Ultrasonography and computer tomography evaluation of hepatocellular carcinoma with cytohistopathological correlation

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Abstract

The prevalence of hepatocellular carcinoma (HCC) in Bangladesh is 35% among all liver diseases. Sonographic examinations were performed for the evaluation of 38 cases of HCC; then, CT examinations were done of these cases subsequently. Expert opinion was taken in each case for both modalities. Age, sex, clinical features, location of the hepatic lesion, multiplicity, echo-character, CT density, and, contrast enhancement were evaluated in all cases. Histocytopathology reports were collected from the patients and were correlated with the ultrasonography and CT findings. Thirty five cases were detected as HCC on ultrasonography and 36 cases in CT scan. In ultrasonography, most of the lesions (82.9%) were found in right lobe, maximum lesions (45.7%) were hypoechoic and lesion showed mosaic pattern in 68.6% cases, lateral shadowing in 34.3% and posterior acoustic enhancement in 45.7% cases. Significant difference found between mosaic pattern and lateral shadowing (p<0.05). On CT scan, majority of lesions (50%) were hypodense, 91.7% lesions were contrast enhanced. Pattern of enhancement was mostly heterogeneous. Both of the modalities found sensitive but CT was found more sensitive, specific and accurate than ultrasonography in detecting HCC.

Introduction

Hepatocellular carcinoma (HCC) causing an estimated 1 million deaths in the world per year. Its incidence in developing country is high. It is the third most malignancy among all types of cancers. Epidemiological study shows that HCC is very common in Asia and Sub-Saharan Africa and uncommon in developed countries[1, 2]. In developing countries, incidence rate is two to three-fold higher than in developed countries. Excess liver cancer incidence among men compare to women is universal[2]. It is also found that HCC has an increasing incidence during the last century[3, 4]. In Bangladesh its prevalence is 35% among all liver diseases[5]. Study shows HBV contribution 47% in causation of HCC[5] and HCV accounts for 56%[6]. Cirrhosis of liver also is a major (18.75%) contributor to HCC in Bangladeshi population[5]. This is similar to other studies in Himalayan sub-continent[7-10].

Significant advances in cross sectional imaging modalities like ultrasonography and CT now allow not only detection but often non-invasive charac-terization of focal and diffuse hepatic processes. Several studies were undertaken regarding the sonographic or CT evaluation of HCC. The sensitivity of real time sonography for detection of small HCCs has been established[11, 12].

Ultrasonography had the highest detection rate (91.2%) for HCC <3 cm in diameter compare to CT (63.2%). For HCC 3-5 cm in diameter, the difference in detection rate becomes smaller which is 92.9% for ultrasonography and 81.8% for CT[13].

For HCC ≤2 cm in diameter delectability rate for ultrasonography is 52% and that of contrast CT is 56%. For HCC ≤3 cm in diameter delectability rate for ultrasonography is 85% and that of contrast CT is 100%[14].

As surgical resection is the most effective treatment of HCC, it needs early detection. Prognosis of HCC is extremely poor because of the difficulty in early detection. But small HCC discovered by a mass screening program have a very good prognosis when successfully resected. Therefore periodical follow up of high risk patients by imaging

techniques is essential for the early detection of HCCs.

Among the modern imaging modalities, ultrasonography and CT scan was used to detect and evaluate HCCs. This study also evaluate whether ultrasonography can effectively used, in detection and follow up of case of HCC, as screening modality.

Materials and Methods

This prospective study was carried out in the Department of Radiology and Imaging, BSMMU, Dhaka from July 2004 to June 2005 based on an ethically cleared approved protocol. Thirty eight patients having complaints suggestive of HCC from 24 years to 70 years of age of either sex with raised serum alpha-fetoprotein beyond 20 ng/ml were included in this study. All patients were informed about the nature, objectives and procedure of the study in understandable language. Written informed consent was taken with the assurance of keeping the personal information concealed. A pre-tested questionnaire was used for data collection. Patients were evaluated by detailed history, clinical examination with emphasis on hepatobiliary system. Sonographic examination was performed for the evaluation of HCC. Then CT scan was done of the same patient, subsequently. Expert opinion was taken in each case for both the modalities.

Ultrasonographic technique: Every patient had been fasting for 8-10 hours previous to sonographic examination. Ultracarbon tablets were given for minimizing abdominal free gas. Ultrasonography intervention was performed by Sonoline Adora machine (SEIMENS) with 3.5 MHz curvilinear transducer. Scanning was performed with the patient in a supine, right and/left anterior oblique and/ right lateral decubitus position. Patient was asked to hold his/her breath at different phase of respiration and sagittal, transverse and oblique scans were done through sub costal, and intercostal spaces, in a symmetrical fashion to screen the whole liver. Number, site, nature, echogenicity, lobar distribution of the lesion were recorded.

