

Cytological Analysis of Body Fluids in A Tertiary Care Hospital of Jammu Region: A One-year Retrospective Observational Study

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ABSTRACT

Introduction: Exfoliative cytology of body fluids involves the analysis of cells present in fluids such as cerebrospinal fluid, pleural fluid, peritoneal fluid, pericardial fluid and synovial fluid. The cytological interpretation of individual cells exfoliated into these fluids provides an insight into the diagnosis, prognosis and therapeutic aspects of various pathological conditions. It also helps in staging of malignancies.

Objective: To evaluate the significance of fluid cytology for various pathological conditions, including malignancies.

Materials and Methods: This observational retrospective study was carried out for a period of one year from 31st May 2023 to 1st June 2024. A total of 392 cases of peritoneal, pleural, cerebrospinal, synovial, and pericardial fluids received during the study period in the cytology section, Department of Pathology, Government Medical College and Hospital, Jammu, J&K, India were included in this study. Gross and clinical findings were noted from the requisition forms. The fluids were centrifuged at 2000 rpm for 5-minutes and the sediment was used to prepare smears that were stained by May-Grunwald-Giemsa (MGG) stain and Papanicolaou (Pap) stain.

Results: A total of 392 cases of serous effusions were studied. The most common fluid was peritoneal fluid, 230 (58.67%) cases, followed by pleural fluid, 145 (36.99%) cases, CSF, 15 (3.83%) and least common were pericardial fluid and synovial fluid, 1 (0.26%) case each. The age ranged from 4-years to 98-years. Most cases, 85 (21.68%) belonged to 51-60 years age group. Female preponderance was observed with M:F ratio of 1:1.23. 43 (10.97%) of the total effusions were malignant, out of which 23 were malignant peritoneal effusions. 23 (5.87%) cases were suspicious of malignancy, which 13 (56.52%) cases were peritoneal fluids. Carcinoma ovary was the most common primary site causing malignant peritoneal effusion.

Conclusions: Exfoliative cytology is a valuable tool in evaluation of body cavity fluids. It is relatively painless, simple, cost effective, rapid technique that yields quick and reliable results. Some cases may present major interpretative challenges to the pathologist like presence of reactive mesothelial cells which at times poses difficulty in diagnosis, being close mimicker of malignancy. It is especially helpful in evaluation and staging of malignancy.

Keywords: Body fluids, Exfoliative cytology, Malignant effusions.

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INTRODUCTION

Exfoliative cytology, the microscopic examination of shed or desquamated cells from body surfaces, offers a diagnostic tool of significant value in medical science. The study of cells within the fluids of serous cavities is known as effusion cytology.¹ This technique, pivotal in the detection and monitoring of various pathological conditions, involves the analysis of cells present in body fluids such as cerebrospinal fluid, pleural fluid, peritoneal fluid, pericardial fluid and synovial fluid.

By examining these cells, pathologists can identify malignancies, infections, inflammatory conditions, and other abnormalities.^{2,3} The diagnostic yield, sensitivity and specificity of effusion fluid is higher than that of needle biopsy, as the cells present in the sediment are representative of a much larger surface area and the sample size is greater.^{1,4,5}

There are three major body cavities, namely peritoneal, pleural and pericardial.⁶ The fluid cavities are lined by single layer of epithelium. Normally these cavities contain minimal fluid that is required for lubrication and protecting the underlying viscera. The dynamics of fluid accumulation is governed by Starling's law, which stated that fluid is accumulated when there is a decrease in the plasma colloidal

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pressure and increase in the hydrostatic pressure. An effusion results in imbalance between fluid formation and removal.⁴ The body fluids, being in constant contact with different tissues and organs, serve as a reservoir of shed cells that mirror the health status of these tissues.¹⁻³ Morphological analysis of these cells helps in understanding the disease process and in reaching a final diagnosis.⁷ For instance, the presence of specific inflammatory cells can signal infection or autoimmune conditions, guiding appropriate therapeutic interventions.^{1,3} The malignant cells exfoliated into body fluids can be an early indicator of neoplastic processes, thus providing crucial, timely information for cancer diagnosis and treatment planning. In 1882, Quincke published a detailed description of cancer cells in pleural and peritoneal fluids, which was the first authenticated description of cancer cells in body fluids.^{6,8}

