

# Role of Fine Needle Aspiration Cytology on Abdominal Ultrasonography in the Diagnosis of Hepatobiliary Masses

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## ABSTRACT

**Aim:** To compare the diagnostic accuracies of ultrasound guided FNAC and ultrasound alone, considering histopathology as gold standard.

**Study design:** Cross Sectional study.

**Setting:** Histopathology Department, AIMCS, Lahore.

**Duration of study:** One year from July 22, 2012 to August 13, 2013.

**Methods:** Abdominal ultrasound, ultrasound guided FNAC and biopsy of 100 patients with clinical diagnosis of hepatobiliary masses were carried out.

**Results:** Histopathologically, 92 masses were malignant (35 metastatic carcinomas, 53 hepatocellular carcinomas (HCC), 03 gallbladder adenocarcinomas and one cholangiocarcinoma) and 08 were benign abscesses. Ultrasound diagnosed 51 cases as HCC, 35 as metastatic, 03 gallbladder cancers, 01 cholangiocarcinoma and 10 as benign. FNAC revealed 91 malignant (35 metastatic, 52 HCC, 03 gallbladder adenocarcinomas, 01 cholangiocarcinoma) and 09 benign (08 abscesses, and 01 benign hepatocytes only). FNAC accurately diagnosed almost all the cases. Ultrasound correctly diagnosed all gallbladder masses, cholangiocarcinoma, and many abscesses, metastatic tumors and HCC but labeled 02 benign abscesses as necrotic HCC, and 04 necrotic HCC as benign abscesses.

**Conclusion:** FNAC is superior to ultrasound alone in the diagnosis of hepatobiliary masses & with the help of cell block, it can even be used for the typing of tumors.

**Keywords:** Comparison, Ultrasound, Ultrasound guided-fine needle aspiration cytology Diagnosis, Hepatic lesions.

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## INTRODUCTION

Fine needle aspiration cytology is frequently used and entails placing a very thin needle inside the mass and extracting cells for microscopic evaluation<sup>1</sup>. FNAC is simple, quick, safe, tolerable, cosmetically acceptable, reliable and cost-effective method of determining histology<sup>2</sup>. It has a pivotal role, and is cost-effective tool for establishing tissue diagnosis as a primary investigative modality<sup>3</sup>. FNA-cytology can positively affect the surgical management. It can be utilized to select the patients for frozen section examination and can thus spare the patients from additional procedure of biopsy under separate anesthesia<sup>4</sup>. It is also helpful and accurate in follow-up of patients with a known malignant disease, thereby avoiding surgical intervention<sup>5</sup>. Cytological diagnosis is quite helpful in planning the management of many neoplastic diseases. With

ultrasonographic (USG) and computerized tomography (CT) guided FNAC, deep-seated lesions are being diagnosed more accurately and frequently<sup>6</sup>. Although clinicoradiological parameters themselves have certain limitations in diagnosing benign versus malignant lesions, in conjunction with guided fine needle aspiration they are very accurate and safe in diagnosing deep-seated mass lesions of abdomen<sup>3</sup>. FNAC is a useful technique in evaluating the liver masses especially malignant tumors<sup>7</sup>. The advantages of USSG-FNAC in the diagnosis of liver diseases cannot be overemphasized. The advantages of this technique are its high diagnostic accuracy and low cost, thereby rendering the older technique of blind percutaneous biopsy using a coarse needle obsolete. This procedure can also be used in diagnosing metastases to liver<sup>8</sup>. Most aspirates are performed to confirm suspected malignancy; however, recent technical refinements also allow characterization of many benign lesions especially when used in combination with information derived from clinical examination, laboratory tests, radiology and relevant serologic tests, e.g., alpha-fetoprotein (AFP) levels in cases of Hepatocellular carcinoma. The cytological confirmation of the malignancy thus obtained is very helpful for treatment

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planning and to determine the prognosis. FNAC cannot give precise information about the cell type and origin of the tumor, especially in cases of poorly differentiated tumors and is often not helpful in benign lesions, typing of lymphomas, and some very well-differentiated carcinomas e.g. HCC.

