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Document heading **doi: 10.21276/apjhs.2016.3.4.1** **Research Article**

Ultrasound guided Fine Needle Aspiration cytology of Hepatobiliary and Pancreatic lesions

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ABSTRACT

Aim: To evaluate the reliability of ultrasound(USG) guided fine needle aspiration cytology(FNAC) in distinguishing between benign and malignant lesions of pancreas and hepatobiliary system and report the findings of significance. The cytology findings were correlated with histology, wherever possible. **Materials and Methods:** This study was conducted in the department of Pathology, Jawaharlal Medical College, Aligarh in collaboration with department of radiology from 2001 to 2002.The study included 95 patients out of which 56 were females and 39 were males. Most patients presented with Right hypochondrial mass and others with pain or discomfort in the abdomen. After clinical examination, patients were sent for USG examination and USG guided FNAC of the mass and cytological examination of the smears was done. Subsequent to it, some patients underwent surgery. Tissue obtained from surgery was examined by histopathology. **Results:** Sex distribution of patients showed 58.95% females and 41.05% males. Out of 95 patients, malignant lesions constituted 64 cases(67.37%),benign and inflammatory lesions together comprised 18 cases(18.95%). 9 cases(9.47%) were found inadequate for diagnosis and 4 smears(4.21%) were found to be suspicious for malignancy. In this study, we achieved an overall diagnostic accuracy of 95.65%.No major complications were encountered. **Conclusions:** We concluded that USG guided FNAC is a safe and accurate method for diagnosis of hepatobiliary lesions and sonography is ideally suited as a method of guidance.

Key words: Fine needle aspiration cytology, Hepatobiliary, Pancreatic, Ultrasound

Introduction

Lesions of liver, gall bladder and pancreas are quite common.Gall bladder carcinoma ranks 5th in frequency among gastrointestinal malignancies and is a common malignancy in Northern India.[1]Malignancy in liver is usually inoperable at the time of diagnosis, so a diagnostic modality like fine needle aspiration cytology(FNAC) which offers accuracy with minimum intervention at lowest cost and without complication, warrants consideration early in investigative sequence.[2] Pancreatic carcinoma is difficult to differentiate clinically from chronic pancreatitis and its biopsy carries risk of haemorrhage ,infection and fistula formation. FNAC of pancreas is a rapid,safe and accurate method for diagnosis of malignancy.[3] Ultrasonography(USG) is rapid, inexpensive, versatile method and does not require contrast medium and ionising radiation.[4] CT guided FNAC is time consuming and is limited to transverse plane.[5,6] FNAC has advantage over thin needle core biopsy in very small tumours[7] Complication rate of FNAC of abdominal masses is reported as 0.5%[8]

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Materials and methods

This study was conducted in the department of Pathology, Jawaharlal Nehru Medical College, Aligarh in collaboration with department of radiology from 2001 to 2002.The study included 95 patients out of which 56 were females and 39 were males. Most patients presented with Right hypochondrial mass and others with pain or discomfort in the abdomen. After clinical examination, patients were sent for USG examination and in patients having a mass lesion, USG guided FNAC of the mass and cytological examination of the smears was done. Staining of the cytology

smears was done by Haematoxylin and eosin method ,Papanicolaou method and May Grunwald Giemsa staining method.Subsequent to cytology, some patients underwent surgery.Tissue obtained from surgery was examined by histopathology.Those patients who were not operated included patients with metastases in liver or inoperable tumours who were sent for radiotherapy or patients with non neoplastic lesions.

Results

This study included 95 patients in which 39 were males and 56 were females.

Table 1: Sex distribution of patients

Sex	Number	Percentage
Male	39	41.05
Female	56	58.95
Total	95	100

The percentage of females was much higher mainly because of the inclusion of gall bladder masses.Out of 35 patients with gall bladder masses,28(80%) were females. Tables 2 and 3 depict categorization of patients according to their age and sex.