The cytological interpretation of individual cells, exfoliated into these fluids, is important since they provide an insight into the diagnosis, prognosis and therapeutic aspects of various pathological conditions.^{4,9} Some conditions in effusions may often have overlapping features and mimic one another cytomorphologically. The accurate identification of cells due to these overlapping features, such as malignant and reactive mesothelial cells, can pose a diagnostic challenge.¹⁰⁻¹² Most important is the recognition of a malignant pathology, but many other conditions such as inflammatory diseases, parasitic, fungal, viral and bacterial infections can also be identified.^{4,13}

This study aims to delve into the application of exfoliative cytology in the analysis of body fluids, highlighting its diagnostic relevance for various pathological conditions and malignancies in a tertiary care hospital. Also, to know the trends of different effusions and categorize effusions according to age, gender, predominant cell type and diagnosis.

MATERIALS AND METHODS

The present study was carried out in the Department of Pathology, Government Medical College, Jammu, from 31st May 2023 to 1st June 2024. All effusion samples of pleural, peritoneal, pericardial, synovial, and CSF irrespective of age and sex received in the cytology section of the Department during that period were studied. Other fluids were excluded. All the faded slides and those with inadequate material were excluded from

the study. Ethical permission was duly taken from the institute's ethical committee. The study included 392 cases. All the relevant clinical information regarding age, sex, and accompanying clinical symptoms were documented. Radiological and biochemical data was also obtained from the requisition forms. The gross findings were noted, cell count was done in improved Neubauer's chamber, then centrifuged at 2000 rpm for 5 minutes. For hemorrhagic fluids, glacial acetic acid was used as a hemolysing agent and then processed routinely. Cytospin was also used for some samples. Smears were made from the sediment. Both wet-fixed and air-dried smears were prepared. The air-dried slide was stained with May Grunwald Giemsa stain. The other slide was immediately fixed in 95% alcohol and stained with Papanicolaou stain. The stained smears were studied on light microscopy and evaluated for cellularity, predominant cell type, size, nuclear and cytoplasmic features, chromatin, degree of inflammation, reactive changes and other background features. All the data was analyzed and summarized.

RESULTS

A total of 392 cases of serous effusions were examined cytologically, which included pleural, peritoneal, pericardial, synovial and CSF. The age ranged from 4-years to 98-years. The most common fluid was peritoneal fluid, 230 (58.67%) cases, followed by pleural fluid, 145 (36.99%) cases, CSF, 15 (3.83%), and least common were pericardial fluid and synovial fluid, 1 (0.26%) case of each.

The present study showed a female preponderance with a male to female ratio of 1:1.23. Peritoneal fluid was the most common fluid received. Most Peritoneal fluids were received from the patients who were aged between 51 to 60 years, followed closely by 41 to 50 years age group. Most Pleural fluids were received from patients of age group 61 to 70 years. CSF was received mostly from 61 to 70 years age group. One sample of pericardial fluid was received from a 60-year-old female. One sample of Synovial fluid was received from a 29-year-old male patient.

According to this study, 83.16% of the total cases were benign/non-malignant lesions. Most benign lesions were of peritoneal fluid cases (59.51%). Out of 43 malignant cases, 23 (53.48%) were peritoneal and 20 (46.51%) pleural. 23 cases were diagnosed as suspicious of malignancy, of which 13 (56.52%) were peritoneal and 10 (43.48%) were pleural.

Table 1: Age and gender wise distribution of cases.

