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Original Research Article**Evaluation of guided fine needle aspiration cytology in the diagnosis of hepatic lesions****Akriti Agarwal^{*1}, Ruchee Khandelwal¹, S.N. Singh¹, Hema Pant¹, Piyush Kumar² and Ashish Kumar Gupta³**¹Department of Pathology, Shri Ram Murti Smarak Institute of Medical Sciences (SRMS IMS), Bareilly – Nainital Road, Bhojipura, Bareilly- 243202, Uttar Pradesh, India²Department of Radiotherapy, Shri Ram Murti Smarak Institute of Medical Sciences (SRMS IMS), Bareilly – Nainital Road, Bhojipura, Bareilly- 243202, Uttar Pradesh, India³Department of Radiodiagnosis, Shri Ram Murti Smarak Institute of Medical Sciences (SRMS IMS), Bareilly – Nainital Road, Bhojipura, Bareilly- 243202, Uttar Pradesh, India**QR Code*****Correspondence Info:**

Dr. Akriti Agarwal

Junior Resident,

Department of Pathology,

Shri Ram Murti Smarak Institute of Medical Sciences (SRMS IMS),

Bareilly – Nainital Road, Bhojipura, Bareilly- 243202, Uttar Pradesh, India

Article History:*Received:** 19/01/2017**Accepted:** 11/02/2017**DOI:** <https://dx.doi.org/10.7439/ijbr.v8i2.3880>**Abstract****Objectives:** To categorize the lesions of liver observed on FNAC into malignant or benign, to correlate the radiological observations with cytology findings and to perform histopathological correlation wherever possible.**Material and methods:** A total of 150 cases underwent ultrasonography-guided FNAC, in whom lesion/pathology in the liver was suspected and hepatic mass was confirmed on radiological examination with normal prothrombin time. This study was performed on admitted and OPD patients of SRMS IMS, Bareilly from November 2014 to May 2016.**Results:** Of the total 150 cases, 4 liver aspirates were inadequate for cytological evaluation and were excluded. Most cases (48 cases; 32.87%) were found in the 6th decade. Radiological findings revealed that out of 146 cases, 6(4.10%) were benign and 140(95.9%) were malignant, while cytological examination revealed 13(8.90%) as benign and 133 (90.09%) as malignant. Among malignant cases, 93.2% were metastatic, the commonest being metastatic adenocarcinoma. Correlation between radiodiagnosis and FNAC was evaluated, which revealed a significant change. Sensitivity and specificity of FNAC were 90.00% and 100% respectively. Accuracy of FNAC was observed to be 90.5% when compared with histopathology; however, the latter was available in very small number of cases.**Conclusion:** Categorisation of liver lesions into malignant or benign can be done on FNAC with high accuracy. Guided FNAC is very useful in diagnosis of different hepatic lesions as the procedure is simple and safe. The results are obtained quickly without serious complications related to the procedure.**Keywords:** Fine needle aspiration cytology (FNAC), Liver, Diagnostic, Metastatic, benign.**1. Introduction**

The evaluation and management of discrete hepatic masses is a common clinical problem.[1] Malignancy in the liver, primary or metastatic, is usually inoperable at time of diagnosis and as such, portends an ominous prognosis. A diagnostic modality such as FNA, which offers accuracy without significant complications and which requires minimal intervention at low cost, warrants consideration early in the investigative sequence.[2]

Ultrasound-guided FNAC is a rapid, accurate and safe diagnostic procedure that can be used in diagnosing various neoplastic and non-neoplastic diseases of the liver.[3] The advent of newer modalities possessing the ability of providing cross sectional anatomy, namely computed tomography (CT) and USG have revolutionized the guidance for FNAC.[4]

The study was conducted to evaluate the utility of USG or CT guided FNAC in the diagnosis of liver lesions and to assess the feasibility of using this technique as a routine diagnostic procedure. The purpose of the study was to categorize the lesions of liver observed on FNAC into malignant or benign, to correlate the radiological observations with cytology findings and perform histopathological correlation wherever possible.