Table 2: Distribution of patients with liver masses in relation to age groups and sex

Age group(in years)	No.of patients	% of total	Males	% of total	Females	% of total
0-10	0	0	0	0	0	0
11-20	1	1.75	1	3.12	0	0
21-30	7	12.28	2	6.25	5	20
31-40	11	19.30	3	9.38	8	32
41-50	12	21.05	10	31.25	2	8
51-60	20	35.09	12	37.5	8	32
>60	6	10.53	4	12.5	2	8
Total	57	100	32	100	25	100

Table 3: Distribution of patients with gall bladder and pancreatic masses in relation to age goups and sex

Age group(in years)	No.of patients	% of total	Males	% of total	Females	% of total
0-10	0	0	0	0	0	0
11-20	0	0	0	0	0	0
21-30	0	0	0	0	0	0
31-40	4	10.53	1	14.29	3	9.68
41-50	17	44.74	2	28.56	15	48.39
51-60	6	15.79	1	14.29	5	16.13
>60	11	28.94	3	42.86	8	25.80
Total	38	100	7	100	31	100

Table 4 gives an overview of the general categories formed upon cytologic evaluation of aspirate smears.Suspicious smears were those in which there was a suggestion of malignancy due to cellular atypia,but an unequivocal fulfilment of cytologic criteria for malignancy were not present.

Table 4: Distribution of total number of patients according to cytologic diagnostic category

Diagnostic category	Number	Percentage
Inadequate	9	9.47
Inflammatory	18	18.95
Suspicious	4	4.21
Malignant	64	67.37
Total	95	100

Tables 5 and 6 give overview of morphological distribution of patients with Hepatic, Gall bladder and Pancreatic masses according to cytological diagnostic category.

Table 5: Morphological distribution of patients with hepatic masses according to cytologic diagnostic category

Diagnostic category	Number	Percentage
Adequate	5	8.78
Inflammatory+ Benign	12	21.05
Abscess	6	10.53
Hydatid cyst	1	1.75
Focal Nodular Hyperplasia	1	1.75
Others	4	7.02
Suspicious	3	5.26
Malignant	37	64.91
Primary	13	22.80
Hepatocellular CA(HCC)	12	21.05
Well differentiated	5	8.77
Mod.& poorly differentiated	7	12.28
Undifferentiated	1	1.75
Secondaries	24	42.11
Metastatic adenocarcinoma	20	35.09
Cholangiocarcinoma	3	5.27
Metastatic carcinoid	1	1.75
Total	57	100

In our study, the parameters considered characteristic of well differentiated HCC were-thick cytoplasm,well defined cell borders,eccentric nuclei and increased N:C ratio.Various cellular patterns like trabecular, pseudoacinar, spindle cell, pleomorphic and dispersed were noticed and amongst these trabecular was the most common pattern.(Figs 1,2,3).Amongst the metastatic tumours,metastatic adenocarcinoma and cholangiocarcinoma exhibited lumen forming glandular structures.Metastatic carcinoid had endocrine look and cytoplasmic granularity.(Figs 2,4).Benign lesions of liver included Focal nodular hyperplasia,Hyadatid cyst and Liver abscess.(Figs.5,6,7).

Table 6: Morphological distribution of patients with gall bladder and pancreatic masses according to cytologic diagnostic category

Diagnostic category	Number	Percentage
Inadequate	4	10.53
Inflammatory	6	15.79
Chronic cholecystitis	5	13.16
Xanthogranulomatous cholecystitis	1	2.63
Suspicious	1	2.63
Malignant	27	71.05
Adenocarcinoma Gall Bladder	25	21.05
Not otherwise specified	18	47.37
Mucinous	3	7.89
Papillary	4	10.53
Adenocarcinoma Pancreas	1	2.63
Islet cell tumors of Pancreas	1	2.63
Total	38	

Amongst the inflammatory gall bladder lesions(Fig.10),1 case of Xanthogranulomatous cholecystitis was reported which had mesothelium like cells,foamy histiocytes,giant cells and inflammatory cells in a pink granular background.This case was confirmed on histopathology.Amongst the malignant gall bladder lesions, only adenocarcinoma was observed.(Fig.11)Amongst the malignant pancreatic lesions(Fig.9),1 case of adenocarcinoma was reported.1 case of islet cell tumour was reported which was confirmed by histopathology.One case cytologically reported to be an inflammatory smear turned out to be adenocarcinoma.So there was 1 false negative diagnosis.In our study, there was sensitivity of 92.31%,specificity was 100%,predictive value of positive result was 100%,predictive value of negative result was 90.91% and diagnostic accuracy was 95.65%.

