



CYTOMORPHOLOGICAL EVALUATION OF BODY FLUIDS WITH SPECIAL REFERENCE TO MALIGNANT EFFUSIONS

Pathology

Junu Devi*	Associate Professor Department of Pathology, Gauhati Medical College, Guwahati, Assam, India.*Corresponding Author
Harani Brahma	PGT, Department of Pathology, Gauhati Medical College, Guwahati, Assam, India
Anamika Dutta Adhikary	PGT, Department of Pathology, Gauhati Medical College, Guwahati, Assam, India

ABSTRACT

Background- Cytological evaluation of body fluid help in the diagnosis of neoplastic and non neoplastic conditions specifically malignant pathology. It provides insight on the diagnostic, prognostic and therapeutic aspects of various diseases. **Objective** of present study was cytomorphological analysis and diagnosis of benign and malignant effusion and evaluation of frequency of malignant effusions. **Materials and Methods:** This is a cross-sectional study for a period of 18 months comprising of 870 cases of various body fluids. Centrifuged deposit smears from fluids are stained with Giemsa and Papanicolaou (Pap) stain and diagnosis were made under light microscope. Body fluid included in the study are Pleural, Peritoneal, Cerebrospinal fluid, Bronchoalveolar lavage fluid, Sputum and Synovial fluid. Urine are excluded from the study. **Results and observations:** All total 870 cases were analysed of which 333 cases were Peritoneal fluid, 332 Pleural, 122 CSF, 49 Pericardial, 23 BAL, 9 sputum and 2 synovial fluids. Peritoneal fluid is the most commonly analysed fluid (M-124.256, Median-49.0, SD-147.695). Out of 870 cases 787 (90.45%) were benign, 83 (9.50%) malignant (P<0.0001). Maximum numbers of cases seen in 61-70 years age group (P<0.0001). M:F ratio was M:F=1.2:1 (P<0.0001). Malignant effusions are common in 41-50 years (P<0.0001). Most common malignant effusion is Peritoneal effusion. Malignant effusions were seen most commonly seen in female. Prevalence of malignant effusion is 9.54%. Commonest type of malignancy was adenocarcinoma (P<0.0001). **Conclusion:** Cytomorphological evaluation of body fluid is a simple, rapid, inexpensive, less invasive procedure for diagnosis of various benign and malignant conditions specifically malignant cases which helps in prognostic and therapeutic aspects also and should be advised in all effusion cases.

KEYWORDS

Body Fluid, Cytology, Malignancy

INTRODUCTION:

Cytological evaluation of body fluids is an important diagnostic test for various benign and malignant conditions [1]. Normally main serous body cavities are lined by single layered epithelium (mesothelium) and contain very minimal amount of fluid which is required for lubrication and protection of underlying viscera [2]. In certain pathological conditions there is imbalance between fluid formation and removal which leads to accumulation of fluid in the serous cavities and there is exfoliation and infiltration of cells in to these fluid [2]. Cytological evaluation of these fluids helps in interpretation of both non neoplastic and neoplastic conditions especially malignant pathology [3]. Accurate interpretation of cells is of prime importance since it can provide valuable information for diagnosis and also can help in the prognostic and therapeutic aspects of various pathological processes in the body [1].

Cytological evaluation of body fluid is a simple, safe, rapid, inexpensive and less invasive procedure with high diagnostic accuracy and low false positive rate [3]. The aim and objective of this study is to evaluate the prevalence and significance of fluid cytology in various pathological conditions specifically in malignant neoplastic lesions.

Materials and Methods:

This study was conducted in the department of pathology Gauhati Medical College & Hospital, Assam Guwahati. Study period – The study was conducted for 18 months from January 2019 to June 2020. Study design – Hospital based cross sectional study. Source of data: All body fluid received in the Cytopathology department for analysis during the study period. Sample size : 870 samples were included in the study.

Inclusion criteria- All effusion samples of pleural, peritoneal and pericardial cavities, Cerebrospinal fluid (CSF), Broncho-alveolar Lavage fluid (BAL), Synovial fluid and sputum are included during the study period. Sample received from both the sexes and irrespective of age groups are included in the study. Exclusion criteria- Urine samples are excluded from the study.

