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Both Prospective and Retrospective Role of USG Guided FNAC in Hepatobilliary Pancreatic Lesion in Correlation with Radiological Diagnosis

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ABSTRACT
Background: *First reports of fine-needle aspiration cytology (FNAC) as a technique for obtaining diagnostic material date back to the 19th century when, at St Bartholomew's Hospital, London, aspiration was undertaken on a large mass in the liver by the surgeons Stanley and Earle. USG is operator dependent and has a limitation in obese patients and those with large amount of bowel gas. Computed tomography (CT) is a reliable modality and provides good definition of lesions and facilitates visualization of the entire extent of pancreatic pathology.* ***Aims:*** *To study the role of fine needle aspiration cytology in diagnosis of hepatobilliary and pancreatic lesions of patients attending tertiary care hospital and their correlation with ultra sonography.* ***Materials and Methods:*** *50 patients presented with intra-abdominal lumps attending the outpatient department as well as admitted in Rama Medical College, Hospital & Research Centre, Kanpur and J.K. Cancer Institute, Kanpur. The study was carried out from January 2017 to September 2018.* ***Results:*** *Total 50 patients were suffered with pain abdomen weight loss anemia, and personal history was tobacco and site of swelling was right hypocondrium 50 (100%) each. Out of 50, males were 24 (48%) and females. Male to female ratio was 1:1. Age ranged from 10 to 70 and above years with a mean age of 54 years. Cytological diagnosis out of 50 patients 14 (29.03%) were adenocarcinoma, 3 (3.23%) metastatic adenocarcinoma d/d ?, 2 (3.23%) suggestive of adenocarcinoma /gb, 2 (3.23%) hepatic adenoma, 5 (6.45%) suggestive of metastatic adenocarcinoma d/d hepatocellular carcinoma, 2 (3.23%) suggestive of ? hepatocellular carcinoma d/d ? metastatic adenocarcinoma, 9 (22.58%) metastatic adenocarcinoma, 2 (3.23%) suggestive of neoplastic lesion most likely metastatic adenocarcinoma, 11 (25.81%) metastatic carcinoma. Radiological diagnosis USG out of 50 patients Ca GB 27 (54%), Ca Liver 18 (36%), Ca Liver Sol 3 (6%), Liver Sol 2 (4%).* ***Conclusion:*** *Ultrasound provides a safe, quick, reliable, non-invasive and cost effective tool for screening for hepatobilliary pancreatic lesion.*
Keywords: *Liver, Pancreas, Ultrasound, Ultrasonography, Cytology.*

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I. Introduction

First reports of fine-needle aspiration cytology (FNAC) as a technique for obtaining diagnostic material date back to the 19th century when, at St Bartholomew's Hospital, London, aspiration was undertaken on a large mass in the liver by the surgeons Stanley and Earle [1]. Sir James Paget advocated the use of aspiration as an investigative technique in his lectures [2]. Menetrier was probably the first to use aspiration to investigate lung cancer [3]. Some years later, at the beginning of the 20th century, Griegg and Gray published the results of a lymph node aspirate for tripanosomiasis [4]. In 1921, Guthrie described using a 21-guage needle and a technique similar to that used today, but the first large-scale study was carried out at the Memorial Hospital, New York, by the pioneering team of Martin, Ellis and Stewart [5,6]. Stewart published the results of 2,500 tumours biopsied by an aspiration method using an 18-gauge needle [7]. The historical background of FNAC has been researched by Webb [8] and Grunze and Spriggs [9]. True fine needles for aspiration (22- to 27-gauge vs. 18-gauge) were first introduced in Europe in the 1950s by Lopez-Cardozo in The Netherlands [10] and Soderström in Sweden [11]. It was, however, publications by Zajicek, from the Karolinska Hospital in Stockholm, that brought aspiration cytology to international attention [12, 13] Linsk described the work of the aspiration cytology pioneers Zajicek, Esposti and Lowhagen [14]. At that time, the European clinicians, mainly from the ranks of haematologists developed the Romanowsky and May-Grünwald Giemsa stains for use on air-dried smears to allow for rapid interpretation. Despite their success, it was not until the 1980s that FNAC became widely used. The reasons included lack of confidence in the sensitivity and specificity of the procedure,

fear of tumour implantation in the needle track, apprehension of lawsuits and the reluctance of surgeons to relinquish the use of the formal histological biopsy technique [15].