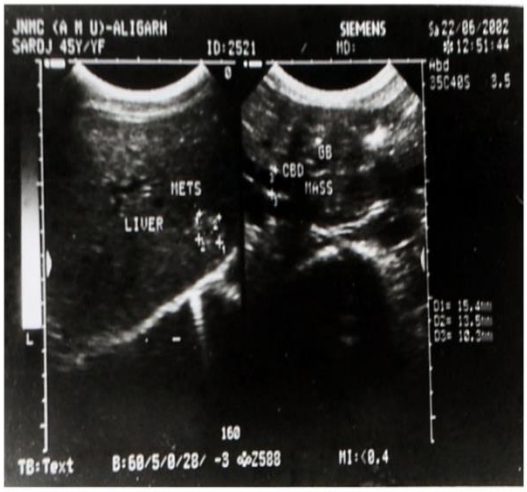
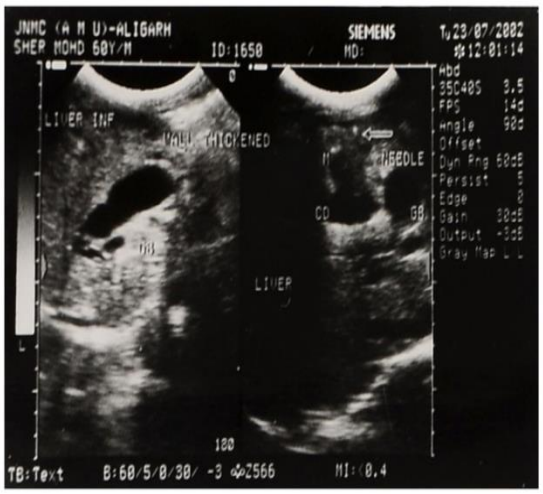
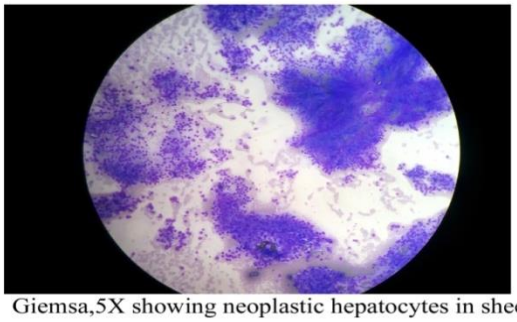


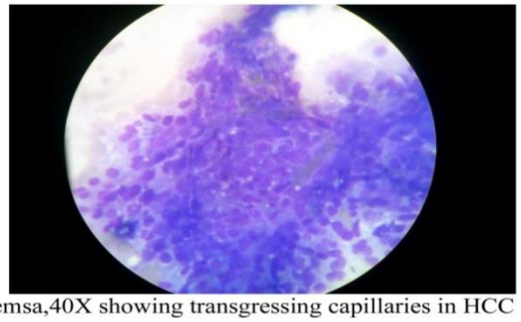
Fig 1:USG showing mass in gall bladder with metastasis in liver proved by cytology



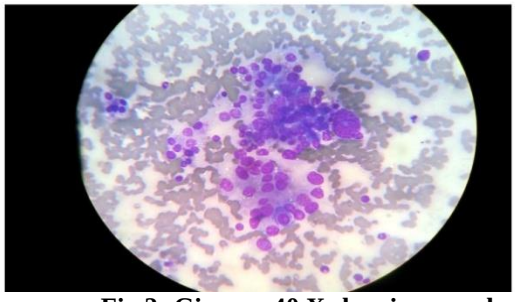
USG showing mass lesion near gall bladder fossa with provisional diagnosos of metastasis proved as hepatocellular carcinoma by cytology



Giemsa,5X showing neoplastic hepatocytes in sheets



Giemsa,40X showing transgressing capillaries in HCC



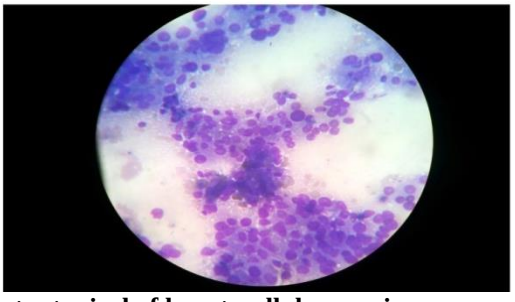
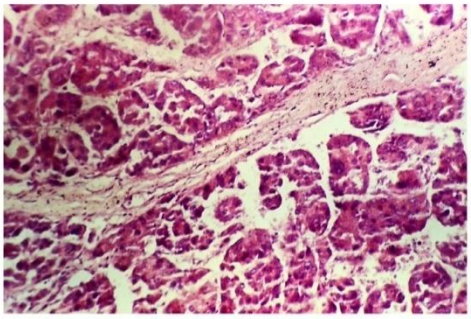
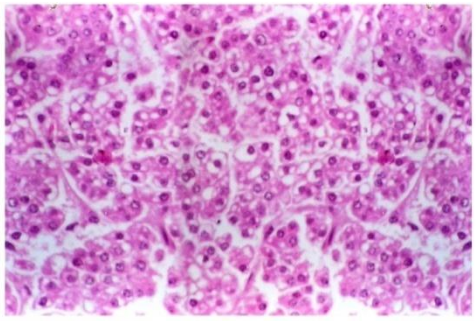


