

*Original Article*

## Role of Ultrasound in the Diagnosis of Hepatocellular Carcinoma in Patients with Chronic Liver Disease

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### *Abstract*

**Background:** Hepatocellular carcinoma (HCC) is a common cancer in humans. Its mortality ranks third among human malignancies. Cirrhosis of liver is a major contributor to hepatocellular carcinoma, about in 80% of the affected individuals. Fine needle aspiration cytology (FNAC) of the liver which is a minimal invasive procedure is essential to sort out primary and secondary neoplasm of the liver. **Objective:** The aim of this cross-sectional study was to determine the accuracy of ultrasound for diagnosis of HCC in comparison with FNAC findings. **Materials and Methods:** This study was done in the Radiology & Imaging Department in Enam Medical College & Hospital, Savar, Dhaka in collaboration with the Department of Pathology of the same institution for FNAC correlation during October 2017 to November 2019. A total number of 50 patients with CLD with known hepatic mass, referred to the department were included in the study. Ultrasound was done with TOSHIBA using low frequency curvilinear probe of 3.5 MHz. USG-guided aspirations was performed using 18G needle under full aseptic measure. USG findings were validated by histopathology reports. Analysis was done by SPSS 19.0. **Results:** Mean age of the study population was  $58.6 \pm 10.9$  years, of whom 37(74%) were male and 13 (26%) were female. Mean size of the hepatic lesions was  $4.7 \pm 1.08$  cm. The lesions were characterized as iso-, hypo- and hyperechoic as compared with hepatic parenchyma. Doppler study shows both central and peripheral vascularity. Compared with FNAC findings, accuracy of USG findings was determined. Sensitivity of USG in detection of HCC was 97.7%, specificity was 66.7%, and positive prediction value 95.6% and negative prediction value 80%. **Conclusion:** Conventional USG can be used as a screening method in patients with CLD having hepatic masses. However, further workup is required for definite diagnosis.

**Key words:** Chronic liver disease; Hepatocellular carcinoma; Fine needle aspiration cytology; Ultrasound

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## Introduction

Liver cancer is the third most common cause of cancer-related death in the world.<sup>1</sup> Among liver cancers, the hepatocellular carcinoma (HCC) is the most common primary liver cancer.<sup>1</sup> It is two to four times more prevalent in men<sup>1</sup>, rarely occurring before the age of 40 years, with the peak incidence at approximately the sixth to seventh decade of life. According to the International Agency for Research on Cancer (IARC), it is the fifth most frequent malignant neoplasm in men and the ninth most frequent in women.<sup>2</sup> Overall prognosis is poor with the average mortality to morbidity rate of 0.95.

Approximately 90% of cases of HCC develop in the setting of chronic liver disease, most commonly approximately 60% of HCC cases in developing countries, while only up to 20% in developed countries.<sup>3</sup> Probability of developing HCC increases with duration of liver cirrhosis and 1/3 of patients with known cirrhosis will develop HCC in due life course.<sup>4</sup> Research conducted on large groups of patients with a long-term follow-up allowed to distinguish factors indicative of increased risk of HCC in patients with liver cirrhosis. Smoking is considered an independent risk factor in development of HCC.<sup>4</sup>

## Materials and Methods

This cross sectional study was carried in the department of Radiology and Imaging of Enam Medical College & Hospital, Savar, Dhaka in collaboration with the department of Pathology of the same institution for histopathological correlation during October 2017 to November 2019. This study was carried out on consecutively selected 50 patients ranging from 41–75 years having chronic liver disease with hepatic SOL and supported by ultrasonogram.

Ultrasonogram was performed by Toshiba Aplio 500 low frequency (3.5 MHz) curvilinear transducer. USG-guided aspiration was performed using 18G needle under full aseptic measure. Finally, ultrasonographic diagnoses of hepatic SOL were correlated with histopathological reports. The following outcome variables were observed.

Demographic: Age of the patient. Gender of the patients.

Imaging variables: Size of mass, site of lesion, type of lesion (solid/cystic), echogenicity, margin and Doppler findings.

The entire relevant data of patients were recorded in a predesigned structured questionnaire. Then all data were checked and edited after collection and entered into computer and analyzed with the help of SPSS (statistical package for social sciences) 19.0 version. For the validity of the study outcome sensitivity, specificity, accuracy, positive and negative predictive values were calculated out after confirmation of the diagnosis histopathologically.

## Results

A total 50 consecutive cases diagnosed clinically as patients with chronic liver disease having hepatic mass who attended the department of Radiology and Imaging of EMCH for ultrasonography during the period from 1<sup>st</sup> October 2017 to 30<sup>th</sup> November 2019 were selected for this study. Mean age of the patients was  $58.6 \pm 10.9$  years, ranging from 41 to 75 years. Among them 37 (74%) were male and 13 (26%) were female.

