Peritoneal Fluid Analysis Clinicocytological Study

Neha Sharma[1], Krishna Dubey[2], H. Gurubasavaraj[3], S.S. Hiremath[4]

ABSTRACT

Introduction: Appropriate peritoneal fluid analysis is the most efficient and effective method of diagnosing the cause of peritoneal effusion. Both nonmalignant and malignant causes of effusion can be identified by cytology in several cases in correlation with clinical history and examination. With this basis, the present study on cytology of peritoneal effusion was taken up. Current research aimed to study the cytology of the peritoneal fluid in various diseases to establish clinicocytological correlation, for proper management of patient.

Material and Methods: 115 samples of peritoneal fluid were subjected to physical, biochemical and cytological examination.

Results: Peritoneal effusion was seen in 62.61% of females and 37.39% of males. 66.96% samples were transudative and 33.04% were exudative. TLC was less than 500 cells/cu.mm in most (74.02%) of transudative effusions. 47.36% of exudative effusion had TLC greater than 1000 cells/cu.mm and 39.47% of exudative effusion had TLC between 500-1000 cells/cumm. 95 (82.60%) samples had predominantly lymphocytes. 18.26% of peritoneal effusions were positive for malignant cells. Most (85.71%) of malignant effusions were exudative. Primary site could be assessed by cytological examination in (57.14%) of malignant effusions.

Conclusion: Cytological study of body effusions is neither a screening test nor a method of early diagnosis of cancer. It is in fact a complete diagnostic modality which aims at pointing out the etiology of effusion as well as in certain cases a means of prognostication of the disease process. Non malignant causes are the more common causes of peritoneal effusion. Metastatic carcinomas are the most common tumors found in effusions.

Keywords: Effusion, Peritoneal Fluid Cytology, Malignant Effusion.

INTRODUCTION

The word ascites is of Greek origin "askos" meaning bag or sac.Ascites is the accumulation of excess fluid in the peritoneal cavity. Ascites usually becomes clinically detectable when at least 500 mL have accumulated.[1]

Ascitic fluid examination provides a valuable clue to the etiological diagnosis of ascites particularly in cases where the clinical picture is not straight forward.

Among many causes of ascites, decompensation of chronic hepatic cirrhosis accounts for 80% of the cases, followed by tumours which account for10% of cases, congestive heart failure and inflammatory conditions account for 3% of cases each whereas other causes such as nephritic syndrome, exudative enteropathy and chylous ascites are less common.[2,3]

The cytologic study of body fluids is one of the oldest applications of cytologic techniques, first investigated in the latter half of the 19th century. The purpose is to determine the cause of fluid accumulation in body cavities, such as the pleura, pericardium (effusions), and the abdominal cavity (ascitic fluid). Primary or metastatic cancer and many infectious processes can be so identified.

The cytologic diagnosis, which is often more difficult than histologic diagnosis, must be based on a synthesis of the entire evidence available, rather than on changes in individual cells. If the cytologic material is adequate and the evidence is complete, a definitive diagnosis should be given. Current research aimed to study the cytology of the peritoneal fluid in various diseases to establish clinicocytological correlation, for proper management of patient.

MATERIAL AND METHODS

This study on Peritoneal fluid cytology was undertaken in the Department of Pathology, J.J.M. Medical College, Davangere over a period of two years from July 2011 to June 2013.

Peritoneal washing samples were also used in the study. All the cases were subjected to detailed clinical examination,

An effort was made in this study to process the peritoneal fluid specimens as expeditiously as possible, the majority were processed immediately but in small number, when there was a delay, these specimens were stored in the refrigerator at 4°C. The fluid was divided into two parts, one part was used for cell count and the other part was poured into centrifuge tubes and centrifuged for 10 minutes at 2000 rpm. The supernatant was poured off. Part of the sediment was transferred to a clean glass slide and mixed with a drop of 1% toluidine blue. After placing the coverslip, slide was observed under the microscope for immediate identification of cell morphology. Then the remaining sediment was transferred with the help of a Pasteur pipette to three slides. One was air dried and stained with Giemsa, the other two were fixed in 95% alcohol for a minimum period of 15 minutes and stained with Haematoxylin and Eosin, Papanicolaou stains.

