

## Cytomorphological Assessment of Different Body Fluids: A 5 Year Retrospective Study!!

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**Abstract:** A scrupulous assesment of body fluids for their cytomorphological properties plays a vital role in diagnosis, prognosis and therapeutic aspect of various neoplastic and nonneoplastic pathological conditions. Hence we conducted a 5 year descriptive, analytical and retrospective study in a tertiary care centre from January 2012 to January 2017. A total of 4197 sample of effusion fluids from various sites were analyzed retrospectively. Pleural fluid cases, 2056(49%) was commonest followed by peritoneal fluid and cerebrospinal fluid with, 1847(44%) and 126(3%) cases respectively. Pericardial and Synovial fluid were least common with only 84(2%) cases each. Majority of cases were Reactive in nature. Metastatic adenocarcinoma was the commonest malignancy encountered in both pleural and peritoneal fluid. Most of the patients were in 5<sup>th</sup> decade with age range between 3 to 87 years. Male preponderance was observed with M: F ratio of 1.11:1. Although fluid cytology poses diagnostic dilemma in few cases, still it is cost effective, quick, relatively painless and simple technique that yields reliable and diagnostically significant results.

Date of Submission: 01-06-2018

Date Of Acceptance: 18-06-2018

### I. Introduction

Cytopathology is an imperative branch that provides key information in a wide spectrum of infective, inflammatory and neoplastic conditions. It deals with study of cells aspirated or imprinted from the lesion as well as cells obtained from effusions at various body cavities. All the body cavities are lined by its native mesothelial cells and are lubricated by small amount of free fluid. These fluids are increased under various pathological conditions. Peritoneal, pleural, cerebrospinal, synovial and pericardial fluids comprise the majority of fluid specimen in pathology laboratories <sup>[1]</sup>. Tapping and analysing these fluids in terms of biochemical parameters and cytology not only serves in therapeutic and diagnostic intervention but also aids in disease monitoring, prognosis, staging of tumors and treatment outcome <sup>[2]</sup>. Our study aims to analyse various body fluids received in our department and correlate individual case clinically.

### II. Material and methods

Ours is a descriptive, analytical and retrospective study, undertaken in the department of Pathology in a tertiary care hospital over a period of five years from January 2012 to January 2017.

**Study Design:** Descriptive, Analytical and Retrospective Observational study

**Study Location:** This study was performed in a tertiary care centre, Department of Pathology, Jawaharlal Nehru medical College, AMU, Aligarh.

**Study Duration:** 5 years from January 2012 to January 2017 .

**Sample Size:** 4197 patients.

**Subjects & selection method:** All the patients, including both male and female presenting with effusion at various sites like pleural, peritoneal, pericardial, synovial and cerebrospinal space were included in our study.

#### Procedure methodology:

Complete Clinical history including duration and progression of disease, clinical examination along with all relevant blood, serum and radiological investigations of the patients were retrieved from the cytopathology form filled at the time of submission. 2-4 slides were obtained in each case, previously wet fixed and stained by Hematoxylin and Eosin and Papanicolaou technique. The slides were studied on light microscopy and evaluated for Cellularity, Predominant cell type, Size, Architecture (Acini / Sheets/ 3D balls/ Papillae/ Rosette, Singly

scattered), Nuclear and Cytoplasmic features, Chromatin, Degree of inflammation, Reactive changes and other background features. All the data was summarized and analyzed.

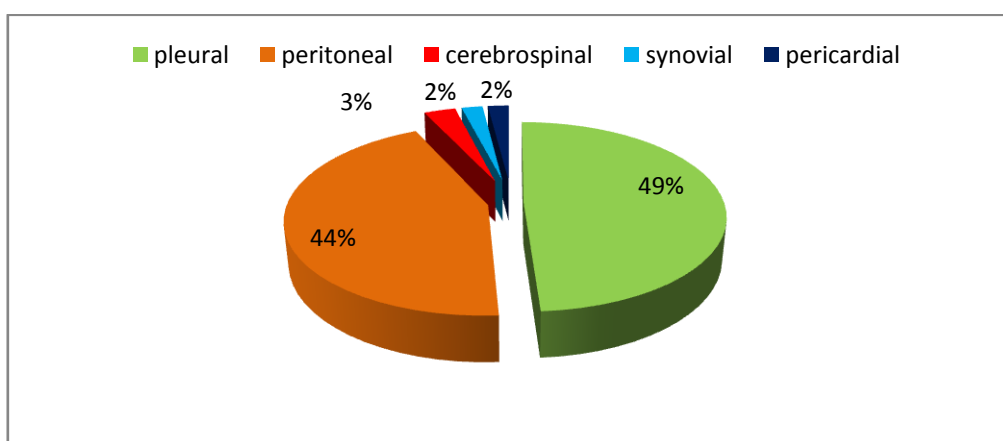
### III. Result

After evaluation of total 4197 patients, following observation was made.

