

## Ultrasound Guided Fine Needle Aspiration (FNA) Cytology in Gall Bladder Lesions at Tertiary Care Centre - A 2 Years Study of 580 Cases

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### Abstract

Gall Bladder Carcinoma (GBC) is the most aggressive and most common malignancy of the biliary tract in the world. GBC is common in India and shows rising trend with 10 times more incidence in northern and north eastern region than Southern region. As most of the patients are diagnosed in the advanced stage of cancer, prognosis is dismally poor and early diagnosis is essential. We aim to study the importance of Ultrasound (US) guided Fine Needle Aspiration Cytology (FNAC) in the early detection and diagnosis of gall bladder malignancy in the suspicious cases of gall bladder lesions. A prospective cytomorphologic analysis of total 580 cases of suspected gall bladder lesions was conducted in the Department of Pathology, SMS Medical College, Jaipur, Rajasthan over a period of 2 years. US guided FNAC of the suspicious lesion was done and diagnosis was made on the basis of their cytomorphological features. The mean age of presentation was 54 years with male: female ratio of 1:2. The most common site for GBC was found to be Fossa (97.4%). According to nature of the smears, 73% were malignant, 18% unsatisfactory, 7% benign and 2% were suspicious. On cytomorphological diagnosis, Adenocarcinoma was found to be the most common of all malignant neoplasm (42%), followed by cholangiocarcinoma (9%), MEN (8%), metastatic (05%), adenosquamous (3%) and squamous cell carcinoma (1.5%). We concluded that US guided FNA is safe, quick and reliable procedure for an early diagnosis and pre therapeutic workup for gall bladder lesions.

**Keywords:** Gall bladder Carcinoma (GBC), ultrasound guided, fine needle aspiration cytology, adenocarcinoma, cytomorphological.

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### INTRODUCTION

Gall Bladder Carcinoma (GBC) is the most common malignancy of the biliary tract in the world. It is known to be the most aggressive cancer and is also said to be the fifth most common cancer of gastrointestinal tract worldwide [1]. Although relatively rare, Gall Bladder cancer is a notoriously lethal malignant neoplasm with marked variation in geographical and ethnic distribution. GBC is common in countries like Japan, India, Chile, Central Europe – Poland, Israel and southern Pakistan. In the Indian subcontinent, it is one of the most common causes of mortality in North India with most prevalence in the northern states of Bihar, Uttar Pradesh, Orissa, West Bengal and Assam [2].

In India, the incidence of gall bladder cancer in females ranges from 1.01/100000 to 10.1/100,000 which is two times higher than in men and indeed is reported to be the leading GIT malignancy in women in north Indian states with age adjusted incidence rate of

8.9/100,000 [1]. It is the most aggressive cancer of the biliary tract having shortest median survival time after diagnosis [3].

The associated risk factors in the development of GBC include female preponderance, gall stones, ethnicity, genetic susceptibility, lifestyle factors and conditions including chronic inflammation and infection.

The presenting complaints are generally vague and usually associated to other diseases such as cholelithiasis and cholecystitis. Patient mostly present in the advanced stage with complaints of constant pain palpable hard lump in the right hypochondrium, anorexia, cachexia, icterus, ascites and left supraclavicular lymphadenopathy with poor performance status. Due to such vague presentation and overlapping symptoms with many common entities, it is often neglected. Hence, the diagnosis is often made at an advanced stage.

Biochemical tests and tumor markers- CEA and CA 19-9 are of not important in early diagnosis of GBC as these are not specific for GBC. Various imaging tools available including Ultrasound (USG), Computed Tomographic (CT) scan, and Magnetic Resonance Imaging (MRI) with Magnetic Resonance Cholangiopancreatography (MRCP) and Magnetic Resonance Angiography (MRA) are used as required to detect structural changes of the gallbladder as well as help in assessment of hepatic reserve [2].

Ultrasound guided FNAC is very safe, reliable and cost effective procedure which can be used as a useful diagnostic tool in all cases of GB mass, so as to enhance early detection

The present study aims to add to the existing literature, the awareness of this potentially treatable disease, with special emphasis on the role of Ultrasound guided FNA in early detection, as most of the cases present late in the course of disease.

## MATERIALS AND METHODS

The present study was a prospective cytomorphologic analysis conducted in the Department of Pathology, SMS Medical College, Jaipur, Rajasthan from January 2016 to December 2017.

