



## Original Research Article

## Cytomorphological study of body fluids- An attempt to know its role in diagnosis

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## ABSTRACT

**Introduction:** Body fluid cytology is a routinely performed procedure. It is simple, cost-effective and acts as a first-line investigation in the evaluation of effusions. The inflow and outflow of fluid in the potential spaces of pleural, peritoneal and pericardial cavities is governed by Starling forces. In case of tumors, study of effusion cytology helps in the diagnosis and staging process.

**Aim:** To study cytomorphology of various body fluids and know their role in diagnosis.

**Materials and Methods:** The present study is a retrospective descriptive study of 100 cases of various body fluids such as pleural, peritoneal, cerebrospinal and synovial fluids which were received in the department of pathology, at a tertiary care center from July 2019 to December 2020. Data was retrieved from records maintained in the department of pathology. Slides were reviewed if considered necessary. In cases positive for malignancy, histopathology records were checked for correlation.

**Results:** 100 fluids were studied. Age group varied between 10 days and 90 years. Maximum number of cases was in the range of 41 to 50 years with 23 cases (23%). Most common fluid was pleural fluid (46%), followed by ascitic fluid (41%), CSF (7%) and synovial fluid (6%).

**Conclusion:** From our study, we could conclude that cytological evaluation of body fluids plays an important role in initial screening for presence of acute and chronic inflammatory cells, tumor cells. It also helps in staging of tumors where the presence of tumor cells increases the stage of tumor.

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## 1. Introduction

Body fluid cytology is a routinely performed procedure. It is simple, cost-effective and acts as a first-line investigation in the evaluation of effusions.<sup>1</sup>

The main serous cavities are pleural, peritoneal and pericardial cavities. They have two layers, the parietal and visceral layers, which are lined by a single layer of mesothelial cells and normally have a minimal amount of fluid. Starling forces govern the process by which there is a balance between the inflow and outflow of fluids and any difference in the pressure results in fluid accumulation.<sup>2</sup>

An abnormal amount of fluid accumulated can be tapped and biochemical, microbiological and cytological analysis can be done on the fluid.

Inflammatory, infective and neoplastic etiologies can be identified in the majority of cases. It also helps in the staging of tumours and prognostication.<sup>3</sup>

Exfoliated cells in the fluid give a better yield and hence represent a larger surface area increasing the diagnostic efficiency when compared to a needle biopsy as focal lesions may be missed. Nonetheless, the cytomorphology of effusion fluids can be challenging at times.<sup>4</sup>

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## 2. Aims and Objectives

The present study was undertaken with the objective of studying the cytomorphology of various body fluids

## 3. Materials and Methods

The present study is a retrospective descriptive study of 100 cases of various body fluids such as pleural, peritoneal, cerebrospinal and synovial fluids which were received in the department of pathology, at a tertiary care centre for a period of one and a half years from July 2019 to December 2020 after obtaining institutional ethical committee clearance (EC 87). The data was obtained by examining the previous reports and registers maintained in the department.

The data pertaining to physical characteristics such as volume, colour and appearance (clear or turbid) were noted. Cell count and cell type were noted. Slides were reviewed if considered necessary. Leishman, Hematoxylin and Eosin, and Papanicolaou stains were used to stain the smears. In cases with positive malignancy, histopathology records were checked for correlation. Pleural, peritoneal, synovial and cerebrospinal fluids were included in the study. No pericardial fluids were received. Other fluids like Bronchoalveolar lavage fluid, sputum and urine were excluded from the study.

A lymphocyte- or neutrophil-predominant effusion was defined as the presence of >50% of that cell type in the absence of  $\geq 10\%$  eosinophils, in which case the effusion was deemed eosinophilic. Any effusion not meeting any of the above criteria was classed “nonspecific”, i.e., which showed both lymphocytes and neutrophils.<sup>5</sup>

## 4. Results

The number of fluids studied were 100 in the present study. Age group varied between 10 days and 90 years. Maximum number of cases was in the range of 41 to 50 years consisting of 23 cases (23%) followed by 2 age groups, 21-30 years and 51 to 60 years having 18 (18%) cases each.

The number of male patients was 57 and the number of female patients was 43. Male: female ratio was 1.32:1

Out of 46 cases of pleural fluid, 44 were non-neoplastic, and 2 were reported as malignant.

Out of 41 cases of ascitic fluid, 39 were non-neoplastic and 2 were reported as positive for malignancy.