Fig 2: Giemsa, 40 X showing neoplastic hepatocytes typical of hepatocellular carcinoma



Section from HCC showing trabecular arrangement of hepatocytes separated by sinusoids(H&E,10X)



Section from HCC showing hepatocytes in tebeculae surrounded by endothelial cells(H&E,40X)

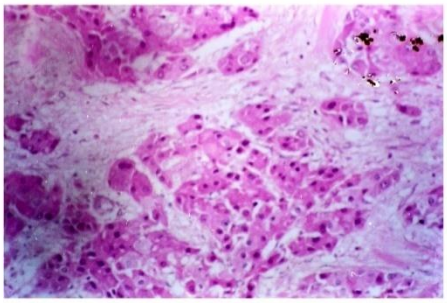
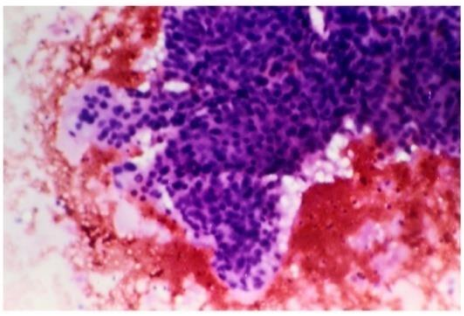
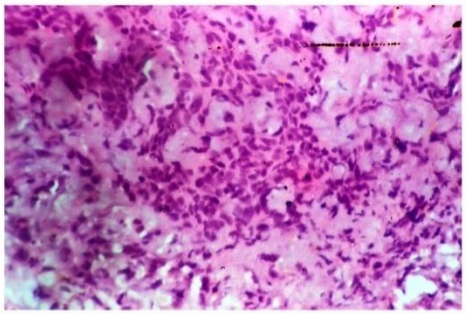


Fig 3: Section from Fibrolamellar HCC showing cords of hepatocytes separated by collagen(H & E,10X)



Smear from metastatic adenocarcinoma liver showing malignant columnar cells forming a papillae(H&E,10X)



Smear from metastatic adenocarcinoma liver showing malignant cells in cords and acini(H&E,10X)

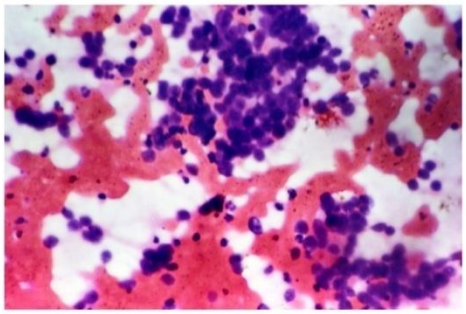


Fig 4: Smear from metastatic carcinoid liver showing cells with ill defined margins and hyperchromatic nuclei (H&E,40X)

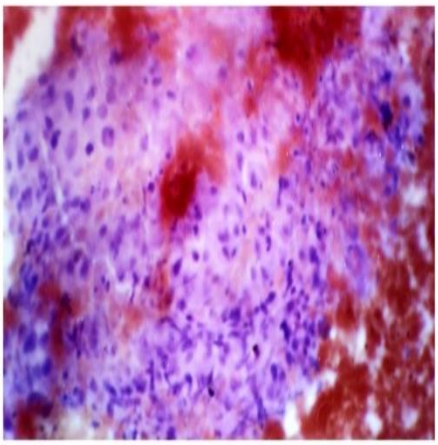
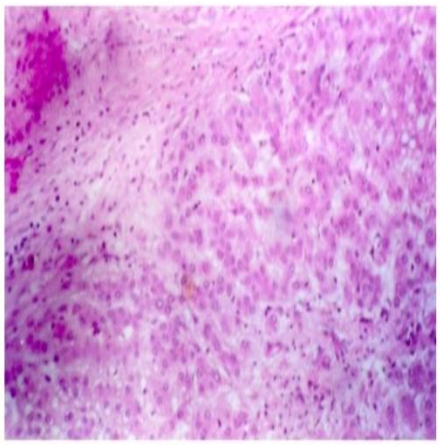


