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Original Article

Evaluation of Patients with Hepatic Masses Using Triphasic Multidetector Computed Tomography and Correlation with Cytohistopathological Findings

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Abstract
Purpose: *The purpose of study was to evaluate the features of various hepatic masses using triple phase multidetector computed tomography and to correlate features of triple phase multidetector computed tomography with cytohistopathological findings. Tumour enhancement subsequent to contrast administration depends on blood supply, thus images are acquired in arterial, portovenous and delayed phases after fixed time interval and helps in characterizing tumours.*
Methods: *It is a descriptive type of observational study done on 100 patients of hepatic masses on basis of clinical findings or on ultrasonography. Axial, coronal and sagittal images of noncontrast, arterial phase, portovenous and delayed phase were taken and imaging findings were correlates with cytohistopathological findings/USG guided biopsy.*
Results: *Study was done in 100 patients (n=100). In our study the youngest patient was of 3 years and the oldest was 92 years, with a mean age of 53.8 years. Majority of the patients were in age group of 41-50 & 51-60 years. Out of 100 patients, half of the patients were male and half were females. Hepatic tumors were detected in all 100 patients. Of these 21 were benign and 79 were malignant tumors. Of 100 cases, 45 cases of metastases, 21 cases of HCC, 18 cases of hemangiomas, 10 cases of intrahepatic cholangiocarcinoma, 2 case of biliary cystadenoma, 1 case of biliary cystadenocarcinoma, 1 case of focal nodular hyperplasia, 1 case of hepatoblastoma and 1 case of epithelioid hemangioendothelioma detected.HCC were prevalent in 51-60 years age group, metastases in 41-50 years age group and hemangioma in 31-40 years age group. High male predilection was noted in Hepatocellular carcinoma and metastases, whereas hemangiomas and cholangiocarcinoma were more common in female. Out of 100 cases right lobe was involved in 37 % cases, left lobe in 11% cases and both lobe involvement was noted in 52% cases. In 11(52.4%) cases out of 21 underlying liver parenchyma is cirrhotic and in 10 (47.6%) cases underlying liver parenchyma is normal. In 12(57.2%) cases out of 21 involvement of portal vein/hepatic vein and IVC is seen. In 17(80.9%) cases of HCC out of 21 level of AFP were raised, however in 4 (19.1%) patients serum AFP level were normal.*
Conclusions: *Hypervascular tumours are better appreciated in arterial phase. Hypovascular tumours are better demonstrated on portovenous phase. Delayed phase helped in demonstrating few tumours like intrahepatic cholangiocarcinoma, hemangioma and HCC. Triple phase MDCT with its arterial, portovenous inflow (late arterial) and portovenous phases is an ideal modality for diagnosis and characterization of HCC. It is helpful to provide additional*

information like vascular invasion, capsular delineation, arterioportal shunts and also provide a vascular road map for surgery and image guided interventions. Pediatric malignant tumors like hepatoblastoma are diagnosed and managed with help of important information provided by triple phase MDCT. Cholangiocarcinoma is diagnosed in delayed phase images acquired during triple phase MDCT protocol. Metastases could be differentiated as hyper or hypovascular type based on triple phase CT characteristics. This further helps to define primary lesion. Compared to other imaging modalities MDCT provides substantial amount of information regarding hepatic tumours and surrounding structures hence it has carved a niche for being a superb diagnostic and follow up modality.