2. Material and methods

USG-guided FNAC was performed on a total of 150 cases, in which lesion/pathology in the liver was suspected and hepatic mass was confirmed on radiological examination. This study was performed on admitted and OPD patients of SRMS IMS, Bareilly from November 2014 to May 2016. The area was sterilized with alcohol and infiltrated with 2% xylocaine. Aspirates were obtained with 22-23 gauge disposable spinal needles attached to a 10 ml disposable syringe and smears were made as quickly as possible. Two smears were allowed to dry in air for May-Grünwald Giemsa (MGG) stain, and two were immediately fixed in 95% alcohol for Papanicolaou stain, respectively. Biopsy was available in 21 cases due to the various reasons: many patients were not giving consent for biopsy, some were uncooperative and some lesions were highly vascular or unapproachable. The received specimens were fixed with 10% formalin and processed for paraffin sectioning and stained with H & E. Various cytological features of the smears were recorded and cytological diagnoses were correlated with radiological diagnosis. A comparison was

made with histopathological diagnosis in cases where a biopsy was available.

2.1 Statistical methods

All the data was entered in a database file and analysis was done using SPSS 23 version. P value less than 0.05 was considered as significant. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were evaluated. Wilcoxon signed ranks test was performed to evaluate correlation of radiodiagnosis with FNAC and FNAC with histopathology.

3. Results

Out of total 150 cases, 4 liver aspirates were inadequate for cytological evaluation and were excluded and the clinical data, radiological findings and cytological interpretation were reviewed for remaining 146 cases. Histopathological correlation was available in 21 cases. Age of the patients ranged from 23 years to 85 years with maximum cases (48 cases; 32.87%) in 6th decade. There was a male predominance with male to female ratio as 1.51:1. The most common clinical presentations were abdominal pain, appetite loss, abdominal mass, breathlessness and weight loss.

Radiological findings revealed solitary lesion in 26 cases (17.80%) and multifocal lesions in 120 cases (82.19%). Out of total 146 cases, 6(4.10%) were categorized as benign and 140(95.9%) as malignant on radiological examination. Cytological examination revealed that out of total 146 aspirates 13(8.90%) were benign and 133 (90.09%) were malignant. (Table 1)

Table 1: Classification of cytological findings in 146 liver aspirates

Cytological diagnosis		No. of cases	Percentage (%)	
BENIGN	Benign cystic lesion	1	0.68	
	Vascular lesion	1	0.68	
	Extramedullary haematopoiesis	1	0.68	
	Pyogenic abscess	1	0.68	
	Benign regenerative nodule	1	0.68	
	Amoebic abscess	1	0.68	
	Negative for malignancy	7	4.79	
MALIGNANT	Primary	Hepatocellular carcinoma	3	2.05
	Secondary	Metastatic adenocarcinoma	82	56.16
		Metastatic malignant epithelial neoplasm	25	17.12
		Metastatic small cell carcinoma	7	4.79
		Metastatic squamous cell carcinoma	6	4.11
		Metastatic GIST (Gastrointestinal stromal tumor)	2	1.37
		Metastatic pleomorphic sarcoma	1	0.68
		Metastatic dysgerminoma	1	0.68
	Unclassified malignancy		4	2.74
	Lymphoma		1	0.68
	Suspicious		1	0.68
Total		146	100.0	

Metastatic tumors constituted 93.2% of malignant cases and adenocarcinoma was the commonest type. In some tumors it was not possible to differentiate squamous carcinoma from adenocarcinoma and they were reported as malignant epithelial neoplasms.

Out of 6 cases which were diagnosed as benign on radiology, 5 were confirmed to be benign on FNAC, while 1 case was given suspicious for malignancy. Out of 140 cases suggested as malignant on radiology, 124 cases were proved

as metastatic malignancies, 4 cases as unclassified, 3 cases as hepatocellular carcinoma (HCC), 1 case as lymphoma, while 7 cases were diagnosed as negative for malignancy and 1 case as benign regenerative nodule on cytological examination.

