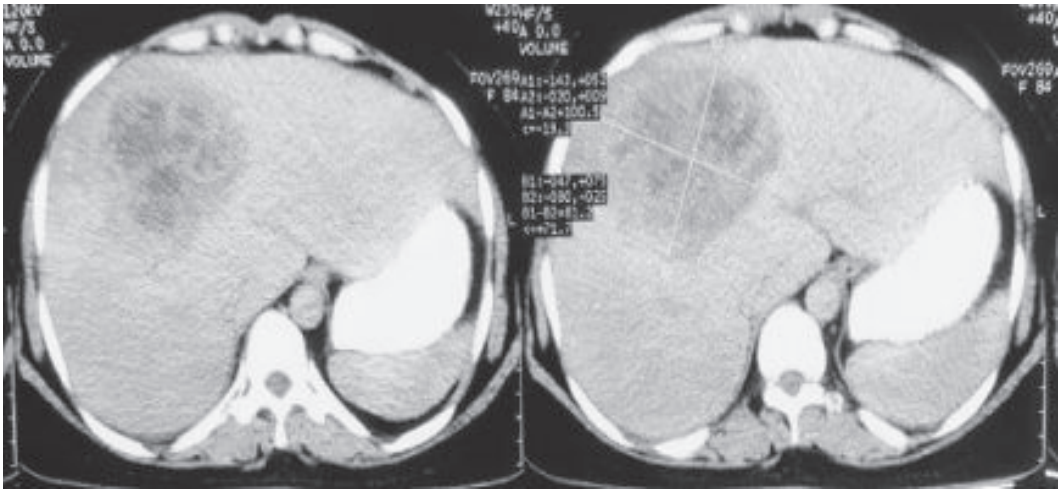

Fig 6: *Axial post-contrast CT scan of the abdomen in a 30-year-old female with HCC shows arterial phase enhancement of the lesion in the liver (Case 47)*

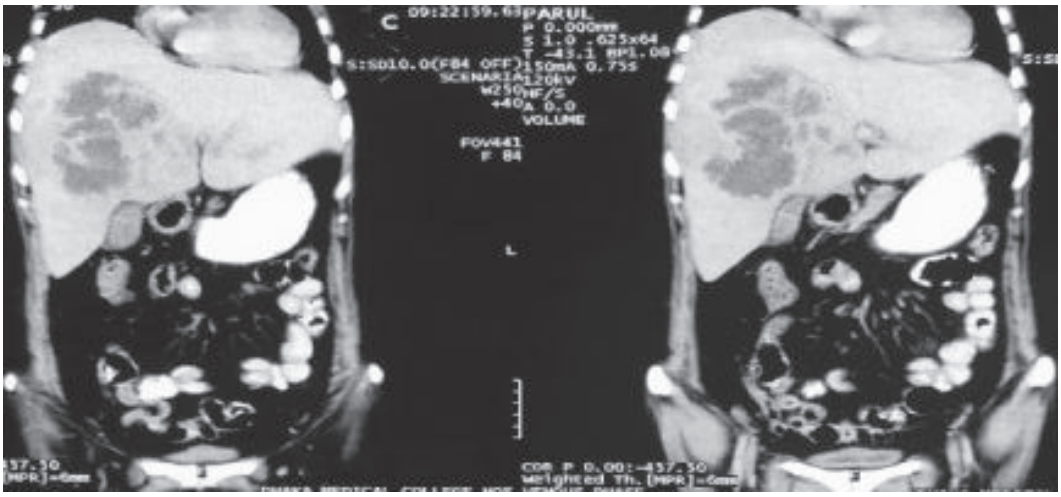

Fig 7: *Coronal post-contrast images of the above patient with HCC shows wash out of contrast in portal venous phase (Case 47)*

