

IMAGE-GUIDED FINE-NEEDLE ASPIRATION CYTOLOGY OF HEPATOBILIARY LESIONS WITH RADIOLOGICAL CORRELATION

PRERNA CHHABRA¹, SARITA NIBHORIA², SAHIL CHHABRA¹, SHIVANI PURI^{3*}

¹Department of Pathology, Adesh Institute of Medical and Research, Bathinda, Punjab, India. ²Department of Pathology, GGS Medical College and Hospital, Faridkot, Punjab, India. ³Department of Pathology, Dr SS Tantia Medical College, Hospital and Research Centre, Sri Ganganagar, Rajasthan, India.

*Corresponding author: Shivani Puri; Email: shivanipuri1612@gmail.com

Received: 07 May 2024, Revised and Accepted: 20 June 2024

ABSTRACT

Objectives: The clinical and radiological presentations of both primary and metastatic hepatobiliary tumors can be similar—as a space-occupying focal mass. Fine-needle aspiration cytology (FNAC) can play a decisive diagnostic role minimizing the requirement of biopsy. Therefore, the present study was undertaken to evaluate various hepatic and gall bladder lesions on the basis of their cytomorphological features on ultrasound (USG)/computed tomography (CT)-guided FNAC and to study their correlation with radiological findings.

Methods: The patients presenting with liver enlargement, gall bladder masses, and radiologic evidence of focal/diffuse and nodular hepatic lesions were subjected to USG-guided fine needle aspiration, which was performed using 22-gauge lumbar puncture needle with 20/50 cc disposable syringe under USG/CT guidance. Subsequently smears were fixed and stained according to standard protocol and cytomorphological examination was done in the department of pathology. Analytical tests (Mc-nemar's test for p-value and kappa test for kappa value) were applied for cytological and radiological correlation.

Results: Among 100 patients, liver lesions accounted for 79 cases and gallbladder lesions accounted for 21 cases. On FNAC, liver lesions were categorized into 91.23% cases of neoplastic lesions, 6.33% as non-neoplastic lesions and 2.53% as indeterminate/non-diagnostic cases. Radiological-cytological correlation was seen in 43/79 cases (54.43%). Gall bladder lesions were categorized into 9.52% as non-neoplastic, 85.71% as neoplastic, and 4.77% as indeterminate/non-diagnostic. Radiological-cytological correlation was seen in 7/21 cases (31.25%).

Conclusion: Radiologically-guided fine-needle aspiration is a very useful test in diagnosing liver and gall bladder lesions as it is simple to perform, cost-effective, safe and a quick procedure leading to early diagnosis.

Keywords: Liver cytology, Hepatocellular carcinoma, Liver metastases, Gallbladder, Liver sol.

© 2024 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>) DOI: <http://dx.doi.org/10.22159/ajpcr.2024v17i78.51342>. Journal homepage: <https://innovareacademics.in/journals/index.php/ajpcr>

INTRODUCTION

Hepatic diseases are common in our environment, ranging from hepatitis, cirrhosis, and benign space-occupying lesions (SOLs) to malignant tumors, affecting relatively all age groups with the peak in the 5th and 6th decades of life [1]. Liver remains one of the most common organs for the lodgment of metastasis. Differentiation between benign and malignant, primary, or secondary tumors is extremely important from the management point of view. The presence of metastases usually rules out surgery whereas; if hepatocellular carcinoma (HCC) is diagnosed at an early stage, surgical resection is possible and may assure cure. The latter group is the target of fine-needle aspiration cytology (FNAC), which is performed under imaging guidance (USG or CT). Gall bladder enlargement may have many causes, such as acute or chronic cholecystitis or cholelithiasis, which usually causes clinical symptoms. Lack of specific signs and symptoms prevents early detection of gall bladder carcinomas [2]. The purpose of cytologic sampling of the gall bladder is to rule out a primary malignant tumor.

It is not difficult to find out hepatobiliary SOLs with wide application of imaging methods, but it is still troublesome to make an accurate and definite diagnosis of tumors, therefore, ultrasound (USG)/computed tomography (CT)-guided fine needle aspiration should be advocated for the diagnosis of SOLs to improve the accuracy of its diagnosis.

In the present study, the focus lies on diagnosing various liver and gallbladder lesions on USG/CT-guided FNAC on the basis of their cytomorphological features and establishing their correlation with the radiological diagnostic findings.