Wilcoxon Signed-Rank Test showed that radio diagnosis and fine needle aspiration cytology did elicit a statistically significant change ($Z = -2.333$, $p = 0.020$). (Table 2)

Table 2: Wilcoxon Signed Rank Test between Radiology and FNAC.

		Cytological Diagnosis		
		Malignant	Benign	Total
Radiological Diagnosis	Malignant	132	8	140
	Benign	1	5	6
	Total	133	13	146

Ranks				
		N	Mean Rank	Sum of Ranks
Guided FNAC liver – Radio diagnosis	Negative Ranks	1 ^a	7.00	56.00
	Positive Ranks	8 ^b	7.00	35.00
	Ties	137 ^c		
	Total	146		
a. Guided FNAC liver sol < Radiodiagnosis				
b. Guided FNAC liver sol > Radiodiagnosis				
c. Guided FNAC liver sol = Radiodiagnosis				

$Z = -2.333^b$ P value=0.020; DF (degree of freedom) =1

Diagnostic accuracy of FNAC was calculated taking histological diagnosis as the gold standard wherever possible. The statistical analysis showed 90.00% sensitivity, 100% specificity, 90.5% diagnostic accuracy, 100% positive predictive value and 33.33% negative predictive

value of FNAC. A Wilcoxon Signed-Rank Test showed that FNAC and histopathological examination did not elicit a statistically significant change ($Z = -1.414^b$, $p = 0.157$). (Table 3)

Table 3: Wilcoxon Signed Rank Test between FNAC and histopathological examination (HPE)

		Histopathological Diagnosis		
		Malignant	Benign	Total
Cytological Diagnosis	Malignant	18	0	18
	Benign	2	1	3
	Total	20	1	21

Ranks				
		N	Mean Rank	Sum of Ranks
HPE Liver - FNAC liver	Negative Ranks	2 ^a	1.50	3.00
	Positive Ranks	0 ^b	.00	.00
	Ties	19 ^c		
	Total	21		
a HPE < Guided FNAC liver sol				
b. HPE > Guided FNAC liver sol				
c. HPE = Guided FNAC liver sol				

$Z = -1.414^b$, $p = 0.157$, DF =1

Primary sites were detected on the basis of clinicoradiological details and other investigations like fluid cytology, FNAC or histopathology from the suspected lesion. Gall bladder was diagnosed as most prominent

21(16.93%) followed by lung 19(15.32%), gastrointestinal tract (oesophagus, stomach, duodenum, periampullary mass, colon, anorectal) 16(12.90%), breast 9(7.25%) and ovary 7 (5.64%).

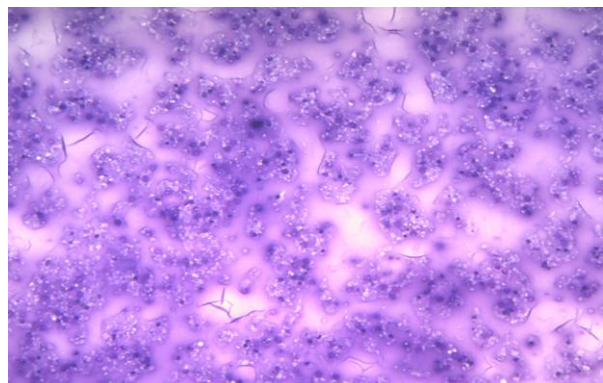


Fig.1. Liver abscess (pyogenic abscess): numerous neutrophils accompanied by necrotic cells and debris (MGG, x400)

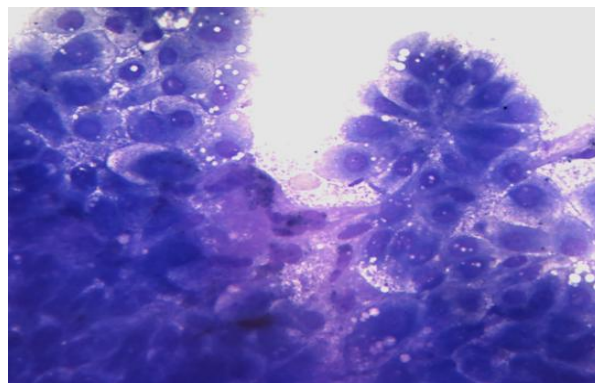


Fig.2. Hepatocellular carcinoma: atypical polygonal cells displaying high N: C ratio, centrally placed nuclei and prominent nucleoli (MGG, x400)

