

## ROLE OF MULTIPHASE STUDY OF LIVER LESIONS ON 128 SLICE DUAL SOURCE COMPUTED TOMOGRAPHY WITH CYTOLOGY OR HISTOPATHOLOGICAL CORRELATION

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### Abstract

**Introduction:** Dual source Multidetector Computed Tomography (MDCT) provides multiphase study of various liver lesions for better detection and characterization. This study aims to detect and characterize the liver lesions in multiphase Computed Tomography (CT) with cytological & histopathological correlation to confirm the diagnosis.

**Material and Methods:** This cross-sectional study included 65 patients who were referred to the Radiology Department of Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, India with clinical features jaundice, pain in abdomen, nausea and vomiting. All patients were evaluated by five phase CT (unenhanced, early & late arterial, portal venous and delayed scan) of liver with Siemens 128 slice dual source spiral CT. Protocols with a scan delay of 06 seconds, 09 seconds, 45 seconds & 180-300 seconds from contrast bolus was preselected for early and late arterial, portovenous and delayed scans.

**Results:** Sixty five (age 10yrs- 90yrs) patients were included in the study. Most common neoplasm was metastases 33(51%). Hepatocellular carcinoma (HCC) were 18(28%), hemangioma 10(15%), peripheral intrahepatic cholangiocarcinoma 1 and 3 were non-neoplastic which included hepatic abscesses and hydatid cyst. Most common pattern of enhancement of metastasis in arterial phase was hypodense with peripheral enhancement and most were hypodense in portal venous phase. Portal venous phase had highest grade for hypovascular metastases & arterial phase had high grade to detect hypervascular metastasis. Delayed scan was better for smaller lesions less than 1cm. The sensitivity to detect metastases was 94%. Most common pattern of enhancement in HCC (variegated or heterogeneous enhancement) in arterial phase with rapid washout in the portal venous phase. Total sensitivity to detect HCC was 83.3%. Hemangioma showed peripheral globular enhancement in arterial phase. In portal venous and delayed phase showed progressive enhancement with more centripetal filling. Sensitivity was 90% in case of hemangiomas.

**Conclusion:** Multiphasic CT scan is a good non-invasive tool and can be used as first line imaging modality for differentiating benign and malignant liver lesions.

**Keywords:** Multidetector Computed Tomography, Liver lesions, Hepatocellular carcinoma

### INTRODUCTION

Multidetector helical acquisition with higher capacity enables multiphase helical examination of about 5-6 seconds each with short time interval and a choice of section thickness post acquisition. The technology permits the examination of the abdomen in multiphases with single monophasic non-ionic iodinated contrast material intravenous bolus, providing the lesion detection and characterization of liver masses. Unenhanced imaging is valuable for assessing diffuse hepatic changes such as fat infiltration and iron deposition and focal changes such as subtle calcification and haemorrhage.

Currently multiphasic (5-phase CT-unenhanced, early arterial/ late arterial/ portal venous & delayed phase study) contrast enhanced dynamic CT of whole liver has shown promise in better characterisation of morphology of hepatic masses.

The hypervascular masses receive their blood from hepatic artery, hence the hypervascular masses like HCC or hypervascular metastasis are more conspicuous in early scanning phase called the arterial phase while hypovascular masses like most of the metastatic lesion become conspicuous in the later phase called the portal venous phase. Late arterial phase images were found to be superior

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as regards tumour conspicuity but a combination of early and late arterial phase together with portal venous phase that is triple phase CT imaging allowed improved detection of the hypervascular neoplasms. Hepatic venous phase also known as the delayed phase or equilibrium phase along with hepatic arterial phase gives information about the vascularity of the lesion, which may further help to clarify the nature of the lesion.<sup>1</sup>

During the delayed phase (e.g. 3-5 minutes after the injection), equilibrium is attained and the concentration of the contrast material in the vascular space and the interstitial space becomes almost equal. On reaching this equilibrium, the increase in the tissue attenuation by the distribution of the contrast material depends chiefly on the volume of interstitial space because it is about three times as large as the vascular space in most tissues. Therefore, enhancement observed on delayed phase images reflects the relative volume of the interstitial space in tissues<sup>2</sup>. Most tumors show hypoattenuation on delayed phase images because they have increased cellularity or decreased interstitial space than the liver parenchyma. Hemangiomas have disproportionately large vascular space and lesions with rich fibrous tissue have a large interstitial space; these are depicted as a hyperattenuating area on delayed phase images.<sup>3</sup>

