



CLINICOPATHOLOGICAL ASSESSMENT OF ASCITIC FLUID CYTOMORPHOLOGY IN A SAMPLE OF IRAQI PATIENTS

Marwa M. Ekraayem*¹, Ban J. Qasim² and Alaa G. Hussein²

¹AL-Emamain Al-Kadhmain AS Medical City.

²Department of Pathology, College of Medicine, Al-Nahrain University. Baghdad Iraq.

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*Corresponding Author: Marwa M. Ekraayem

AL-Emamain Al-Kadhmain AS Medical City.

ABSTRACT

Background: the International System for Reporting Serous Fluid Cytopathology was applied to report serous effusion. Effusion cytopathologic evaluation can be challenging due to multiple, different processes affecting serous cavities, ranging from benign (infectious, autoimmune) to malignant processes (primary or metastatic neoplasms). **Method:** A retrospective study included the analysis of 147 randomly selected samples of ascitic fluid sent to the Teaching Laboratories of Al-Emamain Al-Kadhmain Medical City (AS) from January 2020 to January 2023. **Results:** In this study, Mean age of 47+_19.41 years. Females to male ration 1.5:1, Abdominal distension was the clinical presentation for all cases. Chronic liver disease 38 (25%) was the most common associated diseases. Transudate fluid was the most common ascitic fluid appearance 90(61%), the percentage of hemorrhagic effusion 11(7%). Pleural effusion 12 (8%) was the most common radiological finding As for the international system for reporting serous fluid cytopathology 4(3%) are classified as non-diagnostic or unsatisfactory samples, 92 (63%) are negative for malignancy, 29 (20%) are atypical of undetermined significance, 15 (10%) are suspicious for malignancy, 7 (5%) are malignant, and finally, the most common diagnostic categories was negative for malignancy (IL,NFM) 63%. **Conclusion:** Most of cases were adult Females, Abdominal distension and dyspnea was the most common clinical presentation, Chronic liver disease was the most frequent associated disease ,Pleural effusion was the most common radiological finding negative for malignancy (IL,NFM) was the most common diagnostic categories.

INTRODUCTION

Ascitic fluid cytology is one of the first tests conducted in a patient with ascites, both for confirmation of a suspected malignancy and staging of a known malignancy. The sensitivity of this method in detecting malignancy has been found to be 50%–96.7% in different studies.^[1-4]

Effusion cytopathologic evaluation can be challenging due to multiple, different processes affecting serous cavities, ranging from benign (infectious, autoimmune) to malignant processes (primary or metastatic neoplasms).^[5]

Decompensated hepatic cirrhosis is the leading cause worldwide, and the ascitic fluid is usually transudate in nature with a serum-ascites albumin gradient (SAAG) >1.1 g/dl.^[6-10]

Ascites is the first sign of malignancy in around half of all patients with peritoneal carcinomatosis secondary to malignancies of the gynecological and gastrointestinal

tracts.^[11-14] The detection of malignant cells on effusion cytology in these patients is important for management and disease prognostication.^[15-17] Both architecturally and cytologically reactive mesothelial cells may pose a diagnostic challenge. The reported false-negative rate of ascitic fluid smear cytology for malignancy is as high as 42%.^[18]

Ascites of malignant etiology appear in only 10% of all ascites cases.^[19] Malignant ascites are most frequently present in gynaecological and gastrointestinal carcinomas. A combination of malignant ascites and carcinomatosis of the peritoneum is present in 15–30% of cases.^[20]

Ascites can be exudative or transudative. Transudate make up 90% of ascitic fluids, and they are caused by conditions of non-malignant etiology. This fluid is clear, with a small number of cells and a low level of albumin. An exudate is usually malignant and cloudy, with a greater number of cells and a higher level of proteins than a transudate.^[21]

Although cytomorphology is the foundation of a cytologic diagnosis, ancillary studies are increasingly important in the workup of serous effusion specimens. The most common and widely available approach is immune histochemical (IHC) staining on formalin-fixed, paraffin-embedded (FFPE) cell block sections.^[22]

Aim of study

This study aims to assess ascitic fluid cases in a sample of Iraqi patients according to the International System for Reporting Serous Fluid Cytopathology (TIS) in correlation with age, sex, fluid appearance, radiological findings, and present and associated diseases or surgical history.