METHODS

A prospective study was conducted over a period of 1½ year on patients presenting with liver enlargement, gall bladder masses, and radiologic evidence of focal/diffuse and nodular hepatic lesions, with normal prothrombin time index and irrespective of age and sex in a tertiary care hospital. A non-probability sampling was applied and as per the feasibility, 100 patients were considered for this study. In each patient, a brief clinical history, and radiological and biochemical findings were noted. FNAC was performed using 22-gauge lumbar puncture needle with 20/50 cc disposable syringe under USG/CT guidance. Aspiration was done by applying suction, and subsequent smears were fixed and slides prepared were received in the department of pathology. Dry fixed smears were prepared by air drying and then fixing in methanol followed by staining with May-Grunwald Giemsa stain. Wet fixed smears were prepared by immediately fixing in 95% isopropyl alcohol and then staining by hematoxylin and eosin.

The procedure done was in accordance to ethical committee.

OBSERVATIONS AND RESULTS

Out of 100 cases subjected to USG/CT-guided FNAC, liver lesions accounted for 79% of cases and gall bladder lesions were 21%.

Liver lesions

A total of 79 cases of liver lesions were subjected to USG/CT-guided FNAC over a period of 1½ years. The age of the patients with liver lesions ranged from 37 to 90 years with a mean age of 60.55 years.

Maximum patients (36.7%) were in the age group 51–60 years (36.7%). Male-to-female ratio was 2.3:1.

The most common mode of clinical presentation was weight loss/anorexia and pain abdomen. About 48.1% of cases were alcoholic and 51.9% of cases were non-alcoholic. About 29.1% of the patients presenting with liver lesions were affected by Hepatitis C, whereas Hepatitis B affected patients were 2.5%.

Three out of five non-neoplastic cases were diagnosed as inflammatory pathology and showed the presence of inflammatory cells. The other two cases showed singly scattered and clusters of epithelioid cells along with a few inflammatory cells and necrotic debris and were diagnosed as granulomatous pathology (Table 1).

Twenty-six cases (33.00%) were classified as primary HCC under neoplastic liver lesions (Table 1). All the cases of HCC were in the age group 41 to 80 years with a mean age of 61.38 years and male-to-female ratio was 3.3:1.

About 57.70% of cases of HCC presented predominantly as single SOLs, followed by 26.90% as multiple SOLs. About 7.70% of cases presented as two SOLs in the liver and the same 7.70% as diffuse lesions.

The cytological smears were moderately to markedly cellular. Architectural pattern of all the cases (100%) comprised cell clusters, 88.46% of cases showed widened trabeculae whereas 46.15% of cases also showed singly scattered cells and again 46.15% showed sheet pattern. Most of the smears (88.46%) showed moderate degree of cellular pleomorphism. All the cases (100%) showed a high N: C ratio, prominent nucleoli and transgressing vessels (Figs. 1 and 2). Peripheral endothelial wrapping was seen in 65.38% and intranuclear-cytoplasmic inclusions were present in 50% of cases.

Forty-one cases (51.90%) were classified as secondary metastatic deposits under neoplastic liver lesions (Table 1).

Out of 40 cases of metastatic deposits liver, the majority of the patients (70.73%) presented with multiple SOLs radiologically and 17.07% presented as two SOLs, whereas few cases (12.20%) presented with single SOL radiologically.

Majority of the cytological smears of metastatic liver deposits were moderately cellular. Architectural pattern predominantly comprised cell clusters (95.12%) along with singly scattered cells in 82.93%. Acini or attempted gland formation was seen in 17.07% of cases and papillaroid clusters in 24.40% of cases. Cells of squamoid differentiation were present in 4.88% of cases and spindle-shaped cells in 2.44% of cases. Majority of the smears (78.05%) showed a moderate degree of cellular pleomorphism with a high N: C ratio in 95.12% of cases.

Three cases were diagnosed as malignant, not otherwise specified. Two cases as suspicious of carcinoma and two cases were categorized as non-diagnostic or indeterminate (Table 1).