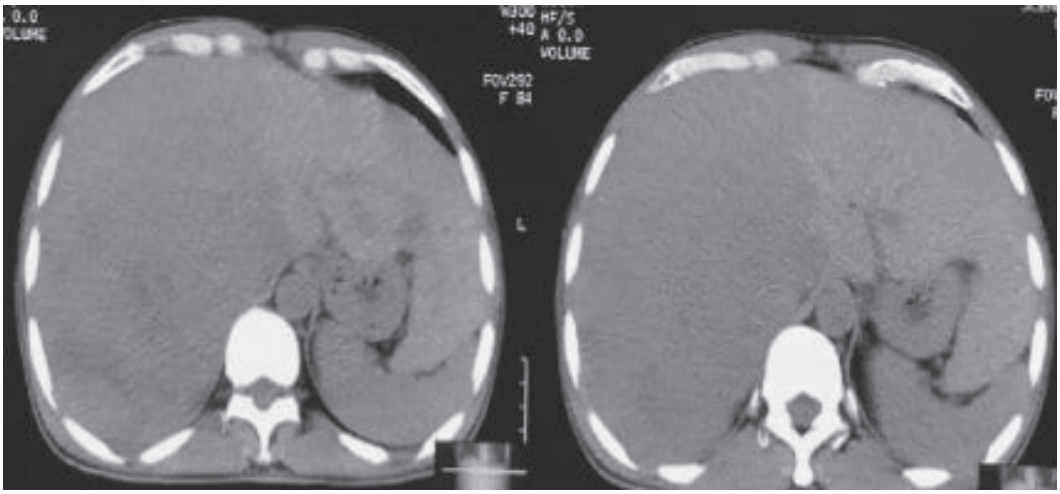

Fig 8: *Axial pre-contrast CT scan of the abdomen in a 45-year-old male with HCC shows diffuse iso to hypodense lesions in the right lobe of the liver (Case 48)*

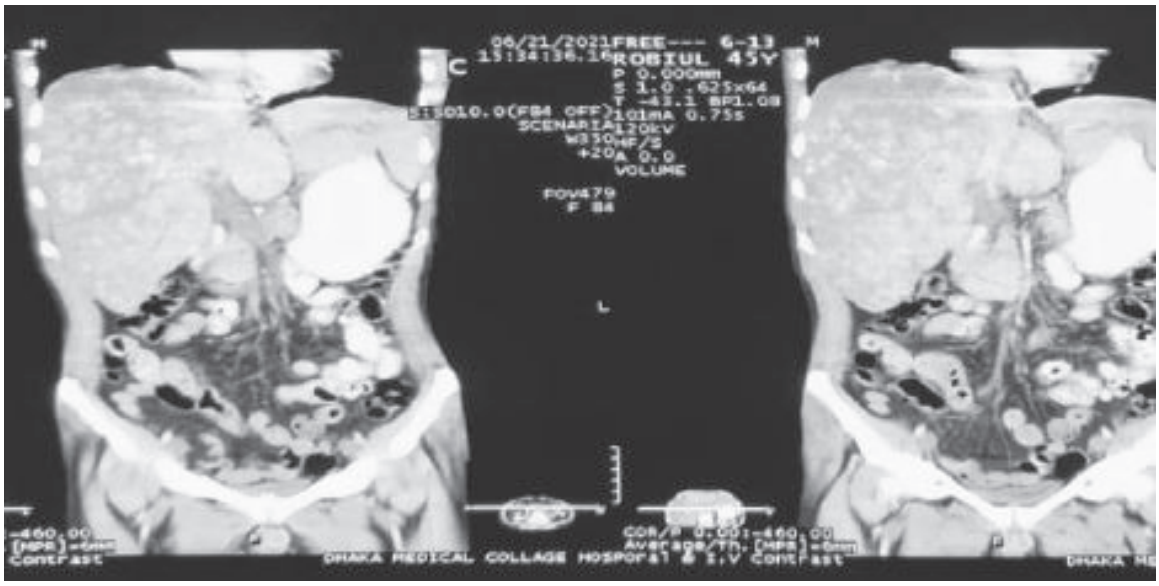

Fig 9: *Coronal post-contrast images of the above patient reveal diffuse arterial phase enhancement of the lesions (Case 48)*