Pancreatic resection continues to carry high morbidity (69%) for total pancreatectomy [16] and (20%) risk of severe complications following pancreaticoduodenectomy [17] and although mortality improved over time from 8% during 1990-1999 era to 2% during 2000- 2007 era [16], the high associated morbidity underscores the importance of a robust pre-operative evaluation prior to considering definitive surgical therapy.

Pancreatic lesions are a difficult diagnostic and therapeutic challenge owing to the deep seated location of pancreas. Acute or chronic pancreatitis may be associated with pancreatic calcification, pseudocysts, extrapancreatic phlegmons, hemorrhage and pancreatic necrosis or abscess formation which can help the radiologist make an accurate diagnosis.[18] Ultrasonography (USG) is a good modality because of its low cost, real time interactions, lack of bioeffects and wide availability. It can provide information about size, site and characteristics of pancreas, pancreatic lesion, diameter of the biliary and pancreatic ducts and site of obstruction. The presence or absence of lymph nodes or liver metastases can also be determined. More recently the use of echo enhanced Doppler sonography (Doppler after injection of contrast agent) has increased the sensitivity and specificity of this diagnostic modality. [19]

USG is operator dependent and has a limitation in obese patients and those with large amount of bowel gas. Computed tomography (CT) is a reliable modality and provides good definition of lesions and facilitates visualization of the entire extent of pancreatic pathology. Multiplanar three dimensional reconstruction techniques including volume rendering, maximum intensity projection and shaded surface display provide comprehensive information about the relationships and possible involvement of vascular structures and demonstrating local extension. [20] But CT is expensive, exposes patient to ionizing radiation, may require long waiting periods for examination and may have difficulty in defining fat planes in lean patients. In addition USG-guided invasive manipulations of cystic pancreatic lesions or guided fine needle aspiration cytology (FNAC) of pancreatic masses are also easy to perform, quick and effective diagnostic methods but in some cases punctures and biopsies under CT control appear to be the imaging modality of choice. CT and USG are the most common utilized imaging modalities for evaluation of pancreatic pathologies. [21]

Space occupying lesions (SOLs) of pancreas, both cystic or solid are detected during ultrasound screening in either a symptomatic patient with obstructive jaundice, recurrent pancreatitis, or unprecedented loss of weight and appetite or as an incidental finding in an asymptomatic individual. Computed tomography (CT) and magnetic resonance imaging (MRI) confirm and stage the lesion and also provide morphological interpretation. CT-guided aspiration cytology is not recommended for fear of needle track seeding.

Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is a safe and complimentary investigation to CT/MRI imaging. The major advantage is the feasibility of tissue diagnosis. Fine-needle aspiration cytology (FNAC) and fluid analysis together with morphological characteristics helps differentiate malignant/premalignant pancreatic lesions from those that are benign. [22] The reported sensitivity and specificity of EUS-FNAC for various SOLs in pancreas are as high as 97%. [23]

Few case reports from India have highlighted the role of EUS-FNA in diagnosis of pancreatic tuberculosis [24-28] and other SOLs of pancreas. [29-31] However, there are no large series reporting the validity and accuracy of EUS-FNAC for various SOLs of pancreas from major tertiary centers in India, possibly due to lack of follow-up data.

Since fine-needle aspiration (FNA) has assumed a primary diagnostic role in the evaluation of hepatic masses, this prospective study has been done focussing on the value of percutaneous FNA in the diagnosis of focal pancreatic lesions and their radiological and cytological correlation.

II. Materials And Methods

The present study was carried out on 50 patients presented with intra-abdominal lumps attending the outpatient department as well as admitted in Rama Medical College, Hospital & Research Centre, Kanpur and J.K. Cancer Institute, Kanpur. The study was carried out from January 2017 to September 2018.