**MATERIALS AND METHODS**

The cross sectional study was conducted in the Department of Histopathology, Sheikh Zayed Hospital, Lahore which is a 600 plus bedded teaching hospital. The study comprised one hundred cases, judged clinically and with radiological evidence of mass in the hepatobiliary region. These cases were collected in a period of one year after approval of synopsis. Both males and females clinically judged and with radiological evidence of mass of more than 1 cm in the hepatobiliary region were included in this study. Patients with abnormality in the clotting profile were not included.

One Hundred cases of hepatobiliary masses judged clinically and proved radio- logically were analyzed. The fine needle aspiration cytology was done in Radiology Department by an expert radiologist under ultrasound guidance. An informed consent was taken, confidentiality ensured and the patients were explained about the purpose, procedure, risks and the benefits. The data collected was entered in SPSS 10.

The patient’s descriptive data was expressed as mean±Standard deviation. As the outcome variables, which were (tumor location, benign/malignant nature and histological type) diagnosed by ultrasonography, FNAC and histopathology are correlated with each other and also with histopathology, screening tests were applied. Sensitivity, specificity, positive predictive values, negative predictive values and diagnostic accuracy were calculated by applying their respective formulas. P value of <0.05 was considered statistically significant. Chi-square was used to compare my results with other studies.

**RESULTS**

A total of hundred patients were studied with a mean age of 55.5±14.3 years and range between 18 and 80 years. The peak age incidence was between 40 and 60 years age groups. The study revealed more males 71(71%) patients with hepatobiliary masses than females 29 (29%). Eighty percent of the patients presented with upper abdominal pain. Abdominal distension remained the most common clinical sign (66%) of the patients. The results of the ultrasound diagnosis and the USSG-FNAC as shown in (Table 1) were the same for gallbladder carcinomas and

cholangiocarcinoma. Out of 100 patients diagnosed by histopathology, 92 were malignant (35 metastatic carcinomas, 53 primary hepatocellular carcinomas (HCC), 03 gallbladder adenocarcinomas and one cholangiocarcinoma) and 08 were benign (two amoebic liver abscesses and 06 non-specific abscesses). The ultrasound diagnosed 51 cases as primary HCC, 35 as metastatic, 03 gallbladder cancers, 01 cholangiocarcinoma and 10 cases as benign (abscesses). The results of FNAC were 91 malignant (35 metastatic, 52 primary HCC, 03 gallbladder adenocarcinomas, 01 cholangiocarcinoma) and 09 benign (02 amoebic liver abscesses, 06 non specific abscesses, and 01 revealing benign hepatocytes only, probably regenerating nodule). Fine needle aspiration cytology accurately diagnosed all the cases except one well differentiated HCC. Ultrasound diagnosed the gallbladder masses, cholangiocarcinoma, abscesses, many metastatic and primary HCC correctly as FNAC, but labeled 02 benign abscesses as necrotic HCC, and 04 necrotic HCC as benign abscesses. Ultrasound (US) also confused multifocal HCC with metastatic lesions (diagnosed 02 multifocal HCC as metastatic and 02 metastatic carcinomas as Primary multifocal hepatocellular carcinomas). The primary hepatocellular carcinoma (Hepatoma) remained the commonest finding. Serum Alpha fetoprotein was elevated in 35(66%) out of 53 patients with HCC. Viral hepatitis (Hepatitis C-62.3%, Hepatitis B-37.7 %) remained the main etiological factors of Hepatocellular carcinoma in our study. Among the 35 metastatic tumors, adenocarcinomas were the most common. Seven were colorectal carcinomas, 05 gall bladder adenocarcinomas, 05 ampullary carcinomas, 03 breast carcinomas, 03 ovarian tumors, 03 lung carcinomas, 02 pancreatic adenocarcinomas and 02 prostatic adenocarcinomas. Four metastatic tumors were diagnosed as Non Hodgkin’s Lymphoma and 01 was diagnosed as spindle cell sarcoma. Fine needle aspiration cytology correctly diagnosed all adenocarcinomas, Non Hodgkin’s Lymphomas and spindle cell sarcoma. FNAC gave exact diagnosis of adenocarcinomas in cases where the primary neoplasms were known. In the remaining cases, differential diagnoses were suggested.

