

Role of Ultrasound And Multiphase Contrast Enhanced Computed Tomography in The Evaluation of Hepatobiliary Neoplasms

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Abstract:

Aims And Objectives: To demonstrate the role of USG and triple phase CE-MDCT in accurate diagnosis, staging of hepatobiliary neoplasms and to study their epidemiology, risk factors and imaging findings.

Materials And Methods: It was a hospital based, observational, descriptive and cross sectional study with a sample size of 120 cases during the period of 2 yrs. in the department of radio diagnosis, VIMSAR. Patients referred to our department with symptoms and imaging findings s/o malignancy were included. Non-neoplastic pathologies were excluded from the study. The patients were subjected to USG with Doppler, MDCT and FNAC.

Results: Of the total 120 cases, the distribution was Liver metastasis- 45 cases, Carcinoma gall bladder-35, hepatocellular carcinoma – 20, Cholangiocarcinoma- 14, Hemangioma- 5, Hemangioendothelioma -1 case.

Conclusion: The fact that most of the hepatobiliary neoplasms are malignant should be kept in mind. Malignant lesions constituted 95% of the cases. Liver metastasis was the most common liver tumor and carcinoma GB was the most common biliary tumor. Both USG and CECT are highly sensitive and specific and often complementary. Ultrasound with doppler should be the initial modality because of its real time high resolution images, cost effective nature. Regular ultrasound and CT screening programs in high risk patients like cholelithiasis, cirrhosis can help in early detection of malignant change.

Keywords: Hepatobiliary neoplasms, Ultrasound, Computed tomography

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I. Introduction

Tumors of the liver and biliary tree, mainly hepatocellular carcinoma and cholangiocarcinoma, are the second leading cause of cancer related death worldwide. Recent developments in biomarkers and imaging modalities have enhanced early detection and accurate diagnosis of these highly fatal malignancies. Notable differences exist between Asian and Western regions in guidelines on surveillance, diagnosis of hepatobiliary tumors, which reflect differences in the epidemiological and etiological factors underlying the large disease burden in Asia¹. The most common adult malignant liver tumors are HCC, metastases to the liver, fibro lamellar HCC, epithelioid hemangioendothelioma (EHE), and angiosarcoma. Benign liver tumors include focal nodular hyperplasia, hepatic adenomas, and hemangiomas. Biliary tract malignancies include cholangiocarcinoma (CCA), both intra- and extrahepatic, gallbladder cancer and cancer of the ampulla of Vater. Benign biliary neoplasms include biliary cystadenoma, biliary hamartoma, and granular cell tumors. The epidemiology, risk factors, imaging features and effectiveness of ultrasound and CT scan in the diagnosis of hepatobiliary benign and malignant masses will be discussed. There are large number of cases being referred to the radiodiagnosis department with the complaints of abdominal pain, jaundice and mass per abdomen. Major problem is that detecting and characterization of focal liver masses in all standard non-invasive imaging modalities are less sensitive than generally perceived. These sensitivity problems are such that the focal hepatic lesions are frequently missed with one modality, then detected with another². This justifies the use of ultrasound and CT scan as complementary investigations in our study.

II. Material S And Methods

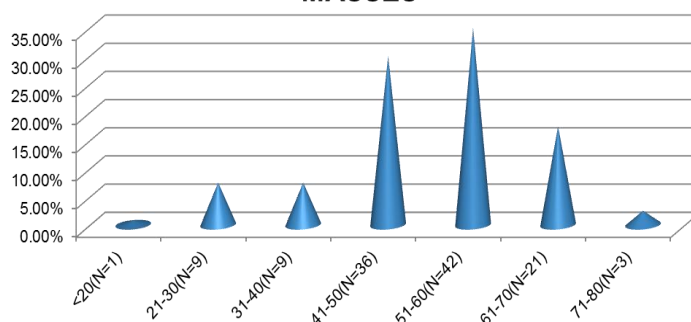
The study is a hospital based study conducted in VIMSAR, Burla, Dist- Sambalpur, Odisha, during the period of December 2015 to November 2017. It was an observational, descriptive and cross sectional study. The sample size is 120 cases with patients being referred to our department with abdominal pain, jaundice, mass per abdomen and abdominal distension and having imaging findings consistent with neoplasm and patients with a known history of a primary neoplasm to screen for metastatic deposits in liver. When in doubt the patients were subjected to FNAC and the imaging suspicion of neoplasm was cross verified.