Keywords: *Hepatocellular carcinoma, Cholangiocarcinoma, Epithelioid hemangioendothelioma, Biliary cystadenoma /cystadenocarcinoma & Diffuse hepatic hemangiomatosis.*

Introduction

Neoplastic disorders (benign & malignant tumours) affect wide range of population i.e. pediatric, adolescents, adults and geriatric population. E.g. Hemangioma is the most common benign liver lesion affecting almost all age groups; hepatocellular carcinoma is the commonest primary malignancy of the liver.[1]The subsequent text will be pertaining only to the neoplastic disorders (benign &malignant tumours) of liver, excluding the infectious disorders (e.g. abscess). The most common causes of cancer death are cancers of: Lung (1.69 million deaths), Liver (788 000 deaths), Colorectal (774 000 deaths), Stomach (754 000 deaths) and Breast (571 000 deaths).[2] Over the time various modalities (USG, CT, MRI, nuclear imaging) have been developed to diagnose these conditions and help in the management. CT (computed tomography) is a widely available and thus well-utilized modality to characterize and describing the extent of the hepatic tumours. Multiphasic studies have begun with the advent of helical CT scan units. The helical CT overcame the constraints of conventional CT by reducing scan duration. With single slice helical CT, multiphase imaging of liver included a hepatic arterial phase and a portal venous phase after beginning of intravenous contrast material injection.[3] The current generations of multidetector row CT scanners have helped further reduce scan time and improve resolution in different planes. This allows increase distance of coverage or increase resolution in Z axis.[3,4] The entire liver can be scanned in a single breath hold without respiratory misregistration.[3] Thereafter the different phases of hepatic enhancement are better defined. Contrast enhanced Triphasic studies (in arterial, venous and delayed phases) using CT are performed to characterize the hepatic tumours. Thus we need to evaluate the role of multidetector row computed tomography hepatic Triphasic studies in characterization of hepatic tumours with a secondary objective to stage the tumour for further management.

Material and Methods

The study was conducted in the department of Radiodiagnosis, Dr. S.N. Medical College and Associated MDM and MGH Hospital, Jodhpur in close association with Department of Gastroenterology from January 2018 to November 2018.

The study was comprises of patients with hepatic masses on basis of clinical findings or on ultrasonography. A minimum of 100 patients will be included in the study.

Each patient included in the study after obtaining an informed consent, will be subjected to a detailed history, clinical examination and diagnostic work up plan. Technique of triple phase will be individualized as per the case. Findings were correlated with histopathology findings obtained from USG guided Biopsy/FNAC.

Patients of all age groups with clinically suspected or ultrasound proven cases of hepatic tumours.

Excluded patients

Already proven cases of hepatic tumours by CT scans or histopathology previously, pregnant patients, patients with renal failure, bleeding diathesis & previous case of anaphylactic reaction to iodinated contrast.

Methodology

In the present study, hepatic triphasic examination was carried out using Philips 64 slices multidetector row computed tomography (MDCT).USG guided biopsy/FNAC is done in association with gastroenterology department MDM Jodhpur.

Observation and Results

This study was carried out in the department of radio-diagnosis, Dr. S. N. medical college Jodhpur, Rajasthan, India. In the present study, 100 patients clinically suspected of having hepatic tumours or sonographically proven cases of hepatic tumours were studied for a period of 11 months and were subjected to computed tomography study of abdomen using triphasic hepatic study protocol and correlates with cytohistopathological findings.

Table No. 1: Age Distribution of Liver Tumours (n=100)

Age Group (Years)	No.of Cases	Percentage
0-10	3	3%
11- 20	2	2%
21-30	6	6%
31-40	12	12%
41-50	23	23%
51-60	19	19%
61-70	16	16%
71-80	12	12%
81-90	6	6%
91-100	1	1%
Total	100	100%

Table No. 2: Sex wise distribution of cases (n=100)

Sex	No of Cases	Percentage
Male	50	50%
Female	50	50%

Table No.3: Age wise distribution of the specific tumor (n=100)

Age group	Hemangioma	B. Cyst adenoma	FNH	HCC	Cholangiocarcinoma	Hepatoblastoma	Metastasis	B.Cystadenocarcinoma	EHA
0-10				1		1	1		
11-20	1			1					
21-30	3		1	1			1		
31-40	5				2		4		1
41-50	4	1		4	2		12		
51-60	2	1		6	2		7	1	
61-70	2			2	2		10		
71-80	1			3	2		6		
81-90				3			3		
91-100							1		
Total	18	2	1	21	10	1	45	1	1