Among the 44 cases of non-neoplastic pleural fluids, 31 cases showed lymphocytes as the predominant cell type, 6 cases showed neutrophils as the predominant cell type, 1 case showed eosinophils as the predominant cell type and 6 cases showed a mixed population of neutrophils, lymphocytes and mesothelial cells.

Among the 39 cases of non-neoplastic ascitic fluids, 24 cases showed lymphocytes as the predominant cell type, 5 cases showed neutrophils as the predominant cell type, and 10 cases showed a mixed population of neutrophils,

lymphocytes and mesothelial cells.

Among the 7 CSF samples, 5 showed lymphocytes as the predominant cell type and the remaining 2 were acellular. No malignancy was detected in any of the CSF samples. All 6 cases of synovial fluid were non-neoplastic and 4 out of 6 samples showed lymphocytes as the predominant cell type and the remaining 2 had neutrophils as the predominant cell type.

## 5. Discussion

Historically, cancer cells were detected in ascitic fluid in the year 1867 by Lucke and Klebs. Since then, it is a practice to study the cytology of effusions to detect the presence of abnormal cells.<sup>6</sup> However, the study of effusion cytology is not only helpful for neoplastic conditions but also for non-neoplastic conditions. They can also yield adequate material for molecular testing, especially in malignancy.<sup>7</sup> On cytology, serous fluid effusions can show a predominance of inflammatory cells or predominance of mesothelial cells which can show a variety of reactive changes or can have malignant cells. It can be challenging to interpret the morphology of reactive mesothelial cells that have a tremendous capacity to proliferate and mimic malignancy, leading to a diagnostic dilemma.<sup>8</sup>

All effusions can be categorised as transudates or exudates based on their protein levels; transudates have protein levels of less than 3 g/dl and exudates have protein levels of more than 3g/dl. Transudates are formed when there is increased venous pressure as in congestive heart failure or cirrhosis of the liver, or due to hypoproteinemia, for example in renal failure. The serum is filtered through an intact capillary wall. Cellularity is usually low in transudates, whereas in exudates, cellularity is usually high. Exudates are generally caused by inflammatory processes like pneumonia, pulmonary infarct, lung abscess, pleuritis, peritonitis, pelvic inflammatory disease in women, or neoplastic processes.<sup>8</sup>

The present study was undertaken to know the cytomorphology of various fluids and to analyse the incidence of neoplastic and non-neoplastic effusions. In our study, there were more male patients with effusion when compared to females, similar to a study by Kushwaha et al.<sup>9</sup>

In our study, the most common age group in which we received a maximum number of fluids was between 41 to 50 years of age, similar to a study by Ayyagari Sudha.<sup>10</sup>

In our study, pleural fluid was the most common, comprising of 46 cases out of 100 cases. There was no mention of whether pleural effusion was unilateral or bilateral in the records reviewed. In a UK-based study, sensitivity by cytological examination was low in picking up cases of clinically suspected mesothelioma, necessitating more definitive investigations to be performed at the earliest. Kumavat et al<sup>11</sup> and Pramod et al,<sup>12</sup> Piyush et al,<sup>13</sup> Ayyagari Sudha,<sup>10</sup> priavadhana et al<sup>14</sup> also found the most common

**Table 1:** Showing age wise distribution of cases

Age (in years)	Pleural fluid	Ascitic fluid	Cerebrospinal fluid	Synovial fluid	Total
0-10	0	0	2	1	2
11-20	3	2	0	1	6
21-30	7	9	1	1	18
31-40	6	6	1	0	13
41-50	9	13	1	0	23
51-60	10	4	1	3	18
61-70	7	7	1	1	16
71-80	3	0	0	0	3
81-90	1	0	0	0	1
Total	46	41	7	6	100

**Table 2:** Showing gender wise distribution of cases

Nature of fluid	Number of various fluids	Number of Males	Number of Females
Pleural fluid	46	27	19
Ascitic fluid	41	22	19
Cerebrospinal fluid	7	6	1
Synovial fluid	6	3	3