Well-differentiated HCCs are usually small, in fact, most are less than 2cm. Their vascular supply and vascularity are variable and dependent on grade of malignancy. HCCs less than 2cm were usually more conspicuous on delayed phase (fourth phase) images than on portal venous phase images and some were detected only on delayed phase images. As the grade of malignancy increases, HCC neovascularity develops and arterial blood supply increases in tumors.<sup>4,5</sup>

Purpose of this study is to characterize the hepatic masses depending on the pattern of enhancement in various phases & to make confident diagnosis. Advantage of 128 slice dual source CT is small breath hold time for each phase 5-6 sec.

## **MATERIAL AND METHODS**

The Ethical Committee of our Institute approved this cross-sectional study. Informed consent was taken from all patients undergoing this study. We prospectively studied 65 patients (43 males and 22 females) in the age range 10-90 years over a period from November 2014 to May 2016 at Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, India. Multiphase CT study was done in all patients on 128 Dual source CT Somatom definition flash of Siemens.

All patients were evaluated by 5 phase CT (unenhanced, early & late arterial, portal venous and delayed scan) of liver with Siemens 128 slice dual source spiral CT in SRMS medical college and hospital.

Water was given as an oral contrast before scanning. All patients underwent a non-contrast enhanced liver CT (Phase-1). A dual-syringe injector system (stellantmedrad) was used for intravenous administration of 80 ml non-ionic contrast media (370mg /mL) at 5 ml per seconds followed by 30 to 40 ml saline chaser bolus. A bolus-tracking technique with automated scan-triggering software was used.

A circular region of interest (ROI) was placed within the abdominal aorta just below the diaphragm. The threshold CT value was preset at 100 Hounsfield unit (HU). The following protocols with a scan delay of 06 seconds, 09 seconds, 45 seconds & 180-300 seconds (from the time when threshold enhancement was detected in aorta to the beginning of the early arterial phase scan) was preselected for early and late arterial, portovenous and delayed scans for each patient prior to the examination.

Helical scan for the early arterial phase of the liver was performed in a cephalo-caudal direction. The late arterial phase (Phase 3) was taken following the early arterial phase scan, in a caudo-cephalic direction. The portal venous (Phase 4) and delayed scan (Phase 5) in cranio-caudal direction. Patient was instructed to hold their breath in full inspiration during each scan phase.

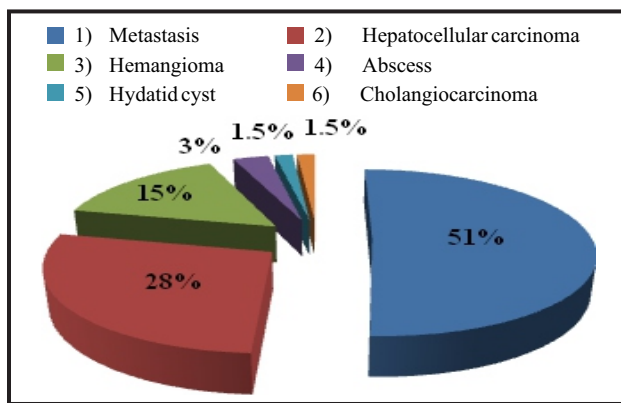
The images acquired in different phases were evaluated in detail to identify the lesions, classify according to the age, clinical background and other imaging/ biochemical findings. Further the findings were classified as benign or malignant by correlating with cytological /histopathological findings.

## **RESULTS**

Multiphase CT study was done for a total of 65 patients who were clinically diagnosed as having liver lesions. In present study there is male predominance. The study group comprised of 43 (66%) males and 22 (34%) females. The majority of patients with liver lesions were in age group of 51-60 years.