SELECTION OF PATIENTS

The patients presented with intra-abdominal lumps clinically and were advised ultrasonography for exact localization of lesion. All the patients were included irrespective of their sex and age. The written consent for the procedure was obtained from the patients.

HISTORY AND PHYSICAL EXAMINATION

Patients clinically diagnosed as cases of intra-abdominal lumps were studied thoroughly and investigated as follows:

- Detailed clinical history including history of present past illness with special reference to age, occupation, ea habits and history of smoking and any other addiction.

- Thorough clinical examination with special reference abdominal examination, and lymph nodes draining the area
- Local examination including consistency of lump tenderness, pulsation and mobility of lump was done. Complete examination of genital system and superficial lymph nodes was also done.

INVESTIGATIONS:
All, the concerned patients were subjected to routine investigations like Hb%, TLC, DLC, BT, CT, PT, SGOT, SGPT, Alkaline phosphate, serum creatinine, and serum Alpha fetoprotein (AFP) were also done whenever indicated. Radiological investigations like USG and CT scan was done to know the exact site and origin of lesions.

MATERIAL NEEDED FOR FINE NEEDLE ASPIRATION CYTOLOGY
- Complete laboratory request form giving pertinent clinical details of patients.
- Skin disinfectant.
- Disposable long 21-23G needle with 10 ml or 20 ml syringes.
- Several 76x26 mm glass slides labelled with patients name and number.
- Fixatives (95%) ethyl alcohol in a jar.
- Sterilized disposable gloves.
- Informed written consent for the procedure.

TECHNIQUE OF FINE NEEDLE ASPIRATION CYTOLOGY:
After taking consent for the procedure patients were placed in a comfortable and most suitable position for aspiration. Taking all aseptic precautions aspirations were done without any kind of anaesthesia under US guidance. After through clinical examination, USG examination was performed on Medison SA 8000 ultrasound machine having 3.5 MHz sector (mechanical) probe; and subjected to fine nee those found to have a mass were dle aspiration biopsy by a 20-22 G needle attached to a 20 ml disposable syringe for superficial masses and a 9 cm, 20-22 G spinal needle was passed into deep seated masses. Needle the proper site within the target organ and plunger is pulled to apply negative pressure. Needle was moved to and fro for a distance of about 2 cm for 3-5 times to cut tissue fragments and dislodge cells and tissue fragments to be aspirated in syringe. Needle is withdrawn carefully. The procedure was repeated in the same site in different direction to ensure adequate representative tissue sample. Image guided FNAC under ultrasound guidance was done in all of the cases.

PROCESSING OF MATERIAL
After obtaining the material, aspirates were smeared between two closely opposed slides. In cases of cystic lesions where fluid was aspirated, smears were made after centrifugation of fluid. Prepared slides were fixed in 95% alcohol or air dried case of May Grunwald Giemsa stain and subsequently stained with Haematoxylin and Eosin and May Grunwald Giemsa Technique
After making fine needle aspiration smears patients were followed by biopsy of the lesion which after receiving, were fixed in 10% formalin. Paraffin embedded blocks were made an sections were cut and stained by Haematoxylin and Eosin Stain **Bancroft** (1982).

HISTOLOGICAL DIAGNOSIS:
These cases were then subjected for histological examination and finally the findings are correlated with that of cytological findings.

III. Results

Table 1: Showing Sex wise distribution.