After receiving the fluid samples, information written in accompanying form is checked properly to identify the details. Gross description of fluid including volume, colour, turbidity, appearance was noted and immediately sent for centrifugation at 2000-3000 rpm for 5 minutes and smears were prepared from the sediment obtained.

Smears were stained with Papanicolaou (PAP) and Giemsa stains. Cells blocks were prepared whenever required.

Cytomorphology of the cells were studied and documented paying attention to cellular arrangement, cytoplasmic features and nuclear characteristics.

Statistical analysis was done in Microsoft excel work sheet. The categorical data were expressed as rate, ratio, and proportion. Statistical significance is expressed in P value.

RESULTS AND OBSERVATIONS:

The sample size in the study is 870 cases. Age group ranged from 0->70 years. Maximum number of cases are in the 61->70 years age group (table 1) (P<0.0001). Male constituted 55.17% (480) cases and female comprised of 44.83% (390) cases. Male to female ratio was 1.2:1 (P<0.0001) (table 3).

The most common fluid was the peritoneal fluid 38.28% (333) followed by Pleural fluid 38.16%

(332), CSF 14.02% (122), BAL 5.6% (49), Pericardial 2.6% (23), sputum 1.03% (09), synovial 0.22% (02). [M-123.256, Median-49.0, SD-147.695]

Out of 870 cases 787 were benign and 83 cases were malignant. Benign effusions are more common than malignant effusion. Prevalence of malignant effusions was 9.5%.

It was seen that out of 870 cases 480 were from male patients. 92.29% (n-443) were benign and 7.71% (n-37) cases were malignant. In case of females, out of 390 cases 88.21% (n-344) cases were benign and 11.79% (n-46) cases were malignant. It shows that malignancy is more common in females in our study.

Malignant effusions are common in 41-50 years age group (P<0.0001) (Table 6) Among all malignant effusions most of the cases were adenocarcinoma infiltrating the peritoneal fluid (P<0.0001).

Out of 333 peritoneal fluid 86.18% (n-287) cases were non-neoplastic and 5.29% (n-46) cases were neoplastic. Male to female ratio was 0.5:1 (M=119, F=214) Most common malignancy observed in peritoneal fluid was adenocarcinoma seen in 97.8% (n-45) cases. One

2.1%(n-1) case was squamous cell carcinoma. Out of 46 neoplastic cases 82.60%(n-38) cases had known primary and 17.39%(n-8) case had unknown primary. Most of the cases of known primary were from ovaries. Adenocarcinoma was most common malignant peritoneal effusion. Ovary was found to be the most common primary site.

Out of 332 cases of pleural fluids 91.86%(n-305) were nonneoplastic 7.53%(n-25) cases were neoplastic, one case (0.30%) was suspicious for malignant cells, another one had scanty cellular elements and comprised of few atypical cells. Male to female ratio was 2.32:1 (M=232, F=100). Out of 25 malignant cases 16.0%(n-4) were squamous cell carcinoma, 76.0%(n-19) cases were adenocarcinoma, one case (4.0%) was Non-Hodgkin's lymphoma, another one (4.0%) was multiple myeloma. Adenocarcinoma was the most common type of malignancy. Out of 25 malignant cases 64.0%(n-16) cases had known primaries and 36.0%(n-9) cases with unknown primary. Lung was found to be the most common primary site.

Out of 122 cases of CSF, 95.08%(n-116) cases showed normal findings 4.92%(n-6) cases were malignant. Male to female ratio 0.8:1 (M=38, F=44). All these 6 malignant cases showed infiltration of Acute Lymphoblastic leukemia (ALL). All the patients were already diagnosed and on treatment.

We analysed 49 cases of BAL fluids of which 89.8%(n-44) cases were benign and 10.2%(n-5) cases were malignant. Male to female ratio 3.4:1 (M=38, F=11). Out of 5 malignant cases 40.0%(n-2) were squamous cell carcinoma, 60.0%(n-3) were adenocarcinoma. Lung was the primary site in all 5 cases.