CT technique: CT scan was done after US detection of the HCC. Scan was done by third generation helical CT machine (Hitachi/W2000). CT obtained in cranio-caudal direction with the following parameters- 165 effective mA, 120 KVp, 1:1.5 pitch, collimation- 5 mm, effective section thickness 3-5 mm at 5-10 mm interval. IV injection was given by 18G needle in ante-cubital vein. Contrast was used Iopamiro 60 ml. CT was interpreted by the researchers' panel and reviewed by professors of the department. Number, nature, density (after and before contrast), and lobar distribution of the lesion was recorded.

Cytopathology technique: Ultrasonography guided aspiration from the lesion was done by 18G needle under full aseptic precaution. Then the aspirate spread in a glass slide and fixed in absolute alcohol. Slides then sent for laboratory examination. The Papaniculaus' stain is done and examined under microscope.

Age, sex, clinical features, location of the lesion, multiplicity, echo character/CT density and contrast enhancement were evaluated in all cases. Data were tabulated and analyzed by SPSS by using computer. Cyto-histopathology reports were correlated with the ultrasonography/CT findings. Sensitivity, specificity, accuracy, along with positive/negative predictive values of both modalities was calculated by standard statistical formulae.

Results

Among 38 patients, the mean (±SD) age was 50 (±13.69) years. No significant age group preponderance was noted for HCC incidence. There were 32 males and 6 females. Male female ratio was 5.3:1. In this study, highest number of HCC patients (34.2%) was small scale businessman. Cultivator (23.7%), housewife (15.8%), serviceman (10.5%) and miscellaneous (15.8%) profession were also included in this study. No significance preponderance between different occupation groups was noted. Among studied patients, most frequent symptom was upper abdominal pain (73.7%) followed by (right) abdominal mass (57.9%). Ascites (31.6%), anorexia (26.3%), weight loss (23.6%) and fever (21.2%) were also found.

Among 38 cases, 35 cases were detected by ultrasonography as HCC. Most of the patients got right lobe lesions (82.9%). Lesions in left lobe were in 11.4% and in both lobes in 5.7% cases (Table I).

Table I: Location and numeral of HCC

	Ultrasonography (n=35)	CT (n=36)
Location		
Right Lobe	29	29
Left Lobe	4	4
Both Lobes	2	3
Numeral		
Unifocal	25	25
Multifocal	10	11

Maximum lesions (71.4%) were found unifocal; 10 (28%) lesions were multifocal.

Hypoechoic lesions (45.7%) top the table. In 13 patients (37.1%) lesion showed mixed echogenicity and in 6 (17.2%) patients' lesions were hyperechoic (Table II). Mosaic pattern and lateral shadowing was characteristic in 24 (68.6%) and 12 (34.3%) cases respectively; whereas 16 (45.7%) cases showed posterior acoustic enhancement. Significant difference is noted between mosaic pattern and lateral shadowing (z=2.1; p<0.05).

In CT evaluation, 36 cases were detected as HCC. Twenty nine (80.6%) patients got lesions in right lobe. Lesions in left lobe were found in 4 patients. Lesions in both lobes of liver were found in 3 cases. Maximum (25 cases) lesions were observed unifocal where as multifocal lesions were detected in 11 patients. Eighteen patients got hypodense lesion (Table II). Ten lesions showed mixed density. After injection of contrast agent 33 (91.7%) lesions were enhanced, which was mostly heterogenous. Three (8.3%) lesions were un-enhanced.

Comparing both the modalities in detecting HCC with cyto-histopathological reports (Table III), it was found that, sensitivity, specificity, accuracy, positive predictive value and negative predictive value for ultrasonography were 94.5%, 100%, 94.7%, 100% and 33.3% respectively. Sensitivity, specificity, accuracy, positive predictive value and negative predictive value for CT were 97.3%, 100%, 97.4%, 100% and 50% respectively.

Table II: Distribution of HCC patients by pattern of lesions

Echogenicity/ Density	Ultrasonography (n=35)	CT (n=36)
Hypo	16	18
Iso	0	2
Hyper	6	6
Mixed	13	10

Table III: Comparison of ultrasonography and CT with histo-cytopathological findings

		Histocytopathology	
		Positive	Negative
Ultrasonography	Positive	35	0
	Negative	2	1
CT	Positive	36	0
	Negative	1	1

Discussion

The purpose of the study was the determine accuracy of ultrasonography and CT in detection and evaluation of HCC. As the patients of HCC have rapidly deterioration courses, early detection is essential for surgical treatment[15]. Early detection of HCC has improved with non invasive imaging modalities, such as ultrasonography, CT and magnetic resonance imaging.

Ultrasonography is one of the useful tool for detecting focal liver diseases and its advantages over other modalities in early detection and characterization of HCC. It is safe, cheap, easily available, can be done rapidly and repeatedly without any radiation hazards. Real time imaging is also possible.