Fig 5: Smear from focal nodular hyperplasia showing benign hepatocytes and many Kupffer cells (H & E,40X)



Section from focal nodular hyperplasia showing fibrous scar at one end and normal hepatocytes on the other end (H & E, 10X)

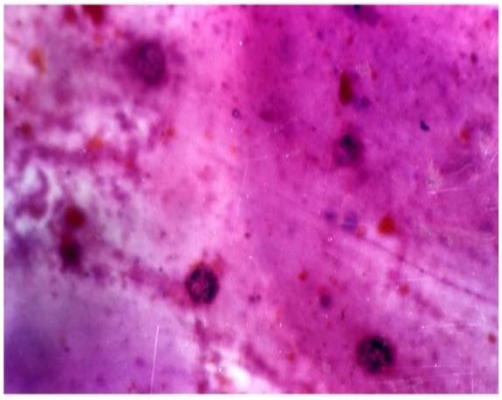
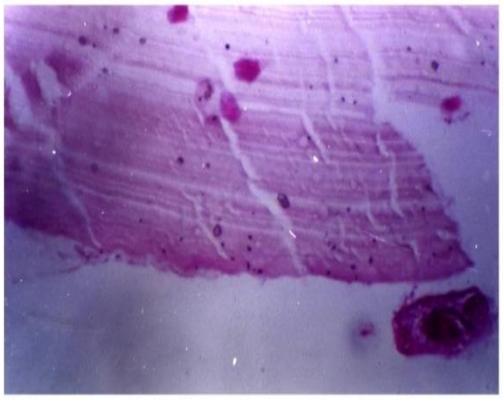


Fig 6: Smear from hydatid cyst showing debris and hooklets in a ring like manner(H &E,10X)



Section from hydatid cyst showing outer chitinous layer and an intact scolex(H &E,10X)

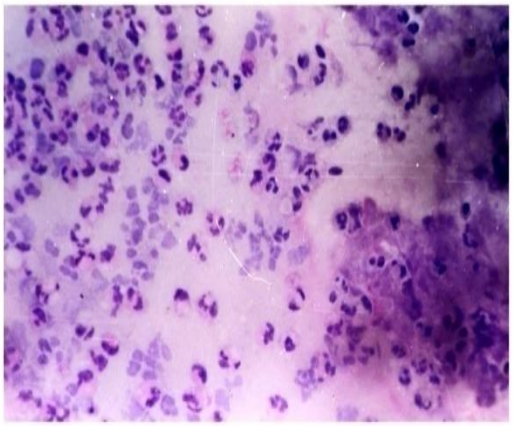
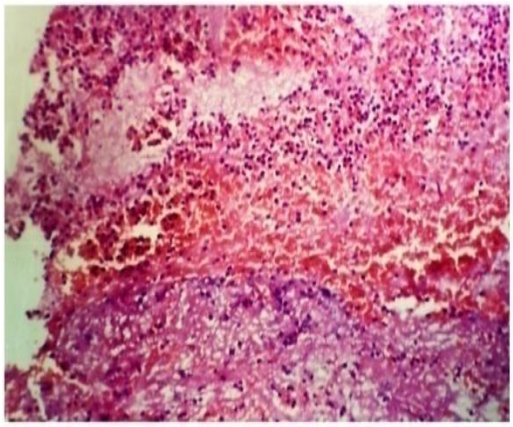


Fig 7: Smear from liver abscess showing acute inflammatory cells,degenerated cells and necrosis(H &E,40 X)



Section from liver abscess showing acute inflammatory cells and RBCs in a necrotic background(H &E,10X)