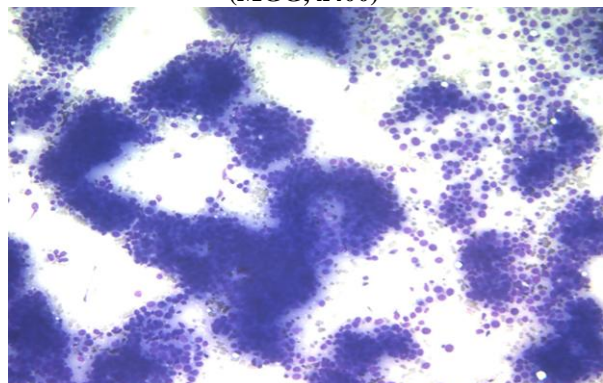


Fig.3. Metastatic adenocarcinoma: richly cellular smears showing acinar and papillary pattern (MGG, x100)

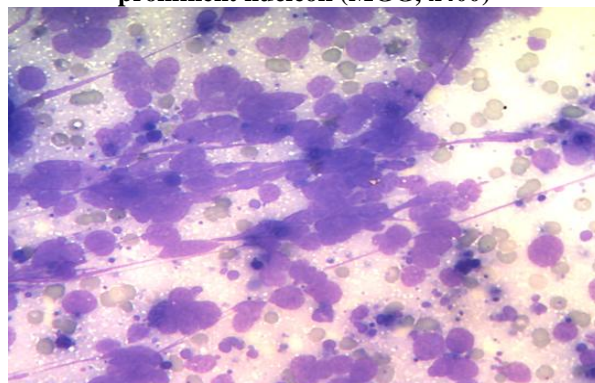


Fig.4. Metastatic small cell carcinoma: singly scattered small cells with little to no cytoplasm, stippled chromatin. Nuclear streaking is evident (MGG, x400)

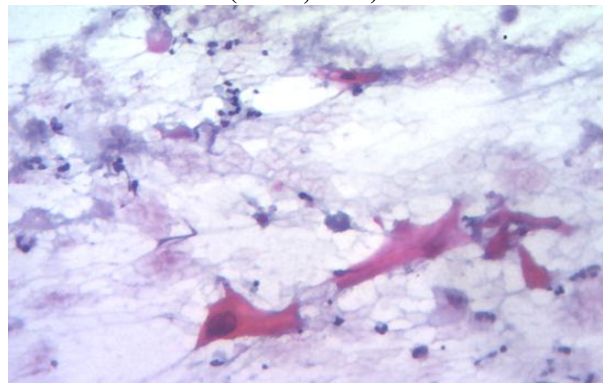


Fig.5. Metastatic squamous cell carcinoma: neoplastic cells showing keratinization (PAP, x400)

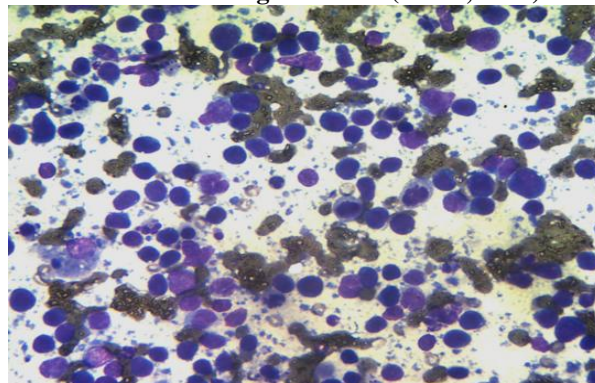


Fig.6. Lymphoma: dispersed large lymphoid cells with scanty cytoplasm (MGG, x400)