MATERIAL AND METHODS

A retrospective study included the analysis of 147 randomly selected samples of ascitic fluid sent to the Teaching Laboratories of Al-Emamain Al-Kadhmain Medical City (AS) from January 2020 to January 2023.

The clinico-cytological data that was collected from patients cytological reports included:

1. Age
2. Sex
3. Clinical presentation
4. Fluid type and appearance
5. Radiological findings
6. Associated diseases or surgical history

Fluid cytological Diagnosis is according to the International System for Reporting Serous Fluid Cytopathology (TIS). A total of five reporting categories are suggested as mentioned below.^[23]

1. Nondiagnostic (ND): The cellular constituents of the fluid are not adequate to draw any conclusive diagnosis.
2. Negative for malignancy (NFM): Total absence of any evidence of mesothelial or non mesothelial malignancy.
3. Atypia of undetermined significance (AUS): Atypical cells are present in the smear. However, there is not enough quantitative or qualitative evidences to suggest these cells as malignant. Overall, the cells simulate benign reactive cells. The atypical cells may be mesothelial macrophages or malignant cells with relatively bland monomorphic nuclei.
4. Suspicious for malignancy (SFM): The smears show atypical cells that are strongly suggestive of malignancy. However, quantitative or qualitative evidence is not adequate enough to reach conclusive evidence of malignancy. The probable type of malignancy, such as carcinoma, lymphoma or mesothelioma should be mentioned in such group. The risk of malignancy in SFM is reported as high as 91.7% in the recently reported cases.

Malignant (MAL) primary and secondary

In this category, the cytological features alone or in combination with other ancillary investigation confirm the diagnosis of malignancy.

Exclusion Criteria

Incomplete clinical or cytopathological data from referring physicians.

All samples had previously been fixed in 95% ethyl alcohol, stained with Hematoxyline and Eosin and the diagnosis was revised by two cytopathologist.

All statistical analysis was performed utilizing SPSS, version 26, and included mean, standard deviation, frequency, and percentage using Yates Chi square, with a p-value <0.05 regarded as statistically significant.

RESULT

1. Distribution of age and sex

Regarding age most of the studied sample cases were in the age group 1-90 years old. As for sex the female to male ratio was 1.5:1, as illustrated in table (1)

Table (1): Distribution of age and sex.

Parameter	Median (Range)	Mean±SD
Age (yr)	50 (1-90)	47.9±19.41
1-10	6	4
11-20	9	6
21-30	14	10
31-40	16	11
41-50	37	25
51-60	31	21
61-70	19	13
>70	15	10
	N	%
Sex	Male	55 37.4
	Female	92 62.6

2. Clinico-cytological characteristic of studied sample as illustrated

In this study, Abdominal distension was the clinical presentation for all cases Chronic liver disease 38 (25%) was the most common associated diseases The percentage of neoplasia in the associated diseases 10(14%). Gastric carcinoma was the most common secondary metastases in effusion (60%). Transudate fluid was the most common ascitic fluid appearance 90(61%), the percentage of hemorrhagic effusion 11(7%). Pleural effusion 12 (8%) was the most common radiological finding. As for the international system for reporting serous fluid cytopathology, 4(3%) are classified as non-diagnostic or unsatisfactory samples, 92 (63%) are negative for malignancy, 29 (20%) are atypical of undetermined significance, 15 (10%) are suspicious for malignancy, 7 (5%) are malignant, and finally, the most common diagnostic categories was negative for malignancy (II,NFM) 63%.