In present study, the most common malignant lesion is metastasis, hepatocellular carcinoma and the most common benign lesion is hemangioma, abscesses and hydatid cyst. The spectrum of diseases is given. (Fig-1)

Present study included 65 patients with hepatic lesions; most common neoplasm was metastases which accounted



**Figure-1:** Spectrum of Disease

for 33 of our cases followed by HCC which accounted for 18 and hemangioma which accounted 10 in total cases. Peripheral intrahepatic cholangiocarcinoma accounted for 1 case and 3 were non-neoplastic. The size of the hepatic neoplasm was evaluated in two dimensions.

In present study 33 cases of metastatic lesions of liver from varying primary sites. Age group ranged from 34 yrs to 85 yrs with mean age being 59 yrs. The mean size of metastatic lesions encountered in present study was 4.2cm with a size range of 1-10cm. The male to female ratio encountered in present study was 19:14 (1.3:1) with male dominance. Out of 33 cases of metastases, most common known primary was from colorectal malignancy constituting 11 (33%) cases, followed by pancreatic malignancy 5 (15%), gall bladder (GB) carcinoma 2 (6%), stomach 1(3%) and ovarian malignancy 1(3%). Other causes of secondaries include renal transitional cell carcinoma, bronchogenic carcinoma and unknown origin. Pattern of enhancement was studied in 33 cases in hepatic metastases by categorizing the pattern as hypodense, heterogeneous, peripheral or isodense to the liver. (Table-1, Fig-2)

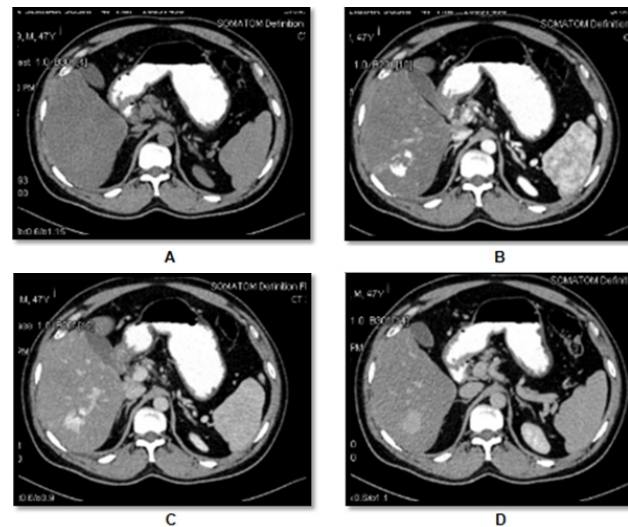
Second most common neoplasm was hepatocellular carcinoma. Total 18 patients with HCC were included in present study. Age of the patients ranged from 35 to 75 yrs with mean age of 55 yrs. HCC had a size range of 1-11cm with a mean size of 4.7cm. In present study no female patients was found to have HCC. Most common pattern of HCC was enhancement in arterial was variegated or heterogeneous enhancement with rapid washout in the portal venous phase. (Table-2) & (Fig.-3)

Alpha fetoprotein level was normal in 5(28%) patients, mildly elevated in 3(17%) patient and highly elevated in 10(55%) patients.

Most common benign lesion was hemangioma. Age group ranged from 30-70 years with mean age of 50 years. The mean size of hemangioma encountered in present study

**Table-1:** Enhancement pattern of metastases

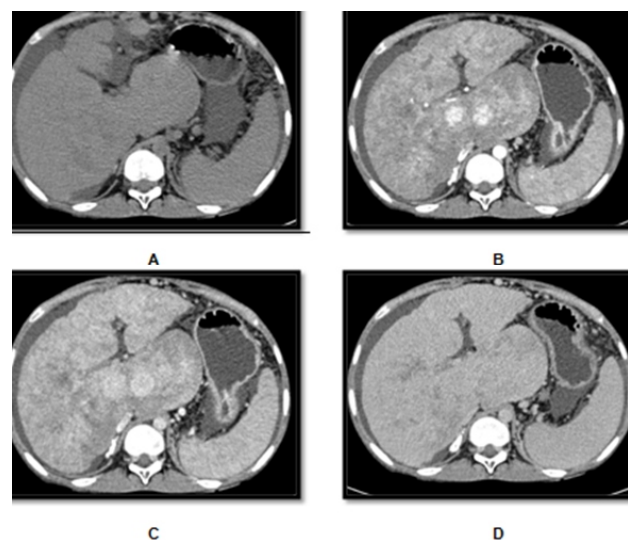
PHASES	HYPODENSE	HYPERDENSE		ISODENSE
		PERIPHERAL	HETEROGENOUS	
NCCT	20	-	-	13
ARTERIAL	17	8	2	6
PORTAL VENOUS	29	-	2	2
DELAYED	21	1	2	9