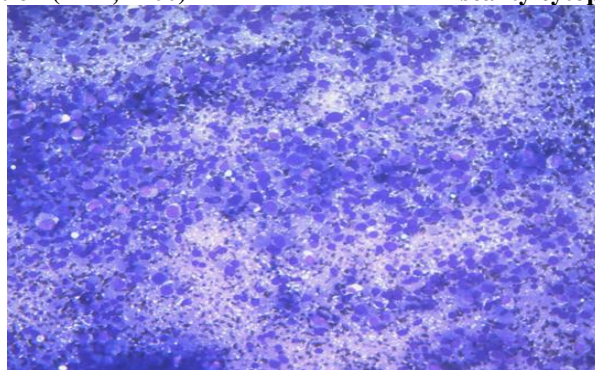


Fig.7. Metastatic dysgerminoma: large poorly cohesive cells in "tigroid" background (MGG, x100)

4. Discussion

Focal hepatic lesions range from cysts and inflammatory processes to neoplasms, be they benign or malignant, primary or metastatic.[5] Clinical, radiological and serological findings cannot reliably distinguish a benign from a malignant lesion, but they can help to narrow the differential diagnosis. In such instances, FNAC under image guidance has gained increasing acceptance as the diagnostic procedure of choice. [6,7] It offers accuracy at low cost without major complication. The contraindications of FNAC are hemorrhagic diathesis, prolonged prothrombin time, vascular structure in the path and suspected extrahepatic obstructive jaundice.[7-9] The main advantage of FNAC is the possibility of multiple passes, which increases the chances of obtaining adequate viable cells.

The age range of the patients and male predominance were comparable with other studies.[10, 11]. The patients' main complaints were abdominal pain in right upper quadrant, loss of appetite, weight loss and abdominal mass, similar to that found in the studies done by Ali *et al*. [12] and Rasanian *et al*. [8]

In our study, the inadequacy rate was 2.66%. Bell *et al*. [13] and Talukdar *et al*. [14] in their studies, reported inadequacy rate of 13% and 6.5%, respectively, using 22 gauge needle technique. Lowest inadequacy rate of 1% is reported by Guo *et al*. [15] using 22 gauge chiba needle.

Correlation between radiodiagnosis and FNAC revealed a significant association i.e. P-value<0.05. But we are unable to conclude the superiority of one of the two diagnostic tests in the present study as biopsy was not available in all the cases. Appropriate results were interpreted by Nggada *et al*. [16] who reported significant statistical difference between ultrasound diagnosis and US guided FNAC in the diagnosis of hepatic lesions. Due to paucity of literatures, we were not able to compare our results with other studies. However, we conclude that although radiological findings cannot reliably distinguish a primary hepatic malignancy from a metastatic disease, they can help to narrow the differential diagnosis.[7]

FNAC results in our study revealed predominantly malignant lesions (91.09%). This is in accordance with the study by Nazir *et al*. [9] (81%). Cytological evaluation revealed 13(8.90%) cases as benign which correlates with the incidence reported by Goel *et al*. [17] (2%) and Ali *et al*. [12] (12%). In our study, the primary malignancies included 2.05% hepatocellular carcinoma while Swamy *et al*. [6] found primary malignancies more common than metastatic lesions.

Out of all hepatic malignancies, 93.2% were metastatic neoplasms, which is similar to some studies that have shown metastatic liver malignancy as high as 90%. [18] But our figures are quite high in comparison to

those reported by [19, 20] who found the frequency of metastatic lesion as 75% and 74.9% respectively. Metastatic adenocarcinoma was most prominent in the present study (56.16%) which correlates with the incidence reported by several other authors. [3, 8, 12, 20, 21]

Incidence of cases reported as metastatic malignant epithelial neoplasms, which could not be further classified was 17.12% which is comparable to 24.53% observed by Goel *et al*. [17] In our study, 2.74% cases were designated as unclassified whereas 0.68% were suspicious for malignancy and lymphoma each; similar results have been reported by Rasanian *et al*. [8]

Gall bladder was the most common primary site of metastatic tumors in liver followed by lung, gastrointestinal tract, breast, and ovary in that order. In the studies by Nasit *et al*. [11] and Singh *et al*. [22] gastrointestinal tract was the most common primary site.