It included 580 cases of suspected Gall Bladder lesions.

All the cases had a clinical, biochemical or radiological suspicion of gall bladder malignancy. All FNAs were performed under ultrasound guidance as an outdoor procedure after work up for prothrombin time, platelet count and with informed consent, taken from each patient for FNAC.

US guided FNAC of the suspicious lesion was done using Spinocan needle 20G, attached to 20 ml of syringe. After withdrawing the needle, the aspirated material was expressed on pre-labeled clean slides and smeared. Few of the smears were air dried and then stained with May Grunwald Geimsa (MGG) and few were fixed with 95% alcohol and subsequently stained by Haematoxylin and Eosin (H&E). Both MGG and H&E stained cytology smears were available for examination in all cases. Diagnosis was made using cytomorphological features and analysed and tabulated according to age, gender, site and cytomorphological diagnosis.

The objective of the study was to determine the importance of US guided FNAC for the diagnosis of carcinoma gallbladder in the suspicious gall bladder lesions.

## RESULTS

In this study of 580 cases, the age of the patients ranged from 13 to 86 years with maximum

number of cases falling in the 5th decade and the mean age was found to be of 54 years. The present study showed higher female preponderance (394 cases, 70%) with male: female ratio of 1:2. The most common site for GBC was Fossa, comprising of 565 cases (97.4%), followed by neck, comprising of 11 cases (1.9%) and least common being fundus comprising of 4 cases (0.7%).

On the basis of the nature of smears, out of 580 cases, 73% were malignant, 18% unsatisfactory, 7% benign and 2% were suspicious.

On cytomorphological diagnosis, Adenocarcinoma was found to be the most common of all malignant neoplasm (42%), followed by cholangiocarcinoma (9%), Malignant Epithelial Neoplasm, MEN (8%), metastatic (5%), adenosquamous (3%) and Squamous cell carcinoma (1.5%).

The cytomorphological spectrum was categorised as-

Unsatisfactory smears were acellular or paucicellular or haemorrhagic (blood obscuring the cells) and did not show any malignant cells. There were 104 cases, which were grouped under unsatisfactory smears.

Benign showed presence of normal epithelial cells and inflammatory cells. 38 cases fall into the benign category.

Suspicious due to scant cellularity with only few clusters (2 clusters with <5 cells) showing atypical morphology with nuclear enlargement and hyperchromasia or there is pronounced secondary changes like necrosis, mucinous change, clotting or air drying artefact in the background. Our study had 14 such cases, which were reported as suspicious for malignancy.

Malignant Out of 580 cases, 390 cases were malignant accounting for 67.24% of all lesions. These malignant lesions were further divided into various subtypes histologically as-

Malignant Epithelial Neoplasm was considered when the subtyping of the malignant lesion was not possible due to absence of characteristic features. 45 cases were reported as Malignant Epithelial Neoplasm.

Poorly Differentiated Carcinoma showed high cellularity with poorly differentiated features of discohesive clusters or isolated dispersed cells having overlapping, bizarre nuclear features. 7 cases were diagnosed under this category.

Poorly Differentiated Adenocarcinoma- 16 cases were reported under this category showing focal

acinar pattern with high grade nuclear anaplasia and signet ring cells.

Adenocarcinoma was the most common malignant neoplasm encountered in the study with 242 cases (41.72%) out of total 580 cases. The smears were cellular showing clusters or acini or sheets of malignant cells showing hyperchromasia, nuclear enlargement and prominent nucleoli with scant to moderate amount of cytoplasm. Some cells also showed mucin in the cytoplasm.

Cholangiocarcinoma showed presence of clusters and sheets of cuboidal or columnar cells with varying degrees of nuclear enlargement and pleomorphism showing more than 10 proliferating ductules. 50 cases were reported as cholangiocarcinoma.

Adenosquamous carcinoma-18 cases were diagnosed as adenosquamous carcinoma which constitutes 3.10% of all the cases. Smears showed the features of both adenocarcinoma and squamous carcinoma.

Squamous Carcinoma comprised of dispersed isolated degenerated atypical cells with hyperchromatic, pyknotic nuclei and moderate to abundant amount of cytoplasm. 9 cases were labelled as squamous cell carcinoma, 1.55% of total cases.

Metastatic Carcinoma- 32 cases were metastatic with primary being in liver.