Correlation of radiological findings with cytological diagnosis was present in a total of 43 out of 79 cases (54.43%) of liver lesions. Radiological and cytological findings were similar in 16/26 cases (61.53%) of HCC. Kappa test of measure of agreement was applied, and it showed kappa value of 0.47, which indicates moderate strength of correlation, and $p < 0.001$ which shows significant correlation. 25/41 cases (61.00%) of metastatic deposits showed the same diagnosis on FNAC and radiology. Kappa value was 0.422, that is, moderate strength of correlation and $p < 0.01$, that is, significant correlation. In 2/3 cases (66.67%) of inflammatory pathology, radiological findings correlated with cytological diagnosis. Kappa value was 0.794, that is, good strength of correlation and $p < 0.001$, that is, a significant correlation (Table 3).

Gall-bladder lesions

Twenty-one patients presented with gall bladder lesions (21.00%) (Table 2). Majority of the patients (52.38%) were in the age group 41–60 years, followed by 42.86% of cases in the age group 61–80 years with a mean age of 58.62 years. Male-to-female ratio was 3:1.

Two cases were diagnosed as inflammatory pathology (Table 2). Smears of both cases showed the presence of polymorphonuclear neutrophils and degenerated cells, along with hemorrhage.

Sixteen cases were diagnosed as adenocarcinoma of the gall bladder (Table 2). Majority of the smears were moderately cellular, and the architectural pattern predominantly comprised cell clusters in 87.50% along with singly scattered cells in 62.50%. Characteristic features, acini, and papillaroid structures were present in 50.00% smears each (Fig. 3). About 75% of the smears showed a moderate degree of cellular pleomorphism and 25.00% of smears showed marked degree of cellular pleomorphism. All the smears showed a high N: C ratio of malignant cells while prominent nucleoli were seen in 43.75% of smears.

Two cases were diagnosed as malignant pathology – not otherwise specified and one case was diagnosed as non-diagnostic as it showed mainly the presence of blood along with reactive hepatocytes (Table 2).

All the cases (2/2) of inflammatory pathology, radiological, and cytological diagnosis were similar to each other. Kappa value was 0.77, which indicates good strength of correlation and $p < 0.001$, that is, a significant correlation. In 5/16 cases diagnosed as adenocarcinoma-gall bladder, radiological findings showed correlation with cytology in 5 cases (31.25%). Kappa value was 0.178, that is, poor correlation and p value were 0.15, that is, an insignificant correlation.

RESULT AND DISCUSSION

Clinical, serological, and radiological findings are not reliable to differentiate between a benign and malignant lesion but are useful in making differential diagnosis of various hepatic and gall bladder lesions. Thus, FNAC under image guidance has been considered as a diagnostic modality early in the investigative sequence as it has the advantages of minimal invasion, safety, minimal complication rate and cost-effectiveness along with possibility of multiple passes, which increases the chances of obtaining adequate viable cells.

Table 1: Cytological diagnosis of liver FNAC (n=79)

Diagnosis	Number	Percentage
Non-neoplastic lesions	05	6.33
Inflammatory pathology	03	3.80
Granulomatous pathology	02	2.53
Neoplastic lesions	72	91.14
Primary – Hepatocellular carcinoma	26	33.00
Secondary – Metastatic deposits	41	51.90
Malignant pathology – NOS	03	3.80
Suspicious of malignancy	02	2.53
Indeterminate/non-diagnostic	02	2.53
Total	79	100.00

FNAC: Fine-needle aspiration cytology

Table 2: Cytological diagnosis of gall bladder FNAC (n=21)

Diagnosis	Number	Percentage
Non-neoplastic lesions	02	09.52
Inflammatory pathology	02	09.52
Neoplastic lesions	18	85.71
Adenocarcinoma	16	76.20
Malignant pathology – NOS	02	09.51
Indeterminate/non-diagnostic	01	04.77
Total	21	100.00

FNAC: Fine-needle aspiration cytology

Table 3: Correlation of cytomorphological findings with radiological findings in liver lesions (n=79)

Cytology diagnosis	Radiological diagnosis					Total
	HCC	Liver metastatic	Neoplastic liver mass	Abscess/inflammation	Chronic liver disease	
HCC	16	6	3	0	1	26
Liver metastatic	6	25	9	1	0	41
Malignant-Nos	0	0	2	0	1	3
Suspicious of malignancy	0	1	1	0	0	2
Granulomatous pathology	1	0	1	0	0	2
Inflammatory pathology	0	0	1	2	0	3
Indeterminate/non-diagnostic	1	0	0	0	1	2