Gender	No.	Percentages
Male	24	48%
Female	26	52%
Total	50	100%

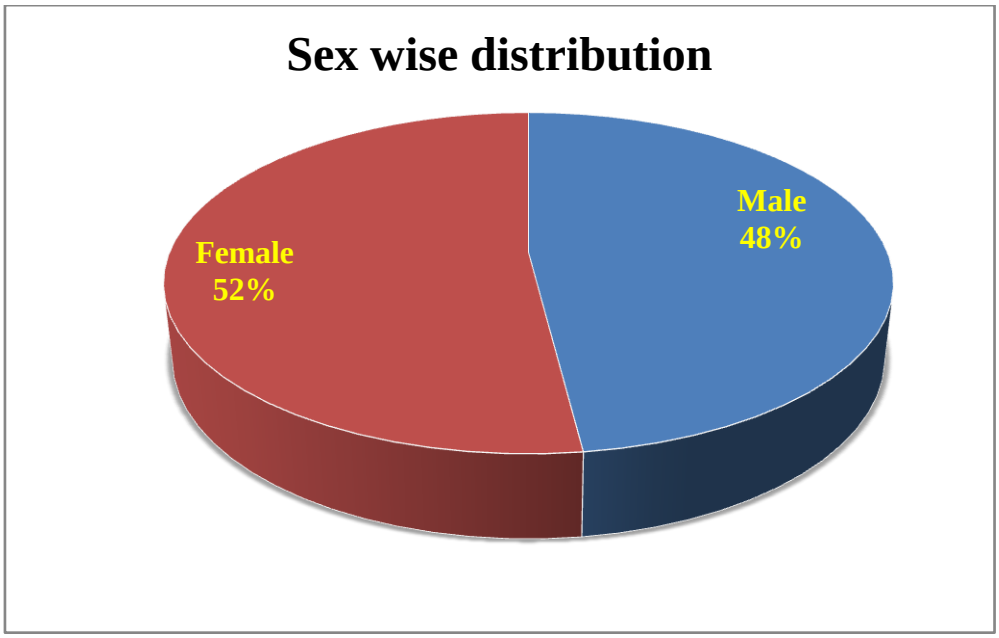

Fig. 1: Showing Sex wise distribution

Table 2: Showing age wise distribution

Age group (in years)	No. of cases	Percentages (%)
10-20	4	8%
21-30	6	12%
31-40	8	16%
41-50	9	18%
51-60	12	24%
61-70	8	16%
71 and above	7	14%
Total	50	100%

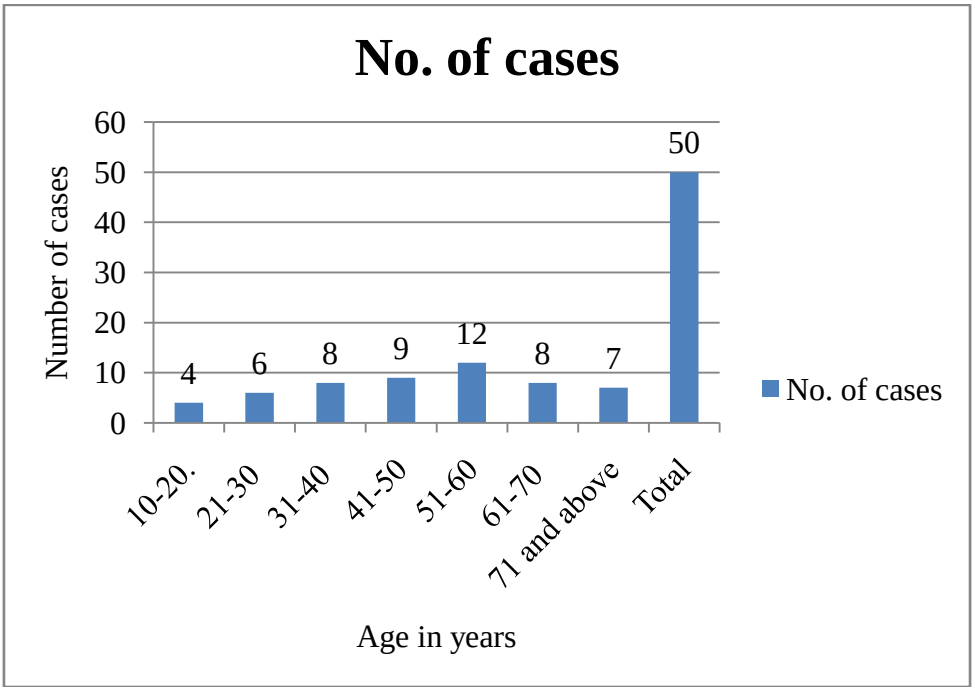

Fig. 2: Showing age wise distribution

Table 3: Showing clinical diagnosis and history of the patients.