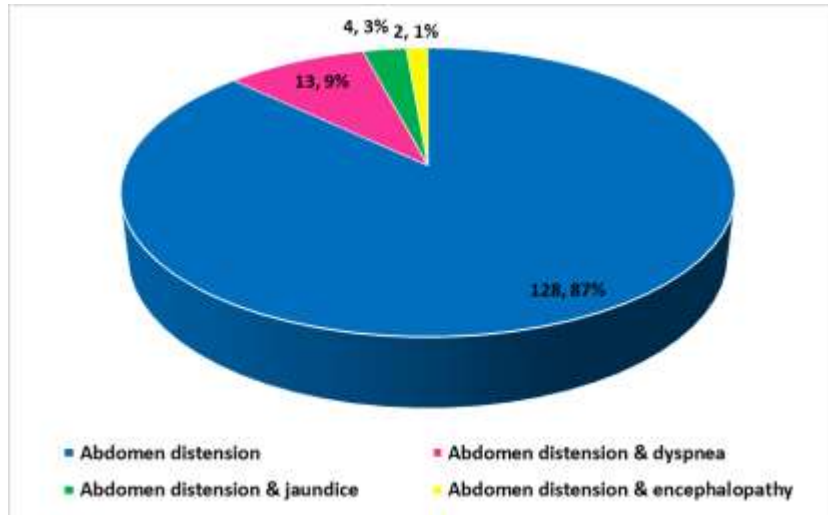


Figure (1): Clinical presentation of cases.

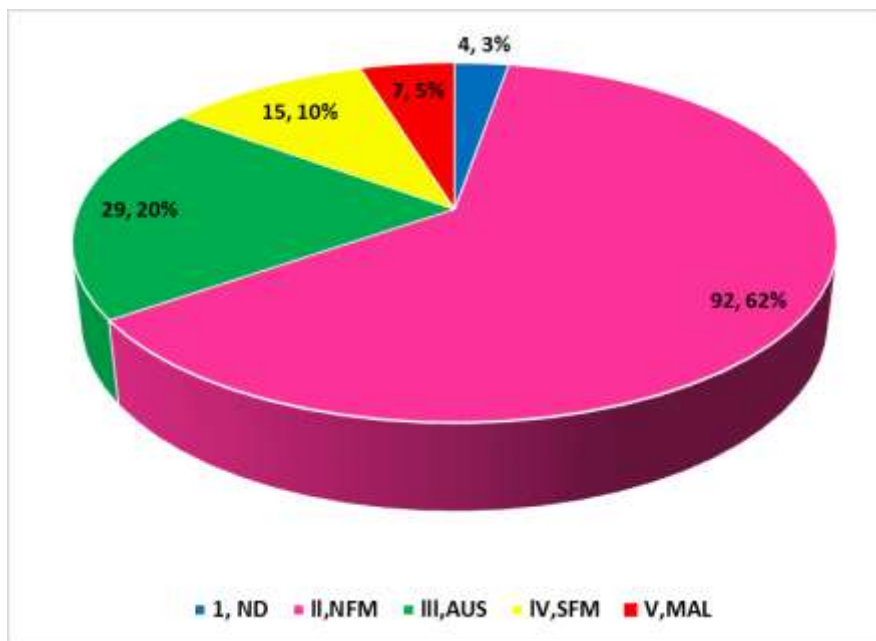


Figure 2: Diagnostic categories according to the international system of reporting serous cytology.

Table 2: Type of ascitic fluid.

Type of effusion	Frequency	percentage
Transudate	90	61
exudate	57	39
hemorrhagic	11	7
Non hemorrhagic	136	93

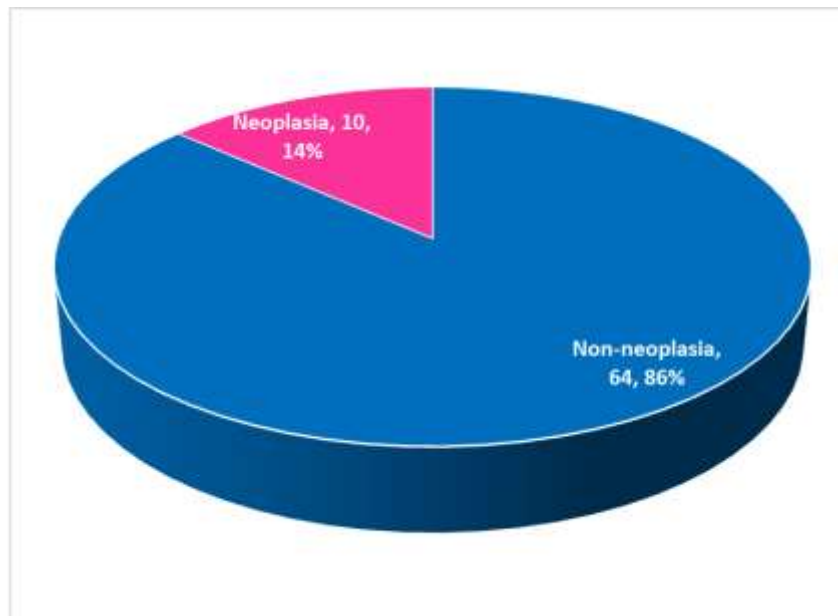


Figure 3: Percentage of the neoplasia and non-neoplasia of associated diseases in cases of ascitic effusion.