A wide range of patients between the age group of 3 to 87 years were seen in our study. Most common age group affected was 5<sup>th</sup> decade followed by 4<sup>th</sup> decade. Mean age of presentation in both the sexes was 49.1 years. Mean age of presentation in non malignant cases was 46.9 years while that in malignant cases was 56.4 years.

Male constituted 2210 (52.6%) cases while 1987 (47.3%) cases were that of female. Slight male preponderance was seen with M: F ratio of 1.11:1.

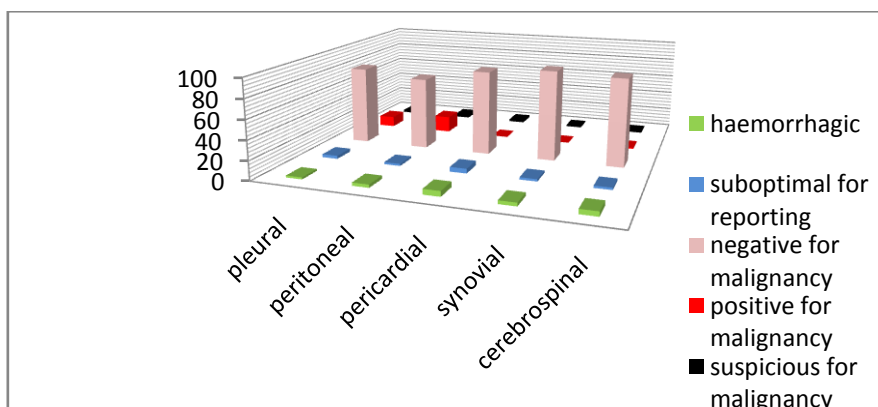
Out of total 4197 cases Pleural fluid, 2056(49%) was commonest followed by peritoneal fluid and cerebrospinal fluid with, 1847(44%) and 126(3%) cases respectively. Pericardial and Synovial fluid were least common with only 84(2%) cases in each.



All the individual fluids were categorised into 5 major categories-1) Haemorrhagic (smear shows only blood), 2) Suboptimal for reporting (acellular smear/ low cellularity smear/ smear with degenerative changes/smear with artifactual changes), 3) Negative for malignancy, 4) Positive for malignancy, 5) Suspicious for malignancy. The smears which were positive for malignancy were further typed on the basis of morphology. Those which could not be typed were followed and the diagnosis was made on the basis of histopathology and immunohistochemistry, wherever necessary. Following distribution of diagnosis was observed among different fluids.

Table 1: Distribution of cases according to diagnosis

Fluid type	Haemorrhagic	Suboptimal for reporting	Negative for malignancy	Positive for malignancy	Suspicious for malignancy
Pleural (2056)	41(2%)	65(3.2%)	1670(81.2%)	229(11.1%)	51(2.5%)
Peritoneal (1847)	59(3.2%)	39(2.1%)	1377(74.6%)	315(17%)	57(3.1%)
Pericardial (126)	7(5.5%)	6(4.8%)	110(87.3%)	0	3(2.4%)
Synovial (84)	3(3.5%)	2(2.3%)	78(93%)	0	1(1.2%)
Cerebrospinal (84)	4(4.8%)	2(2.3%)	76(90.5%)	1(1.2%)	1(1.2%)
Total (4197)	114(2.7%)	114(2.7%)	3311(79%)	545(13%)	113(2.6%)



Out of total 4197 cases, 114(2.7%) cases were predominantly haemorrhagic with absence of desired cellularity (figure-2). Haemorrhagic smears were maximum in pericardial and cerebrospinal space due to difficulty encountered in accessing these region.

Equal number of cases were suboptimal for reporting due to poor preservation of sample, inadequate/delay in processing and other factors, all leading to degenerative and artifactual changes rendering the smear inappropriate to report.