HCC: Hepatocellular carcinoma

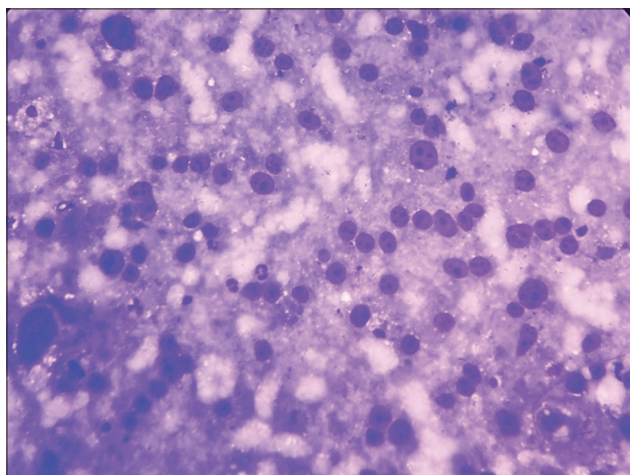


Fig. 1: Prominent nucleoli in hepatocellular carcinoma tumor cells (May-Grunwald Giemsa; ×400)

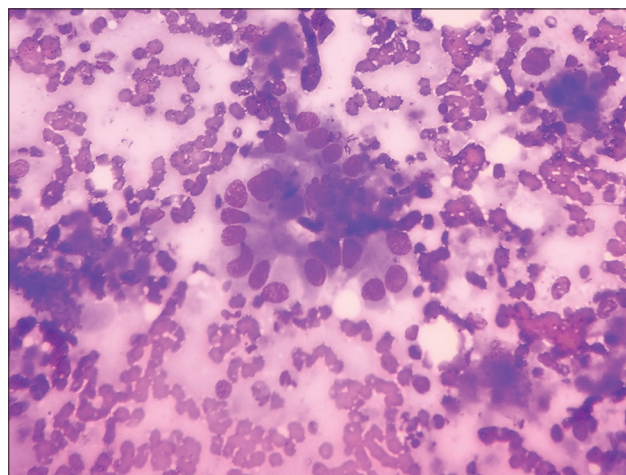


Fig. 3: Acini formation adenocarcinoma-gallbladder (H&E; ×400)

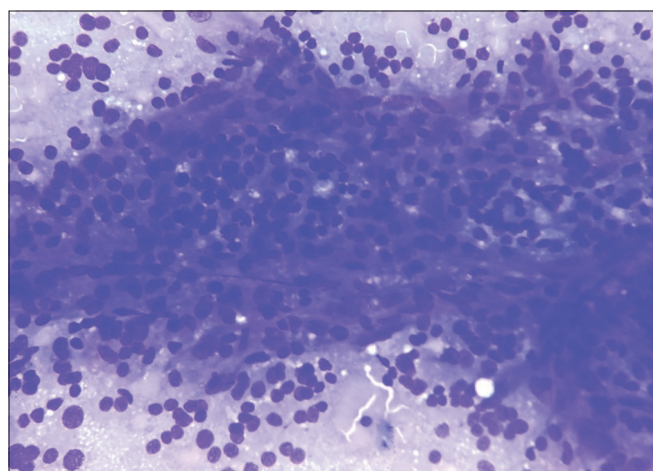


Fig. 2: Transgressing vessel through tumor cells – hepatocellular carcinoma (May-Grunwald Giemsa; ×400)

In the present study, it was found that hepatic lesions were more common in comparison to gall bladder lesions. Maximum number of patients with liver lesions were seen in the age range of 51–60 years. This was also the observation made by Roy *et al.* [3] and Meena *et al.* [4]. Male-to-female ratio was 2.3:1 which is in concordance with the results of studies done by Goel *et al.* [5] and Roy *et al.* [3]. In our study, the majority of the liver lesions (91.14%) were neoplastic and 6.33% were non-neoplastic. About 2.3% were reported as indeterminate/non-diagnostic. These results were concordant with studies done by Nazir *et al.* [14] and Goel *et al.* [5] which also showed the majority of the cases of liver lesions categorized as neoplastic.