Table No 4 : Sex wise distribution of the specific tumor (n=100)

Tumor	Male	Female	Total
Benign			
Hemangioma	7	11	18
Biliary cystadenoma	1	1	2
Focal nodular hyperplasia	0	1	1
Malignant			
Hepatocellular Carcinoma	17	4	21
Cholangiocarcinoma	3	7	10
Hepatoblastoma	0	1	1
Metastasis	24	21	45
Epithelioid hemangioendothelioma	1	0	1
Biliary cyst adenocarcinoma	1	0	1

Table No.6: Alfa-fetoprotein (AFP) correlation with HCC (n=21)

HCC	No. of cases	Percentage
HCC with Raised AFP	17	80.9 %
HCC with normal AFP	4	19.1%
Total no. of cases	21	100%

Hemangioma

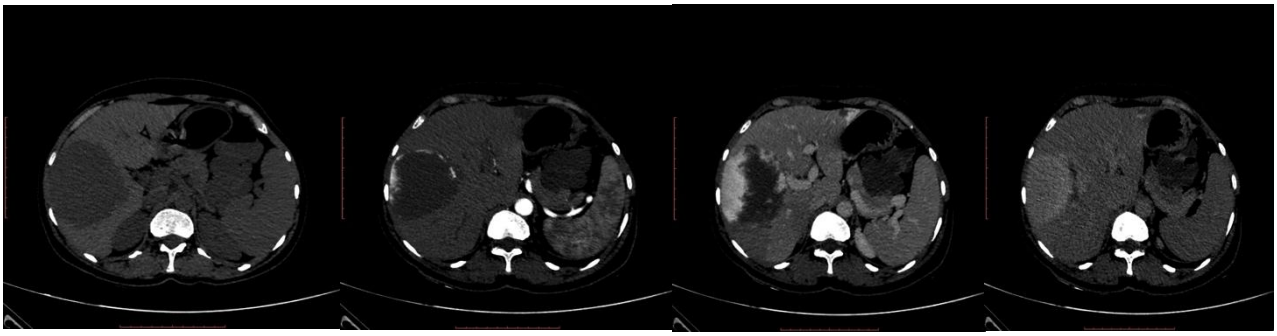

Fig.1: Classical hemangioma in a 50 year female patient, images A,B,C&D Non contrast, arterial ,venous and delayed phase respectively showing peripheral nodular enhancement in arterial phase and centripetal filling in portovenous phase

Hepatocellular Carcinoma (HCC):

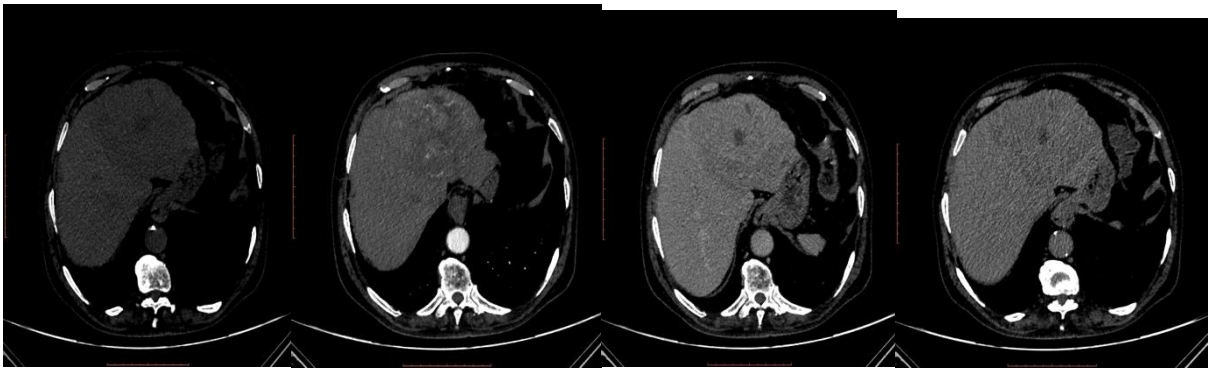

Fig. 2: Classical Hepatocellular carcinoma in left lobe in a 87 year male patient, images A, B, C & D Non contrast, arterial, portovenous & delayed phase respectively showing early arterial enhancement and washout