Clinical diagnosis	No.	Percentages
Pain Abdomen Weight Loss Anemia	50	100%
Personal history (Tobacco)	50	100%
Site of Swelling (RT. Hypocondrium)	50	100%

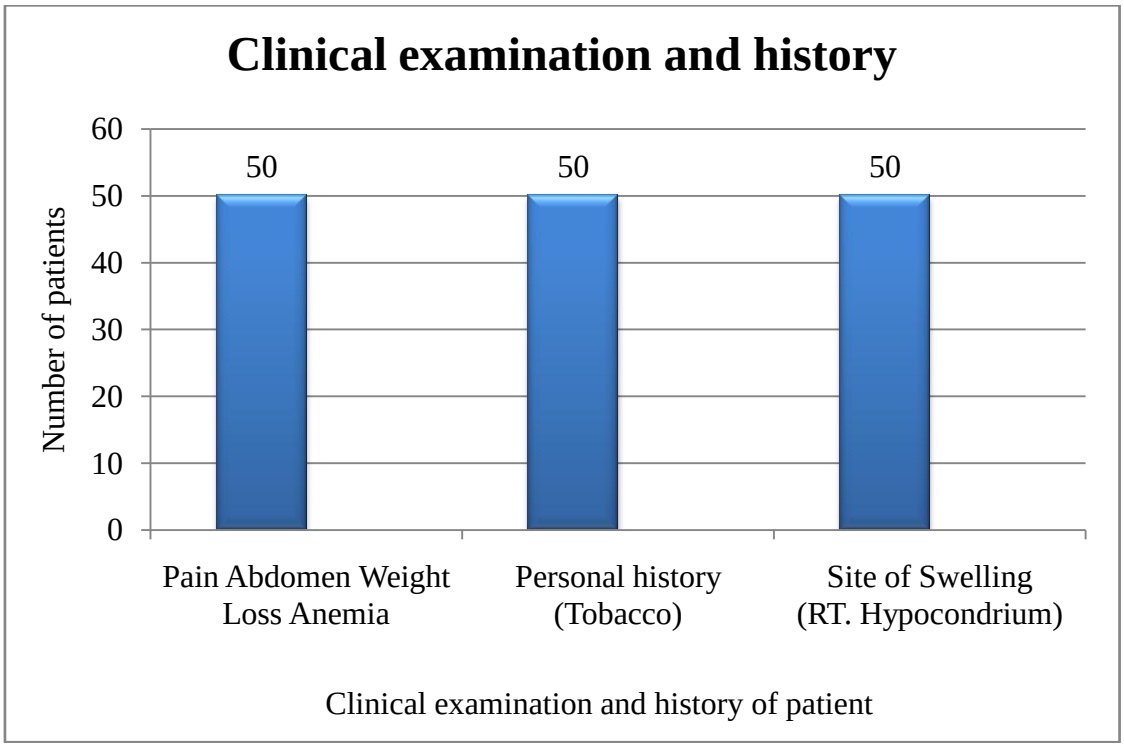

Fig. 3: Showing clinical diagnosis and history of the patients.

Table 4: Shows cytological finding of patients

Cytological Diagnosis	No. of patients	Percentages
Adenocarcinoma	14	29.03%
Metastatic Adenocarcinoma D/D ?	3	3.23%
Suggestive of Adenocarcinoma /GB	2	3.23%
Hepatic Adenoma	2	3.23%
Suggestive of Metastatic Adenocarcinoma D/D Hepatocellular Carcinoma	5	6.45%
Suggestive of ? Hepatocellular Carcinoma D/D ? Metastatic Adenocarcinoma	2	3.23%
Metastatic Adenocarcinoma	9	22.58%
Suggestive of Neoplastic lesion most likely Metastatic Adenocarcinoma	2	3.23%
Metastatic carcinoma	11	25.81%
Total	50	100%