We had 23 cases of pericardial effusion and all were benign. Male to female ratio was 0.4:1 (M=7, F=16)

Nine cases were analysed for sputum cytology, all were negative for malignant cells. Male to female ratio was 1.2:1 (M=5, F=4)

Two cases of synovial fluid were analysed both of them came out as benign. Male to female ratio was 1 (M=1, F=1)

DISCUSSION:

Cytomorphological evaluation of body fluid has distinct value in confirming presence or absence of malignant cells in serous effusions[3]. It has been playing an important role as a diagnostic aid in establishing a definitive diagnosis predicting prognosis and planning or monitoring therapy[1]. It is a safe simple and inexpensive procedure which can give lots of information.

In the present study total 870 cases were analysed. Most common fluid was ascetic fluid (333) followed by Pleural fluid (332) which is similar to the studies done by Gupta R et al [4]. 49.7%, Sulbha VS et al [2] 45.1%, Khatib WM et al [5] 45.65%. The disparity observed between the frequency of type of fluid in the present study other studies may be because of large sample size of our study and more cases arising from pelvic organs.

In the present study most of the fluid sample belonged to male 480 (55.17%) and 390 (44.82%) of the samples belonged to females. The male to female ratio was 1.2:1 suggesting male preponderance. Findings are comparable to Mahoyan S et al [6], Sobha SN et al [7]. In contrast Khatib WM et al [5] reported almost equal incidence with male (50.24%) cases being slightly more than female (49.5%) cases.

In the present study age group ranged between 0 to ≥ 70 years. In our study maximum numbers of cases are in the 61-70 years age group. In

contrast to this other authors reported that 41-60 year age group is the commonly affected age group. In the present study minimum numbers of cases observed in 0-10 years age group. It was similar to the observation done by Poorna Priya [8] and Mahima Sarma et al [1].

Ascitic fluid is the most common type of fluid referred for analysis followed by pleural fluid. Cerebrospinal fluid is the most common fluid in the age group 0-10 and 11-20 years. 23 Pericardial fluid were received and all cases were benign. 49 cases of broncho-alveolar lavage fluid received and maximum cases were in the age group 61-70. Out of 49 cases 5 cases were malignant. 9 cases of sputum and 2 cases of synovial fluid were received for analysis and all were benign effusions.

In the present study, in case of males most commonly received fluid for analysis is the pleural fluid. Ascitic fluid is the most commonly received fluid in case of female. Khatib WM et al [5] reported that pleural fluid was the most common fluid received for analysis in both males and females.

Out of 83 malignant cases maximum numbers of cases were ascetic fluid (n-46) followed by Pleural fluid (n-25) which is similar to the studies done by Saba H et al [3] and Sharma M et al [9], Kol PC et al [10] and Khatib WM et al [5]

Cerebrospinal fluid showed 6 malignant lesions out of 122 cases, BAL showed 5 malignant lesions out of 49 cases.

In the present study there are 787 benign cases, one atypical case and one suspicious for malignancy. In our study adenocarcinoma was the common malignant diagnosis (64/83) seen commonly in ascetic fluid (45/83). Our findings are similar with the study done by Shubha VS et al [2], Jha R et al [11], Sears and Hajdu [12]. Out of 83 malignant cases 46 were female 37 were male. Ovary was the most common primary site in our study. Parson et al [13] found ovary was the most common primary site which is similar with our study.

The goal of fluid cytology is to detect malignant cells. Sometimes fluid cytology used as a first line of investigation specially in metastatic disease [11,14,15]. Presence of malignant cells in body fluid indicates spread of the disease beyond the primary site and analysis of it has both therapeutic and prognostic significance.

However, there are some drawbacks of fluid cytology. Sometimes, interpretation of malignant cells is difficult due to less numbers of malignant cells which may go undetected on cytological examination and leads to false negative diagnosis. Again sometimes because of extensive haemorrhagic fluid there may be difficulty in interpretation of malignant cells which leads to false negative diagnosis. Glacial ascetic acid should be added to the haemorrhagic fluid to lyse the RBC for better visualization.

