



Fine Needle Aspiration Cytology in Lesions of Gall Bladder - Experience in a Primary Care Setting

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Authors' contributions

This work was carried out in collaboration by both authors. Both authors have contributed in study design and analysis of the results. Author PT has managed the literature search and wrote the first draft of the manuscript. Both authors have read and approved the final manuscript.

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ABSTRACT

Aims: In certain regions of India, cancer of gall bladder (GBCa) is a common form of malignancy. In the Gangetic belt, its incidence is up to 10 times greater as compared to some other parts of the country. The aim of the present study is to study the diagnostic utility of guided fine needle aspiration cytology (FNAC) in patients of carcinoma of gall bladder. Whether use of this technique can help in segregating patients requiring palliative care only, was also analyzed. The demographic profile of these patients was also studied in a primary care setting.

Study Design: All patients referred with a gall bladder mass underwent guided fine needle aspiration procedure for purpose of establishing a morphological diagnosis. Ultrasonographic examination was used for cancer staging and delineating inoperable cases.

Place and Duration of Study: The study was conducted at Ama diagnostic centre, Lucknow, in collaboration with the department of Pathology, Integral Institute of Medical Sciences, Lucknow,

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India. The period of study is from August 2010 to March 2016.

Methodology: FNAC was performed under ultrasound guidance on all patients having a gall bladder mass. Clinical details of the patients were recorded and their demographic profile was studied.

Results: Forty five patients having a gall bladder mass underwent FNAC for diagnostic purposes. Adequate material was obtained in 44 patients. It was possible to provide a definite diagnosis in 38 cases (86.3% of cases). Adenocarcinoma NOS was the commonest diagnosis (86.8% of cases). Amongst patients with malignancy, 73.7% of cases were in advanced stage of the disease. Palliative care represents suitable treatment option in such patients in our clinical set up.

Conclusion: Utilizing guided FNAC, it was possible to provide a definite diagnosis of malignancy in 86.3% of cases. It was also possible to segregate patients requiring either definitive or palliative treatment.

Keywords: Cancer of gall bladder; adenocarcinoma gall bladder; aspiration cytology of gallbladder.

1. INTRODUCTION

Cancer of the gall bladder (GBCa) - although uncommon in many parts of the world – is a common malignancy in India [1]. Even within India, it shows marked regional variation. In females, it is about 10 times more common in North India as compared to southern parts of the country [2]. It is about 4 times more common in North Indian males as compared to their counterparts in southern parts of the country.

Of greater significance is the universally dismal prognosis of GBCa [3]. Primary nature of this malignancy and presentation of patients at an advanced stage of the disease is responsible for poor prognosis. Apart from medical resource deficiency and lack of awareness, reasons proposed for late presentation are - GBCa often remains asymptomatic for a long period of time, patients have non-specific symptoms or symptoms mimicking benign gall bladder disease. Correct diagnosis is suspected only after invasion of surrounding structures has taken place [4].

Now days, staging of cancer is easily feasible using non-invasive radiological and radio-isotopic techniques. Since survival of patients having GBCa in advanced stage is usually less than a year, realization of morphological diagnosis with provision of palliative care, often becomes the central objective for the clinician [5, 6]. Therefore delineating patients requiring definitive treatment from those needing palliative care only - at the level of primary medical care service - is an attractive option. Such an approach to patient management, apart from providing relief to the sufferer, helps in conserving scarce medical resources of the country.

Therefore the present study was planned to –

1. Study the utility of guided FNAC in diagnosing GBCa at the level of primary medical care service.
2. Analyzing whether use of guided FNAC helps in delineating two groups of patients outlined above.
3. Study the demographic profile of patients of GBCa presenting for FNAC.

2. MATERIALS AND METHODS

2.1 Study Area

The study was conducted at Ama diagnostic centre, Lucknow, in collaboration with the department of Pathology, Integral Institute of Medical Sciences and Research, Lucknow, India. The period of study is from August 2010 to March 2016.

2.2 Sample Collection

FNAC was performed under ultrasound guidance on all patients with a gall bladder mass that was clinically suspicious of malignancy. After explaining the risks associated with the procedure, a written consent was obtained from the patient. Prior to performing the procedure, the patient was investigated for any hemorrhagic diathesis. FNAC was performed using a 21 or 23 gauge needle attached to a 10 ml syringe. Skin overlying the site of aspiration was thoroughly cleaned to achieve asepsis. Under ultrasonographic (US) guidance, the needle was inserted into the lesion by the radiologist. All efforts were made to place the needle in the peripheral part of the lesion avoiding necrotic or hemorrhagic areas. The patient was asked to

withhold breath and aspiration was performed by the pathologist.