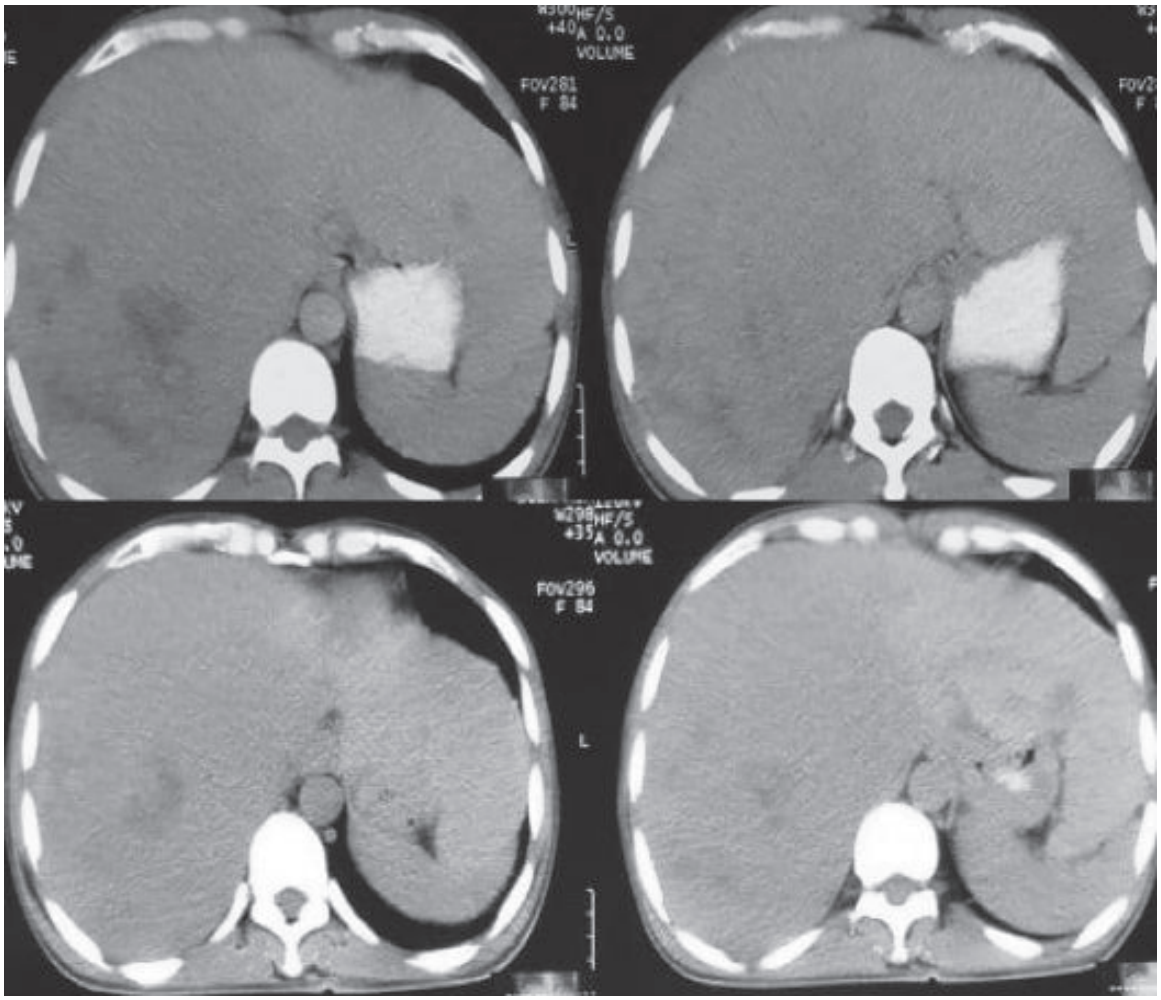

Fig 10: *Multiple axial post-contrast images of the same patient showing subsequent washout of contrast in portal venous (above) and delay (below) phases consistent with HCC (Case 48)*

Discussion:

This cross-sectional study was carried out to assess the diagnostic performance of computed tomography scan in hepatocellular carcinoma. A total of 50 patients with suspected hepatic mass of both sexes above 20 years of age referring to the Department of Radiology and Imaging, DMCH were enrolled in this study during July 2019 to June 2021. They all underwent triple-phase MDCT of the abdomen and biopsy for histopathology of the same lesion. Validity tests were performed by calculating sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) respectively.

In this study, it was observed that 30% of patients having hepatocellular carcinoma were in the 6th decade, the mean age was 51.5±5.3 years with a range of 25 to 79 years. Liu *et al.*[13] showed in a study, the mean age of the patients developing hepatocellular carcinoma was 52.4 ranged from 26 to 80 years. Yapali and Tozun[14] observed in another study, the mean age of HCC was 55-59 years in China and 63-65 years in Europe and North America. In our country, Hossain and Yusuf [15] found the youngest patient with HCC was 22 years and the eldest one was 75 years. The mean age of their study population was 49 years. The above findings are comparable with the current study.

It was observed that male patients were 82% and female 18% in this current study. The male to female ratio was 4.5:1. Ratana-Amornpin *et al.*[16] have shown the prevalence of HCC was significantly higher in men than in women, and the ratios of males to females with HCC vary from 2:1 to 4:1, depending on the geographic region. Similarly, Plaz Torres *et al.*[17] observed the male to female ratio between 3:1 and 5:1. These findings are very close to our findings in the present study.

Regarding pre-contrast findings of triple-phase MDCT of the abdomen, it was observed that normal size liver was found 26% cases, enlarged liver in 66% cases, small & irregular liver in 8% cases. More than half (52%) of patients had a single focal lesion. Almost half 48% of patients had right lobe lesions. Isodense lesion was found in 24% cases, hypodense in 52% cases, hyperdense in 4% cases and mixed density in 20% cases.