Miscellaneous- 5 cases were miscellaneous with 2 being neuroendocrine neoplasms, 1 case was reported as small round cell tumor, one was diagnosed as Undifferentiated carcinoma and 1 as Pleomorphic giant cell Adenocarcinoma of gall bladder.

**Table-1: Distribution of cases according to the location of lesion**

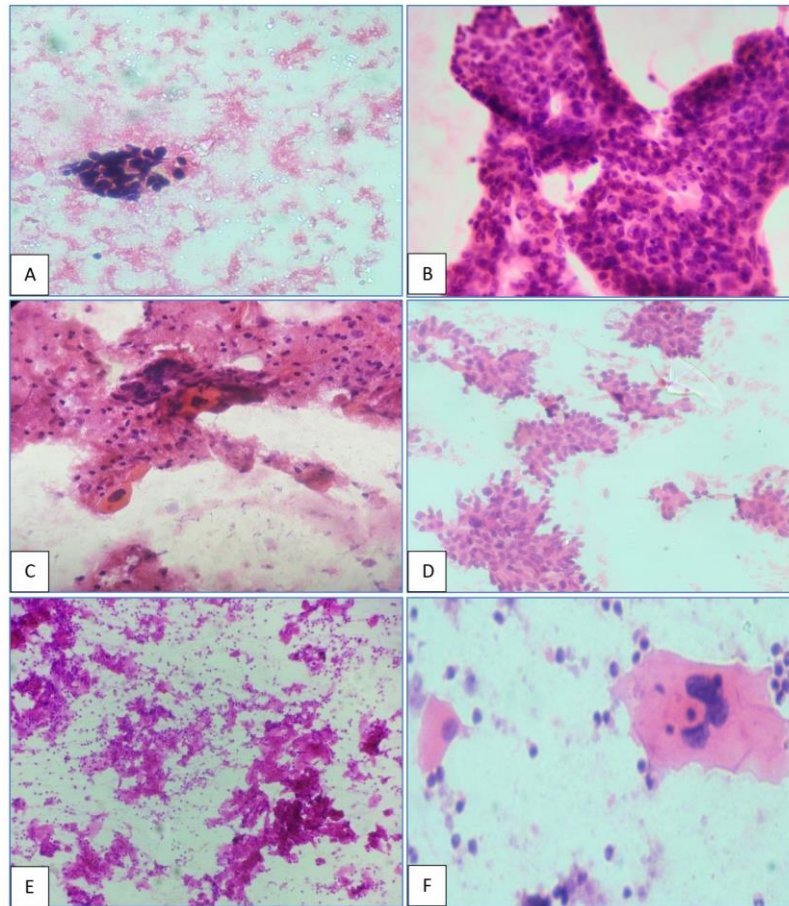
Site of lesion	Cases	Percentage (%)
Fossa	565	97.4
Neck	4	0.68
Fundus	11	1.89
Total	580	

**Table-2: Distribution of the cases according to the nature of smears**

Nature of Smears	No. of Patients	Percentage (%)
Unsatisfactory	104	17.9
Benign	38	6.55
Suspicious	14	2.41
Neoplastic/Malignant	394	73.14
Total	580	

**Table-3: Gender distribution of the cases according to the cytomorphological diagnosis**

Cytomorphological Diagnosis	Female	Male	Total %
Unsatisfactory	65	39	104(17.90%)
Benign	24	14	38(6.55%)
Suspicious	10	04	14(2.41%)
Malignant Epithelial Neoplasm	32	13	45(7.70%)
Poorly differentiated Carcinoma	03	04	07(1.21%)
Poorly differentiated Adenocarcinoma	11	05	16(2.75%)
Adenocarcinoma	178	64	242(41.72%)
Cholangiocarcinoma	34	16	50(8.62%)
Adenosquamous carcinoma	09	09	18(3.10%)
Squamous Cell carcinoma	06	03	9(1.55%)
Metastatic Carcinoma	18	14	32(5.51%)
Miscellaneous	04	01	05(0.86%)



**Fig-1: Photomicrographs of H&E stained smears of Gall Bladder lesions :- A) Low power view (100X) of Malignant Epithelial Neoplasm, B) High power view (400X) of Adenocarcinoma showing cells arranged in acinar pattern with nuclear enlargement and pleomorphism. C) Low power view (100X) of Adenosquamous carcinoma showing squamous cells intermixed with cuboidal cells and scattered neutrophils. D) Low power view (100X) of Cholangiocarcinoma showing acini and sheets of ductal cells. E) Scanner view (40X) of Squamous cell carcinoma showing clusters of squamous cells and F) presence of tumor giant cell.**