**Table 3:** Showing non-neoplastic and neoplastic effusions

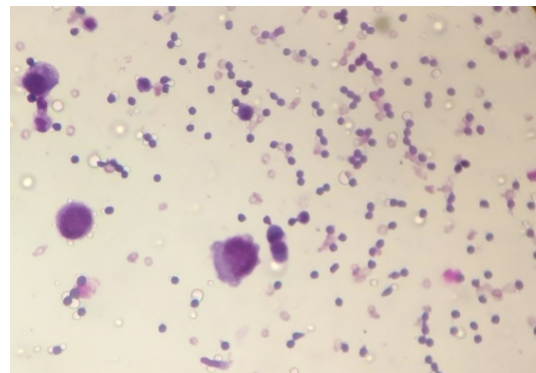
	Pleural	Ascitic	Cerebrospinal	Synovial	Total
Non-neoplastic	44	39	7	6	96
Neoplastic	2	2	0	0	4
Total	46	41	7	6	100

fluid to be pleural fluid. In a study by Shulbha et al,<sup>15</sup> peritoneal fluid was the most common fluid received.

44 out of 46 cases were non-neoplastic. 30 cases were exudates and 12 cases were transudates. Protein level was not done in 4 cases. 32 were non-suppurative out of which one had eosinophils as the predominant cell type and 6 were suppurative. 6 cases showed mixed inflammatory cells with reactive mesothelial cells. Shulbha et al<sup>15</sup> and priavadhana et al,<sup>14</sup> Saba H et al<sup>16</sup> also had similar findings with most cases being non-suppurative. Causes for fluids with a predominance of lymphocytes could be chronic inflammation or neoplastic aetiology. If malignancy is strongly suspected, and the smears are negative the first time, then it is recommended that two more consecutive samples be examined for the presence of malignant cells.<sup>17</sup>

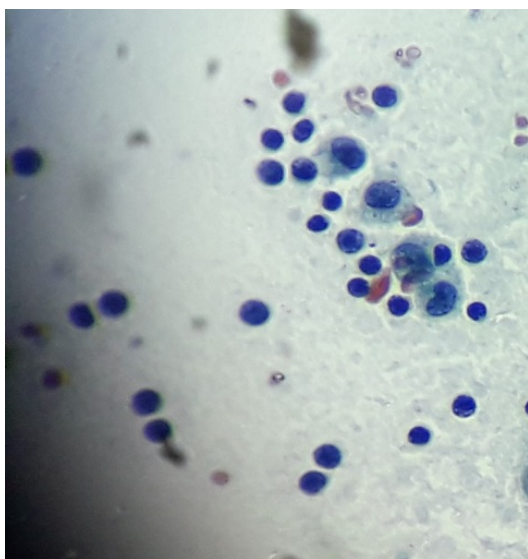
1 case was reported as malignant of adenocarcinoma type and correlated with histopathological findings which showed adenocarcinoma of the lung. Kumavat et al<sup>11</sup> found adenocarcinoma of lung to be the most common primary in their study. In most cases, they are adenocarcinoma cells, with the remainder being squamous cell carcinoma or small-cell carcinoma.<sup>8</sup> The other case had an unknown primary.

Among ascitic fluids, 39 were non-neoplastic and 24 showed lymphocytes as the predominant cell type, 5 cases showed neutrophils and 10 cases showed mixed inflammatory cells. 2 cases were positive for malignant cells, both adenocarcinoma type and one correlated with histopathology which showed mucinous adenocarcinoma

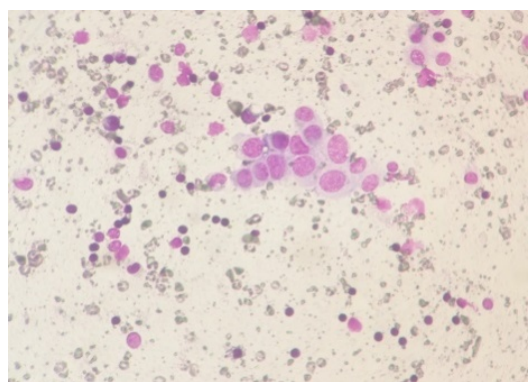
**Figure 1:** Microphotograph I: 40x magnification of Leishman stained smear of pleural fluid showing larger malignant cells compared to smaller lymphocytes.

with predominant signet ring cell component with Rectum being the primary. Other case had unknown primary.