Fig.3: Fat containing Hepatocellular carcinoma in a 50 year male patient, images A,B C&D Non contrast, arterial & portovenous phase respectively

Metastases

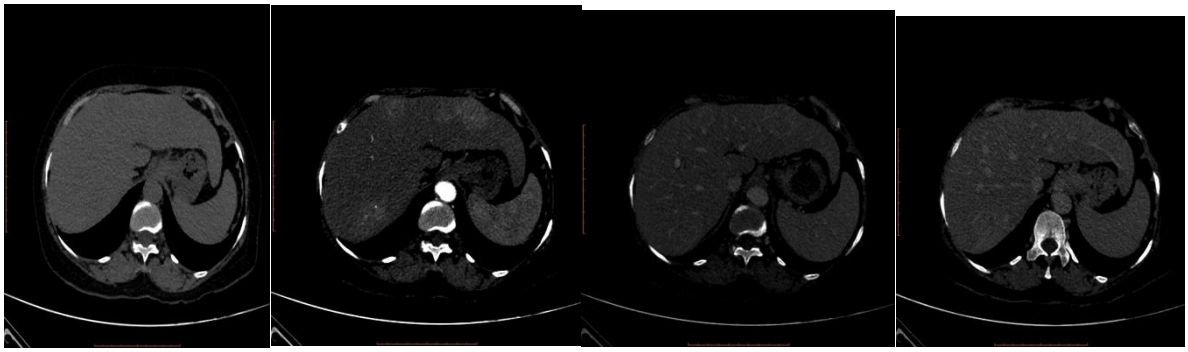

Fig. 4: Hypervascular metastasis from ca stomach in a 69 year female patient, images A, B, C & D non contrast, arterial portovenous & delayed phase respectively showing multiple isodense lesion in both lobe with homogenous arterial enhancement

Fig. 5 : Hypovascular metastasis from ca GB in a 65 year female patient, images A, B & C non contrast, arterial& portovenous phase respectively showing multiple hypodense lesions in right lobe with peripheral enhancement

Intrahepatic Cholangiocarcinoma

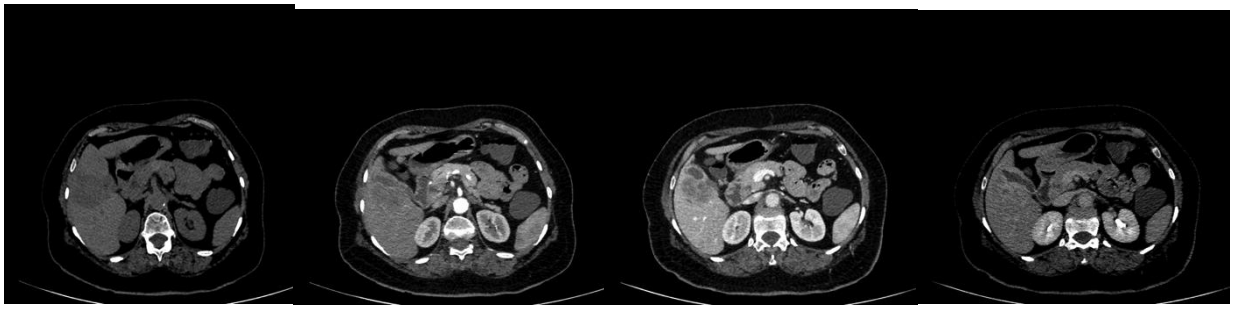

Fig. 6: Intrahepatic cholangiocarcinoma in a 38 year female patient, images A, B, C & D non contrast, arterial portovenous & delayed phase respectively showing hypodense lesion with mild arterial & delayed central enhancement and IHBR dilatation

