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Diagnostic Utility of Body Fluid Cytology: A Retrospective Study in a Tertiary Care Hospital.

Dr. Het Prajapati[1], Dr. Ami Shah[2], Dr. Hansa Goswami[3]
[1]Third Year Resident, [2]Associate Professor,[3]Professor & Head, all authors are affiliated with Department of Pathology, B. J. Medical College and Civil Hospital, Asarwa, Ahmedabad, Gujarat, India.
Corresponding Author: Dr. Het Prajapati, Third Year Resident, Department of Pathology, B. J. Medical College and Civil Hospital, Ahmedabad, Gujarat, India.

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ABSTRACT
Cytological examination of body fluids is an inexpensive and useful tool to assist in diagnosis of neoplastic and non–neoplastic lesions in the body, understanding course of a disease or monitoring response to therapy. The present study aims at studying the morphological spectrum and evaluating the utility of this simple procedure on various body fluids received and processed at the Department of Cytopathology, B.J. Medical College, Ahmedabad, Gujarat.**Materials and Methods:**It is a retrospective study conducted on all the fluid samples received at the Department of Cytopathology from October 2021 to September 2022. Cerebrospinal fluid and urine samples were processed by cytospin method and all other body fluids were centrifuged. The sediment separated from the above procedure was used in preparation of smears on glass slides with frosted ends and stained with Papanicolaou's, Hematoxylin and Eosin and May Grunwald Giemsa stains. The stained slides were then examined under binocular microscope and reported. **Result:**The total number of body fluids received during the above-mentioned study period was 588, out of which the most common aspirated fluid was Peritoneal fluid (54.76%), followed by Pleural fluid (27.21%), Urine (5.27%), Cerebrospinal fluid (4.42%), Sputum (3.40 %), Broncho-alveolar lavage fluid (2.55%),Ovarian cyst fluid (1.36%), and Nipple discharge fluid (1.02%).Out of the total, 21(3.57%) were reported as 'positive for malignancy' and 23 (3.91%) were reported as 'suspicious for malignancy', maximum being reported in peritoneal fluid. Adenocarcinoma was the most common malignancy in our study. Most of the fluid samples belonged to males (59.18%) and the male to female ratio was 1.45:1. Chronic Inflammation was the most common pathology noted in Peritoneal as well as Pleural fluid. **Conclusion:**Cytological study of body fluids helps in differentiating Non-neoplastic and Neoplastic lesions. It is a rapid, effective and inexpensive method of diagnosis and evaluation, and it further helps in making clinical decision regarding management of the underlying pathology. Further typing of neoplastic lesionscan be done using special stains and immunohistochemical stains.
KEY WORDS: Body Fluids, Cytology, Malignancy, Adenocarcinoma.

I. INTRODUCTION

Body fluid cytology is an important diagnostic test for various malignant and benign conditions. Effusions can be caused by inflammatory, infectious, and benign; neoplastic or malignant; and primary or metastatic diseases. Such conditions in effusions may often have overlapping features and mimic one another both cytomorphologically and clinically, presenting diagnostic challenges [1]. Body cavities (pleura, peritoneum) have a common embryologic origin in the mesenchymal embryonic layer and are lined by mesothelial cells. Their support system is appropriate connective tissue, vascular and nervous apparatus. Parietal and visceral layer are separated by thin layer of lubricating fluid that provides the movement of two membranes against each other in the absence of disease. [2]

The history of serous effusion cytology can be tracked back to 19th century. Lucke and Klebs were apparently the first investigators who recognized the presence of malignant cells in an ascitic fluid in 1867. In 1882 Quincke was credited for detailed descriptions of ovarian and lung cancer cells in serous effusions.Since that time reports on effusion cytology have started to appear in the medical literature, and serous effusion cytology now is a diagnostic procedure worldwide [3]. The incidence of patients with effusion has increased in past few years. It has thus become mandatory to study the cytological features of the effusions and provide reliable results for the future treatment[4,5]. Cytological study of body fluids is an inexpensive and simple procedure less invasive tool having a high accuracy with low incidence of