Majority of cases, 3311(79%) were negative for malignancy. 80-90 % cases in almost all fluid were included in this category. These cases included smears which were predominantly inflammatory (acute, chronic as well as mixed) or reactive, having mesothelial cells in abundance. Almost all Synovial fluid belonged to former category having abundant neutrophilic infiltrate in cases of acute synovitis (figure-1) and lymphoplasmacytic infiltrate in cases of chronic synovitis. Similarly, cerebrospinal fluid in 31 cases of pyogenic meningitis had neutrophilic infiltrate, while 14 cases of viral meningitis yielded lymphocytic infiltrate. Rest of the cases had mixed infiltrate. Majority of cerebrospinal fluid was received in pediatric population. Maximum cases in both pleural as well as peritoneal fluid were reactive in nature, with presence of reactive mesothelial cells in abundance along with inflammatory infiltrate (figure-6). These findings were seen in many acute and chronic infective as well as inflammatory conditions like liver disorders, cardiac failure, pancreatitis, tuberculosis, pneumonia etc.

545 of 4197 i.e, 13% of total cases were malignant in nature, with majority of malignancy seen in peritoneal fluid (315cases/17% of all peritoneal fluid). Pleural fluid was second commonest with 229 (11% of all pleural fluid) cases being malignant. No malignant case was observed in case of pericardial and synovial fluid. Only 1malignant case was noticed in cerebrospinal fluid.

Metastatic Adenocarcinoma was the commonest malignant lesion that comprised 87% (475 of 545) of total malignant cases followed by Squamous cell carcinoma with 22(4%) cases.

Most of the adenocarcinomas in males came from gastrointestinal tract and lung, while in case of females, ovary was the commonest primary site. Figure 4&5 shows characteristic features of adenocarcinoma showing acini, clusters, 3D balls made of atypical cells having vacuolated cytoplasm, eccentric nuclei showing features of anisonucleosis and hyperchromasia.

There were 16( 3%) cases of lymphoma as well as of small cell carcinoma. Figure-3 shows smear of lymphoproliferative lesion having monomorphic cell population of atypical cells with scant cytoplasm and hyperchromatic nucleus, histopathology confirmed it to be a case of non-hodgkins lymphoma.3% of cases could not be typed and a report of positive for malignancy was given. These cases were further confirmed on the basis of histopathology and immunohistochemistry.

6<sup>th</sup> decade was the commonest age group involved in malignant cases followed by 5<sup>th</sup> decade. Almost 50% of lymphoma cases were seen in age group of 4-15.

113 of 4197 cases were categorised as suspicious of malignancy. These cases showed presence of atypical looking cells, either obscured by too much of haemorrhage, inflammation, necrosis, etc or had low cellularity with changes rendering only a doubt of malignancy. Presence of reactive mesothelial cells, close mimickers of malignancy also raised suspicion of malignancy in few cases. These cases were further followed and a definite diagnosis was given, in cases which underwent repeat cytological or histopathological test.

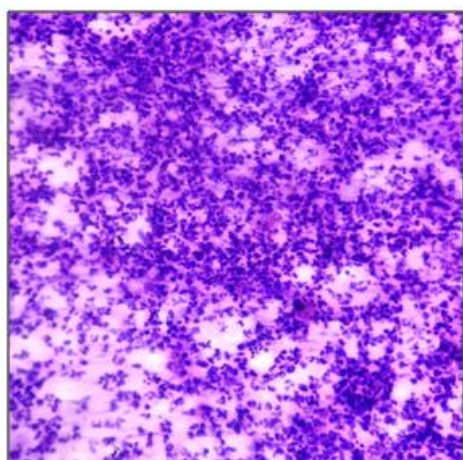


Figure-1: Effusion showing predominantly acute inflammatory infiltrate and necrotic debris, H&E x100