Biliary Cystadenoma and Cystadenocarcinoma

Fig.7: Biliary Cystadenoma in a 55 year female patient, images A,B&C Non contrast, arterial & portal phase respectively showing multiloculated cystic lesion with enhancing septations

Hepatoblastoma

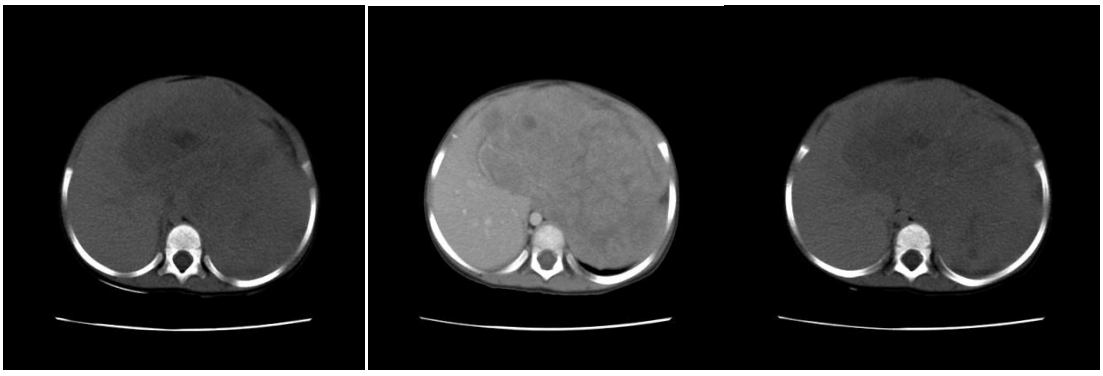

Fig.8 : Hepatoblastoma in a 4 year female patient, images A, B& C Non contrast, arterial & delayed phase respectively showing large heterogeneous enhancing lobulated mass showing no contrast retention on delayed phase

Epitheloid Hemangioendothelioma:

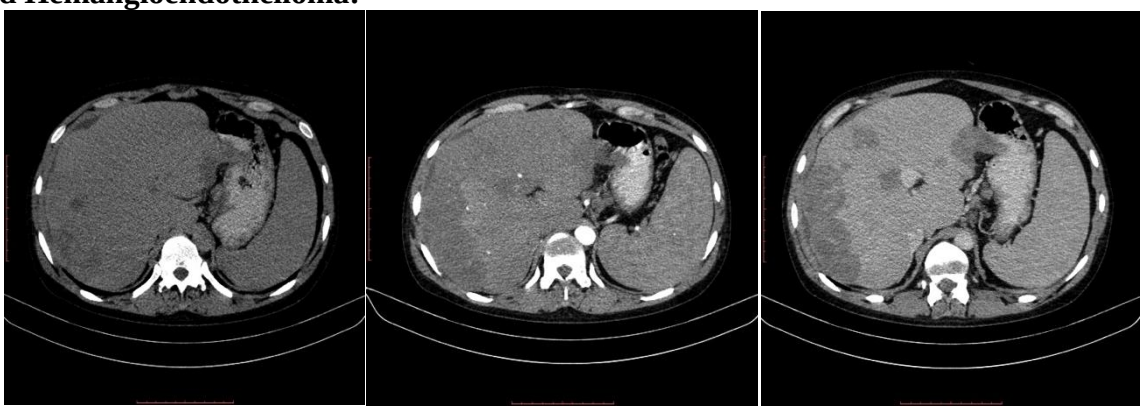

Fig. 9: Epithelioid hemangioendothelioma in a 35 year male patient, images A, B&C Non contrast, arterial & portovenous phase respectively showing multiple subcapsular hypodense lesion with mild enhancement

Discussion

Out of 120 patients referred from various clinical departments a total of 20 patients were excluded. 8 patients were excluded as USG features suggested abscess, 6 patients had USG features suggestive of hydatid cyst and 6 patients had USG features suggestive of simple cyst of liver.