2.3 Laboratory Procedure

Aspirated material was smeared onto glass slides. Air dried smears for MGG stain and wet fixed smears for H&E and Papanicolaou stain were prepared. An initial on site evaluation of one smear was carried out using Leishman stain. If the aspirate was found inadequate, re-aspiration was performed in the same sitting. A maximum of three attempts were made to obtain adequate material. Every case was examined individually by both pathologists. Results were recorded separately. If discordant opinion existed for any particular case, a final consensus diagnosis was attempted for purpose of analysis, Diagnosis was rendered based on cytological criteria enumerated in standard textbooks of cytology [7].

3. RESULTS

FNAC was performed on 45 cases presenting with a gall bladder mass. In one case, sufficient material could not be obtained and it is excluded from further analysis. The diagnosis rendered in remaining 44 patients is shown in Table 1.

Table 1. Disease distribution of 44 patients with gall bladder mass

Nature of cellular aspirate	Number of patients
Adenocarcinoma NOS	33
Papillary adenocarcinoma	01
Poorly differentiated carcinoma	03
Adenosquamous cell carcinoma	01
Cellular atypia	03
Acute inflammatory exudate	03

Table 1 reveals that definite diagnosis of malignancy was possible in 38 cases. Cellular atypia and acute inflammatory exudate was seen in 3 cases each. Amongst 38 cases of malignancy, adenocarcinoma NOS was present in 33 patients (86.8% of cases). Poorly differentiated malignancy was seen in 3 patients. Papillary adenocarcinoma and adenosquamous cell carcinoma was seen in one patient each.

Cellular aspirate from patients with adenocarcinoma NOS showed three dimensional cell clusters. Cell nuclei were irregular and pleomorphic with increased N/C ratio. Nucleoli were prominent. The solitary case of adenosquamous cell carcinoma, apart from

having features of adenocarcinoma also revealed squamous differentiation in form of pyknotic nuclei, thick cytoplasm, angulated cell borders and orangeophilia on Pap staining. Cellular aspirate from patient having poorly differentiated carcinoma showed dispersed cell population with presence of highly pleomorphic cells. The case of papillary adenocarcinoma showed papillae formation with minimal cellular pleomorphism.

In our series, no case of mucinous carcinoma, signet ring cell carcinoma, pure squamous cell carcinoma, small cell carcinoma or neuroendocrine tumour was seen. We were unable to confirm the diagnosis in patients whose cellular aspirate revealed cellular atypia only or presence of mixed inflammatory exudate, as follow up histological biopsies were unavailable.

The age and sex distribution of patients with gall bladder malignancy is shown in Table 2. The youngest patient in our series was a 35 years old female and the oldest was 75 years of age. Our results indicate that gall bladder malignancy is seen more often during 5th and 6th decade of life (65.8% of cases). GBCa is about 2.5 times more common in females as compared to males.

Table 2. Age and sex distribution of gall bladder malignancy (n=38)

Age group	Male patients (n)	Female patients (n)
31- 40 years	2	4
41- 50 years	4	9
51- 60 years	4	8
61- 70 years	1	5
71- 80 years	0	1

Ultrasound examination of the liver showed presence of metastasis in 28 cases. In rest of the patients, metastasis was not detected.

4. DISCUSSION

In many parts of the world, GBCa is an uncommon malignancy. In USA, its frequency is 1.43/hundred thousand population [4]. However in certain regions of the world, it ranks amongst ten commonest malignancies. High incidence of GBCa is seen in persons living in western parts of the Andes, in North American Indians, in Mexican Americans and amongst inhabitants of northern India. In these areas, the incidence may reach up to 7.5/hundred thousand for men and 23/hundred thousand for women [8]. In northern parts of India, cancer registry of Indian Council of

Medical Research, records an incidence of 4.5/hundred thousand for men and 10.1/hundred thousand for women [1]. In Delhi, GBCa with an incidence rate of 6.6/hundred thousand females, is the fourth most common cancer overall and the most common gastrointestinal cancer [9]. In north Indian city of Lucknow, GBCa happens to be the most common cause of obstructive jaundice caused by a malignant disorder [10]. That this cancer shows marked geographical variation is further illustrated by the fact that in southern India, its incidence is only 1.2/ hundred thousand females. From Mumbai, an incidence rate of 1.6 and 2.3 per hundred thousand is recorded for men and women respectively [11]. However one fact common to GBCa all over the world is its definite predilection for the females.