CT is quite valuable in diagnosing and evaluating HCC. However, the presence of isodense tumor should always by kept in mind false positive examination may result from very small lesion, low contrast between tumor and surroundings liver tissue or due to technical failure. In this study there are two false negative in ultrasonography and one in CT. With the spiral CT diagnostic decision tree for the management of HCC has dramatically changed[16]. Ultrasonography, CT, magnetic resonance imaging techniques seem to have a strong potential to improve detection and characterization techniques seen to have a strong potential to improve detection and characterization of HCC[30]. CT has been highly useful in detecting liver tumors and determining their extent[17].

In this study, out of 38 cases 35 were diagnosed as HCC by ultrasonography and 36 cases were diagnosed by CT. Right lobe of the liver alone involved in 82.9% cases in ultrasonography and 80.5% cases in CT. In ultrasonography 11.4% lesions detected in left lobe, which was 11.1% in CT. Ultrasonography detects 5.7% lesions in both lobes whereas with CT 8.3% cases are detected.

Saad et al 1996 found 59% right lobe lesion and 23% left lobe lesion. This study is not similar to our findings, probably because of variation in patient selection[18].

In ultrasonography 71.4% cases found as unifocal lesion, where as in CT 69.4% lesions were found unifocal. Ultrasonography detected 28.6% multi-focal lesions; CT showed 30.6% lesions as multifocal. Yoshida et al 1987 in an ultrasono-graphy study found 68.8% as unifocal lesion[19]. Sarder et al 1997 found 71.4% unifocal and 27.6% multifocal lesions[20]. Colombo et al., 1991 found 71% HCC lesion as unifocal in sonography and

28% as multifocal[21]. Our study is more or less similar with these studies.

Types and patterns of echogenicity is an important characteristic of tumor, which helps in detection and differentiations of HCC from other hepatic masses. Tanaka et al., 1993 studied 23 patients of HCC, sonographically. They found 26.1% hypo-echoic, 60.8% complex or mixed and 13.04% hyperechoic[22]. Giorgi et al., 2004 found 60.8% hypoechoic tumors in sonographic scan of HCC patients[23]. Tanaka et al., 1993 found HCC lesion hypoechoic in less percent than our study but Giorgi et al., 2004 found more that us. This may be due to lesion size.

In our study 50% lesion were hypodense, 27.7% were mixed, 5.6% were isodense, and 16.7% were hyperdense. Total 91.7% cases were enhanced after contrast injection.

In a CT study with 13 HCC patients by Saad et al., 1996, 76% lesions were hypodense, 7.6% were hyperdense[18]. In another CT study with 51 HCC patients. Valls et al., 2003 found 88% of HCC nodules enhanced at arterial phase[24]. Our study findings were close to the findings of other researchers.

An ultrasonography study of HCC 64 patients Yoshida et al., 1987 found mosaic pattern in 65.6%, posterior echo-enhancement in 53.1% and lateral shadowing in 32.8%[19]. In our study, mosaic pattern is found in 68.6% cases, posterior echo-enhancement in 45.7% cases and lateral shadowing in 34.3%. Our study was in alignment with Yoshida et al.

In our study, sensitivity, specificity, accuracy, PPV and NPV for ultrasonography were 94.5%, 100%, 94.7%, 100% and 33.3% respectively. Sensitivity, specificity, accuracy, PPV and NPV for CT was 97.3%, 100%, 97.4%, 100% and 50% respectively.

Sinagawa et al., 1984 found overall Ultrasono-graphy sensitivity in detecting HCC is 92.2% which is closely similar to our findings. They found CT sensitivity 73.2%[13]. But Giorgio et al., 2003 found CECT sensitivity 91.9%[23]. Snow et al., 1979 found CT sensitivity 96%, specificity 86%, accuracy 91% and ultrasonography sensitivity 75%, specificity 50%, and accuracy 90%[17].

Ultrasonography and CT have been used as modality for screening and evaluation. In regular survillance program it is found that, 75% to 90% of HCCs occur as a single lesion less than 5cm. The sensitivity of ultrasonography for detecting small HCC ranges from 55%-85% and specificity is between 90%-94%. The sensitivity and specificity of CT in detecting HCC varies from size to size of the lesion. Sensitivity of CT is greater than 90% for tumors greater than 1 cm in size. In general, sensitivity of contrast enhanced CT ranges from 53% to 95%. CT scan specificity in detecting HCC is approximately 94%[25]. Sensitivity, specificity, accuracy for CT and ultrasonography found in our study were in alignment with other studies.

CT is found more sensitive and accurate. But ultrasonography is the modality which is easily available in most areas of the country. As a screening modality ultrasonography may be used but for proper characterization of the hepatic lesion CT is necessary.

Authors' contribution

HWH: Study planning, design, data collection, compiling, analysis and manuscript writing.

ShA: Study planning, design, data collection and analysis.

SA: Study planning, design and data collection.

MNI: Study planning, design, and data collection.

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