## DISCUSSION

GBC is the most aggressive cancer of the biliary tract with shortest median survival from the time of diagnosis because of lack of sensitive screening methods for early detection. Incidence of GBC is 10 times higher in northern and north eastern states of India. Although it is not recommended to perform FNAC for fear of developing biliary peritonitis, still we feel that for early and accurate diagnosis, this is a relatively safe and sensitive method and can prevent radiological overdiagnosis in inflammatory conditions. Importance of FNAC of gall bladder was recognised from 1990s.

In 1998, Das et al., [4] in a 5 year study of 82 cases shows the diagnostic utility of US guided FNAC in gall bladder lesions. They diagnosed 48 cases of malignancy, 12 cases of inflammatory lesions and 22 inadequate cases. Out of all malignancies, Adenocarcinoma was the most common malignancy with 83.3% which is consistent with our study in which Adenocarcinoma is the most common of all malignancies (61%). However, in our study the number

of unsatisfactory smears was high because many smears were prepared by clinicians.

In 2000, Krishnani et al., [5] in a retrospective 7 years study on diagnostic efficacy of FNAC in gall bladder lesions showed that overall sensitivity for detecting the carcinoma is 90.63% and specificity 94.74% [2].

In 2011, Roa et al [6] found squamous differentiation in 41(7%) cases out of 606 cases. Pure SCC constitutes only 8 cases (1%) [3]. In our study, squamous and adenosquamous carcinomas together forms 4% of total.

Rana et al., in 2015 studied 596 cases and evaluated the diagnostic application of US guided FNAC in preoperative diagnosis of gall bladder lesions and revealed malignancy in 462, 23 cases suspicious of malignancy, 23 inflammatory lesions, 29 negative and 56 cases were inadequate for opinion [1]. Our study revealed 424 cases of malignancy, 14 cases suspicious

of malignancy, 38 cases benign and 104 cases as unsatisfactory.

In 2017, Bhartiya R et al., [7] in the retrospective study of 3 years determined the accuracy of US guided FNAC of gall bladder lesions and classified them cytologically. The sensitivity and specificity was found to be 98.6% and 97.3% respectively.

In 2017, Kumar R et al., [8] in 5 years retrospective study of 791 cases of gall bladder malignancies showed adenocarcinomas as the most common malignancy with 96% cases and 26 cases with unusual malignancies were noted. Out of which 8 cases were of adeno squamous and 7 were squamous cell carcinoma, 9 were small cell neuroendocrine, one case each of undifferentiated and non hodgkins lymphoma. Our study also revealed adenocarcinoma as the most common malignancy with 41.72% of all the gall bladder lesions. In our study we also encountered some unusual and rare tumors like adenosquamous carcinoma in 18 cases, squamous carcinomas in 9 cases and 2 cases of neuroendocrine neoplasms, 2 cases of lymphoma and one case of pleomorphic giant cell adenocarcinoma.

US guided FNAC has an upper hand over open biopsy because it is an outdoor procedure and patient does not require any admission or general anaesthesia.

The overall prognosis of GB cancer is dismal, with median survival of less than 6 months and 5 year survival rate is 5%- 10% [9]. This is because most patients become symptomatic when they have an advanced disease.

The treatment guidelines include surgical resection with simple cholecystectomy or extended radical cholecystectomy with or without radiotherapy or chemotherapy. Palliative treatment is given for symptomatic relief in advanced cancer patients.

#### Limitations

We could not correlate with histopathology which is gold standard because nearly all the patients presented in advanced stage and were treated with radiotherapy or/and chemotherapy.

#### CONCLUSION

As the incidence of GBC is very high (10.1/100000) in India and owing to its late presentation, US guided FNAC plays an important role in early diagnosis and pre therapeutic workup and operative management.

Although US guided FNA is reasonably sensitive method for detecting GBC, the status of cancer has still not shown any significant improvement

in overall survival in the present century due to lack of sensitive screening modalities.

The future therefore will depend on research directed towards development of higher sensitive and specific screening strategies and relevant improved molecular understanding of underlying pathogenesis for which targeted therapy can be employed.

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