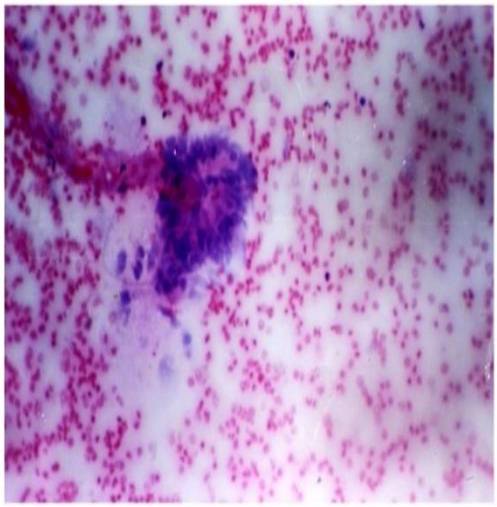
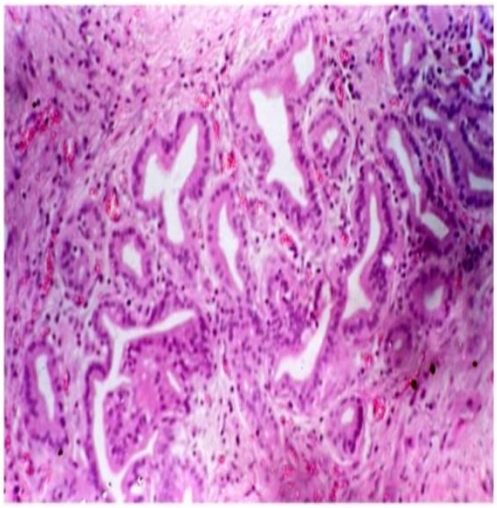
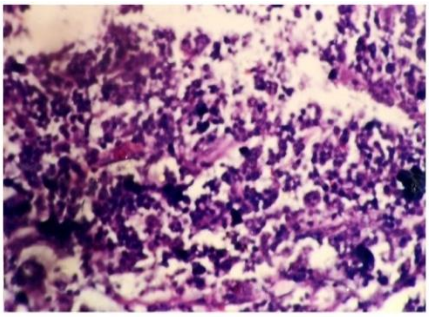


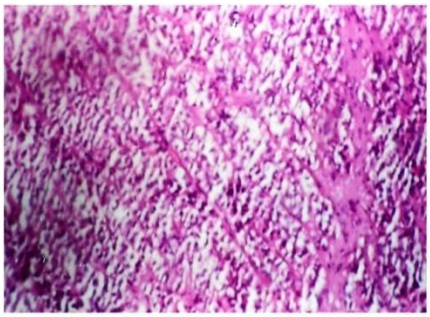
Fig 8: Smear from cholangiocarcinoma showing acinar arrangement of ductal cells (H &E,10X)



Section from cholangiocarcinoma showing neoplastic ducts and glands in a desmoplastic stroma (H &E,10X)



Smear from islet cell tumour of Pancreas showing cords & neats of cells with granular cytoplasm , round nuclei and acinar formations(H&E,40X)



Section from Islet cell tumour of Pancreas showing cords and trabeculae of cells with granular or vacuolated cytoplasm,& round nucleus(H&E,10X)

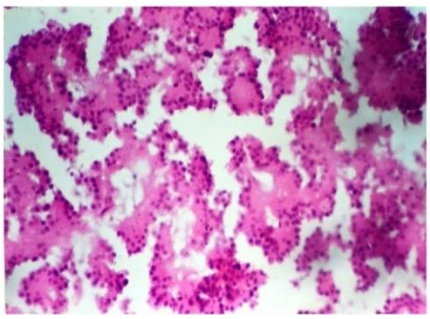
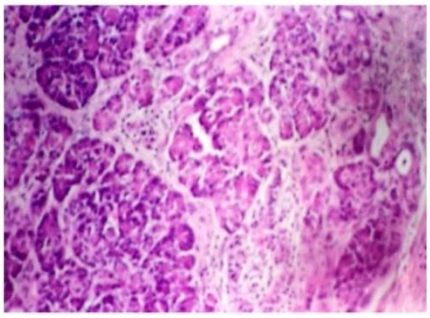
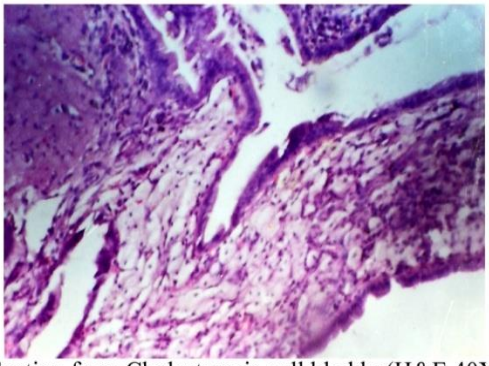