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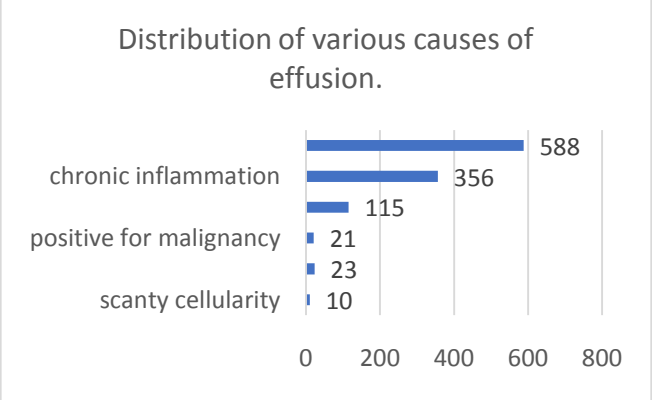
false positive diagnosis useful in making diagnosis regarding etiology, understanding course of disease and to monitor the response to therapy. It helps in diagnosing of both non neoplastic and neoplastic conditions. Most important is the recognition of a malignant pathology. Many other conditions such as inflammatory diseases, parasitic infestations, bacteria, fungi and viruses can also be identified[6]. Thus, the number of samples received in Cytopathology lab is increasing[7]. Body fluids are considered diagnostic rather than screening-type specimens in cytology[8].The purpose of present study is to evaluate the significance of fluid cytology for various pathological condition and classify them into neoplastic and non-neoplastic types in a tertiary care hospital. It is a complete diagnostic modality. First, it assists the clinician in formulating and pointing out the etiology of effusion and list of differential diagnoses, secondly it allows one to follow the results of therapy and prognosis.

II. MATERIALS AND METHODS

The fluid samples were received at the Department of Cytopathology, B.J. Medical college and Civil Hospital, Ahmedabad. It was a retrospective study of one year duration from October 1, 2021, to September 30, 2022. A total of 588 samples were included in the study.The age, sex, date and time of collection, relevant clinical history, volume, colour and clarity of the received fluid were documented. Samples received from those patients who were already on treatment were excluded.Cerebrospinal fluid and urine samples were processed by cytospin method (at 2500 rpm for 5 minutes) and all other body fluids were centrifuged (2000 rpm for 10 minutes). The sediment separated from the above procedure was used in preparation of smears on glass slides with frosted ends. The smears were fixed in alcohol which is followed by staining with Papanicolaou's and Hematoxylin and Eosin stains. Air dried smears were stained with May Grunwald Giemsa stain. The stained slides were then examined under binocular microscope and reported.

III. OBSERVATION AND RESULT:

A total of 588 body fluids were studied in the given time period. The most common aspirated fluid was Peritoneal fluid-322 (54.76%), followed by Pleural fluid-160 (27.21%), Urine-31 (5.27%), Cerebrospinal fluid-26 (4.42%), Sputum-20 (3.40%), Broncho-alveolar lavage fluid-15 (2.55%), Ovarian cyst fluid-7 (1.36%) and Nipple discharge fluid- 6 (1.02%) (Table-1).The number of males were 348 and the number of females were 240. Overall male to female ratio was 1.45:1 (Table 2). The most common aspirated fluid in both male and female population was peritoneal fluid (Table-2, Table-3). The age ranged from <1 years to >75 years with maximum bulk being in the age group of 41 – 60 years. In this study CSF was the common type of fluid referred for analysis in those specimens which belonged to age < 1 year (Table 4).



In the present study, majority of effusion were non neoplastic accounting to 544 cases (92.51%) and neoplastic effusion accounting to 21 cases (3.57%). Among non-neoplastic lesions maximum cases were of chronic inflammation followed by changes of acute inflammation and reactive changes. Out of 356 cases of chronic inflammation 43 cases were suggestive of tuberculous inflammation characterized by lymphocytes rich effusion.

Out of the total 588 fluids, 21 (3.57%) body fluids were reported as 'Positive for malignancy' and 23 (3.91%) were reported as 'Suspicious for malignancy'. The maximum number of malignancies was reported in peritoneal fluid (Table-5).

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From the 21 body fluids reported as positive, 12 (57.14%) were reported in Females and 9 (42.85 %) were reported in males and from the 23 body fluids reported as suspicious, 13 (56.52 %) were reported in males and 10 (43.47%) were reported in females.

Table 1 : Distribution of types and percentages of various body fluids.