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How to cite this article: Neha Sharma, Krishna Dubey, H. Gurubasavaraj, S.S. Hiremath. Peritoneal fluid analysis clinicocytological study. International Journal of Contemporary Medical Research 2019;6(9):I12-I16.

DOI: http://dx.doi.org/10.21276/ijcmr.2019.6.9.27

For cell count one drop of fluid was mixed with a drop of toluidine blue and cells were counted in improved Neubauer counting chamber.

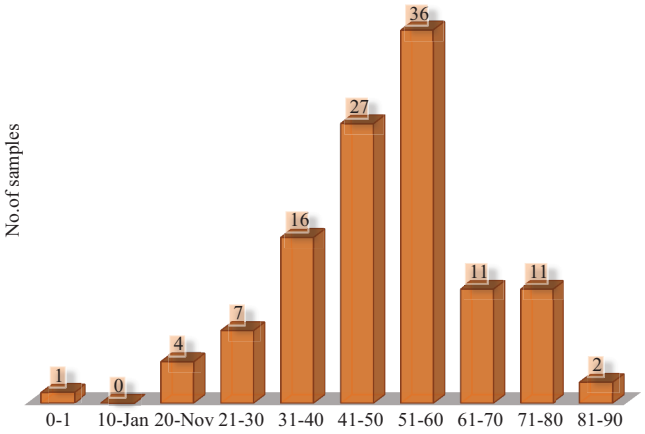
Cytospin was used to increase the cell recovery, when the sample is hypocellular and less in amount.

When possible, the remaining (or separated centrifuged) cell sediment was also fixed in 10% formalin processed and embedded in paraffin as a cell block. For all cases biochemical analysis of protein, sugar and chloride was done. Wherever possible bacteriological culture of peritoneal fluid was also done.

RESULTS

A total of 115 samples of peritoneal fluid were received for cytological examination. Out of total 115 samples 94 (81.74%) samples were cytologically non malignant and 21(18.26%) samples were malignant.

36 (31.30%) samples were from patients in 6th decade followed by 27 (23.48%) samples from patients in 4th decade (graph-1).



Graph-1: Age distribution of peritoneal effusion

Out of 115 samples, 72 (62.61%) samples were from females and 43 (37.39%) were from males. 77 samples were transudative and 38 samples were exudative effusions (Table-1).

Transudative effusion was seen in 36 (31.30%) samples of

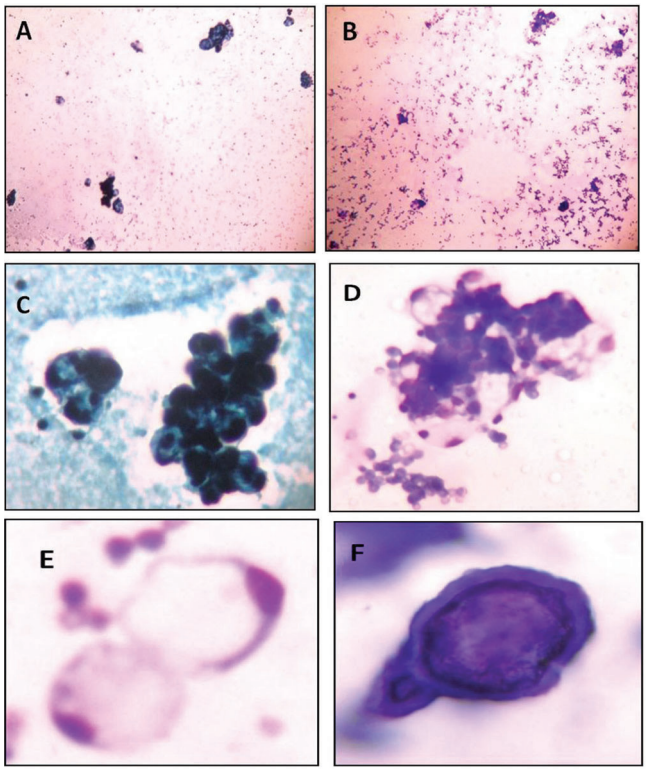


Figure-2: Metastatic papillary adenocarcinoma

(A) Papillary clusters seen, Pap(low power); (B) Papillary clusters seen, Giemsa(low power); (C) Papillar clusters, Pap (high power); (D) Papillary cluster, cells with abundant vacuolated cytoplasm, Giemsa(high power); (E) Signet ring cells, Giemsa(high power), (F) Psammoma body, Giemsa (high power).