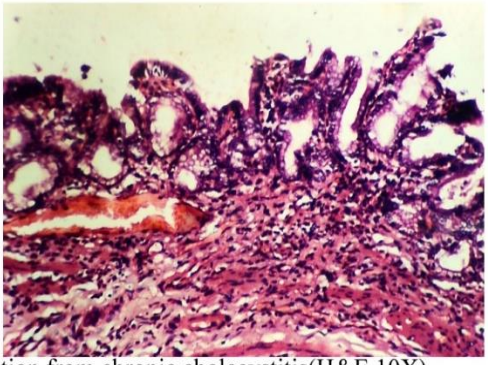
Fig 9: Section from acinar cell carcinoma pancreas showing acini and nests formed by cells with granular , eosinophilic cytoplasm(H &E,40 X)



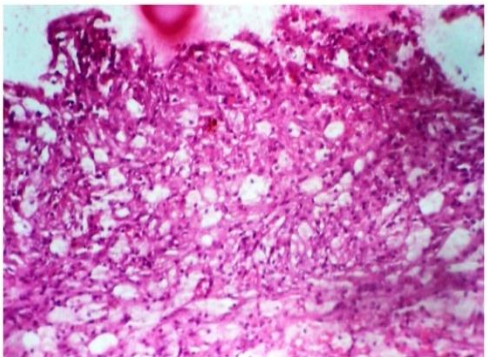
Section from ductal adenocarcinoma of pancreas glands lined by neoplastic cells separated by connective tissue (H & E,10 X)



Section from Cholesterosis gall bladder(H&E,40X)



Section from chronic cholecystitis(H&E,10X)



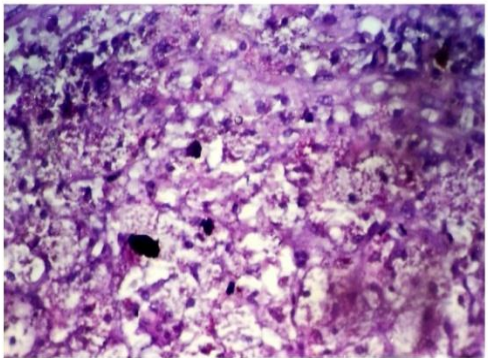
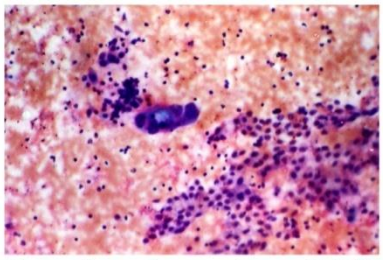
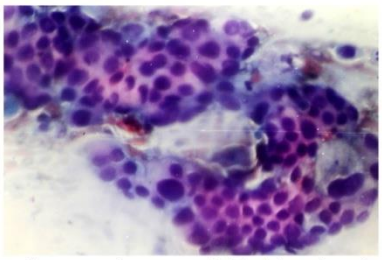


Fig 10: Section from xanthogranulomatous cholecystitis (H & E,10 X) and smear from same showing PAS positive granules of lipofuscin(PAS,10 X)



Smear from adenocarcinoma Gall bladder showing malignant cells with eccentric nuclei,clear cytoplasm (H&E,10X)



Smear from adenocarcinoma gall bladder showing malignant cells forming papillae (Pap,10X)

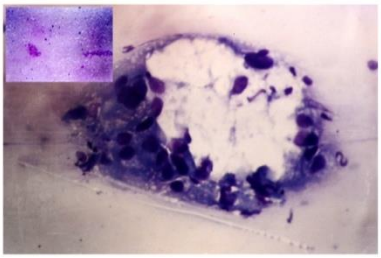
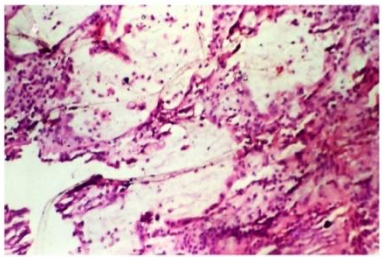


Fig 11: Smear from mucin secreting adenocarcinoma GB showing malignant cells with abundant mucin (Pap ,40 X).Inset shows PAS positive cells



Section from mucin secreting adenocarcinoma showing mucin filled spaces lined by neoplastic cells(H & E,10 X)