Patients who were pregnant, allergic to contrast media, pathologies like simple hepatic cyst, diffuse fatty infiltration, infective pathologies like hepatic abscess, hydatid cyst were excluded from the study. Patients with end stage liver disease, coagulopathy, gross ascites in whom pathological intervention cannot be done. Patients with raised urea and creatinine in whom contrast administration is contraindicated. The patients were subjected to ultrasound with colour Doppler using Philips HD 7 colour Doppler, Computed tomography using Siemens Somatom Emotion scanner and ultrasound guided FNAC/Biopsy.

III. Results

Epidemiology

AGE DISTRIBUTION OF HEPATOBIILIARY MASSES



Most of the hepatobiliary neoplasms presented between the age group of 41-60 years (65%). 65% cases of HCC and carcinoma gall bladder were noted in the age group of 41-60 years. 64% cases of cholangiocarcinoma were noted in the 51-60 age group. 60% of hemangiomas were found in 31-40 year-younger age group

There was a slight female predominance (55.63%) overall in the distribution of hepatobiliary neoplasms. However individually there is male predominance in hepatocellular carcinoma and slightly in cholangiocarcinoma. Female predominance was noted in metastasis, carcinoma gall bladder and in benign neoplasms like hemangioma. The most common symptom in hepatobiliary masses overall is abdominal pain (33.3%) followed by abdominal distension (27.5%) and jaundice (23.3%) and the least common symptom is fever (3.3%). Jaundice was the predominant symptom in cases of cholangiocarcinomas (98%). Most hemangiomas (95%) were asymptomatic except a giant hemangioma which presented with mass abdomen

Pathological distribution:

The most common pathology was liver metastasis. Benign tumours constituted very less percentage (5%). Haemangioma was the most common benign tumor identified.

Staging of malignant hbn:

The observation in our study was that most commonly the hepatobiliary neoplasms presented in stage IV (51.4%) f/b stage III (19.2%). Carcinoma gall bladder presented majority in stage III/IV (72.9%). Extrahepatic cholangiocarcinoma in our study presented early in stage I/II (92.85%) due to CBD obstruction. Presentation of HCC was variable in our study with majority cases in Stage IV (45%) and in Stage I (30%).

Hepatic neoplasms:

Malignant neoplasms:

Liver metastasis:

Hypoechoic (59.2%) liver metastasis constituted the most common followed by hyperechoic and target pattern. Necrotic was the least common. Nodular metastatic disease (92.5%) was the most common pattern observed. Most of the liver metastasis were hypovascular (61.1%) on CECT followed by scirrhous pattern (21%) and hypervascular (14%). Most common source of liver metastasis was from the hepatobiliary source (35%) followed by Gastrointestinal source (14.7%). Most of the malignant metastatic deposits (80%) in our study had a hypoechoic halo.

S.No.	Source Of Metastasis- Primary Neoplasms	No Of Cases	Percentage
1.	Carcinoma Gall Bladder	11	20.3%
2.	Hepatocellular Carcinoma	9	16%
3.	Breast	4	7.4%
4.	Pancreas	4	7.4%
5.	Ovary	4	7.4%
6.	Stomach	4	7.4%
7.	Unknown Primary- Needs Evaluation	4	7.4%
8.	Lymphoma	2	3.7%
9.	Carcinoma Colon	2	3.7%
10.	Lung	2	3.7%
11.	Gist,Cholangio Ca,Small Intestine,Thyroid,Prostate,Testis,Retroperitoneal Mass, Melanoma Of Anal Canal	8(1 Each)	14.4

The sensitivity and specificity of ultrasound in the detection of liver metastasis was 95% and 96% respectively. CECT was superior in the detection of additional number of metastasis and in assessing the vascularity pattern. The sensitivity and specificity was 98% and 92% respectively.