Five cases were diagnosed as non-neoplastic liver diseases precising to two cases of inflammatory pathology and three cases of granulomatous pathology on the basis of cytomorphological features which include the presence of inflammatory cells and epithelioid cell clusters along with necrotic debris. Goel *et al.* [5] studied 360 cases of liver FNAC and reported 7 cases (2%) as non-neoplastic lesions, out of which 3 cases (42.86%) were further categorized as liver abscess, 2 cases (28.57%) as granulomatous lesions and 2 cases 28.57% cases as regenerating nodule.

It was found in our study that metastatic deposits in liver were more common in comparison to primary HCC. These results were similar to that reported by Goel *et al.*, Dalsaniya *et al.* and Balani *et al.* [5-7]. However, it was discordant with the studies done by Nazir *et al.* [14] and Swamy *et al.* [5,8].

Cytological smears of all the cases diagnosed as HCC in our study were cellular, being moderately cellular in 61.54% of cases and markedly cellular in the rest. The most important architectural pattern considered was cell clusters and the formation of widened trabeculae. In our study, the persistent features in all the HCC cases (100%) along with hypercellularity were a high N: C ratio, prominent nucleoli, and transgressing capillaries. Swamy *et al.* [8] in their study also stated that hypercellular aspirates comprising cohesive clusters of atypical hepatocytes with arborescent broad trabeculae, with or without peripheral endothelial rimming are pathognomonic of classic HCC.

The characteristic cytological findings in HCC relate to cell groupings, relationship to endothelium and cell morphology. The features in any individual FNA sample were extremely variable. Many smears were typically cellular with large fragments, clusters, and dispersed cells. Neoplastic cells form widened trabeculae, acini, multi-layered sheets,

or lying as many striped atypical nuclei. N: C ratio was increased and the nuclei showed increased atypia, macronucleoli, and intranuclear inclusions. Microfragments of tumor cells surrounded by a distinct layer of endothelial cells were also seen. Mitosis, multinucleation, and necrosis were seen in many cases.

Cytological smears of cases diagnosed as liver metastatic deposits comprised predominantly of cell clusters along with singly scattered cells. Wide array of cytomorphological features was noted, pinpointing toward the origin of primary tumor in 20 cases. Majority of the cases (17/41 cases) showed acini or attempted gland formation (17.07%) and papillaroid clusters (24.40%) giving clues toward metastasis from adenocarcinoma. 2/41 cases showed cells with squamoid differentiation, thus possibility of metastasis of squamous cell carcinoma was suggested. One case with spindle cell morphology was also noted, giving the possibility of metastatic sarcoma. Benign hepatocytes were present in all the cases.

The correlation between radiological findings and cytological diagnosis was found in 43/79 cases (54.43%) of liver lesions, which included 02 cases (66.67%) of inflammatory pathology, 16 cases (61.53%) of HCC and 25 cases (61.00%) of metastatic deposits. The study done by Arathi and Giriyan [9] showed that radiological studies correlated with cytological diagnosis in 81% of cases, respectively.

The age of presentation of gall bladder lesions in the present study ranged from 37 to 80 years with a mean age of 58.62 years. Bhartiya *et al.* [10] reported the mean age of 53 years. There was a female preponderance noted in our study with male-to-female ratio of 1:3. It was comparable with studies done by Ahmad *et al.* [11] and Kumar *et al.* [12]. Majority of the gallbladder lesions were reported as neoplastic. Similar results were reported by Handa *et al.* [13] and Kumar *et al.* [12].

Two cases of gallbladder lesions were reported as inflammatory pathology, cytological smears of both the cases showed presence of polymorphonuclear neutrophils along with degenerated cells. Sixteen cases showed glandular differentiation on cytological smears which suggested the possibility of adenocarcinoma. Cytological smears of these cases were moderately cellular with the presence of cell clusters and singly scattered cells along with typical acinar and papillary patterns of cells having a high N: C ratio and exhibiting moderate to marked degree of pleomorphism.

Out of 21 gallbladder lesions, there were a total of 7 cases (33.33%) where radiological findings found correlation with cytological diagnosis, which included two cases of inflammatory pathology and five cases of adenocarcinoma gallbladder. Thus, the majority of the cases were misleading radiologically.

CONCLUSION

Thus, it is concluded that the present study shows that radiologically-guided fine-needle aspiration is an excellent tool for diagnosing liver and gallbladder lesions. Guided FNAC is a great diagnostic tool particularly in absence of liver biopsy and other ancillary studies. Well stained and accurately sampled cytological smears can help in reaching the accurate diagnosis with minimum cost, thereby, helping in further management of the patient.