Therefore a total of 100 cases were included in the study.

In our study 100 Patients, who were clinically suspected of having focal hepatic lesions or lesions detected by ultrasound were included. The age group of the subjects ranged from 3 to 92 years. Study group compromised males as well as female in equal proportion i.e. 50 (50%) male and 50 (50%) females. Most lesions were found in the age group of 41 to 50 with 23 patients, followed by 51 to 60 with 19 patients.

Out of 100 patients 92 had hypodense appearing, 7 isodense, 1 mixed density and none hyperdense appearing tumours on non-enhanced CT (NECT). At least 10 HU of difference in attenuation is required for a lesion to be visualized. Such tumors were typically those with a density differing from that of liver because of necrosis, cystic changes, vascularity and fluid content, or calcification. Tumors lacking these characteristics are not sufficiently different in density from liver to be detected on unenhanced CT scans.

In our study many lesions were not satisfactorily identified on NECT images and were better appreciated on contrast enhanced CT studies. Contrast enhanced studies detected tumours in all 100 patients. Unenhanced scans have lower sensitivity for identification of small lesions because of difficulty in differentiation from unopacified vessels or biliary dilatation, which may be difficult even with contrast- enhanced CT available for comparison.Thus, the IV contrast material is added to increase the inherent contrast differences between the liver and the tumour, and show enhancement patterns in different phases pertaining to blood supply. NECT detected areas of calcification in tumours or hepatic parenchyma in 1 patient of biliary cystadenoma.

Arterial phase of study helped in detecting multiple tumours, which were inconspicuous on NECT, portal venous phase images suggesting significant arterial supply. In our study we detected HCC, metastases as malignant hypervascular tumours. Many of these tumours become isodense on portovenous phase of study.

In patients with hypervascular malignancies, detection of small lesions especially if solitary is important because these lesions are more likely to be resectable or respond to therapy than are large lesions. These are consistent with few studies, which reported advantages of arterial phase in detection of tumours.[5,9]

Out of 100 patients we detected 21 (21 %) cases of HCC. The peak incidence was noted in 51-60 years age group. Overall HCC showed male preponderance i.e. out of 21 cases, 17 (81%) male patients and 4 (19%) female patients. Observation is consistent with tumour demographics.[2] 13 (61.9%) cases showed peak enhancement in arterial phase with rapid wash out in portovenous phases.

Oliver & co workers reported that the combined review of hepatic arterial and portovenous phases detected 98 % of lesions, where as review of each phase alone detect 76 and 81% lesions respectively.[15]

Metastases were the commonest tumour detected in our study. Out of 100 patients, 45(45 %) had metastases with peak incidence in 41-50 years age group.

Metastases were slightly more common in males i.e. 24 (54.3%) patients. Rest 21 (46.7%) were female patients. 35(77.8%) cases had multiple metastatic lesions and 10 (22.2%) were solitary lesions with known primaries. No specific lobar predilection was noted. Out of these 45 cases, hypervascular metastases were detected in 8 (17.8%). These tumours showed enhancement in the arterial phase, and were isodense on portovenous and delayed phased images. Out of 8 cases of hypervascular metastases 3 cases had hypervascular secondary metastases from neuroendocrine tumor of stomach, 2 cases from carcinoma thyroid, 1 case from carcinoma stomach, 1 case from GIST and 1 case from chondrosarcoma.

In addition to detection of HCC, metastases other tumours that were detected on arterial phase images were hemangiomas, intrahepatic cholangiocarcinoma, hepatoblastoma, focal

nodular hyperplasia, epithelioid hemangioendothelioma, biliary cystadenoma and cystadenocarcinoma.