Table 1: Overall Results of U/S, FNAC and Histopathology

Hepatobiliary masses	u/s	FNAC	Histo- pathology
Primary Hepatocellular ca	51	52	53
Metastatic Neoplasm	35	35	35
Gall bladder carcinomas	03	03	03
Cholangiocarcinoma	01	01	01
Abscesses	10	08	08
Regenerating nodules (Benign hepatocytes)	0	01	0

## DISCUSSION

Hepatobiliary masses refer to the liver, gall bladder and bile ducts. Hepatobiliary tumors are abnormal growths occurring on or in the liver, bile ducts, and biliary tract, the tubes that carry bile from the liver or gallbladder to the small intestine. Tumors of the liver are classified as primary (originating in the liver) or metastatic (spread from another body organ to the liver). Metastatic tumors of the liver originate in the lung, colon, prostate, gallbladder, breast, pancreas, stomach or from skin (malignant melanoma). These metastases tend to gain access to the liver via the bloodstream, either through the portal vein or the hepatic artery. Hepatobiliary masses are common in our environment and it affects relatively all age groups with the peak age in the 4<sup>th</sup> to 6<sup>th</sup> decades of life. Male, female ratio is 2.5:1. It has become a routine practice over the past sixteen years in our hospital for any patient suspected with hepatic lesion to undergo ultrasound guided FNAC technique to localize the tumor so that a high precision of the lesion aspirate is obtained. The technique is done once or twice for most of the patients to obtain adequate aspirates for cytopathological diagnosis. Our study is focused on the role of ultrasound and fine needle aspiration cytology in the diagnosis of hepatobiliary masses. Our study was compared with similar studies conducted in Pakistan and abroad. The peak age incidence is between 40 and 60 years i.e. 68%. The mean age was 55.5±14.3 years and age range between 18 and 80 years. This is comparable to a study by Nggada in which the mean age was 47.04±14.24 and range between 14 and 75 years. This is also comparable to a study in Taiwan by Chen in which the mean age detected was 56±10. Regarding sex, our study is comparable with three other studies. In our study, hepatobiliary masses are more common in males (71%). The study by Nggada also revealed more male patients with hepatic diseases (80.9%) than females (19.1%). In the studies by Sharma and Das again, hepatobiliary masses are more common in males. As far as symptoms and signs of hepatobiliary masses are concerned, our study is comparable with the studies by Joshi and Pandey in which abdominal pain (82.8%) and abdominal distention were the main presenting features. In our study 80% patients presented with abdominal pain and 66% with abdominal distention. In our study serum Alpha-fetoprotein was elevated in 35 out of 53 patients with hepatocellular carcinoma i.e. in 66% of patients, which indicates that this screening test should not be used as the only test for screening and surveillance for hepatocellular carcinoma. This is comparable with studies by Yoon Tong and Lopez. The fact that

hepatocellular malignancies can also present without elevated serum AFP was also proved by another study by Tsui. In our study viral infection was the main etiological factor for hepatocellular carcinoma comparable with the studies by Amin But Qasmi and Joshi but in these studies Hepatitis B virus infection was more common than Hepatitis C virus. In our study the incidence of Hepatitis C was more as compared to Hepatitis B because of the recent increase in the incidence of Hepatitis C and its association with hepatocellular carcinoma worldwide especially in Pakistan, comparable to studies by Anwar Raja and Chen. Another study by Raza revealed a predominance of HBsAg in hepatocellular carcinoma from most Asian, African and Latin American countries, but anti-HCV predominated in Japan, Pakistan, Mongolia and Egypt. Primary hepatocellular carcinoma was the commonest tumor among hepatobiliary masses in our study, which is comparable with the study by Ngadda in which 43 out of 47 hepatic masses were primary hepatocellular carcinomas (hepatomas). This is also comparable with studies by Parvez and Molmenti in which Hepatocellular carcinoma (HCC) was the most frequent tumor of the liver in adults. Kwok-Chai in his study proved that metastatic tumors were the most common malignancies of liver. The reason for high incidence of primary hepatocellular carcinomas in our study is the increase spread of hepatitis B and C and the association of HCC with these viruses. The Gastroenterology unit of AMICS, Lahore is well recognized all over Pakistan and most of the patients with hepatic disease are referred here from different cities; this is another reason of increase incidence of hepatocellular carcinomas in our study. In our study, 35 cases were diagnosed as metastatic tumors, and among these most cases were metastatic adenocarcinomas. This is comparable with the study by Tsui and Das in which 43 out of 61 metastatic tumors were metastatic adenocarcinomas. Our study recorded a sensitivity of 98.9% and specificity of 100% of ultrasound guided FNAC, which is comparable with the study by Soyuer<sup>18</sup> in which sensitivity of FNAC for diagnosing hepatic malignancies was 99.5% and the specificity was 100%. This result is also comparable with studies by Jain and Metcalfe in which specificity and positive predictive value of FNAC were very high and sensitivity of FNAC was reported as 90-93%. A study by Ceyhan recorded high sensitivity, specificity and positive predictive value of FNAC and according to that study the diagnostic accuracy of FNAC for hepatic tumors approach 100%. The same study proved that the combine use of conventional cytological smears and cell block significantly improved the diagnostic and sub typing accuracy of