**Figure-2:** Case of metastases. A) non contrast lesion was hypodense. B) arterial phase showed peripheral enhancement. C) portal venous shows heterogeneous enhancement. D) delayed phase lesion was hypodense.

**Table-2:** Enhancement pattern of HCC

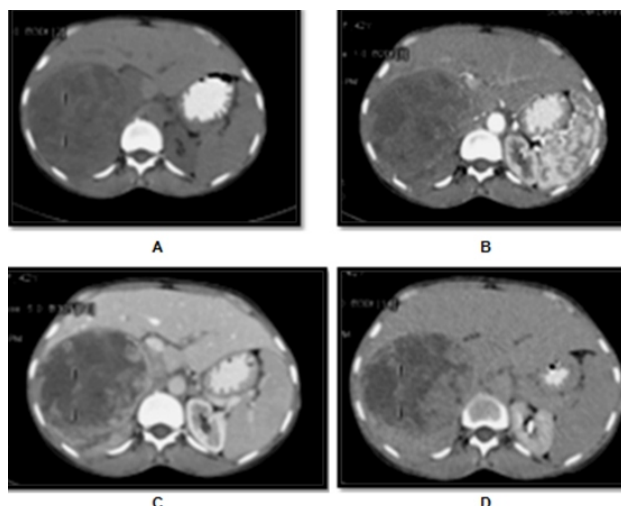
PHASES	HYPODENSE	TOTAL NO. OF CASES = 18			ISODENSE
		HOMO	HETRO	PERIPHERAL	
NCCT	18	-	-	-	-
EARLY	-	3	15	-	-
ARTERIAL	-	-	18	-	-
LATE ARTERIAL	15	-	2	-	1
PORTAL VENOUS	15	-	-	-	3
DELAYED	15	-	-	-	3



**Figure-3:** Case of Hepato Cellular Carcinoma. Liver shows irregular surface with mild ascitis. On post contrast study multiple nodules of varying sizes are noted in bilateral lobes of liver. A) non contrast nodules are hypodense. B) arterial phase shows heterogeneous enhancement. C) portal venous shows homogenous enhancement. D) delayed phase shows complete wash out and appears to be hypodense.

**Table-3:** Enhancement pattern of Hemangioma

PHASES	HYPD	PERIPHERAL GLOBULAR	PERIPHERAL (INCOMPLETE RING)	PROGRESSIVE HYPERDENSE	ISODENSE
NCCT	10	-	-	-	-
EARLY ARTERIAL	-	7	3	-	-
LATE ARTERIAL	-	7	3	-	-
PORTAL VENOUS	-	7 (Increased)	2 (Increased)	-	1
DELAYED	1	-	-	8	1

**Figure-4:** Case of hemangioma. A) non contrast it showed heterogenous appearance. B) arterial phase showed peripheral enhancement c) portal venous phase showed peripheral globular enhancement. D) delayed phase enhancement persists peripherally.

was 3.4 cm with a size range of 1.8-8.4cm. Females were more affected in present study with ratio being 6:4. Common pattern of enhancement was peripheral globular enhancement (also known as peripheral nodular) in arterial phase. In portal venous and delayed phase these showed progressive peripheral enhancement with more centripetal filling with iso or hyperattenuating to liver parenchyma. (Table-3) & (Fig.-4)

Present study had one case of intrahepatic cholangiocarcinoma which displayed peripheral enhancement with no much intratumoral density changes in arterial & portal venous phases and showed hyperattenuation in delayed phase. It was associated intrahepatic biliary dilatations.