Fluid cytology is useful in classifying benign and malignant lesions and helps in rapid diagnosis of various lesions. Prevalence of malignancy in our study is 9.54%. Adenocarcinoma is the most common neoplastic lesion. Peritoneal fluid is the most commonly involved fluid in malignant lesions followed by pleural fluid. Rate of malignancy is high in case of female.

CONCLUSION:

Fluid cytology is a rapid easy, cost effective method of detection of malignant as well as benign conditions. From fluid cytology we can not only detect malignancy but also know about the type and primary site of the lesions which helps in diagnosis, therapeutics and in prognostic aspects.

Table 1: Distribution of age in different types of fluids

Age group	Pleural	Peritoneal	CSF	BAL	Pericardial	Sputum	Synovial Fluid	Total
0-10	07	08	44	00	00	00	00	59 (6.78%)
11-20	05	15	43	01	03	00	00	67 (7.70%)
21-30	24	25	18	04	02	00	00	73 (8.39%)
31-40	52	43	08	02	05	01	01	112 (12.87%)
41-50	68	82	06	11	04	02	00	173 (19.89%)
51-60	78	89	03	12	05	02	00	189 (21.72%)
61= $\geq$ 70	98	71	00	19	04	04	01	197 (22.64%)
Total	332	333	122	49	23	09	02	870 (100%)

Maximum numbers of cases are seen in 61-70 years age group which is statistically significant (P<0.0001)

Table 2: Distribution of fluids in male and female

Sex	Pleural	Peritoneal	CSF	BAL	Pericardial	Sputum	Synovial	Total
Male	232	119	78	38	07	05	01	480(55.17%)
Female	100	214	44	11	16	04	01	390(44.82%)
Total	332	333	122	49	23	09	02	870(100%)

M:F= 1.2:1 which is statistically significant($P<0.0001$)

Table 3: Distribution of different types of fluid

Type of fluid	Number	Percentage
Pleural	332	38.16%
Peritoneal	333	38.27%
CSF	122	14.02%

BAL	49	05.63%
Pericardial	23	02.64%
Sputum	09	1.03%
Synovial	02	0.22%
Total	870	100%

Mean- 124.286 Median-49.0. SD- 147.695

Table 4: Distribution of cell types in different categories of fluid

Cytology	Pleural	Peritoneal	CSF	Pericardial	BAL	Sputum	Synovial	Total
Benign	305	287	116	23	44	09	02	787(90.45%)
Malignant	25	46	06	00	05	00	00	83(9.54%)
Atypical	01	00	00	00	00	00	00	01(0.11%)
Suspicious	01	00	00	00	00	00	00	01(0.11%)
Total	332	333	122	23	49	09	02	870(100%)

P= 0.41 Statistically insignificant

Table 5: Distribution of different types of malignancies in various body fluids

Cytological Category	Pleural	Peritoneal	CSF	Pericardial	BAL	Sputum	Synovial	Total
SCC	04	01	00	00	02	01	00	08(9.64%)
Adenocarcinoma	19	45	00	00	03	00	00	67(80.72%)
Lymphoma(1)/ Leukemia(6)/Multiple myeloma(1)	02	00	06	00	00	00	00	08(9.64%)
Melanoma	00	00	00	00	00	00	00	00(00%)
Total	25	46	06	00	05	01	00	83(100%)

Adenocarcinoma is the most commonly encountered malignant neoplastic effusion in pleural, Peritoneal and in BAL fluid which is statistically significant ($P<0.0001$)

Table 6: Relationship between age and malignancy in different type of fluid

Age in years	Pleura	Peritoneal	CSF	BAL	Sputum	Total
0-10	00	00	01	00	00	01(1.2%)
11-30	00	01	05	00	00	06(7.2%)
21-30	01	01	00	00	00	02(2.4%)
31-40	03	04	00	00	00	07(8.4%)
41-50	05	18	00	02	00	25(30.1%)
51- 60	08	11	00	01	00	20(24.09%)
61->70	08	11	00	02	01	22(26.50%)
Total	25	46	06	05	01	83(100%)