Age Group	CSF n (%)		Pericardial n (%)		Peritoneal n (%)		Pleural n (%)		Synovial n (%)		Total n (%)		Grand Total n (%)
Sex	M	F	M	F	M	F	M	F	M	F	M	F	
0–10	0	2	0	0	0	1	0	1	0	0	0	4	4 (1.03%)
11–20	0	0	0	0	2	1	5	0	0	0	7	1	8 (2.04%)
21–30	0	1	0	0	2	22	8	2	1	0	11	25	36 (9.18%)
31–40	1	0	0	0	8	26	8	5	0	0	17	31	48 (12.24%)
41–50	0	1	0	0	15	36	11	10	0	0	26	47	73 (18.62%)
51–60	0	0	0	1	25	32	18	9	0	0	43	42	85 (21.68%)
61–70	2	4	0	0	11	25	23	12	0	0	36	41	77 (19.64%)
71–80	2	1	0	0	7	9	11	10	0	0	20	20	40 (10.20%)
81–90	1	0	0	0	1	3	9	1	0	0	11	4	15 (3.83%)
91–100	0	0	0	0	3	1	2	0	0	0	5	1	6 (1.54%)
Total	6 40%	9 60%	0	1 100%	74 32.17%	156 67.83%	95 65.52%	50 34.48%	1 100%	0	176 44.90%	216 55.10%	392 (100%)
Grand Total	15 (3.84%)		1 (0.25%)		230 (58.67%)		145 (36.99%)		1 (0.25%)		392 (100.00%)		

*n = number

Table 2: Distribution of effusions on the basis of cytological examination.

Fluid	Malignant n (%)	Non-Malignant			Suspicious Of Malignancy n (%)	Total n (%)
		Lymphocyte Rich n (%)	Mixed Inflammatory Infiltrate n (%)	Neutrophil Rich n (%)		
CSF	0	7 (46.67%)	5 (33.33%)	3 (20%)	0	15 (3.83%)
Pericardial	0	1 (100%)	0	0	0	1 (0.26%)
Peritoneal	23 (10%)	74 (32.17%)	92 (40%)	28 (12.18%)	13 (5.65%)	230 (58.67%)
Pleural	20 (13.80%)	57 (39.31%)	40 (27.58%)	18 (12.41%)	10 (6.90%)	145 (36.99%)
Synovial	0	0	1 (100%)	0	0	1 (0.26%)
Total	43 (10.97%)	139 (35.46%)	138 (35.20%)	49 (12.50%)	23 (5.87%)	392 (100%)

*n = number

Table 3: Distribution of peritoneal fluid according to the diagnosis and the associated malignancies.

Primary site n (%)	Malignant n (%)	Non Malignant n (%)	Suspicious Of Malignancy n (%)	Total n (%)
Acute Lymphocytic Leukemia	0 (0.00%)	1 (4.35%)	0 (0.00%)	1 (1.69%)
Anal Canal	0 (0.00%)	1 (4.35%)	0 (0.00%)	1 (1.69%)
Bladder	0 (0.00%)	1 (4.35%)	0 (0.00%)	1 (1.69%)
Breast	0 (0.00%)	1 (4.35%)	0 (0.00%)	1 (1.69%)
Cervix	1 (4.35%)	0 (0.00%)	0 (0.00%)	1 (1.69%)
Colon	1 (4.35%)	4 (17.38%)	0 (0.00%)	5 (8.47%)
Gall Bladder	2 (8.70%)	2 (8.70%)	0 (0.00%)	4 (6.78%)
Gastroesophageal Junction	0 (0.00%)	1 (4.35%)	0 (0.00%)	1 (1.69%)
Kidney	0 (0.00%)	1 (4.35%)	0 (0.00%)	1 (1.69%)
Lung	1 (4.35%)	0 (0.00%)	0 (0.00%)	1 (1.69%)
Ovary	9 (39.13%)	3 (13.04%)	3 (23.08%)	15 (25.42%)
Pancreas	0 (0.00%)	3 (13.04%)	0 (0.00%)	3 (5.08%)
Rectum	1 (4.35%)	1 (4.35%)	0 (0.00%)	2 (3.39%)
Stomach	1 (4.35%)	3 (13.04%)	0 (0.00%)	4 (6.78%)
Unknown Primary	7 (30.42%)	0 (0.00%)	10 (76.92%)	17 (28.81%)
Uterus	0 (0.00%)	1 (4.35%)	0 (0.00%)	1 (1.69%)
Total	23 (38.99%)	23 (38.99%)	13 (22.02%)	59 (100%)

*n = number

Table 4: Distribution of pleural fluid according to the diagnosis and the associated malignancies.