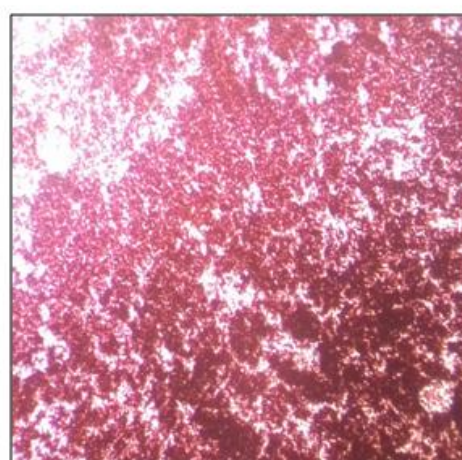


Figure-2: Haemorrhagic smear showing only blood, H&E x100

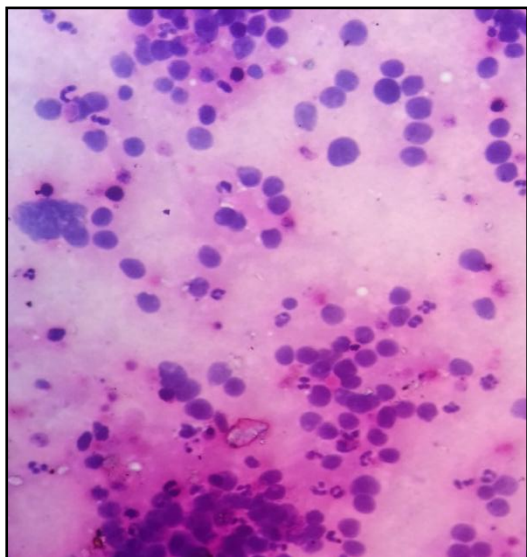


Figure 3: Pleural effusion showing monomorphic population of atypical cells in a case of Non-Hodgkins lymphoma. H&E x400.

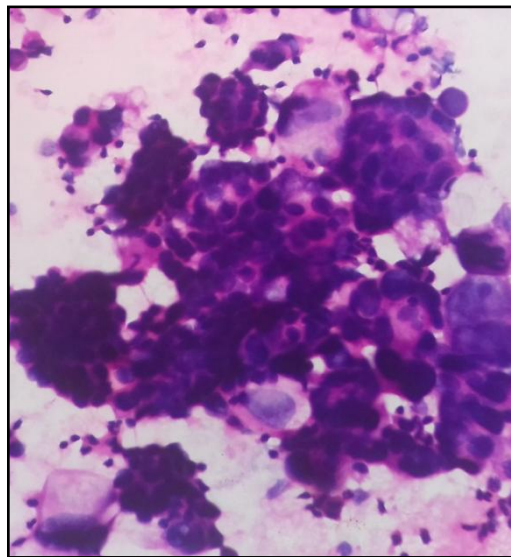


Figure 4: Pleural effusion in a 55-year-old male showing 3-D clusters and acini of malignant cells in a case of mucin secreting adenocarcinoma. H&E x400.

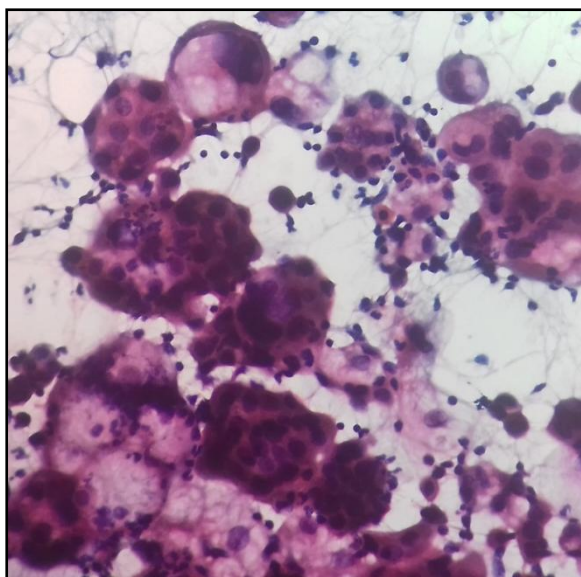


Figure-5 : Peritoneal fluid from 66 yrs old female in a case of mucinous cystadenocarcinoma showing clusters of multi vacuolated malignant cells with anisonucleosis and hyperchromatic nucleus. H&E x400.

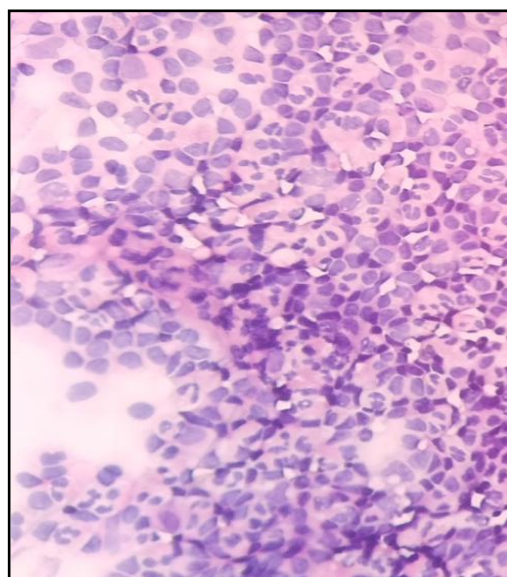


Figure-6 : Peritoneal fluid having reactive mesothelial cells as well as mixed inflammatory infiltrate ,H&E x400.