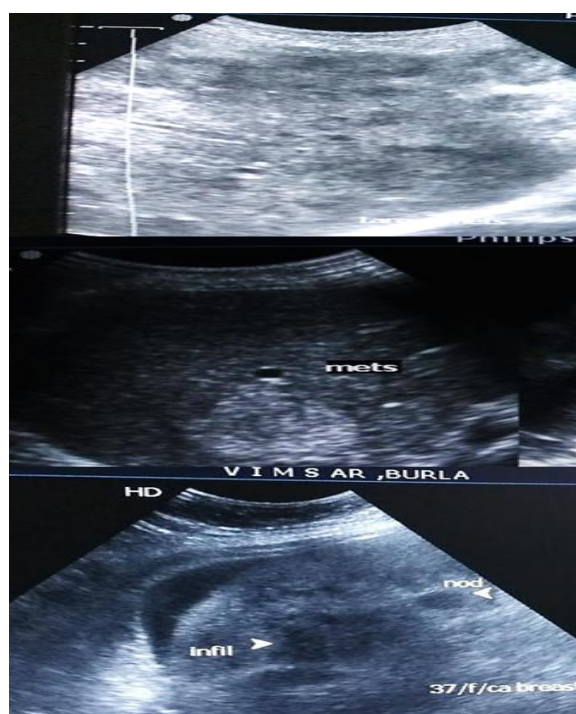
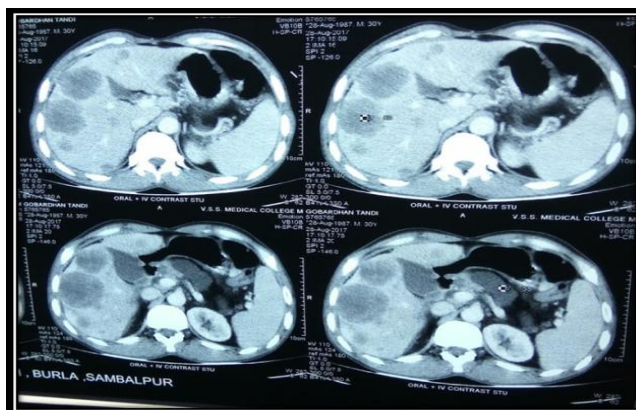


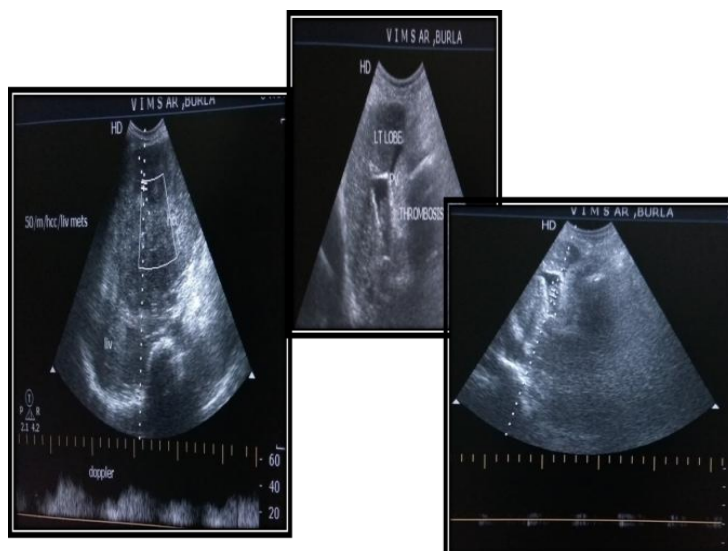
Fig showing target metastasis in a case of carcinoma pancreas at the top, echogenic liver metastasis in case of carcinoma colon in the middle and infiltrative and nodular hypoechoic metastatic deposits in as case of carcinoma of breast, below.



CT scan figure showing scirrhus metastatic deposits in a case of carcinoma pancreas. The deposits took rim enhancement in the arterial phase followed by centripetal filling in the delayed phase due to the fibrotic nature of the metastatic deposits

IV. Hepatocellular Carcinoma

Alcoholism (75%) and cirrhosis (45%) were associated with the majority of cases of HCC. Single nodular pattern (50%) was the most common imaging morphological pattern of HCC in ultrasound and CT. Multinodular HCC (45%) was most commonly found in patients with cirrhosis. Most of the HCC (90%) were heterogeneously hypoechoic in ultrasound and were localised to the right lobe of the liver. Ultrasound with Doppler that showed arterial flow on colour doppler was highly sensitive and specific with values of 88% and 86% in the diagnosis. Complications included portal vein thrombosis (25%), ascites, necrosis (15%) and fatty degeneration of the tumor. CT scan was effective in the confirmation of diagnosis as in all the cases showed arterial phase enhancement followed by rapid washout in the portal venous phase and demonstration of capsule in the equilibrium phase. The sensitivity and specificity was 85% and 100% respectively. Also, CT scan was more effective in the diagnosis and differentiation of HCC from regenerative nodules in cirrhotic liver and in staging.