Sonographically hepatic SOLs were diagnosed as hepatocellular carcinoma having following criteria – irregular shaped in 86% cases, margin were irregular in 90% cases, hypoechoic in 80% cases and central necrosis in 92% cases. Doppler study shows central and peripheral vascularity in 84% cases (Table I).

On ultrasonography, lesions were diagnosed as HCC in 90.0% cases and other than HCC in 10%. Among other lesions FNH was found in 2.0%, metastasis in 4.0%, abscess in 2.0%, hemangioma in 2.0% cases (Table II).

On histopathology, lesions were diagnosed as HCC in 88.0% cases and other than HCC in 12%. Among other lesions metastases were found in 44.0%, abscess in 6.0%, hemangioma in 8.0%, FNH in 4.0% and Hydatid cyst in 4% cases (Table III).

Table I: Distribution of the respondents by ultrasonographic findings (n=50)

USG findings	USG diagnosis	Frequency	Percentage
<i>Shape</i>			
Oval and round	Others	7	14
Irregular	HCC	43	86
<i>Margin</i>			
Well circumscribed	Others	5	10
Irregular	HCC	45	90
<i>Echogenicity</i>			
Hypoechoic	HCC	30	60
Hyperechoic /anechoic	Others	10	20
More hypoechoic	HCC	10	20
<i>Lesion size</i>			
3 cm	8		16
4 cm	15		30
5 cm	15		30
6 cm	12		24
<i>Internal echoes</i>			
Homogeneous	Others	3	6
Heterogeneous	HCC	47	94
<i>Central necrosis</i>			
Present	HCC	46	92
Absent	Others	4	8
<i>Multiplicity</i>			
Solitary lesion	HCC	37	74
Multiple lesions	Other than HCC	13	26
<i>Doppler study</i>			
Central vascularity	HCC	42	84
Peripheral vascularity	Others	8	16

Table II: Distribution of the respondents by ultrasonographic diagnosis (n=50)

USG diagnosis	Frequency	Percentage
HCC	45	90
Metastases	2	4
Abscess	1	2
Hemangioma	1	2
FNH	1	2
Total	50	100.0

Table III: Distribution of respondents by histopathological findings (n=50)

Histopathological diagnosis	Frequency	Percentage
HCC	44	88.0
Abscess	1	2.0
Metastases	2	4.0
FNH	1	2.0
Hemangioma	1	2.0
Hydatid cyst	1	2.0
Total	50	100.0

Table IV: Distribution of HCC by ultrasonographic diagnosis and histopathological diagnosis (n=50)

Ultrasonographic findings	Histopathological findings		Total
	HCC	Not HCC	
HCC (45)	43 (95.5%)	2 (4.4%)	45 (90%)
Not HCC (5)	1 (20%)	4 (80%)	5 (10%)
Total	44 (88%)	6 (12%)	50 (100%)

Sonographically 45 lesions were HCC; out of these 43 (95.5%) were also proved HCC histopathologically, and 2 (4.4%) other than HCC. Out of 5 cases who were sonographically diagnosed as other than HCC, one (20%) was diagnosed as HCC and 4 (80%) were proved other than HCC (Table IV).

Ultrasonographic findings were correlated with histopathological findings to evaluate the ultrasonographic characteristics of Hepatic SOL. Table V shows that in diagnosis of HCC by ultrasonogram, sensitivity was 97.7%, specificity 66.7%, positive predictive value (PPV) 95.6%, negative predictive value 80% and accuracy was 94.0%.

Table V: Validity test for HCC (n=50)

	Value	95% CI
Sensitivity	97.7	89.9-99.7
Specificity	66.7	60.3-80.6
PPV	95.6	88.9-96.7
NPV	80	78.3-91.6
Accuracy	94	87.1-95.9

PPV = Positive Predictive Value, NPV = Negative Predictive Value

### Discussion

Chronic liver diseases are common in our environment. It usually affects all age groups with peak age in 5<sup>th</sup> and 6<sup>th</sup> decades of life.<sup>2</sup> In the present study patients' age ranged from 41–75 years with mean age of 58 years which is similar to Franca et al.<sup>5</sup> M : F ratio was 3 : 1 showing male predominance. Franca et al<sup>5</sup> and Gatphoh et al<sup>6</sup> observed male preponderance, while Siddalinga reddy et al<sup>7</sup> observed slight female preponderance. The neoplastic lesions were common between 40–70 years, similar to that of study by Rasania et al.<sup>8</sup>

On ultrasound, normal liver appears as homogenous echogenicity. Fatty liver shows increased echogenicity and decreased vascular architecture. Cirrhosis shows irregular nodular surface with heterogenous echotexture. HCC appears as isoechoic or slightly hypoechoic or hyperechoic lesion. Thus the appearances are variable. Necrotic tumors are typically heterogeneous.<sup>9,10</sup> Tumor masses, primary or secondary, undergo extensive necrosis, with the resultant radiologic image of the cavitory neoplasm mimicking abscesses, making radiologic diagnosis difficult. Here aspiration cytology plays an important role and ultrasonography enhances proper sampling and hence proper yield of material which will aid in accurate diagnosis.<sup>11</sup> In 2007, Rasania et al<sup>8</sup> discussed that FNAC is a very useful procedure for diagnosis of various hepatic lesions.