AUTHORS' CONTRIBUTIONS

Dr. Prerna Chhabra – Developing concept for research, designing study, literature search, data acquisition, analysis and conclusion, manuscript preparation. Dr. Sarita Nibhoria – Data analysis and conclusion, manuscript preparation, editing and reviewing. Dr. Sahil Chhabra – Data analysis and reviewing. Dr. Shivani Puri – Data statistical analysis, and editing.

CONFLICTS OF INTERESTS

Nil.

AUTHORS' FUNDING

Not applicable.

REFERENCES

- Naggada HA, Ahidjo A, Ajagi N. 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):1-5.
- Das DK, Tripathi RP, Bhambhani S, Chachra KL, Sodhani P, Malhotra V. Ultrasound-guided fine-needle aspiration cytology diagnosis of gallbladder lesions: A study of 82 cases. *Diagn Cytopathol.* 1998;18(4):258-64. doi: 10.1002/(sici)1097-0339(199804)18:4<258:aid-dc2>3.0.co;2-8, PMID: 9557259
- Roy SK, Sultana S, Mollah NU, Yasmin T, Sarker A, Jahan MU. Role of ultrasonography in diagnosis of solid space occupying lesion in the liver correlation with FNAC. *Bangladesh Med Res Counc Bull.* 2015;41(2):81-8. doi: 10.3329/bmrcb.v41i2.29986, PMID: 29624286
- Meena SP, Patangia P, Rai NN. Diagnostic utility of USG-guided FNAC in hepatic lesions. *J Evid Based Med Healthc.* 2016;3(52):2699-702. doi: 10.18410/jebmh/2016/591
- Goel S, Hemrajani D, Sharma M. Ultrasound guided fine needle aspiration cytology (FNAC) in diagnosis of space occupying lesions (SOL) of liver. *J Evol Med Dent Sci.* 2014;3(27):7480-6.
- Dalsaniya SB, Shah MG, Patel TS, Gandhi JS, Jetly DH, Trivedi PP. Evaluation of liver space occupying lesions by fine needle aspiration cytology. *Int J Curr Res Rev.* 2016;8(24):13-8.
- Balani S, Malik R, Malik R, Kapoor N. Cytomorphological variables of hepatic malignancies in fine needle aspiration smears with special reference to grading of hepatocellular carcinoma. *J Cytol.* 2013;30(2):116-20. doi: 10.4103/0970-9371.112655, PMID: 23833401
- Swamy MC, Arathi CA, Kodandaswamy C. Value of ultrasonography-guided fine needle aspiration cytology in the investigative sequence of hepatic lesions with an emphasis on hepatocellular carcinoma. *J Cytol.* 2011;28(4):178-84. doi: 10.4103/0970-9371.86344, PMID: 22090691
- Arathi S, Giriyan S. Ultrasound guided FNAC in diagnosis of space occupying lesions of Liver. *Indian J Pathol Res Pract.* 2017;6(2):360-4.
- Bhartiya R, Mallick S, Mallik M, Agrawal P, Singh R, Singh RV. Ultrasound-guided fine-needle aspiration cytology diagnosis of gall bladder lesions with the application of WHO histological classification of tumors on cytoaspirate material. *Ann Trop Med Public Health.* 2017;10(1):138-42. doi: 10.4103/1755-6783.196595
- Ahmad SS, Akhtar K, Akhtar SS, Nasir AA, Mansoor T. Ultrasound guided FNA biopsy of abdominal masses. *JK Sci.* 2006;8:200-4.
- Kumar N, Singhal P, Agarwal A, Khan MA. Cytopathological diagnosis of gallbladder mass and mural thickening based on imaging findings: A prospective study of 51 cases. *J Cytol.* 2015;32(4):234-7. doi: 10.4103/0970-9371.171231, PMID: 26811570
- Handa U, Nanda A, Mohan H, Kochhar S, Sachdeva A. Cytologic diagnosis of gallbladder lesions - a study of 150 cases. *Indian J Surg.* 2010;72(3):181-4. doi: 10.1007/s12262-010-0047-y, PMID: 23133243
- Nazir RT, Sharif MA, Iqbal M, Amin MS. Diagnostic accuracy of fine needle aspiration cytology in hepatic tumours. *J Coll Physicians Surg Pak* 2010;20(6):373-76.