USG shows a heterogeneously hypoechoic mass in liver with arterial flow on colour Doppler and the same case also showed portal vein thrombosis with internal vascularity suggesting a malignant thrombus.

Benign tumors of liver:

Hemangioma was the most common and was most commonly (90%) located in the RT lobe of liver. In CECT they all showed peripheral nodular enhancement in arterial phase followed by gradual centripetal filling in the delayed phase. There was one case of a giant hemangioma which showed necrosis and a central scar and incomplete filling on contrast administration. Infantile hemangioendothelioma in our case presented with cardiac failure, distension of abdomen. On ultrasound multiple hypoechoic nodules were identified which showed internal vascularity. On CT scan the nodules were shown to take enhancement as per the contrast changes in the aorta.

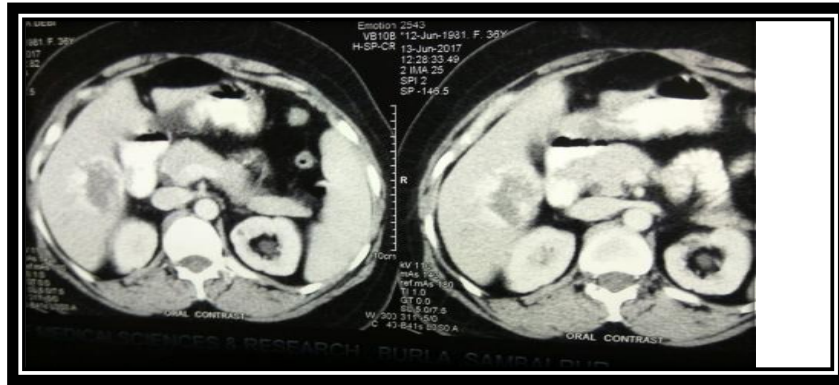


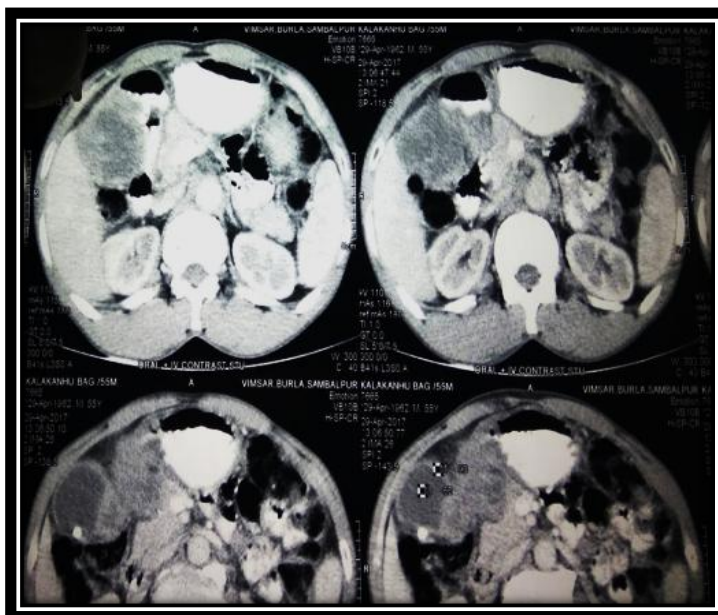
Fig showing Hemangioma in the Right lobe of liver in segment 6 taking nodular discontinuous enhancement in the arterial phase followed by filling and isodensity in the delayed phase

Carcinoma gall bladder:

Mass forming type (52%) was the most common imaging appearance of carcinoma gall bladder and polypoidal (19.5%) type was the least common. Most common location of gall bladder carcinoma was from the fundus (60.8%) and the least common was from the neck (13.0%). Most cases of carcinoma gall bladder took mild enhancement (82.6%) in CECT in arterial phase and delayed enhancement. Less percent of cases especially polypoidal type (17.3%) showed intense enhancement in the arterial phase. Calculus disease (65%) and female gender (60%) contributed to the major risk factors for carcinoma gall bladder. Ultrasound was better in delineating the presence of stone and polypoidal growths while CT scan was better in cases where the wall could not be assessed due to acoustic shadowing caused by calculus. CT scan was also better at delineating the mass forming type.



Figure showing ultrasound and CT scan images of carcinoma of gall bladder of mass forming type and exophytic invasion of duodenum.



Hilar and distal cholangiocarcinoma were the most common anatomical locations (35.7% each) of cholangiocarcinoma. The most common morphological pattern of cholangiocarcinoma is mass forming type (78.5%).