In our study, it was possible to provide a definite diagnosis of malignancy in 38 out of 45 patients in whom guided aspiration was performed. Thus, success rate of aspiration in our series is 84.4%. Success rate of guided aspiration in patients of GBCa reported by other workers from India varies from 60% to 90% [12,13].

In our series, out of 38 cases of confirmed malignancy, 27 patients were females. Thus female to male ratio is 2.45:1. Fig. 1 illustrates female to male ratio in some other series from India. In all of these, GBCa is seen more often in females. In one series, figures reveal nearly five

times greater propensity of this disease amongst females [8]. Reasons proposed for female preponderance of this disease include - higher incidence of gall stone disease and putative role of oestrogen/progesterone receptors in the gall bladder epithelium. That cholelithiasis plays a role in pathogenesis of GBCa is based on observations which show high incidence GBCa in populations with higher prevalence of gall stone disease [8,9]. However, causal role of gall stone disease is still far from established. Role of oestrogen/progesterone receptors is suspected based on observations which show that the disease is more common in females exhibiting following features - younger age of menarche, early age of first pregnancy, multiple pregnancies, and prolonged fertility span with higher number of live births [13-15]. All these conditions are associated with increased duration of exposure to estrogens and progesterone [8]. If this hypothesis is found to be true, then anti-oestrogen therapies like tamoxifen should play a role in treatment.

In our series, GBCa was seen more frequently in the age group of 41 to 60 years (65.8% of cases). Less commonly, it was seen in 4th and 7th decades of life (15.8% cases each).The decade wise incidence of GBCa in some other series from India [16-19] is shown in Fig. 2. All these series show high incidence of GBCa in the age group of 41 to 60 years.

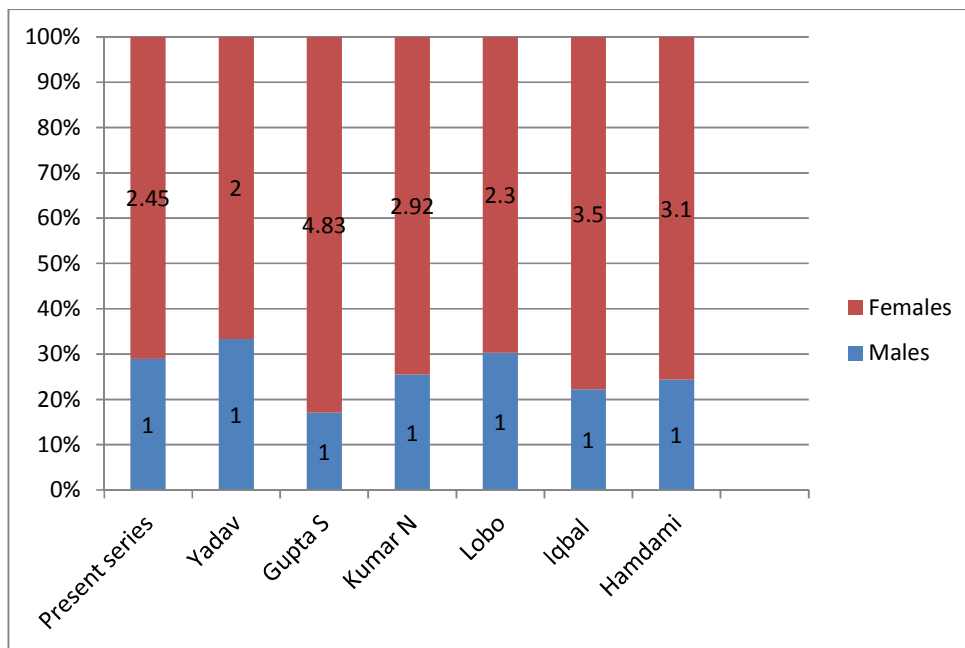


Fig. 1. Comparison of sex ratio of carcinoma gall bladder in different series from India