Nature of Fluid	Causative Factor	No. of Samples	Percentage
Transudative	Cirrhosis	36	31.30
	Portal HTN	5	4.35
	CCF	12	10.43
	Chronic kidney disease	2	1.74
	Chronic pancreatitis	1	0.87
	Intestinal obstruction	5	4.35
	Intestinal perforation	1	0.87
	Blunt trauma	1	0.87
	Malignancy	3	2.61
	Meig's Syndrome	1	0.87
	Cytologically negative for malignant cells in known malignancy	10	8.70
Exudative	Tuberculosis	7	6.09
	Malignancy	18	15.65
	Cirrhosis+TB	5	4.35
	Chylous ascites	1	0.87
	Pseudomyxoma peritonei (PMP)	2	1.74
	Intestinal obstruction	1	0.87
	CCF+TB	1	0.87
	Cytologically negative for malignant cells in known malignancy	3	2.61
	Total	115	100

Table-1: Effusions and the Underlying Causative Factors

cirrhosis, 12 (10.43%) samples of CCF, 5 (4.35%) samples of portal hypertension, 5(4.35%) samples of intestinal obstruction, 1 (0.87%) sample of intestinal perforation, 1 (0.87%) sample of blunt trauma, 3 (2.61%) samples of malignancy and 1 (0.87%) sample of Meig's syndrome, 10 (8.70%) samples of negative for malignant cells in known

Causative Factor	No. of Samples	TLC Cells/ cu.mm			Predominant Cell						Protein (gm%)	
		0-500	500-1000	> 1000	Polymorphs	Lymphocytes	Eosinophils	Macrophages	Mesothelial	Malignant Cells	<3	> 3
Cirrhosis	36	32	3	1	-	36	-	-	-	-	36	-
Cirrhosis+TB	5	-	2	3	-	5	-	-	-	-	-	5
Portal HTN	5	4	1	-	-	5					5	-
CCF	12	10	2	-	-	12	-	-	-	-	12	-
CCF+TB	1	-	1	-	-	1	-	-	-	-	-	-
tuberculosis	7	2	4	1	-	6	-	1	-	-	-	7
Chronic pancreatitis	1	1	-	-	-	1	-	-	-	-	1	-
Chronic kidney diseases	2	2	-	-	-	2	-	-	-	-	2	-
Intestinal obstruction	6	1	2	3	1	3	-	-	2	-	5	1
Appendicularperforation and pelvic abscess	1	-	1	-	1	-	-	-	-	-	1	-
Blunt trauma	1	-	1	-	1	-	-	-	-	-	1	-
Chylous ascites	1	1		-		1						1
Cytologically negative for malignant cells in a known malignancy	13	7	6	-	3	9	-	-	1	-	10	3
Meigs Syndrome	1	1	-	-	-	1	-	-	-	-	1	-
Pseudomyxoma peritonei (PMP)	2	1	1	-	-	1	-	1	-	-	-	2
Malignant	21	-	5	16	1	12	-	-	-	8	3	18

Table-2: Causative factors of Peritoneal effusion, total and differential cell count and biochemical features

Primary Site (Number)	Cytology Positive		Cytology Negative	
	Male	Female	Male	Female
Ovary	-	9	-	7
Breast	-	-	-	1
Liver	-	-	-	3
Cervix	-	-	-	1
GIT	1	-	-	-
Lymph node	2	-	-	-
Unknown primary	-	9	-	1
	3	18	-	13
	21		13	

Table-3: Site of origin of primary malignancy and effusion cytology findings in males and female

Study	Female	Male	Ratio
Karoo RO et al[5] (2003)	153	87	1.75:1
Present study 2013	72	43	1.67:1