There were 2 cases of abscesses and size of the abscesses was approximately 7.5cms and 8cms in the right lobe of liver. These were hypodense showing peripheral enhancement in arterial and portal venous phase. Abscess was aspirated using ultrasound guidance.

The hydatid cyst was 6.5cms in size, high attenuation wall on NCCT without calcification, no perifocal edema or daughter cyst but showed wall enhancement in arterial and portal venous phase.

## DISCUSSION

The present study group comprised of 65 patients ranging from 10 year to 90 years with the mean age of 50 years. The

largest numbers of cases were in the age group of 51 to 60 years..

In present study pattern of enhancement was studied in 33 cases in hepatic metastases among metastases, 24% (8 of 33) showed peripheral ring enhancement and 6% (2 of 33) showed heterogeneous enhancement in the arterial phase suggestive of hypervascular lesions and 70% (23/33) was hypo/ isodense suggestive of hypovascular lesions. Present study correlated with Honda et al<sup>6</sup> who studied 28 cases and found most common appearance of metastases was hypodensity in arterial phase (60%) followed by peripheral ring enhancement accounting to 29%.

In present study, in portal venous phase, the majority of metastatic lesions was hypodense accounting to 29(88%), followed by isodense appearance accounting to 2(6%) and heterogeneously hyperdense 2(6%). According to Honda et al<sup>6</sup> 16(58%) were hypodense and 6(22%) showed isodensity. In present study portal venous phase was better for hypovascular lesions conspicuity and detection. 94% cases were better delineated and characterized on portal venous phase whereas NCCT & arterial dominant phase together were better for only 78% cases.

In present study out of 33 metastases 21(64%) were hypodense, 9(27%) were isodense, 2 (6%) showed central hyperdensity and 1(3%) showed peripheral hyperdensity in delayed phase. Honda et al<sup>6</sup> concluded in his study that in delayed phases, total hypodensity was the most common pattern seen in 16(57%) out of 28 metastases followed by total isodensity in 6(21%) which correlated with present study.

In present study 33 metastases out of 65 cases, 31 proved to be malignant on cytological/histopathological examination, 2 came out to be benign (hemangioma). Thus there were 31 true positive and 2 false positive cases on CT based assessment of liver lesions. The sensitivity to detect metastases was 94%. Our findings correlated with Soyer et al<sup>7</sup> who demonstrated sensitivity of 91%.

Total 18 cases of patient with cirrhotic liver was studied for HCC. In early arterial phases all the lesions showed hyperattenuation, 15(84%) being heterogeneous and 3(16%) homogenous. None of the case in present study was hypo or isodense. Present study correlated with Baron et al<sup>8</sup> out of 66 cases 26(46%) and Karahan et al<sup>9</sup> out of 32 cases 14(44%) both showed hyperattenuation of HCC in arterial phase was the most common pattern of enhancement. Discrepancy was noted in pattern of heterogeneous and homogeneous enhancement from their study and may be due to size of the lesions. In present study characteristic enhancement pattern noted in arterial phase was heterogeneous variegated pattern which accounted for



84% of cases and the presence of abnormal internal vessel was the most common feature (6/15,40%) which correlates with study series of 51 patients by K.H.Y Lee et al<sup>10</sup> which has 86% variegated enhancement with 53% depicting abnormal internal vessel. In present study, all 18 HCC's was hypervascular in early arterial phase and degree of enhancement increased in late arterial phase which correlated with Andrea Laghi et al<sup>11</sup> who concluded that the late arterial phase images depicted 58 tumors (hyperdense) out of total 58 patients.

Foley et al<sup>12</sup> in their study concluded that although hypervascular neoplasms are best seen during the late arterial phase, the use of an early arterial phase allows for CT Arteriography, which can be important for pre-operative detection of vascular anomalies in patients who were candidates for hepatic resection/ tumor cryoablation or arterial chemoembolization.

Although Murakami et al<sup>1</sup> reported a distinct benefit of early arterial phase imaging for less than 1 cm size tumor detection and reduction of false positive diagnosis.