In the present study, on ultrasound examination, solitary space occupying lesions were seen in 42 cases (44.7%), multiple/multifocal lesions in 38 cases (40.4%) and diffuse lesions in 14 cases (14.9%). Lesions showed mixed echogenicity in 35 cases (37.2%), hypoechoic in 32 cases (34%) and hyperechoic in 27 cases (28.7%). Swamy et al<sup>12</sup> in their study observed solitary lesions in over half (51.38%) of his patients followed by multifocal lesions in 26 (36.12%) cases. All neoplastic lesions 44 cases (88%) in the present study were malignant which is same as 34 cases (89.4%) that observed by Khurana et al.<sup>13</sup>

It has become a routine practice over the past four years in our hospital for any patient suspected with hepatic lesion to undergo a FNAC technique. The USSG-FNAC technique localized the tumour so that a high precision of the lesion aspirate is obtained. USSG-FNAC of the liver plays more roles in diagnosis and classification of liver disease than ultrasound alone, as it requires greater precision to reach diagnostic accuracy.<sup>14</sup> Huber & Heuhold<sup>15</sup> recorded a sensitivity

of 93% and specificity of 87% of ultrasound guided-fine needle aspiration biopsy.

The present study observed to have sensitivity 97.7%, specificity 66.7%, positive predictive value (PPV) 95.6%, negative predictive value 80% and accuracy 94.0%. According to Naincy et al<sup>16</sup> found specificity (100%), sensitivity (97.61%), NPV (97.82%), PPV (100%) and diagnostic accuracy (98.85%). The studies of Yang et al and Bakshi et al have mentioned high values for FNAC for the diagnosis of SOL of liver which is comparable with observations of present study.<sup>17,18</sup>

The studies of Saem et al got a sensitivity of 66.7% and specificity of 85.18% for ultrasound in diagnosis of SOL of liver which is unparallel or incomparable with results in present study.<sup>19</sup> Kuo et al reported sensitivity of 78.4% which is low as compared to other published studies and present study.<sup>20</sup>

In another study by Tanaka et al<sup>21</sup> the overall sensitivity, specificity and accuracy of US was found to be 58.9%, 99.9%, and 99.3% respectively. In a study by Sbolli et al<sup>22</sup> 138 patients underwent ultrasound followed by fine needle aspiration biopsy. The diagnosis of HCC was obtained in 132 cases with sensitivity of 95.6% and specificity of almost 100% and in this study the sensitivity closely resembles to this study. In a study by Takayasu et al<sup>23</sup> the sensitivity of ultrasound was found to be more sensitive (86%) and less specific (82%) in diagnosing HCC. The overall accuracy of procedure in the present study was 94.0%, which was comparable to the rate of accuracy reported in literature (78% to 97.82%).<sup>2,14,24,25</sup>

The findings of the present study show that because of increased sensitivity conventional ultrasonography can be used as a screening tool in patients with chronic liver disease for surveillance purpose.