Regarding the post-contrast findings of triple-phase MDCT in this study, it was observed that in the arterial phase, the hyperdense lesion was found in 74% of cases, isodense was 18% cases and hypodense was 8% cases. In portal venous phase, hypodense was 64% cases, isodense was 30%, hypodense with enhancing rim was 6% cases. In the hepatic venous phase, hypodense was 84% cases and isodense was 16% cases. A hypervascular component in the arterial phase was found in 74% of cases. Intralesional contrast washout in the portal venous phase was found in 84% of cases. The Wall of the lesion was well defined in 22% of cases, ill-defined in 78% of cases. Abdominal lymphadenopathy was seen in only 8%. The pattern of enhancement was heterogeneous (e.g. mosaic) in 88% of cases. Lee *et al.*[18] reported 78.2% of lesions showed hyperdense in the arterial phase, and 72.1% of the lesion showed washout during either portal venous or delayed phase.

Costentin *et al.*[19] showed that the hepatic and/or portal vein invasion was present in about 10–40% of the patients at the diagnosis of HCC. In this current study, the vascular invasion was 36% that is comparable.

In this study, triple-phase MDCT scan findings showed that out of 50 cases, 42 (84%) were diagnosed as hepatocellular carcinoma, 04 (8%) were diagnosed as a cirrhotic nodule, metastases 03(6%), and hepatocellular adenoma 01 (2%). According to a histopathology report, patients have HCC 41(82%), cirrhotic nodule 04 (8%), metastases 04(8%), and hepatic adenoma 01(2%). Out of all cases, 42 were diagnosed as hepatocellular carcinoma by MDCT and among them, 40 were confirmed by histopathological evaluation. They were true positive. Two cases were diagnosed as having HCC by CT but not confirmed by histopathological findings. They were false positive. Out of 8 cases of non-HCC which were confirmed by CT, 7 were confirmed as non-HCC and 1 was HCC by histopathological findings. They were true negative and false negative respectively. The sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of the CT in the diagnosis of hepatocellular carcinoma were 97.6%, 77.8%, 94%, 95.2%, and 87.5% respectively. In a previous study, Schwarze *et al.*[20] showed a sensitivity of 94%, a

specificity of 70%, a positive predictive value of 93%, and a negative predictive value of 72% for analyzing HCC. In another study, Iavarone *et al.*[21] found 84 (70%) nodules were HCC in 70 patients, 08(7%) intrahepatic cholangiocarcinoma (ICC), 06(5%) metastases of either colon or lung cancer or lymphoma, and 02(2%) neuroendocrine tumors. They reported that hyper-enhancement in the arterial phase followed by wash-out in venous phases was demonstrated in 62 nodules with a specificity of 97%, a sensitivity of 73%, and diagnostic accuracy of 80%. Tzartzeva *et al.*[8] in a systematic review of test modalities for HCC surveillance found that CT scan has high sensitivity and specificity to detect HCC at any stage. Salvatore *et al.*[22] observed the sensitivity, specificity, and accuracy of 50 masses (43 HCCs, 3 hemangiomas, 2 adenomas, 1 eosinophilic abscess, and 1 metastasis) was respectively 95%, 88%, and 94% for CECT. Pocha *et al.*[10] Showed the overall sensitivity and specificity of triple-phase MDCT ranged from 85% to 90% and 80% to 96% respectively, which was found to be a better diagnostic value in the assessment of hepatocellular carcinoma compared with the ultrasound.

In a meta-analysis by Roberts *et al.*[12] contrast-enhanced CT was compared to both extracellular contrast-enhanced MRI and Eovist MRI for HCC diagnosis. Compared to CT, MRI had a significantly higher sensitivity (82% vs. 66%) with similar specificity (92% vs. 91%). In addition, MRI was more sensitive for the diagnosis of HCC in lesions <1 cm compared to CT (69% vs. 49%), although specificity was lower (46% vs. 69%, respectively). Conversely, MRI was associated with higher cost, greater technical complexity (including longer scan time), and less consistent imaging quality (e.g., difficulty with breath-holding, difficulty holding still, large volume ascites). So the validity parameters of the triple-phase MDCT of this study are more or less very close to that of previous studies. Sensitivity is found slightly higher than the previous studies because the patients seek delayed hospital consultation in our country. So they present with an advanced stage of the disease.

Conclusion:

As the triple-phase multi-detector computed tomography diagnosis of hepatocellular carcinoma in this study is well correlated with histopathology and considering the high validity parameters, it can be concluded that the triple-phase MDCT scan is a useful tool for the diagnosis of HCC.

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