Analysing the cytohistopathological comparison of 21 cases in which biopsy was available, FNAC diagnosed malignancy in 18 cases out of these 21 cases whereas it was negative in 3 cases. While biopsy examination confirmed 20 cases to be malignant and one case as negative for malignancy which was also negative on FNAC.

Diagnostic accuracy of 90.5 % for hepatic lesions in our study, upholds the unquestionable value of guided FNAC as an important diagnostic procedure in the assessment of hepatic lesions and it was comparable to that observed by Cochand-Priollet *et al*. [23] and Tsai *et al*. [24]

Abundant well-prepared material and thorough screening of smears, combined with relevant clinical, radiologic and serologic studies, are the key features to increase the diagnostic accuracy of FNAC. Recent studies have reported good sensitivity of FNAC for liver malignancy, ranging between 67 to 100%, and specificity of 100% or close to it. False-positive diagnoses are rare and positive predictive values approach 100%. [25, 26]

A study by Nasit *et al*. [11], favours FNAC in combination with FNAB (Fine needle aspiration biopsy) as a minimally invasive diagnostic procedure for hepatic masses as both are complimentary to each other and increase diagnostic sensitivity. However, the final choice should be based on the provisional clinical diagnosis, personal experience and expertise.

6. Conclusion

This study concludes that guided FNAC of liver permits the categorization of more frequent benign lesions and neoplastic primary and secondary malignancy in a simple and rational manner which is helpful for the management of hepatic lesions. Correlation of radiological observations with cytology findings revealed a statistically significant change. But we couldn't conclude the superiority

of one of the two diagnostic tests in the study as biopsy was not available in all the cases. However, we feel that guided FNAC is very useful in diagnosis of different hepatic lesions as the procedure is simple and safe. The results are obtained quickly without serious complications related to the procedure. One of the major shortcomings faced in the study was loss of patients for follow up. Moreover, biopsy tissue was available only in few cases, hence statistical analysis may not be exact reflection of actual scenario. Since this was a hospital based study, it cannot be considered wholly as a reflection of entire population, some amount of bias is bound to be introduced. It is, therefore, suggested that a more comprehensive study be performed, taking into account all possible diagnostic modalities.