In our study, 4 fluids which showed malignancy showed a turbid appearance and were exudates. However, they were all not hemorrhagic. Few studies have found that malignancy has to be suspected in hemorrhagic fluids but this is not true for all cases. Hemorrhagic fluids may or may not contain malignant cells and the converse is true that non-hemorrhagic fluids may or may not contain malignant cells.<sup>8</sup>



**Figure 2:** Microphotograph II: 40x view of papanicolaou stained smear of ascitic fluid showing reactive mesothelial cells and lymphocytes

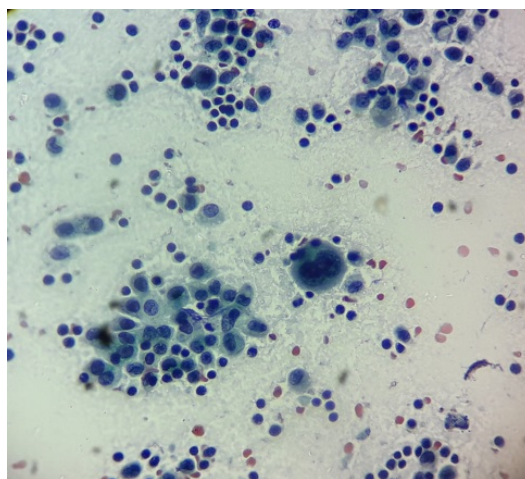


**Figure 3:** Microphotograph III: 40x view of Leishman stained smear of ascitic fluid showing cluster of malignant cells

Also, as in a study by Karoo et al,<sup>18</sup> patients with known malignancy and having effusions need not have malignant cells in the effusion fluid.

In a prospective study by Archana,<sup>3</sup> fluids yielded better results with cytocentrifuge and cell block technique especially in cases of scant cellularity when compared to routine centrifuge preparations.

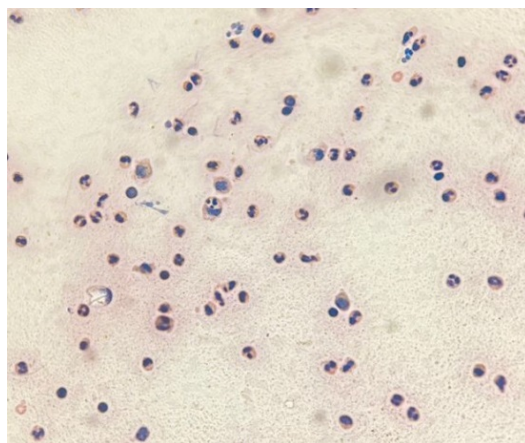
Out of 7 CSF samples, only one showed an increased cell count with predominance of lymphocytes. There were no malignant cells in CSF in any of the samples. CSF is usually obtained by lumbar puncture and the common indication is suspected meningitis, bacterial or viral. Bacterial meningitis shows predominance of neutrophils, viral and tubercular meningitis show predominance of lymphocytes. Opportunistic infections like cryptococcus can be identified by a simple wet mount in which cryptococci appear as



**Figure 4:** Microphotograph IV: 40x view of papanicolaou stained smear of ascitic fluid showing large single malignant cell with pleomorphic hyperchromatic nucleus in a background population of mesothelial cells and lymphocytes.

encapsulated yeast with a clear halo.<sup>15</sup>

In the present study, 2 out of 6 synovial fluids had a count of >10,000 cells/mcL and the differential count showed predominance of neutrophils. Remaining 4 cases showed predominance of lymphocytes. Synovial fluid analysis is generally indicated in cases of suspected Rheumatoid arthritis, Septic arthritis, Tuberculous arthritis, Osteoarthritis, Gout and Pseudogout. Crystal examination requires use of polarising microscopy.



**Figure 5:** Microphotograph V: 40X magnification of Papanicolau stained smear of Synovial fluid showing predominantly neutrophils with few mononuclear cells.

Since this is a retrospective study, data regarding whether the fluid was transudate or exudate could be retrieved only partially, also additional tests like cell block preparation, examination for crystals and immunohistochemistry could not be performed and these were not performed on any

of the samples. Sample size could be increased for better understanding. These are few limitations of this study.

## 6. Conclusion

From our study, we could conclude that cytological evaluation of body fluids plays an important role in initial screening for presence of acute inflammatory cells, chronic inflammatory cells and tumor cells and hence the diagnosis. It also helps in staging of tumors where the presence of tumor cells increases the stage of tumor. Also, it correlated with histopathological confirmation of malignancy. However, being retrospective in nature, we could not find satisfactory clinical correlation for all cases.

## 7. Source of Funding

None.

## 8. Conflict of Interest

None.

## 9. Acknowledgement

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