In present study group of 18 cases of HCC, pattern of enhancement in portal venous phase were as follows: 15(84%) were hypodense, 2(11%) were hyperdense and only 1(5%) of cases became isodense to liver parenchyma. Present findings were similar to the Karahan et al<sup>9</sup> study who observed that 26(88%) out of 30 patients, had tumors being hypodense on portovenous phase and 4(12%) were hyperdense. Studies of Shuichi et al<sup>13</sup>, June Cho Sik et al<sup>14</sup> and Baron et al<sup>8</sup> reported hypo, hyper and isodense pattern in the portovenous study but all reported varied dissimilar percentage patterns on portal venous phase images.

In present study 15(84%) lesions were hypoattenuating and 3(16%) were isoattenuating on delayed phase. Shuichi Monzawa et al<sup>13</sup> described 43(89%) were hypoattenuating and 5(11%) tumors were isoattenuating. The mean sensitivity for the combination of arterial and portal venous phase imaging was 86.8%, that for the combination of arterial and delayed phase imaging was 90.3%, and that for the combination of all three phase imaging was 93.8%. In present study the detection of hypervascular HCC, the arterial phase images were superior to portal and delayed phase images.

Portal vein thrombosis was noted in 5(28%) of our cases, which was less as compared to the Karahan et al<sup>9</sup> who has reported portal vein involvement in 15/30(50%) of his cases. Leeuwen et al<sup>15</sup> however has reported a slightly higher incidence of portal vein involvement 20/57(57%), the discrepancy may be due to lesser number of patient in ours study and size of the lesions.

In present study out of 18 HCC diagnosed on CT 15 were HCCs on cytological/histopathological and 3 were diagnosed as dysplastic nodule and, 8 were poorly differentiated and 5 were undifferentiated and 2 were moderately differentiated on cytological/histopathological examination. Cases of low grade (well and moderately differentiated) HCC showed all patterns of enhancement. Cases of high grade (poorly and undifferentiated) HCC showed only pattern 3 of enhancement. Discrepancy in present study from Ahmed Shokry is likely to be due that there are only limited number of studies that correlate between dynamic MDCT of HCC and pathological tumor grades and also depends on the severity of the disease.

In total 18 cases of HCC, on cytological/histopathological examination 15 was diagnosed as moderately, poorly and ill differentiated HCCs and 3 lesions was diagnosed as dysplastic nodule. Thus there were 15 true positive and 3 were false positive. Hence, total sensitivity to detect HCC was 83.3%.

In present study out of total 10 hemangiomas, 7(70%) showed peripheral globular (also known as peripheral nodular enhancement equivalent to the aorta), enhancement and 3(30%) showed discontinuous peripheral enhancement in arterial phase. In portal venous and delayed phase 1(10%) was hypodense and rest showed progressive peripheral enhancement with more centripetal filling. In delayed phase showed further irregular filling with iso or hyperattenuating to liver parenchyma.

Matilde et al<sup>16</sup> studied 9 cases and Tonsok Kim et al<sup>17</sup> studied 37 cases showed in their studies that peripheral globular enhancement in arterial phase was specific for hemangioma accounting to 66% and 68% respectively, which was similar to present study findings.

In portal venous phase, present study showed globular enhancement with centripetal filling in 7(70%) of cases, 2(20%) cases showed further peripheral ring with increasing centripetal fill in and was 1(10%) was hypoattenuating. Present study correlated with Tonsok Kim et al<sup>17</sup> who out of 37 cases showed that maximum number (18-49%) of their cases showed globular enhancement with centripetal filling. However in his study 43% cases showed isodense attenuation to the liver where as none of cases were isodense to the liver parenchyma but 1 case was hypodense. Discrepancy may be due to difference in the size of study.

In present study out of 10, 8(80%) was hyperdense in delayed phase and 1(10%) hemangiomas were isodense and 1(10%) was hypodense which was correlating with Leeuwen et al<sup>15</sup> study who concluded that hyperdensity was

the most common pattern of hemangiomas seen in 54(91%) out of 59 hemangiomas.