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References

- [1] Kuo FY, Chen WJ, Lu SN, Wang JH, Eng HL. Fine needle aspiration cytodiagnosis of liver tumors. *Acta Cytol* 2004; 48:142-8.
- [2] deBoer B. Liver and Spleen. In: Orell SR, Sterrett GF, editors. Fine needle aspiration cytology. 5th ed. New Delhi: Churchill Livingstone; 2012.p.271-296.
- [3] Das DK, Tripathi RP, Kumar N, Chachra KL, Sodhani P, Parkash S *et al.* Role of guided FNAC in diagnosis and classification of liver malignancies. *Trop Gastroenterol* 1997; 18(3):101-106.
- [4] Bobhate S, Kumbhalkar DT, Nayak SP. Guided (US&CT) FNAC of abdominal masses and spinal lesions. *J Cytol* 2001; 18(3):137-14-25.
- [5] Wee A. FNA biopsy of the liver: Algorithmic approach and current issues in the diagnosis of hepatocellular carcinoma. *Cyto Journal* 2005; 2:7.
- [6] Swamy MCM, Arathi C, Kodandaswamy C. Value of USG-guided FNAC in the investigative sequence of hepatic lesions with an emphasis on hepatocellular carcinoma. *J Cytol* 2011; 28:178-84.
- [7] Chhieng DC. FNA biopsy of liver- an update. *World Journal of Surgical Oncology* 2004; 2:5.
- [8] Rasanía A, Pandey CL, Joshi N. Evaluation of FNAC in diagnosis of hepatic lesion. *J Cytol* 2007; 24:51-54.
- [9] Nazir RT, Sharif MA, Iqbal M, Amin MS. Diagnostic accuracy of FNAC in hepatic tumors. *J Coll Physicians Surg Pak* 2010; 20:373-6.
- [10] Franca AV, Valeric HM, Trevisan M, Escanhoela C, Seva-Pereira T, Zucoloto S, *et al.* FNA biopsy for improving the diagnostic accuracy of cut needle biopsy of focal liver lesions. *Acta Cytol* 2003; 47(3):332-36.
- [11] Nasit JG, Patel V, Parikh B, Shah M, Davara K. FNAC and biopsy in hepatic masses: A minimally invasive diagnostic approach. *Clin Cancer Investig J* 2013; 2:132-42.
- [12] Ali SR, Jayabackthan L, Rahim S, Sharel MB, Prasad K, Hegdekatte N. Role FNAC in the diagnosis of hepatic lesions. *Muller J Med Sci Res*, 2015; 6:125-8.
- [13] Bell DA, Carr CP, Szyfelbein WM. FNAC of focal liver lesions: Results obtained with examination of both cytologic and histologic preparations. *Acta Cytol* 1986; 30:397-402.
- [14] Talukder SI, Huq MH, Haque MA. USG guided FNAC for diagnosis of mass lesions of liver. *Mymensingh Med J* 2004; 13:25-9.
- [15] Guo Z, Kurtycz DF, Salem R, De Las Casas LE, Caya JG, Hoerl HD. Radiology guided percutaneous FNA biopsy of the liver: Retrospective study of 119 cases evaluating diagnostic effectiveness and clinical complications. *Diagn Cytopathol* 2002; 26(5):283-9.
- [16] Nggada HA, Ahidjo A, Ajagi NA. Correlation between ultrasound findings and ultrasound guided FNAC in the diagnosis of hepatic lesions: A Nigerian tertiary hospital experience. *Int J Gastroenterol* 2006; 5(2):1-7.
- [17] Goel S, Hemrajani D, Sharma M. USG guided FNAC in diagnosis of space occupying lesions of liver. *Journal of Evolution of Med and Dent Sci* 2014; 3(27):7480-7486.
- [18] Orell SR, Sterrett GF, Walters MN, Whitaker D. Retroperitoneum, liver and spleen. In: Manual and atlas of FNAC. 2nd ed. Hong Kong: Churchill Livingstone 1992:217-266.
- [19] Tao LC, Donat EE, Ho CS, McLoughlin MJ. Percutaneous FNA biopsy of the liver: Cytodiagnosis of hepatic cancer. *Acta Cytol* 1979; 23:287-91.
- [20] Barbhuiya M, Bhunia S, Kakkar M, Shrivastava B, Tiwari PK, Gupta S. FNAC of lesions of liver and gallbladder: An analysis of 400 consecutive aspirations. *J Cytol* 2014; 31:20-4.
- [21] Kapadiya DN, Varadharajaperumal R, Santwani PM. USG guided FNAC of liver: four year study. *IJAR* 2015; 3(12):523-527.
- [22] Singh S, Sen R, Kumar S, *et al.* Profile of Liver FNA in Tertiary Care Hospital. *Euroasian J Hepato Gastroenterol* 2013; 3(1):31-35.
- [23] Cochand-Prisollet B, Chagnon S, Ferrand J, Blery M, Hoang C, Galian A. Comparison of cytologic examination of smears and histologic examination of tissue cores obtained by FNA biopsy of the liver. *Acta Cytol* 1987; 31:476-80.
- [24] Tsai YY, Lu SN, Changchien CS, Wang JH, Lee CM, Eng HL, *et al.* Combined cytologic and histologic diagnosis of liver tumors via one-shot aspiration. *Hepato-Gastroenterol* 2002; 49:644-7.
- [25] Jenssen C, Dietrich C. Endoscopic USG-guided FNA biopsy and trucut biopsy in gastroenterology- an overview. *Best Pract Res Clin Gastroenterol* 2009; 23:743-59.
- [26] Maheshwari A, Kantsevov S, Jagannath S, Thuluvath PJ. Endoscopic ultrasound and FNA for the diagnosis of hepatocellular carcinoma. *Clin Liver Dis* 2010; 14(2):325-32.