In Porto-venous phase hepatic parenchyma depicted peak enhancement, thus rendering multiple tumours readily visible. In our study, 18(18%) cases of hemangiomas, 10(10%) cases of intrahepatic cholangiocarcinoma were detected on portovenous phase images. Out of total 45 cases of metastases 37 cases of hypovascular metastases were detected on portovenous phase images.

Foley and co workers,[11] Francis and co workers,[12]have proven in their respective studies the efficacy of portovenous phase in detecting hypovascular tumours.

Delayed phase images were acquired after a delay of 7-10 minutes after contrast injection. Hemangiomas depicted peripheral nodular enhancement in arterial phase with persistent centripetal filling in portovenous and delayed phases. 9 out of 10 cases of intrahepatic cholangiocarcinoma depicted contrast enhancement in the delayed images. Out of 21 cases of HCC, 1 case depicted isodensity to hepatic parenchyma on delayed phase images, rest 20 cases of HCC revealed hypodensity relative to hepatic parenchyma.

Delayed images helped in detection of hemangiomas, cholangiocarcinoma pertaining to their blood supply.

Keogan et al[13] have stated in their respective studies that delayed phase images are helpful in better delineation of certain pathologies like cholangiocarcinoma and certain HCC's.

Hemangiomas were the most common benign tumour detected in our study i.e. 18 (18%) cases out of total 100 cases. Female sex predilection was noted i.e. 11 cases in female and 7 cases in male out of 18 cases. In our study 12 (66.7%) hemangiomas were solitary lesions and 6 (33.3%) presented with multiple lesions. A giant hemangioma was detected in a 30 years female patient with size measuring 18x18x23 cm. One case of diffuse hepatic hemangiomatosis (DHH) was detected in a 30 year male showing multiple ill defined hypodense lesion in right lobe of liver showing enhancement in arterial phase and centripetal filling in portovenous phase.

Intrahepatic cholangiocarcinoma constituted 10 (10%) of total 100 cases. 7 cases occurred in female patients and 3 cases in male with age group of 31-80 years. 9 out of 10 cases depicted delayed contrast enhancement in delayed images.[13,14] Intrahepatic biliary radical dilatation was noted in 5 cases and capsular retraction in 3 cases.

Out of 100 patients, F.N.A.C was done 83 patients. The results of F.N.A.C. matched the diagnosis given by triphasic hepatic studies. Out of these 83 cases, HCC was diagnosed in 21 cases, ICC in 10 cases, FNH in 1 case, EHE in 1 case, hepatoblastoma in 1 case, biliary cystadenoma in 2 cases and cystadenocarcinoma in 1 case and metastasis in 45cases which correlated with radiological diagnosis.

During the course of the study we overcame 3 different cases of hepatic tumours in pediatric age group, which did not fit the CT triphasic study protocol because in these cases contrast was injected manually and in present study it was injected by automatic pre-programmed pressure injector. Out of these 3 cases, 2females and 1 male patient was noted with ages of 3-4 years. One case of metastases to the liver was noted from wilm's tumour as primaries. One case of HCC of liver was detected in a 3 years male child.

One case of hepatoblastoma was noted in a 4 years female child. The tumour revealed heterogenous enhancement in arterial phase and portovenous and no contrast retention on delayed phase images. Hepatoblastoma is the most common congenital hepatic malignancy and occurs within first three years of life with male predilection 3:2.

Clinical application

Multidetector Computed Tomography in correlation with triphasic hepatic studies an excellent non-invasive investigation of detecting, characterizing and staging liver tumours. Best characterization of lesions from arterial,

portovenous and delayed phases. It helps to reduce the number of biopsies in patients. MDCT gives excellent tumor characterization, additional features such as ascites, portal vein thrombosis, IVC thrombosis, primary source of malignancy, secondaries in the abdomen, splenomegaly, pleural effusion and bony metastases can be evaluated so staging of tumor can be done which is helpful in planning surgery, image guided interventions, neoadjuvant chemotherapy and further management. Follow up studies can suggest remission, residual or recurrent tumour.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee.

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