Type of body fluid	No of samples	%
Peritoneal fluid	322	54.76
Pleural fluid	160	27.21
Urine	31	5.27
Cerebrospinal fluid	26	4.42
Sputum	20	3.40
Bronchoalveolar lavage	15	2.55
Ovarian cyst fluid	8	1.36
Nipple discharge fluid	6	1.02
Total	**588**	**100**

Table 2 : Distribution of total fluids according to the gender

Gender	Distribution	
	Number	Percentage %
Male	348	59.18 %
Female	240	40.81 %
Total	588	100 %

Table 3: Distribution of various fluidsamongst Males and Females.

Sex	Peritoneal fluid	Pleural fluid	Cerebrospinal fluid	Bronchoalveolar lavage fluid	Urine	Ovarian cyst fluid	Nipple discharge	Total
Male	225	96	15	10	24	-	-	370
Female	97	64	11	5	7	6	8	198

Table 4: Distribution of cases according to age and fluid type

Age (years)	Peritoneal	Pleural	Cerebrospinal fluid	Sputum	Bronchoalveolar lavage fluid	Urine	Ovarian cyst fluid	Nipple discharge	Total
1 or less	-	-	5	-	-	-	-	-	5
2-10	1	2	5	1	1	2	-	-	12
11-20	-	4	3	2	1	1	-	-	11
21-30	10	13	2	2	1	4	2	1	35
31-40	34	26	3	3	2	5	2	2	77
41-50	98	42	2	5	4	8	2	1	162
51-60	116	54	3	3	3	6	1	1	187
61-74	57	16	2	2	2	3	1	1	84
75 or more	6	3	1	2	1	2	-	-	15
Total	322	160	26	20	15	31	8	6	588

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Table 5:Number of cases reported as 'positive for malignancy' and 'suspicious for malignancy'

	Peritoneal Fluid	Pleural fluid	CSF	Sputum	Broncho - alveolar lavage fluid	Urine	Nipple discharge	Ovarian cyst fluid	Total
Positive for malignancy	7	6	0	2	2	4	0	0	21
Suspicious for malignancy	5	4	1	3	4	3	1	2	23
Total	12	10	1	5	6	7	1	2	44

Table 6 : Percentage of malignancy in Males and Females

Gender	Positive for malignancy		Suspicious for malignancy	
	No	Percentage	No	Percentage
Male	9	42.85 %	13	56.52 %
Female	12	57.14 %	10	43.47 %
Total	21	100 %	23	100%

IV. DISCUSSION.

In our study out of the total of 588 maximum cases were of peritoneal fluid followed by pleural fluid. Males were more as compared to females. Similar findings were observed in other studies. [6,8] Overall, maximum number of cases were observed in the age group of 51-60 years followed by 41-50 years. Majority of fluids in our study were found to be non-suppurative. Similar pattern was observed by other authors[4,6]. Majority of non-neoplastic fluids including pleural, peritoneal and cerebrospinal fluid showed lymphocytic predominance and few of them also showed macrophages along with lymphocytes on a proteinaceous background. The cause of such chronic inflammatory exudates is usually infection of the organs enclosed by the serous membranes and sometimes because of the presence of tumors in these organs. Hence it is advisable that those cases that are reported as chronic inflammation need a repeat sample analysis at least for three consecutive times to exclude a suspicion of malignancy [6,9]. Majority of CSF showed lymphocytic predominance. Many other conditions such as inflammatory diseases, parasitic infestations, bacteria, fungi and viruses can also be identified [10]. A sample of hydatid cyst fluid was also received which showed presence of protoscolices.Most of the fluids obtained through nipple discharge which were reported as nonneoplastic, showed presence of cysticmacrophages over proteinaceous background.Similar finding was observed by Shirish Chandanwale et al and Paulo Mendoza et al in their studies [11,12]. No atypical or malignant cells were observed in most of the smears prepared from ovarian cyst fluids. In another study, out of total 459, Zhou AG et al reported 90.6% of all ovarian cyst fluids as benign, 7% as atypical, 0.9% as suspicious and 7% as malignant [16]. The neoplastic or non-neoplastic nature for each of the ovarian cyst, undertaken in our study, was confirmed by histopathological examination. Out of the total 8, on histopathology, 5 werereported as Benign serous cystadenoma of ovary, 1 was reported as Mature cystic teratoma of ovary, 1 was reported as Mucinous cystadenoma of ovary and 1was reported as Simple haemorrhagic cyst of ovary. Thus, 7(85.7%) out of total 8 were found to be neoplastic (benign) and 1(14.3%) was found to be non-neoplastic on histopathologic examination, Benign serous cystadenoma being the most common benign ovarian neoplasm. Reactive mesothelial cells were observed in 52 (8.84%) fluid samples. Gupta R et al. in their study reported 4% of non-neoplastic effusions demonstrating reactive changes in mesothelial cells[6]. In 2 out of the 52 fluid samples mentioned above, reactive mesothelial cells were recorded as a finding besides presence of malignant cells. In 4 out of the 52 fluid samples mentioned above, reactive mesothelial cells were recorded as a finding besides presence of cells suspicious of malignancy.