Discussion

This study was conducted over a period of 2 years on a group of 95 patients with right hypochondrial and epigastric masses. Presenting symptoms were lump abdomen,pain abdomen,anorexia,weight loss,jaundice and gall stones etc.In our study, Carcinoma gall bladder was associated with gall stones in 68% cases whereas Shukla et al.1999[9] reported 62.6% association, Venkataramu et.al.1999[1] reported 54.33% association, Gupta,Misra et.al.2000 [10] reported 63% association and Pandey et.al.2001[11] reported 69.7% association.In our study, the youngest patient of gall bladder lump was a female aged 32 years and the oldest a female aged 70 years.Maximum females were in the age groups 41-50 and >60 years. Maximum males were in the age groups 41-50 and >60 years. 28(80%) patients with gall bladder masses were females and 7(20%) were males. Such female preponderance in gall bladder malignancy is reported in various studies Akosa et.al[12],Gupta et al[10] and Pandey et.al[11].In this study the mean age for gall bladder disease was 40.38 years and average age for gall bladder malignancy was 50 years.Zargar et al[13] reported average age as 53 years, Venkataramu et.al.[1] reported 52-54 years, Akosa et.al.[12] reported 6th -7th decade and Pandey et.al. [11] reported 49.9 years.In our study,amongst the gall bladder lesions,71.43% patients had malignancy,2.86% were suspicious,8.57% were acellular and 17.14% were inflammatory.Shukla et.al[9],while performing USG guided FNAB of gall bladder masses found 53.3% malignant,23.3% suspicious,16.6% inflammatory and 6.6% acellular cases. Similar statistics were also obtained by Venkataramu et.al[1] and Zargar et.al[13].In our study the adequacy of USG guided FNAC of gall bladder and pancreatic aspirates was 89.47% whereas the sensitivity of USG guided FNAC was 94.5% by Pandey et.al.[11].In our study ,57 patients had mass in hepatic region. Out of 57 cases,56.14% were males and 43.86% were females giving a M:F ratio of 1.28:1.Youngest male patient was a child aged 14 years and oldest a man of 80 years. Youngest female was aged 22 years and oldest 61 years..Average age of patients with liver masses was 41 years in males and slightly higher i.e.45 years in females. Average age for liver malignancy was 50 years. On cytology, 64.91% patients were found to have malignancy,9.47% were inadequate,18.95% were inflammatory and benign and 4.21% were suspicious.Pedio et.al.[14] reported 15.28% inflammatory or benign,4.17% inadequate and 80.55% to be malignant. Probably suspicious cases were included in malignant category. In our study, metastatic adenocarcinoma was the commonest liver malignancy. This correlates with the findings of Whitlach et.al [15].Amongst the primary cancers of liver, hepatocellular carcinoma was the commonest having the trabecular pattern most commonly. This correlates with findings of Devi et.al.[16].The various cellular characteristics observed in our study were consistent with that observed by Devi et.al. and Pedio et. al.[16,14].In our study ,the adequacy of USG guided FNAC of liver aspirates was 91.22%. We found 2 cases suspected of being secondaries in liver on USG which turned out to be hepatocellular carcinomas as has been observed by Kedar et. al .[8].No major complications were encountered as has been observed by Shukla et.al. and Venkataramu et.al.[9,1].Cytohistological correlation could be done in 23 patients only because rest of them were sent directly for radio or chemotherapy. Out of these 23 patients,12 were true positive for malignancy,10 were true negative,1 was false negative but none were false positive. The false negative case was of an empyema gall bladder on cytology. We believe that such false negative result was because of incorrect area sampled or limited material aspirated due to fibrosis and necrosis. A negative result should therefore, be interpreted with caution, especially when clinical suspicion of malignancy is high. We obtained sensitivity of 92.31% whereas it was 88.5% by Zargar et.al.,86.9% by Whitlach et.al.[13,15].Specificity and predictive values of positive result were 100% each, exactly similar to that obtained by Whitlach et.al., Zargar et.al.[15,13] ; Predictive value of negative result was 90.91% and diagnostic accuracy was 95.65% closest to that of Esteve et.al[17] who obtained diagnostic accuracy of 91%. We recommend the performance of a maximum of 2 passes for each lesion since diagnostic yield did not improve with more passes.

Conclusion

Thus, Ultrasound guided FNAC is a safe and accurate method for diagnosis of hepatobiliary lesions and sonography is ideally suited as the method of guidance. Pathological diagnosis of malignancy in a patient showing advanced malignancy on imaging can obviate unnecessary laparotomy and can beneficially influence therapy.A negative FNAC result should be disregarded when the suspicion of malignancy is high and either a repeat FNAC or surgical biopsy should be performed to establish the diagnosis.

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