One hemangioma reported on CT was proved to be metastases on cytological/histopathological examination. Hence, it was false positive. The sensitivity was 90% in case of hemangiomas. It was 1.5cm in size and showed peripheral incomplete ring enhancement and was hypodense in portal venous phase & delayed study. This pattern of enhancement was described by Jang et al.<sup>18</sup> But according to present study needs further confirmation by FNAC.

Present study had one case of intrahepatic cholangiocarcinoma which displayed peripheral enhancement with no much intratumoral density changes in arterial & portal venous phases and showed hyperattenuation in delayed phase. It was associated with intra hepatic biliary dilatations. Tay Kim et al<sup>19</sup> in their study of 34 cases of cholangiocarcinoma showed 76% showed associated intrahepatic biliary dilatation. These findings were well correlated with Valls C et al<sup>20</sup> in their series of 25 cases cholangiocarcinomas. According to his study increased CT numbers in delayed phase which is taken after 5-8 minutes can signify slow diffusion of contrast due to presence of intratumoral abundant stroma, which is seen in cholangiocarcinoma. He concluded that hypodense lesion with peripheral enhancement, biliary dilatation, and increasing contrast enhancement on delayed images are highly suggestive of peripheral intrahepatic cholangiocarcinoma. He further emphasized that an infiltrating mass with capsular retraction and delayed persistent enhancement is typical for cholangiocarcinoma. Honda et al<sup>6</sup> in their study of 20 patients also says that along with these features presence of ancillary findings like lymphadenopathy (69%) can help in diagnosis.

Present study had case of 1 case of hydatid cyst and 2 cases of hepatic abscesses. The case of hydatid cyst was 6.5cms in size, high attenuation wall on NCCT without calcification, no perifocal edema or daughter cyst but showed wall enhancement in arterial and portal venous phase. As per study of Ivan Pedrosa et al<sup>21</sup> calcification is seen in 20% - 30% in radiography which is curvilinear or ring-like pattern. It was diagnosed as cystadenoma/hydatid cyst. Microbiological examination revealed hydatid cyst.

We also had 2 cases of abscesses. In present case the size of the abscesses was approximately 7.5cms and 8cms in the right lobe of liver. These were hypodense showing peripheral enhancement in arterial and portal venous phase. With clinical background of fever, Abscesses were aspirated using ultrasound guidance.

Cytological/Histopathological correlation: False Positive cases in present study were defined as lesions deemed malignant on multiphasic CT scan but turned out to be benign on Cytological/histopathology.

Similarly, False Negative case can be defined as lesions reported benign on multiphasic CT scan but were malignant on Cytological/histopathology.

In present study of 65 cases, we had 06 false positive results. These lesions were labelled as malignant because of hypervascularity and patient's history of gastrointestinal malignancy. These lesions proved to be hemangioma, dysplastic nodule and not metastases/HCC.

Based on these findings, multiphasic CT scan was found to have a sensitivity of 100%, positive predictive value of 92.1%, and diagnostic accuracy of 90% in differentiating benign from malignant liver lesions which correlated with study conducted by Saima et al<sup>22</sup>.

Present study has some limitations like small sample size especially for benign lesions. In cases of multifocal lesion, only biopsy of largest and most approachable lesion was performed.

In present study there was no case of true negative because our inclusion criteria included all patients with clinical suspicion of liver disease or with lesion detected on ultrasound/ conventional CT. Hence, specificity could not be calculated.

## CONCLUSION

Multiphase Computed Tomography proved to be a valuable tool in the diagnosis of liver lesions by studying the pattern of enhancement in early/ late arterial, portal venous and delayed phases and helped in detection and better characterization of the lesions.

Focal lesions such as HCC, vascular metastasis which derive blood supply from hepatic artery are better detected in arterial phase of multiphase scan. Portal venous phase/ delayed phase has better conspicuity for hypovascular metastases. Multiphase scans are also helpful in detection of tumor thrombus and arterio portal shunts. Addition of delayed phase was also valuable in diagnosing hemangioma and cholangiocarcinoma.

Present study showed diagnostic accuracy of 90% in diagnosing various lesions by confirming these diagnoses using image guided FNAC/FNAB. This shows excellent correlation between radiological diagnosis and histological/cytological diagnosis of various liver lesions.

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