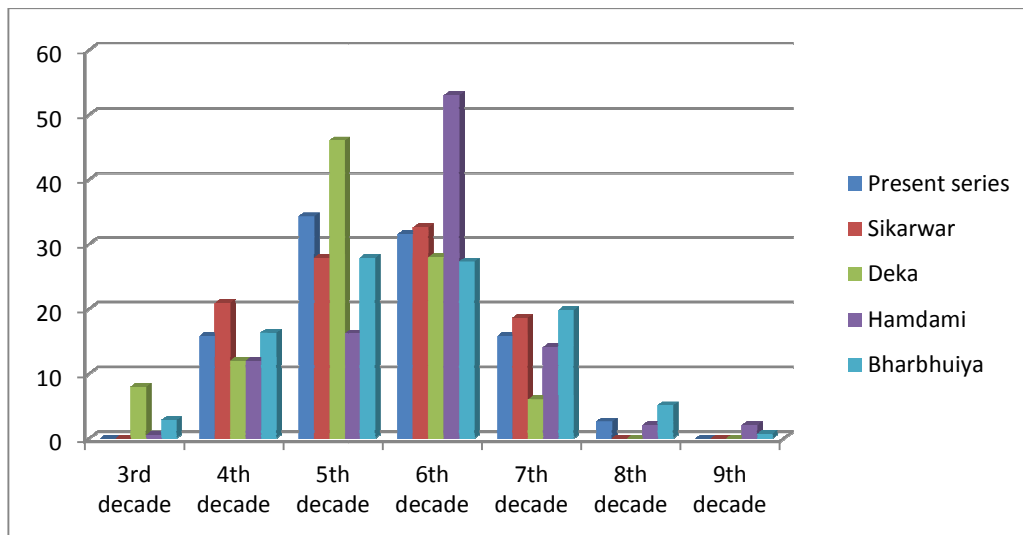


Fig. 2. Comparison of distribution of GBCa in different decades of life in different series from India

The median age of patients of GBCa reported from India by some workers ranges between 49 to 54 years [9,13,20-22]. This figure is much lower than what is reported in western literature. The median age reported from UK is 70-74 years [23]. From USA, it is 73 years [24] and from Sweden [25] Poland [26] and Italy [27] it is 66 years.

In our series, adenocarcinoma was the commonest form of GBCa (86.8% of cases). Other workers from India have reported similar findings in their series [8,12,18,22]. World over, adenocarcinoma is the most frequent histological subtype of GBCa. It is seen in approximately 90-95% of cases [28].

GBCa is seen more commonly in migrant population from India to other countries like US, UK, Australia and Kuwait [29,30]. Genetic factors or retention of cultural practices in migrant population may be responsible for this finding. Further work is required in this field. It may shed light on the role of dietary practices in causation of GBCa. One study from India proposes the role of fried food as an aetiological factor for GBCa [22].

GBCa has one of the poorest prognoses amongst all cancers. Mean survival of patients in TNM stage II, III, and IV is 7.5, 5.2, and 3.7 months, respectively [5]. Survival rate in stages II, III and IV are approximately 25%, 12%, and 1-2% respectively [6]. In one of the largest studies on GBCa involving 490 cases from north India,

52% of patients presented in stage IVB, 27% in stage IIIB and IVA and 18% in stages I - IIIA [8]. In another large study from east India, at the time of presentation, 12.6% patients were in stage I, 16.2% in stage II, 14.1% in stage III and 57.1% in stage IV [18]. Reasons proposed for rapid spread of this malignancy include - absence of submucosa in the GB wall and presence of important organs like liver, duodenum and pancreas in near vicinity to a very thin gall bladder wall (< 3 mm). The hepatic surface of gall bladder has no serosa. This facilitates easy infiltration of the tumour into the liver parenchyma [3].

In our series, 28 out of 38 patients (73.7% of cases) were having metastatic deposits in liver. As elaborated above, cure rates are dismal for such patients. For these patients 'palliative care only' would be in his/her best interest as well as of his/her family.

5. CONCLUSION

FNAC is a useful diagnostic technique in patients presenting with a gall bladder mass. In many patients of malignancy of gall bladder, it obviates the need of performing surgery. Since patients of GBCa in stage II-IV have a dismal prognosis with a short life span, 'palliative care only' becomes the treatment of choice in our country. For such patients, FNAC provides a definitive morphological diagnosis and contributes to staging of the disease.

CONSENT

The study is a retrospective analysis of a laboratory investigative procedure. No personal data of any patient is being presented. An informed consent of all patients was obtained prior to performing the investigative procedure.

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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