liver malignancies. Another study by Tsui proved FNAC a cost effective and safe procedure that could be employed to differentiate benign from malignant processes with accuracy rate as high as 96%. Chai in his study recorded very high specificity and positive predictive value of FNAC, but according to that study the sensitivity of FNAC varies widely between 76-93%. Regarding ultrasound, the sensitivity, positive predictive value, specificity and diagnostic accuracy of ultrasound in diagnosing hepatobiliary masses in our study were 95.6%, 97.7%, 75% and 94% respectively, comparable with the studies by Torzilli et al which reported high accuracy of imaging for HCC, with sensitivity of 100%. Another study by Pasanen reported sensitivity of 63% of ultrasound in diagnosing malignant extra-hepatic masses, but the sensitivity reached 100% in diagnosing intra-hepatic malignant lesions, positive predictive value reaching 96-99% and low negative predictive values ranging between 38-60%.

In our study ultrasound failed to discriminate between multifocal HCC and metastases in four cases which is comparable to a study by Sahani which reported that sensitivity of US for the detection of liver metastases varies from 40-70%. The main limitations of ultrasound noted in that study were high operator dependency, inability to detect lesions <1cm in size and low specificity. The specificity of ultrasound in our study was 75% comparable with study by Shahid R in which the reported specificity of ultrasound for benign lesions was 68.75%. On the other hand, the specificity of Ultrasound guided FNAC was 100%. In our study, out of 100, only three cases were of gallbladder mass and one was diagnosed as cholangiocarcinoma because the tumors of bile duct and gallbladder are relatively rare. This is also proved by study by Goldberg in which it is stated that cancers of the bile duct and gallbladder are rare. Ultrasound correctly diagnosed all these four cases; all of these were advanced cancers. Literature and several studies as the studies by Smits and Boberg proved that visualization is sufficient in more than 90% of cases for adequate diagnosis and staging of gallbladder cancers and cholangiocarcinomas. A few studies, however reported that the ultrasonographic diagnosis of early gallbladder carcinoma was not accurate enough, but ultrasonography was reaching a sensitivity of 70% to 80% for advanced gallbladder cancers. Ultrasonography no doubt plays an important role in

diagnosing hepatobiliary masses but it is obvious that the diagnostic accuracy of ultrasound may vary between institutions because of the variance in the local experiences and expertise, and because of the differences in the diseases. On the other hand, FNAC missed only one case of well differentiated HCC in our study.

## CONCLUSION

- Primary hepatocellular carcinoma was the commonest malignancy, followed by metastatic tumors of liver.
- Alpha fetoprotein was elevated in 35 out of 53 primary hepatocellular carcinomas (66%).
- Most of the patients (33) with primary hepatocellular carcinoma had hepatitis C.
- Both US guided FNAC and ultrasounds alone have high sensitivity, specificity, positive predictive values and diagnostic accuracies in diagnosis of hepatobiliary masses.
- Ultrasound guided FNAC is superior to ultrasound alone in the diagnosis of hepatobiliary masses & with the help of cell block it can be used for typing of tumors. However, the histological diagnosis remains the gold standard for any hepatobiliary mass.

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