Primary site n (%)	Malignant n (%)	Non Malignant n (%)	Suspicious Of Malignancy n (%)	Total n (%)
Breast	3 (15.79%)	1 (16.67%)	1 (10.00%)	5 (14.29%)
CML	1 (5.26%)	0 (0.00%)	0 (0.00%)	1 (2.86%)
Colon	0 (0.00%)	1 (16.67%)	0 (0.00%)	1 (2.86%)
Lung	9 (47.37%)	1 (16.67%)	1 (10.00%)	11 (31.43%)
Multiple Myeloma	0 (0.00%)	1 (16.67%)	0 (0.00%)	1 (2.86%)
NHL	1 (5.26%)	0 (0.00%)	0 (0.00%)	1 (2.86%)
Ovary	2 (10.53%)	0 (0.00%)	0 (0.00%)	2 (5.71%)
Pyriiform Fossa	0 (0.00%)	1 (16.67%)	0 (0.00%)	1 (2.86%)
Tongue	0 (0.00%)	1 (16.67%)	0 (0.00%)	1 (2.86%)
Unknown Primary	3 (15.79%)	0 (0.00%)	8 (80.00%)	11 (31.43%)
Total	19 (54.29%)	6 (17.14%)	10 (28.57%)	35 (100%)

*n = number

Out of 194 cases of non-malignant peritoneal effusion, mixed inflammatory infiltrate was most common (47.42%) followed by lymphocyte-rich exudates (38.14%). Out of 115 cases of non-malignant pleural effusion, maximum number of cases were lymphocyte-rich (49.56%) followed by mixed inflammatory infiltrate (34.78%). Out of 15 CSF cases, all were non-malignant with most (46.67%) lymphocyte rich effusions. The single case of pericardial effusion received was lymphocyte rich and the only case of synovial fluid showed mixed inflammatory infiltrate.

Out of 230 peritoneal effusions, 59 were associated with a known case of malignancy. Out of these cases, 23 (38.99%) were diagnosed as malignant effusion with carcinoma ovary being the most common primary site; 23 (38.99%) were diagnosed as non-malignant with colon as the most common primary site of malignancy and 13 (22.02%) diagnosed as suspicious of malignancy with 76.92% from an unknown primary site.

Out of 145 cases of pleural effusion, 35 were known cases of primary malignancy amongst which 19 (54.29%) were diagnosed as malignant effusions. Most common primary site of malignancy for malignant pleural effusion cases was lung. 6 (17.14%) cases of pleural effusion were diagnosed as non-malignant and 10 (28.57%) were diagnosed as suspicious of malignancy.

DISCUSSION

Main body fluids like pleural, peritoneal, pericardial, cerebrospinal fluid (CSF) and synovial fluid are normally present within respective body cavities in minimal quantities with their constituents in specific proportions. These fluids during a disease process undergo qualitative and quantitative changes.^{4,5,9,14} The cytological examination of effusion fluids in body cavities is a simple procedure and yields vital information of the cell population involving the cavities thereby suggesting the etiology.^{2,10} The advantages of this method are that it is a relatively simple, rapid, inexpensive and less invasive tool having a high accuracy with low incidence of false positive diagnosis.^{4,15} It helps in diagnosing of both non neoplastic and neoplastic conditions.¹⁻⁶