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In this study majority of the fluid specimens that is 92.51% of the specimens were diagnosed as benign lesions while diagnosis of malignant lesions was noted in 3.57% of the fluid specimens and 3.91% of the fluid specimens were diagnosed as suspicious of malignancy. Hence the frequency of malignancy in this study was 3.57%. The rate of malignancy observed in the present study is compared to various studies (Table 7).

Table-7: Comparison of our study results with similar studies

Author	Year	Benign lesions (%)	Malignant lesions (%)	Suspicious of malignancy (%)
Kol PC et al. [13]	2016	77.77 %	16.66 %	5.50 %
Sharma M. et al. [14]	2017	90.40 %	5.40 %	4.20 %
Saba H, Prakash C.J, Sharmila P.S, Vinitra. K. et al [15]	2018	93.60 %	5.20 %	1.20 %
Present study	2022	92.51 %	3.57 %	3.91 %

In the present study, the rate of malignancy was high in females (57.14%), and it was common in the age group of 41 to 60 years. Similar findings were observed in study by Saba H, Prakash C.J, Sharmila. In contrast to these observations, EI-Sheikh SA et al [17] (2012) reported significantly higher number of malignant lesions in males than females.

Table 8: Comparison of male to female ratio in malignancy

Author	Year	Male:Female Ratio
El-Sheikh SA et al. [17]	2012	1.1:1
Saba H, Prakash C.J, Sharmila P.S, Vinitra. K. et al [15]	2018	1:2.25
Present study	2022	1:1.3

21 out of total 588 fluid samples were reported as positive for malignancy. 23 out of the total 588 fluid samples were reported as suspicious for malignancy (Table 5).Most common malignancy observed in our study was adenocarcinoma which is in concordance with other studies. [9,18,19] Adenocarcinoma was the most common malignancy in both peritoneal and pleural fluids. Findings from other studies [5,18] show pleural fluid to be having the highest proportion of positivity for malignant cells. This contrasts with the finding in our study which shows peritoneal fluid to be having the highest proportion of positivity for malignant cells (Table 5). Majority of the malignant effusions (positive as well as suspicious for malignancy) were haemorrhagic effusion. Similar finding is found in other studies [6]. Overall, the present study showed that, fluid cytology is very useful in classifying benign conditions, further it plays a very useful role in rapid diagnosis of malignant effusions. Fluid cytology although not a substitute for conventional histopathology but as complementary to it and is useful in categorizing benign conditions as well as in the diagnosis of malignant conditions.

V. CONCLUSION

Based on the findings of this study it may be concluded that, Peritoneal fluids was the most common type of fluid received for analysis. Mostof the fluid samples belonged to males. The frequency of malignancy in the population studies was 3.57 % with adenocarcinoma being the common malignant lesion. Maximum malignant lesions were noted in peritoneal fluid samples followed by pleural fluid samples while no malignancy was diagnosed in CSF samples. Furthermore, the rate of malignancy was high in females and is common in the age group of 41 to 60 years. Thus, Fluid cytologyis an important diagnostic tool and can be applied as first line diagnostic procedure as it is simple, safe, effective, relatively painless, inexpensive, less time consuming, gives quick results and is a useful complementary diagnosis for categorizing benign as well as malignant conditions. It is an asset to both pathologists and clinicians to study the underlying pathology of a disease and hence, helps in further management of the disease.

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