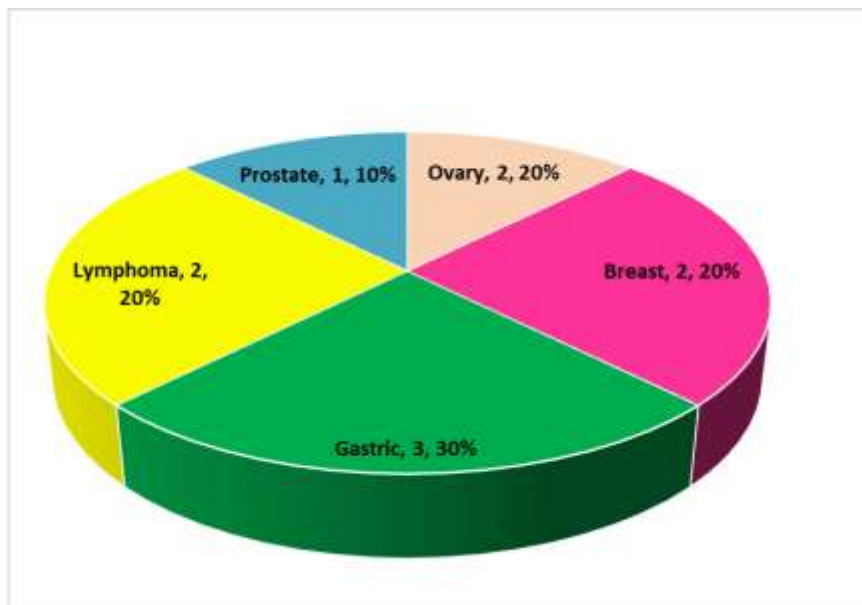


Figure 4: Sources of secondary malignant effusion in cases.

Table 3: Common sources of secondary malignant effusion in female and male.

Sex	Frequency	Percentage
female		
ovary	2	25
breast	2	25
Gastrointestinal tract	3	38
lymphoma	1	12
male		
prostate	1	50
lymphoma	1	50

3. Association between age, sex, type of fluid, clinical presentation, associated disease and radiological finding with diagnostic categories

There is a significant association with type of fluid and associated diseases.

Diagnostic categories	Parameter	P value
	Age	0.398
	Sex	0.937
	Type of ascitic fluid	0.022
	Hemorrhagic vs Non hemorrhagic	0.986
	Clinical presentation	0.952
	Associated diseases	<0.001
	Radiological finding	0.629

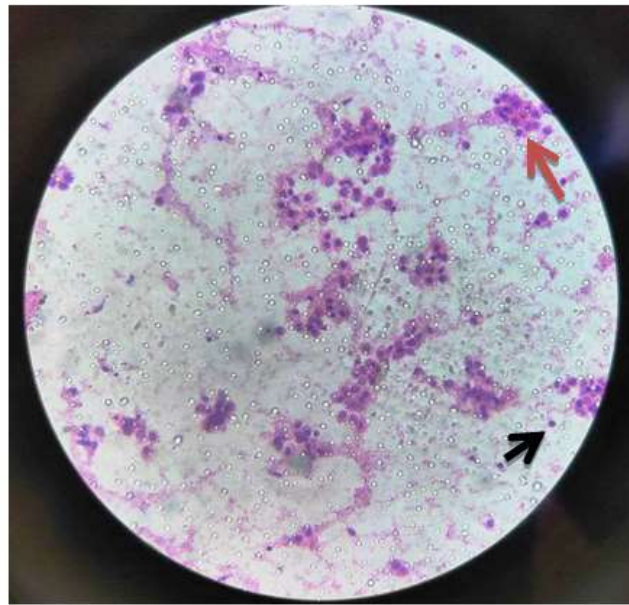


Figure 1: Metastatic hepatocellular adenocarcinoma in ascitic fluid.