Most important is the recognition of a malignant pathology. Since, mesothelial and synovial tumors are rare, this method is useful to detect metastatic malignant cells in the body cavities. The method is more of prognostic value rather than for the early detection or prevention of further tumor growth. It also helps in

staging of the malignancy.^{1,4,16} The development of a malignant pleural effusion is a common complication and indication of advanced stages of cancers like lung, breast and stomach cancer, while development of malignant peritoneal effusion is due to ovary, colon, liver and pancreatic carcinoma. Thus, the examination of body fluids for the presence of malignant cells has been accepted as a routine laboratory procedure for detection of metastasis of unknown primary origin.¹¹

In the present study, a total of 392 cases of serous effusions were studied. The age ranged from 4-years to 98-years. The age range in most of the other studies was

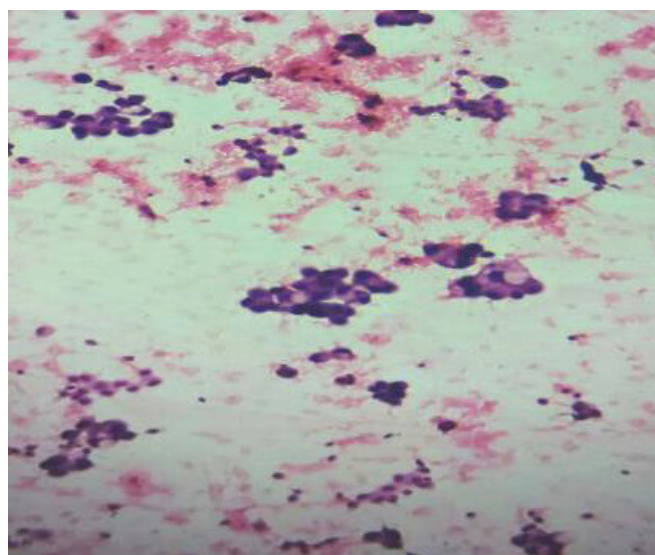


Figure 1: Metastatic ovarian papillary serous cystadenocarcinoma. Malignant cells in cohesive clusters and papillae in peritoneal fluid. (H&E, 100X)

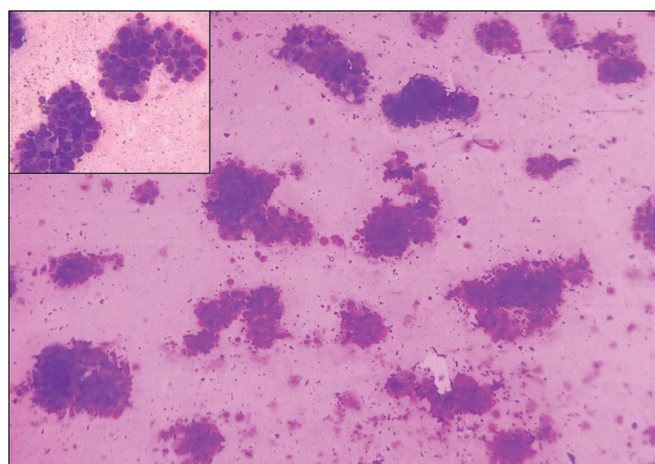


Figure 2: Papillary adenocarcinoma in pleural fluid: Photomicrograph showing clusters with focal acinar arrangement (MGG, 100X). Inset: (MGG, 400X).

from first to ninth decade which is in concordance with our study.^{4,6,8-10,12,14,17-21} Female preponderance was observed with M:F ratio of 1:1.23 in our study, which is similar to the studies carried out by Ayyagari S *et al.*¹⁰, Gupta R *et al.*⁸ and Tiwari A *et al.*⁶

The most common fluid was peritoneal fluid (58.67%), followed by pleural fluid (36.99%), CSF (3.83%), and least common were pericardial fluid and synovial fluid each 0.26%. The findings of the present study correlated with the findings of Chakrabarti PR *et al.*⁵, Shulbha VS *et al.*¹⁴, Bhagat R *et al.*²⁰, Bhade SD *et al.*²¹, Gupta R *et al.*⁸ and Tiwari A *et al.*⁶ Other authors found pleural fluid as the commonest fluid.^{4,9,10,12,17,18}