V. Discussion

Liver Metastasis And Usg Echogenicity Findings

Hypo echoic (59.25%) liver metastasis constitute the most common followed by hyperechoic (18.25%) and target (14.81%) pattern. necrotic is the least common. Similar findings have been noted in other studies carried out by **Jain AK et al**¹⁸ **Viscomi GN et al**¹⁹. Nodular metastatic pattern is the most common pattern observed. Infiltrative pattern was observed only in a minority of cases in carcinoma breast. **Suchanan et al**²⁰ also observed that diffuse parenchymal metastasis is an unusual pattern of liver metastasis and can be seen in cases of metastatic adenocarcinoma of breast. Cystic metastasis was observed in cases of carcinoma ovary. A case of necrotic metastasis was observed in a case of retroperitoneal mass. Calcific metastasis was observed in cases of metastatic thyroid carcinoma and in GIST. Similar findings were noted by **Gregory et al**²¹. Hyperdense metastasis was observed in only one case of metastatic malignant melanoma. Most of the malignant metastatic deposits (80%) had a hypoechoic halo. Similar findings have been documented in Diagnostic ultrasound- Rumack 4 th edition

Liver Metastasis And Their Ct Vascularity

All the cases of liver metastasis in our study washypodense except in one case of metastatic melanoma where it was hyperdense on CT scan. **Gregory T Sica et al**²² also observed that most metastases are revealed as low or isoattenuating masses on CT. In our study, Most of the liver metastasis were hypovascular (61.1%) and hypervascular was 14.8% and scirrhou pattern was 21% on CECT. Scirrhou type metastasis with a central necrosis, rim enhancement in arterial phase and delayed centripetal filling was noted in cases of primaries from the gastrointestinal tract. **Gregory T sica et al**²² noted that most metastases are hypovascular and during the arterial phase show a complete ring of enhancement. Hyper vascular metastases have diffuse enhancement. **Gregory T sica et al**²² also noted that metastases may fill in (centripetally) with contrast material over time

Liver metastasis and their source of primary:

Our findings are that hepatobiliary cancers contributed to 35%, GI source(stomach, small intestine, colon and rectum) contributed 14.7%, breast, pancreas, unknown primary each to 7.4%, lung, lymphoma each to 3.4%. The less common sources were from malignancies like melanoma, GIST, cholangiocarcinoma, small intestine, thyroid, prostate. The most common cause of metastasis however was from the hepatobiliary cancers which contributed to 35% followed by gastrointestinal source. **GhassanKhabbach et al**¹ noted that the most common sites of primary malignancies that metastasize to the liver are gastrointestinal tract cancers (colorectal cancer, pancreatic cancer, gastric cancer, esophageal cancer, etc.), breast cancer, lung cancer, genitourinary cancers, and melanoma. **Ackerman et al**¹³² noted that the liver is one of the most common organs to be involved with metastatic disease, which arises most frequently from primary sites in the colon, breast, lung, pancreas, and stomach.

Risk factors for hcc:

Cirrhosis and alcoholism (40% and 75%) were the major risk factors. Other risk factors were male gender, HBV infection(5%).HBV infection was however noted in less number of cases in our study. Studies have found risk factors as in **PremashisKar's study**²³ "The most important factor responsible for the development of hepatocellular carcinoma in the predominant north Indian population is chronic Hepatitis B virus infection, with tumors developing more often in a cirrhotic (76%) than in a non-cirrhotic liver has been reported in a prospective comprehensive study from the Indian subcontinent. Alcohol consumption has been implicated as a risk factor for developing HCC in many studies.

Hcc And Their Usg Ct Morphology

Single nodular pattern(50%) was the most common imaging morphological pattern of HCC in ultrasound and CT followed by multinodular(45%) and diffuse(5%) patterns. Study by **Fasani P et al**²⁴ in their study also noted that "One hundred twenty-nine (72%) patients had a single tumor nodule detected by US and 49 (28%) patients had multinodular disease" suggesting that single nodular was the most common morphological form of HCC. Most of the HCC (90%) were heterogeneously hypoechoic in ultrasound and were localised to the right lobe of the liver. **Reuss J et al**²⁵ however identified hyperechoic as the most common pattern. Ultrasound with Doppler that showed arterial flow on colour doppler was highly sensitive in the diagnosis. Similar findings were noted by **Omata et al**²⁶. Complications included portal vein thrombosis(5%), ascites, necrosis(15%) and fatty degeneration of the tumor.