Smear of ascitic fluid showing Hypercellularity with mixed inflammatory cells(lymphocyte)(Black arrow), Patchy exudate in back ground frequent groups of large

sized Atypical cells with high grade pleomorphism (Red arrow).(H&E,10X).

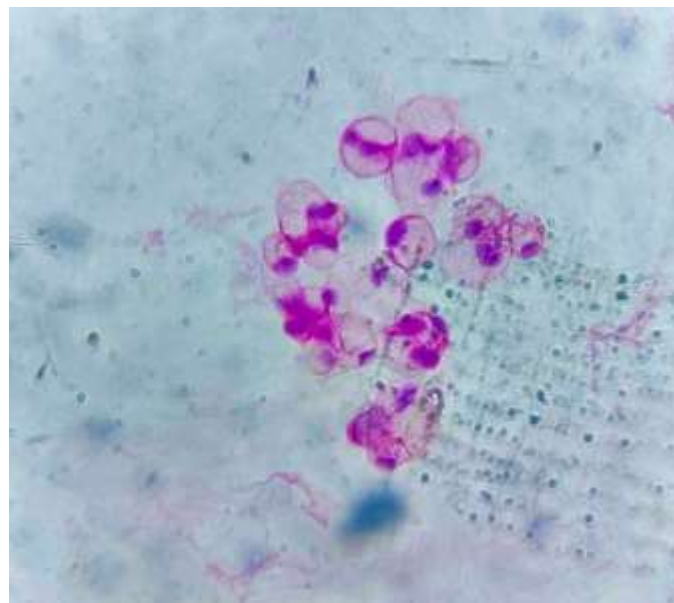


Figure 2: Smear of ascitic fluid showing hypocellularity clear background,few atypical large size cells with eccentric, polymorphic appearance and high grade changes (arrow), (H&E,40x).

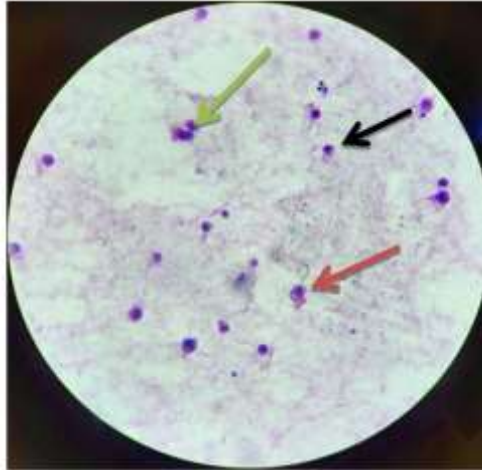


Figure 3: Metastatic gastric carcinoma in ascitic fluid.

Cellular smear shows high count lymphocyte (black arrow) and group of atypical cells (green arrow), and signet ring appearance (red arrow) (H&E,A.10X,B.40X)

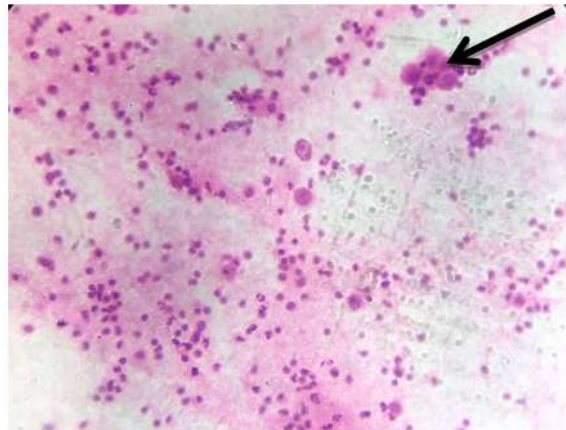


Figure 4: Ascitic smear showing hypercellularity with high count of mixed inflammatory cells with thick exudate, (arrow) frequent large clusters of large size atypical cells with high grade pleomorphism (H&E,40X).



Figure 5: (IV, suspicious for malignancy), hypocellular smear with few inflammatory cells and clear background yet one cluster seen of epithelial cells with high grade atypia (H&E,10X)

DISCUSSION

In this study the mean age of patients was 47.9 ± 19.41 year with age range (1-90) years old, Age group (40-60

year) was the most frequent age group 46% followed by age group (60-70 year)13% the age group (40-60) years

was the most frequent benign effusion the age group(30-60)years was the most frequent malignant effusion.