In 230 cases of peritoneal fluid, most common age group involved was 51-60 years with a female preponderance with M:F ratio of 1:2.1. These findings were in concordance with Ayyagari S *et al.*¹⁰, Chakrabarti PR *et al.*⁵ and Tiwari A *et al.*⁶ who also observed female preponderance. However, age group affected was different.^{5,10} 194 (84.35%) cases of peritoneal effusions were non-malignant showing mainly mixed inflammatory infiltrate. In our study, 23 (10%) cases of peritoneal effusion were malignant in nature with ovarian malignancy (39.13%) being the most common primary site shedding malignant cells into the peritoneal cavity. Most studies showed findings similar to our study.^{5,6,10,12,14} Rest of the malignant peritoneal effusions were from malignancies of unknown primary site (30.42%), malignancies of gall bladder (8.70%), stomach (4.35%), cervix (4.35%), colon (4.35%), rectum (4.35%) and lung (4.35%).

Pleural fluid was found to be the second most common effusion fluid having 145 cases (36.99%). It was similar to the observation by various authors.^{4-6,8,14,20,21} Most common involved age group was 61-70 with male preponderance and M:F of 1.9:1.115 (79.30%) cases of pleural effusion were non-malignant showing lymphocyte rich exudates on microscopy. 20 (13.89%) cases were of malignant pleural effusion with lung as the most common primary site of malignancy. Sudha A *et al.*¹⁰, Chakrabarti PR *et al.*⁵, Gupta S *et al.*²² and Tiwari A *et al.*⁶ also established similar findings. After lung other common primary sites were breast and ovary. We also found a case of Chronic Myeloid Leukemia and a case of Non-Hodgkin Lymphoma infiltrating into the pleural fluid.

CSF remained the third most common fluid in most of the studies including our study.^{4-9,17,20,21-23} 15 cases of CSF were studied with most being in 61-70 age group. Female preponderance was noted with M:F

ratio of 1:1.5. All 15 cases were non-malignant, most commonly showing lymphocyte rich cellularity followed by mixed inflammatory infiltrate. It is important to identify infectious causes of exudative CSF effusion for early diagnosis, prevention of spread of disease and complications. Study done by Shulbha VS *et al.*¹⁴ found Cryptococcus in CSF and Bhade SD *et al.*²¹ found tuberculosis as the cause of exudative effusion. However, we did not find any infective causes in our study. AFB was done and was negative in all cases. One case of Synovial fluid was received from a 29-year-old male, diagnosed as non-malignant showed mixed inflammatory infiltrate. One Pericardial fluid sample of a 60-year-old female was non-malignant showed lymphocyte predominance.

CONCLUSION

We conclude in our study that exfoliative cytology is a valuable tool in evaluation of serous cavity fluids. It is relatively painless, simple, cost effective, rapid technique that yields quick and reliable results. Some cases may present major interpretative challenges to the pathologist like presence of reactive mesothelial cells which at times poses difficulty in diagnosis, being close mimicker of malignancy. In our study, peritoneal fluid was the most common type of fluid received for analysis. Most of the fluid samples belonged to females. The frequency of malignancy in peritoneal fluids studied was 10% with ovarian carcinoma being the common primary malignant lesion to deposit malignant cells into the peritoneal fluid. In pleural fluid, 13.89% cases were malignant with adenocarcinoma of lung being the most common malignant lesion. No malignancy was diagnosed in CSF, pericardial and synovial fluid samples. Thus, fluid cytology is an important diagnostic tool and can be used as first line diagnostic procedure which reduces the need for more invasive investigations. Fluid cytology is useful complementary investigation for categorizing benign as well as malignant conditions. It is especially helpful in evaluating and staging malignancies thereby guiding the clinician in further management. This result in the upstaging or down staging of tumor and thereby affects treatment plan and prognosis for the patient.

Ethical approval: The study was approved by the Institutional Ethics Committee

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