#### **IV. Discussion**

Cytological examination of serous effusion in adults has been widely known and documented in various pathological conditions<sup>[3,4]</sup>. Also, the smear prepared from the cell population present in the fluid sediment is much more representative and has higher sensitivity and specificity than that obtained by needle biopsy<sup>[5,6]</sup>. Taking these things into consideration we conducted a descriptive, analytical and retrospective study in the department of Pathology in a tertiary care hospital over a period of five years on 4197 cases.

Many such studies were performed previously on different number of cases, while few studies focussed on individual fluid. Few of them also performed biochemical analysis of the body fluids. Following table shows comparison of total number of cases and individual proportion of each fluid among various studies, along with mean age of presentation and any gender predisposition

	Our study	Gupta et al <sup>7</sup>	Khatib et al <sup>1</sup>	Pradhan et al <sup>8</sup>	Sharma et al <sup>9</sup>
Mean age	49.1	51.5	46.6		
M : F	1.1:1		1:1	1.1:1	1.9:1
Total no. of cases	4197	11,562	414	584	500
Pleural	49%	43%	33%	40%	45%
Peritoneal	44%	55%	46%	55%	36%
Pericardial	3%	2%		3%	0
Synovial	2%			1%	7%
Cerebrospinal	2%		15%	1%	12%

Above table shows varied number of patients ranging from 500 to 12000 in different studies depending upon the duration of study. Male to female ratio was same in almost all the studies also, studies including non-malignant cases have mean age group in 4<sup>th</sup> decade while studies including malignant cases have mean age in 5<sup>th</sup> decade.

Above table also depicts that Peritoneal fluid was the commonest, in studies of Gupta et al, Khatib et al, Pradhan et al<sup>[7,1,8]</sup>. While our study was in concordance with Sharma et al, Bhanvadia et al, Kumavat et al and Hathila et al who noted pleural effusion to be the commonest fluid<sup>[9,10,11,12]</sup>. This could be attributed to the various epidemiological factors. Also, Khatib et al noted relatively increased number of cases of cerebrospinal fluid as compared to our study<sup>[1]</sup>, this may be due to inclusion of increased number of pediatric population in their study.

Almost all the studies including ours observed 80-90% cases to be negative for malignancy.

We observed 13% of total cases to be malignant in nature, with majority of malignancy seen in peritoneal fluid (17% of all peritoneal fluid). Pleural fluid was second commonest with 229 (11% of all pleural fluid) cases being malignant. Some of the studies noted relatively less percentage of malignant cases like Gupta et al, Khatib et al and Priyanka et al with 7% of their cases to be malignant<sup>[1,2,7]</sup>. Similarly Sharma et al observed 5% of their cases to be malignant, however Pradhan et al noted 19% of their cases to be malignant<sup>[8,9]</sup>.

All the studies conducted so far showed metastatic adenocarcinoma to be the most frequent (80%-90%) cause of malignancy in both peritoneal as well as pleural effusions with variation in rest of the malignancies.

Almost all the studies have encountered difficulty in interpretation of malignancy, due to presence of mesothelial cells which are a close mimicker of malignant cells showing features of rosette formation, pseudoacini or acini, with or without the presence of prominent nucleoli<sup>[13,14,15]</sup>.

Here comes the role of cytocentrifuge and cell block which not only increases the cellularity, but cellular morphology, nuclear and cytoplasmic details, are better appreciated. Also cell block carries advantage of performing Immunohistochemistry which helps in the diagnosis and can also be used for retrospective analysis<sup>[16]</sup>.

## V. Conclusion

Cytology of body fluids are one of the commonest dealt investigation in pathology laboratories yielding diagnostically significant results, both in cases of neoplastic as well as non neoplastic lesions making it a relatively simple, rapid, inexpensive and less invasive tool. However reactive mesothelial cells at times poses difficulty in diagnosis, being close mimicker of malignancy. These limitations are overcome by cell block, histopathology and immunohistochemistry that usually has an upper hand on making the diagnosis.

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A.R.Piyush "Cytomorphological Assessment of Different Body Fluids: A 5 Year Retrospective Study!!IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 6, 2018, pp 62-67.