There was one case of giant HCC which showed central necrosis. One case (5%) showed fatty degeneration of the tumor. CT scan was effective in the confirmation of diagnosis as in all the cases showed arterial phase enhancement followed by rapid washout in the portal venous phase and demonstration of capsule in the equilibrium phase. Also CT scan was more effective in the diagnosis and differentiation of HCC from regenerative nodules in cirrhotic liver and in staging. Similar findings were noted by **Choi B I et al**²⁷. Multinodular disease (45%) was found in patients with cirrhosis. this coincides with **Fasani P et al**²⁸.

Carcinoma gall bladder:

In our study, Mass forming type (52%) was the most common imaging appearance and polypoidal (19.5%) type was the least common. Most common location of gall bladder carcinoma was from the fundus (60.89%) followed by body (27.3%) and the least common was from the neck (13%). **Deshmukh et al**³⁰ also found similar morphological type distribution as "Four patterns of gallbladder cancer have been described on CT scan: (a) a polypoid mass within the gallbladder lumen (15–25%), (b) focal wall thickening, (c) diffuse wall thickening (20% gallbladder cancers), and (d) a mass replacing the gallbladder (40–65%)." **Lim KS et al**³¹ found that Gallbladder cancer may arise in the gallbladder's fundus (60%), body (30%), or neck (10%). Polypoidal type was better assessed by ultrasound whereas the wall thickening type with calculus and acoustic shadowing was better assessed by CT scan where it was difficult to assess with ultrasound. CT scan was also better at delineating the mass forming type. Similar findings were noted by **Baron R L et al**³². Most cases of carcinoma gall bladder took mild enhancement in CECT in arterial phase and delayed enhancement(82.6%). Less percent of cases especially polypoidal type showed intense enhancement in the arterial phase (17.3%)

Yun E J et al³³ noted that Gall bladder carcinoma are usually hypodense on unenhanced CT with up to 40% showing hypervascular foci of enhancement equal or greater than that of the adjacent hepatic parenchyma. Contrast enhancement may be retained in fibrous stromal components of gallbladder carcinoma during the portal venous and delayed phases. **Tiffany et al** noted that appearances on CECT can include a low-attenuation mass, enhancing mass with ill-defined borders, eccentric gallbladder wall thickening or a fungating mass. Calculus 65%, female gender 60.8%, chronic cholecystitis 32.6% were the major risk factors in our study.

Pandey M et al³⁴ also noted similar risk factors for the occurrence of carcinoma gall bladder. Liver infiltration-52.1%,metastatic lymphadenopathy-28.2%,liver metastasis-23.9%,dilated IHBR-10.8%,ascites 6.5% were the major associated features in our study.. Liver infiltration was the most common finding and ascites was the least common. Prevalence of similar findings in varying percentage was noted such as cystic nodes(62.5%),liver metastasis(55%),extension to CBD(45%) and ascites(32.5%),liver infiltration(30%) in another study by **Abdul Qayyum**³⁵ in a high incidence belt in Karachi, Pakistan. **Levy AD et al**³⁶ also noted that "Adjacent organ invasion, primarily involving the liver and biliary obstruction is often present at diagnosis. Periportal and peripancreatic lymph nodes, hematogenous and peritoneal metastases may also be seen"

VI. Conclusion

The fact that most of the neoplasms in hepatobiliary system is malignant should be kept in mind while investigating the patients. Ultrasound should be the initial modality in investigating hepatobiliaryneoplasms due to its high sensitivity, cost effective and non-invasive nature. Ultrasound is superior to CT in cases of stricture

forming cholangiocarcinoma, noting the presence of polypoidal type carcinoma GB and in detecting the presence of stone disease. CECT scan is superior in detecting metastasis that otherwise missed in ultrasound and in noting the presence of lymphadenopathy, extent of the tumor and for staging. It is also superior to ultrasound in assessing the vascularity pattern of HCC which could be a powerful tool for non-invasive diagnosis.

Overall both ultrasound and CT scan are highly sensitive and specific investigations in the investigation of hepatobiliary neoplasms with their own advantages and disadvantages. Ultrasound is non-invasive, real time investigation that could act as a powerful screening modality and also aids in procedures like FNAC . CT scan often adds information that is complementary to ultrasound and helps in preoperative staging. Therefore it is justified to use both of these investigations together for accurate diagnosis.

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