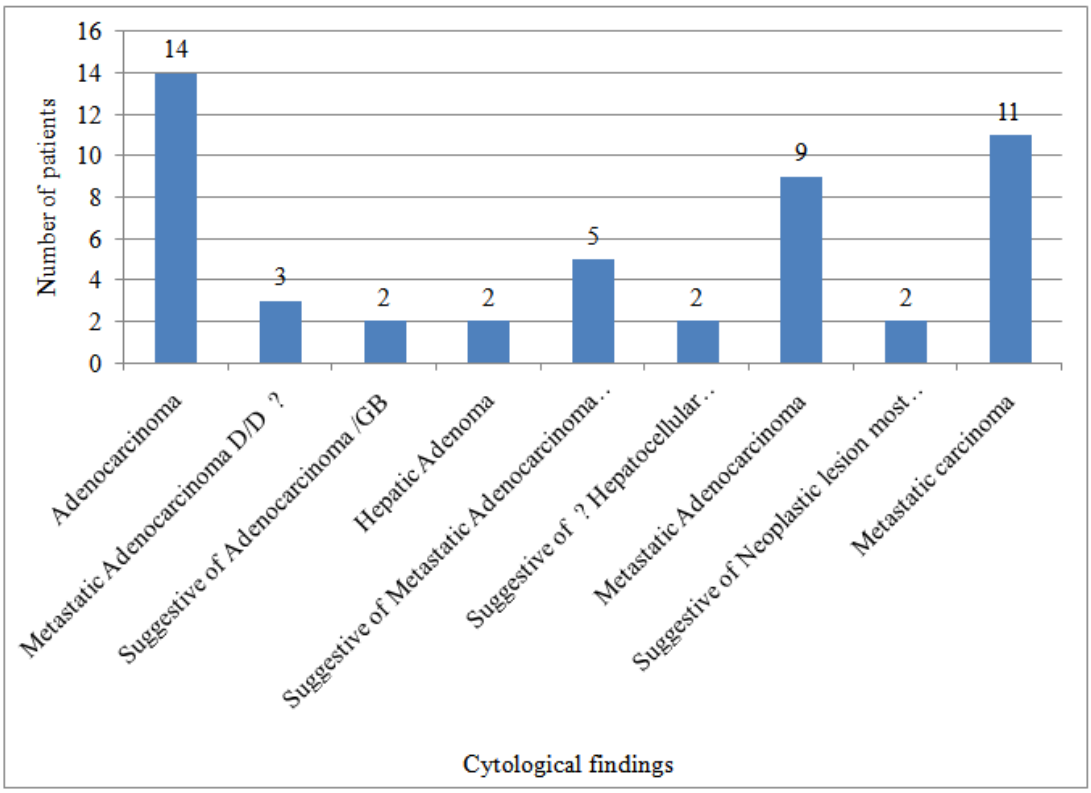

Fig. 4: Shows cytological finding of patients

Table 5: Shows radiological finding of patients

Radiological Diagnosis USG	No. of patients	Percentages
Ca GB	27	54%
Ca Liver	18	36%
Ca Liver Sol	3	6%
Liver Sol	2	4%
Total	50	100%