## References

1. Morris Sherman, Primary malignant neoplasm of the liver. In: James S. Dooley, Anna S.F. Lok, Andrew K. Burroughs, E. Jenny Heathcote (eds). *Sherlock's Diseases of the Liver and Biliary System*; 12<sup>th</sup> edn. New Jersey: John Wiley & Sons, 2011: 705–729.
2. Ahuja A, Gupta N, Srinivasan R, Kalra N, Chawla Y, Rajwanshi A. Differentiation of hepatocellular carcinoma from metastatic carcinoma of the liver – clinical and cytological features. *Journal of Cytology* 2007; 24 (3): 125–129.
3. Jemal A, Bray F, Mellisa M, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin.* 2011; 61(2): 69–90.
4. Naggada HA, Ahidjo A, Ajagi NA. Correlation between ultrasound findings and ultrasound guided FNAC in the diagnosis of hepatic lesions: A Nigerian tertiary hospital experience. *Int J Gastroenterol.* 2007; 5: 2.
5. Franca AVC, Junior JE, Lima BLG. Diagnosis, staging and treatment of hepatocellular carcinoma. *Brazilian J Medical and Biological Research* 2004; 37: 1689–1705.
6. Gathphoh ED, Gaytri S, Babina S, Singh AM. Fine needle aspiration cytology of liver: a study of 202 cases. *Indian J Med Sci* 2003; 57(1): 22–25.
7. Sidhalingreddy AS. Fine needle aspiration cytology of intra-abdominal lesions. *Journal of Clinical and Diagnostic Research* 2011; 5(3): 551–558.
8. Rasanía A, Pandey C L, Joshi N. Evaluation of FNAC in diagnosis of hepatic lesions. *Journal of cytology* 2007; 24(1): 51–54.
9. Talukder SI, Huq MH, Haque MA, Rahman S, Islam SM, Hussain GA et al. Ultrasound guided fine needle aspiration cytology for diagnosis of mass lesions of liver. *Mymensingh Med J* 2004; 13(1): 25–29.
10. Nasir TA, Banu NA, Hussain M, Begum AA, Ali H. Correlation of ultrasonographic findings with ultrasound guided FNA of liver lesion. *Bangladesh Med Res Council Bull.* 2001; 27(3): 84–89.
11. Wee A, Nilsson B, Yap I, Chong SM. Aspiration cytology of liver abscess, with an emphasis on diagnostic pitfalls. *Acta Cytol* 1995; 39(3): 453–462.
12. Swamy MCM, Arathi CM, Kodandaswamy CR. Value of ultrasonography guided fine needle aspiration cytology in the investigative sequence of hepatic lesions with an emphasis on hepatocellular carcinoma.

- J Cytol 2011; 28(4): 178–184.
13. Khurana U, Handa U, Mohan H, Sachdev A. Evaluation of aspiration cytology of the liver space occupying lesions by simultaneous examination of smears and cell blocks. *Diagn Cytopathol* 2009; 37(8): 557–563.
  14. Bell DA, Carr CP, Szyfelbein WM. Fine needle aspiration cytology of focal liver lesions: Results obtained with examination of both cytologic and histologic preparations. *Acta Cytol.* 1986; 30(4): 397–402.
  15. Huber K, Heuhold N. Rapid diagnosis of liver cancer by ultrasound-guided fine needle aspiration biopsy. *Cancer Detect Prev.* 1987; 10(5-6): 383–387.
  16. Naincy R, Arvind B, Deepika A, Akanksha W. Ultrasound guided fine needle aspiration cytology of space occupying lesions of liver. *Int J Res Med Sci* 2019; 7(1): 192–198.
  17. Yang GCH, Yang GY, Tao LC. Distinguishing well-differentiated hepatocellular carcinoma from benign liver by the physical features of fine-needle aspirates. *Mod Pathol* 2004; 17(7): 798–802.
  18. Bakshi P, Srinivasan R, Rao KLN, Marwaha RK, Gupta N, Das A, et al. Fine needle aspiration biopsy in pediatric space-occupying lesions of liver: a retrospective study evaluating its role and diagnostic efficacy. *J Pediatr Surg* 2006; 41(11): 1903–1908.
  19. SaemAM, Saha NK, Begum F, Hey AA, Islam N, Anam T. Fine Needle Aspiration Cytology in the Diagnosis of Focal Liver Lesions. *Journal of Histopathology and Cytology* 2017; 1(2): 110–115.
  20. Kuo FY, Chen WJ, Lu SN, Wang JH, Eng HL. Fine Needle Aspiration Cytodiagnosis of Liver Tumors. *Acta Cytol* 2004; 48(2): 142–148.
  21. Tanaka S, Kitamura T, Ohshima A, Umeda K, Okuda S, Ohtani T et al. Diagnostic accuracy of ultrasonography for hepatocellular carcinoma. *Cancer* 1986; 58(2): 344–347.
  22. Sbolli G, Fornari F, Civardi G, Di Stasi M, Cavanna L, Buscarini E et al. Role of ultrasound guided fine needle aspiration biopsy in the diagnosis of hepatocellular carcinoma. *Gut*, 1990; 31(11): 1303–1305.
  23. Takayasu k, Moriyama N, Muramatsu Y, Makuuchi M, Hasegawa H, Okazaki N et al. The Diagnosis of Small Hepatocellular Carcinoma: Efficacy of Different Imaging Procedures in 100 Patients. *Am J Roentogenol*, 1990; 155(1): 49–54.
  24. Guo Z, Kurtycz DF, Salem R, De Las Casas LE, Caya JG, Hoerl HD et al. Radiology guided percutaneous fine needle aspiration biopsy of the liver: Retrospective study of 119 cases evaluating diagnostic effectiveness and clinical complications. *Diagn Cytopathol* 2002; 26(5): 283–289.
  25. Edoute Y, Tibon-Fisher O, Haim SB, Malberger E. Ultrasound guided fine-needle aspiration of liver lesions. *Am J Gastroenterol* 1992; 87(9): 1138–1141.