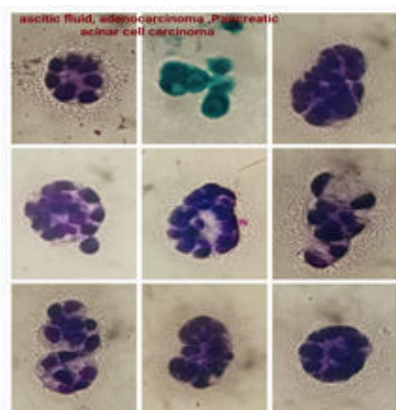
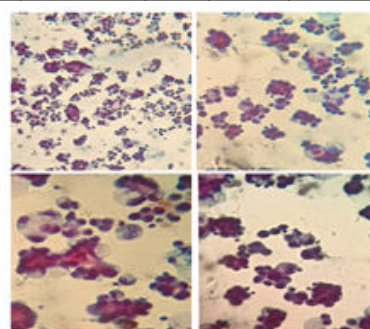
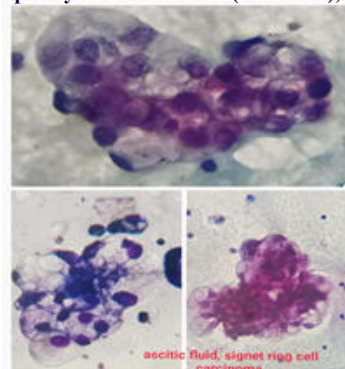
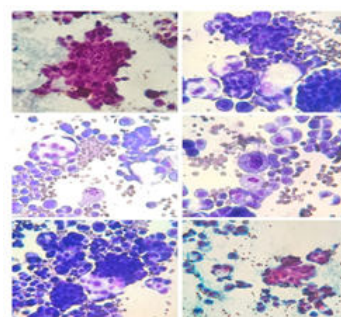
Malignant effusions are common (30.1%) in 41-50 years age group which is statistically significant ($P<0.0001$)

Table 7: Relationship between malignancy and gender

Sex	Benign	Malignant
Male	443(56.28%)	37 (44.57%)
Female	344(43.71%)	46 (55.42%)
Total	787	83

Benign effusions are more common than malignant effusion. Malignant effusions slightly more common in female ($P<0.0001$).

Figures

**Fig 1. Acinar Adeno carcinoma (PAP Stain) , Ascitic fluid****Fig 2 Micropapillary adenocarcinoma (PAP Stain), Pleural fluid****Fig 3, Adenocarcinoma (signet ring cells) (PAP Stain). Ascitic fluid.****Fig 4. Adenocarcinoma (PAP and MGG stains) Ascitic fluid.**

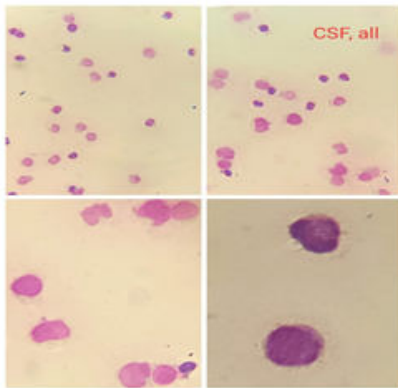


Fig 5. CSFALL (MGG stain)

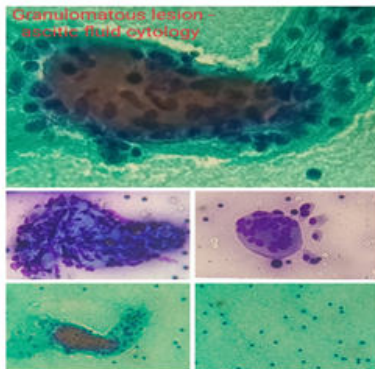


Fig 6. Granuloma in ascitic fluid.(PAP and MGG Stain)

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