Table-4: Comparative study of sex distribution of peritoneal effusion

Causative factors	Runyon B et al[6] 1992	Gurubacharya[7] DL et al 2005	Present study
Hepatic	80%	68 75%	40%
Cardiac	5%	9.3%	11.30
Renal	-	-	1.73%
Pancreatic	-	-	0.86%
Tuberculosis	5%	12.5%	6.0%
Malignancy	10%	9.3%	29.56%
Others	3%	-	7.82%

Table–5: Comparative study of distribution of causative factors of peritoneal effusion

Study	Total	Malignant	Non -malignant	Ratio
Sears D et al[8](1987)	1165	423	742	1:1.7
Junaid TA et al[9](1980)	859	208	651	1:3.1
Karoo RO et al[5](2003)	276	48	228	1:4.75
PradhanSB et al[4](2006)	324	61	263	1:4.3
Present study	115	21	94	1;4.4

Table-6: Comparative study of Distribution of cases according to malignant and non malignant

Primary organ site		Sears D et al[8] (1987)		Monte SA et al[10] (1987)		Jha R et al[11] (2006)		Present study (2013)	
		N	%	N	%	N	%	N	%
Female Genital tract	Ovary	90	28.93	47	47.95	7	18.91	9	42.86
	Uterus Cervix	-	-			1	2.70	-	-
Breast		40	12.86	8	8.16				
GIT		42	13.50	16	16.32	12	32.43	1	4.76
Pancreas		13	4.18	-	-	1	2.70	-	-
liver		2	0.6	-	-	3	8.10	-	-
Biliary tract			-	-	-	7	18.91	-	-
Lung		13	4.18	1	1.0	-	-	-	-
Kidney		4	1.28	-	-	-	-	-	
Prostate		3	0.96	-	-	-	-	-	
Lymphoma / Leukemia		23	7.39	-	-	1	-	2	9.52
Other Non epithelial tumor		22	7.07	-	-	-	-	-	-
Miscellaneous		2	0.64	20	20.40	-	-	-	-
Primary site unknown		33	10.61	6	6.12	5	13.51	9	42.86%
Total		311	100	98	100	37	100	21	100

Table-7: Comparative Study of Primary Organ Site of Neoplasm in Malignant Effusions

malignancy.

Exudative effusion was seen in 7 (6.09%) samples of tuberculosis, 18 (15.65%) samples of malignancy, 5 (4.35%) samples of cirrhosis, 1 (0.87%) samples was chylous, 2 (1.74%) samples of PMP, 1 (0.87%) sample of intestinal obstruction (Table 2),

62 (53.91%) samples had TLC less than 500 cells/cu.mm. 29 (24.21%) had TLC between 500- 1000 cells/cu.mm. In 24 (20.86%) samples TLC was greater than 1000 cells/cu.mm. 95 (82.60%) samples had predominantly lymphocytes. 7(6.08%) samples had predominantly polymorphonuclear leukocytes. 8(6.95%) samples had predominantly malignant cells. 3 (2.60%) samples had predominantly reactive mesothelial cells and 2 (1.73%) sample had macrophages as predominant cells.

77 (66.95%) samples had peritoneal fluid protein level of less than 3 gm% and 38 (33.0%) had peritoneal fluid protein of greater than 3 gm%.

Out of 34 clinically diagnosed cases 21 (61.76%) were cytologically positive for malignant cells and 13(38.23%) were cytologically negative. Clinically diagnosed positive for malignant cells and 7(43.73%) were cytologically negative for malignant cells (Table 3).

DISCUSSION

Diagnostic cytology is the scientific art of interpretation of cells from the human body that exfoliate or are removed from their physiologic milieu.

The value of cytological examination of serous effusion in adults is widely recognized and well documented. The primary role of cytology in this setting is the detection of cancer. In patients without known malignancy, cytological evaluation may not only be able to identify the presence of tumor cells but also be able to classify them according to its type. In patients with known malignancy, the presence of tumor cells in a serous effusion has important prognostic implication and often affects treatment.[4]

In present study, out of 21 clinically diagnosed malignant samples, primary site could be confirmed on cytology in 12 (57.14%) cases, whereas primary site could not be determined in 9 (42.86%) of cases. Most common primary sites were ovary (42.86%) followed by 2 (9.52) samples were lymphoma and 1 sample was from (4.76%) GIT.