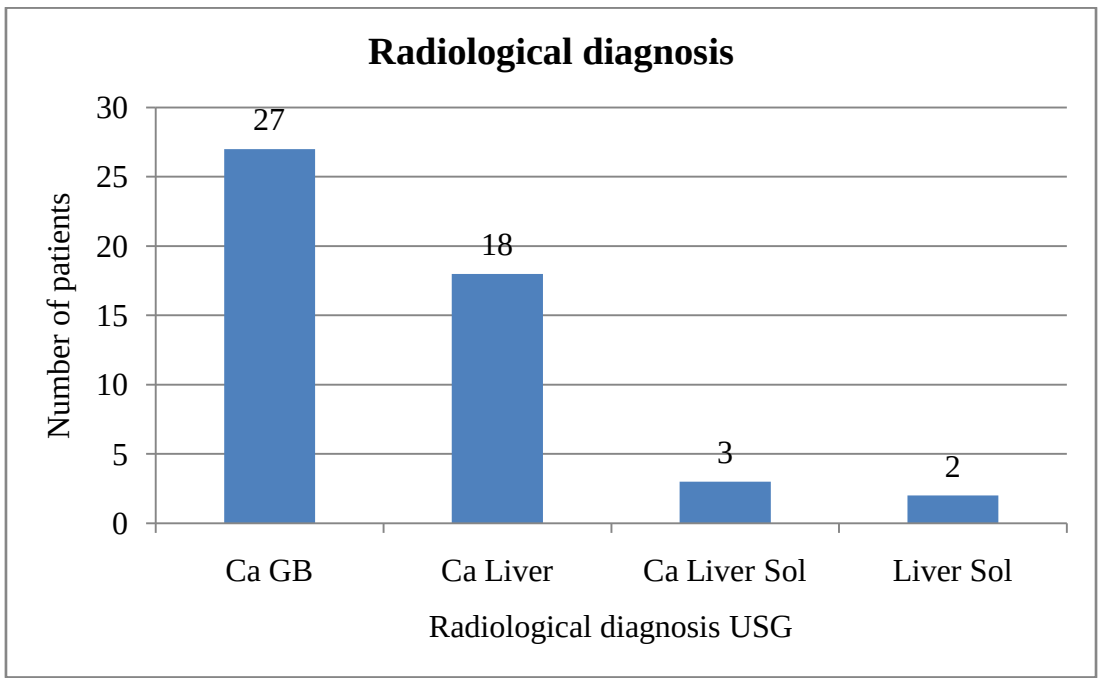

Fig. 5: Shows radiological finding of patients

IV. Discussion

Hepatic aspiration was performed as long ago as in 1833, when Robert and Biet reported its use in the treatment of hepatic suppuration and hydatid disease. [32-33] Needle biopsy using aspiration was first employed in 1883 by Paul Ehrlich in a study of glycogen content of diabetic liver. [34]

Aspiration using very fine needle to evaluate cytological specimens was first used by Lucatello in 1895. [35] At the beginning of 20th century, needle biopsy was accompanied by a high mortality rate. In 1935 Frola in France tried to reduce complications by using a needle which measured 0.5mm in diameter. Since then in 1939 Iverson and Roholm from Denmark, Baron from USA and other workers from northern continental Europe investigated on cytological methods.[36] In 1966, Nils So Derstrom [37] published a series of samples in which his observation on metastatic carcinoma and myeloid metaplasia was helpful in clinical diagnosis. Lundquist published several papers including a thesis on his experience of intrahepatic tumors, acute hepatitis, cirrhosis, iron overload, fatty infiltration and other conditions.

In 1967, Sherlock et al. [38] proved that more neoplasms are detected when cytological examination is performed in addition to histology. This included fluid from needles and syringes and touch preparations of biopsy tissue.

In 1972, Rasmussen et al. [39] described a method for FNA of liver metastases under direct guidance by ultrasonic scanning. They found that FNA cytology had a higher diagnostic rate than routine liver biopsy using the Menghini method.

In 1976, Haaga et al. [40] described a method for precise localization of lesion by US/CT. This allowed accurate positioning of needle when lesions were very small and reduced the rate of false negativity. Over the last 15 to 20 years of the 20th century, it became increasingly clear that percutaneous FNA of single or multiple focal liver lesions demonstrated by palpation, nuclear scan , U/S or CT is both accurate and safe. [41-42] Caution should be exerted when taking a biopsy in a patient with an obstructive biliary tree due to the increased risk of bile leakage. Ascites has also been considered a relative contraindication to biopsy.

FNAC is a procedure available for more than two decades. It is a very useful procedure for the diagnosis of various hepatic lesions. It offers accuracy without major complication and minimal interventions at low cost. The only absolute contraindications are marked haemorrhagic diathesis and suspected vascular lesion. [43] No complications during this study were found. It is of interest to realize that FNAC of the liver guided by ultrasound or C.T. scan has proved to be a safe and an accurate method for diagnosis of focal hepatic lesions.

The main aim of the study is to evaluate the diagnosis of focal liver lesion by FNA guided by radiography.