In other studies the age range 20-39 had the highest prevalence of benign ascites followed by (0-19) and (60-79). The age range (40-59) had the highest prevalence of malignant ascites followed by (20-39).^[24]

Regarding for sex the female to male ratio was 1.5:1, This is similar to observation by Jha et al in kathmandu and Karoo et al in Leicester.^[25,26]

In this study the percentage of hemorrhagic effusion was 11(7%), non hemorrhagic effusion 136 (93%) was the common ascitic fluid appearance with transudate predominant 90(61%).

Abdominal distension was the clinical presentation of all cases, 9(13%) of them presented with dyspnea. chronic liver disease 38(25%) was the most associated diseases followed by gynecological diseases 18(12%).

The non neoplastic was the common etiologies in associated diseases similar to finding in other studies with hepatic cirrhosis being the single most common etiology.^[27]

As of sex gastrointestinal diseases was the most common associated diseases in female, while in male lymphoma (50%) and prostate (50%) was the most common associated diseases.

In other studies the ovary is known to be the most common primary site shedding malignant cells in ascitic fluid in females.^[25,26]

According to radiological finding, pleural effusion 12(8%) was the most radiological finding, The role of ultrasound has been found to have an important role in the investigation of potentially malignant ascites. In 19 of the 32 patients with false negative results the provisional diagnosis was made on ultrasound.^[27]

The study evaluates the application of the recently proposed the international system for reporting serous effusion cytopathology, Cytological evaluation is the most reliable method for detecting malignancy in body cavity fluids, but it cannot determine the exact causes of benign effusions.^[29]

The study included 147 patients being classified into 4(3%) non diagnostic (ND), 92 (63%) negative for malignancy (NFM), 29 (20%) atypia of undetermined significant (AUS), 15 (10%) suspicious for malignancy (SFM), and 7(5%) malignant(MAL)

In this study the malignancy rate (5%) was similar to other studies in the literature, which ranges between 4% and 22.4%.^[30-38] but was lower than that reported in the literature from oncological centers.^[30-37]

In this study the percentage of suspicious for malignancy (SFM) cases (10%) was slightly higher than that in other reported studies (range: SFM, 1.3%–6.3%).^[30-38]

If a case was diagnosed as suspicious for malignancy (SFM) based on tumor history and clinical symptoms they will proceed to do ancillary testing which can lead to reclassified them as malignant or negative for malignancy, if the ancillary tests are noncontributory the diagnosis will remain as suspicious for malignancy (SFM).^[29]

The cases diagnosis as atypia of undetermined significant (AUS) when there is nuclear atypia with overlapping features between reactive changes and malignant appearance but features are closer to benign processes and lack of clinical information.^[29]

In this study the percentage of atypia of undetermined significant (AUS) (20%).

Negative for malignancy (NFM) implies that certain non-malignant cell populations may be present in variable numbers their presence may still indicate disease, but not malignancy.^[29]

In this study the negative for malignancy 92(63%).

Non diagnostic (ND) specimens could be either non-representative for the site (eg, peripheral blood only) or insufficient for interpretation in other ways, as yet to be determined. The sample may consist of blood only.^[29]

In this study the percentage ND cases 4 (3%), The study aligns with previous literature studies indicating non diagnostic rates of 0% to 5.6% in serous effusion.^[25-33]

In this study there was a significant association between diagnostic categories with type of fluid and associated disease (p value 0.022 and <0.001).

There was no significant association between diagnostic and age sex, clinical presentation and radiological finding (p value 0.398, 0.937, 0.952 and 0.629).

The problems encountered in this study is that it was a single center retrospective study, and cytological diagnoses were construed by only two cytopathologists, who, although they reclassified cases according to TIS criteria, may still have individual biases.

CONCLUSION

Most of cases were adult Females Abdominal distension and dyspnea was the most common clinical presentation Chronic liver disease was the most frequent associated disease, Pleural effusion was the most common radiological finding, negative for malignancy(II NFM) was the most common diagnostic categories. A significant association was found between diagnostic categories and (type of ascitic fluid, associated diseases).

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