With this basis the present study was undertaken to identify the various causes of peritoneal effusions. It deals with the accuracy of diagnosis on the basis of contemporary cytologic features and cell count.

Total of 115 samples of peritoneal fluid were studied which constituted 18.4 of 625 samples of body fluid received during study period of two years from June 2011 to June 2013.

Effusion was found to be less common (4.33%) before the age of 20 years. Highest number (31.30%) of cases were seen in 6th decade. This large number in this age group can be attributed to increased incidence of malignancies. Peritoneal effusion was more common in females 72 (65.21%) than in males 43 (37.39%) (Table 4).

Runyon B et al reported that parenchyma liver disease were the most common cause in about 80% and then malignancy 10%, heart failure 5%, tuberculosis 2%, and other causes in

the rest of 3% cases.[6] These findings are similar to our study. Gurubacharya DL et al also reported that peritoneal effusion is caused by hepatic disease 68.75%, cardiac 9.3%, tuberculosis 12.5% and malignancy 10% of cases.[7] In our present study maximum number of cases were due to hepatic disease 40%, followed by 29.56% were malignant, 11.30% were cardiac, 7.82% were due to other causes, 6% were tubercular, 1.32% were renal, 0.86% pancreatic causes pancreatic causes(Table 5).

Sears D et al showed in his study out of 1165, 742 cases were non malignant and 423 cases were malignant, ratio of malignant and non malignant cases was 1 : 1.7.[8] Junaid TA et al showed 208 malignant cases out of 859 cases, ratio of malignant and non malignant cases was 1 : 3.1.[9] Karoo RO et al showed out of 276 cases, 48 cases were malignant and ratio between malignant and non malignant was 1:4.75.[5] Pradhan SB et al in his study showed 61 malignant cases out of 324 cases, ratio between malignant and non malignant was 1:4.3.[4]

In our present study, out of total 115 cases 21 were malignant and 94 were non malignant. The ratio between malignant and non malignant cases was 1 : 4.4. Thus our study was in correlation with all the studies mentioned above (Table 6).

In present study, out of 21 clinically diagnosed malignant samples, primary site could be confirmed on cytology in 12 (57.14%) cases, whereas primary site could not be determined in 9 (42.86%) of cases. Most common primary sites were ovary (42.86%) followed by 2 (9.52) samples were lymphoma and 1 sample was from (4.76%) GIT (Table 7).

In study done by Sears D et al(1987)[8], ovary (28.93%) was most common primary site. Monte SA et al (1987)[10] also showed in his study that female genital tract (47.95%) was the most common primary site of malignancy. Our present study was in concordance with the study done by Sears D et al and Monte SA et al.

Jha R et al (2006)[11] showed that the GIT (32.43%) was the most common primary site for malignancy, followed by ovary and biliary tract (18.91%) each.

CONCLUSION

The present study demonstrates that the most useful tests in establishing the diagnosis of peritoneal effusion are peritoneal fluid cytology and peritoneal fluid cell count. Cytological examination of body effusions is a complete diagnostic modality which aims at pointing out the etiology of effusion as well as in certain cases a means of prognostication of the disease process. The diagnostic performance of cytologic study of the fluid may be attributable to the fact that the cell population present in sediment is representative of much larger surface area than that obtained by needle biopsy.

The value of cytological examination of serous effusions is widely recognized and well documented. The primary role of cytology in this setting is detection of malignancy. In patients without known malignancy, cytological evaluation may not only be able to identify the presence of tumor cells but also may be able to classify them as to type. In patients with known malignancy the presence of tumor cells in serous effusions may have important prognostic implication.

A secondary role of cytological evaluation of effusion is determining non neoplastic causation.

Peritoneal fluid analysis is the most rapid and cost effective method of diagnosing the cause of peritoneal effusion. A negative cytology interpretation is of little value while a positive report is important in the differential diagnosis of the cause of the effusion and in determining the treatment of the patient. Thus peritoneal fluid analysis should be done as a routine procedure in patients with peritoneal effusion.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 09-08-2019; **Accepted:** 30-08-2019; **Published:** 26-09-2019