In our study total patients were 50 out of which males were 24 (48%) and rest females. Male to female ratio was 1:1. [Table 1/ Fig.1] our study is similar with Rasania et al. [44] they reported male to female ratio was 1:1. Another study by Yasin SB et al. [45] reported males 70(53.8%) and females 60(46.2%), male to female ratio was 1.16:1. In their studies by Meena et al. [46] and Nazir et al. [47] male to female ratio of 1.2:1 and 1.7:1 respectively.

In the present study the age ranged from 10 to 70 and above years with a mean age of 54 years. Out of 50 cases in which the diagnosis was made, maximum in age group 51-60 years i.e. 12 (24%), followed by 41-50 years 9 (18%), 61-70 years and 31-40 years 8 (16%) each, 71 and above years 7 (14%), 21-30 years 6 (12%) and lowest in 10-20 years 4 (8%). [Table 2/ Fig.2] Mean age reported by Meena et al. [46] and Nazir et al. [47] was 56 years and 55 years respectively. It is similar to our study.

The most common age group affected was 51-60 years constituting 24% of the patients. Similar results were obtained by Rasania et al [44], Meena et al. [46] and Yasin SB et al. [45] in their studies done in 2006, 2015 and 2017 respectively. Some authors in their studies reported 6th and 7th decades to be the most common age group affected [48-49]

In our study all 50 patients were suffered with pain abdomen weight loss anemia, and personal history was tobacco and site of swelling was right hypocondrium 50 (100%) each. [Table 3/ Fig.3] Examination in most patients revealed spectrum of hepatomegaly, nodular liver, hepatic mass, abdominal mass and some patients with ascites. The most important requirement for such cytodiagnosis is a representative sample from the lesion, and in our case the lesion is located by the guided radiography C.T or U/S, and the operator is expert, so no problem with a representative sample. Patients were subjected to ultrasonography guided FNA which has been reported to be safe useful and accurate technique for making cytological diagnosis of hepatic masses. [50-51]

Our study showed cytological diagnosis out of 50 patients 14 (29.03%) were adenocarcinoma, 3 (3.23%) metastatic adenocarcinoma d/d ?, 2 (3.23%) suggestive of adenocarcinoma /gb, 2 (3.23%) hepatic adenoma, 5 (6.45%) suggestive of metastatic adenocarcinoma d/d hepatocellular carcinoma, 2 (3.23%) suggestive of ? hepatocellular carcinoma d/d ? metastatic adenocarcinoma, 9 (22.58%) metastatic adenocarcinoma, 2 (3.23%) suggestive of neoplastic lesion most likely metastatic adenocarcinoma, 11 (25.81%) metastatic carcinoma. [Table 4 / Fig.4].

Radiological diagnosis USG out of 50 patients Ca GB 27 (54%), Ca Liver 18 (36%), Ca Liver Sol 3 (6%), Liver Sol 2 (4%) [Table 5 / Fig.5]

V. Conclusion

Ultrasound or C.T guided fine needle aspiration cytology (F.N.A.C) is a useful clues test for diagnosis and evaluation of patient with focal liver lesion (unifocal or multifocal), with presence of an expert radiologist and cytopathologist it helps in making a correct diagnosis of focal liver lesions. The role of correlation between discipline of medicine in diagnosis and management of patients with focal liver lesion should be established to advocate the multidisciplinary approach in handling of patients. Not only malignancy can be proved by such a procedure, a number of other conditions as pyogenic liver abscess, tuberculosis and liver hemangioma etc. Radiographic guided FNAC can differentiate benign focal liver lesions against malignancy and also in many cases can verify secondary deposits with help of others features for example finding same cytological pattern in other masses. Ultrasound guided FNAC is useful diagnostic test for evaluation of patients with discrete hepatic mass and superior to CT guided FNAC except for very small lesion. It is concluded that fine needle aspiration cytology under image guidance has increasing acceptance as a means of evaluation of focal liver lesions, and in evaluating liver mass, however there are some difficulties which can be overcome by more experience in aspiration, and better coordination between radiologists, pathologists and clinicians. Further study in this aspect is recommended with a large number of patients with focal liver lesion with stress on cell block and immunohistochemistry techniques.

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