

## Original Research Article

# An observational study of cytopathological analysis of ascitic fluid or peritoneal washings cytology in ovarian neoplasms: correlation with histopathological parameters

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### ABSTRACT

**Background:** Analysis of ascitic fluid and peritoneal washing cytology serves as a useful predictor of ovarian surface involvement and peritoneal metastasis even in the absence of clinical omental spread. The aim of the current study is to correlate peritoneal cytology with various histologic features of ovarian cancers.

**Methods:** It is a retrospective study. A total of 30 cases of ovarian neoplasms were included in the study. Results of peritoneal cytology were correlated with various histologic features of ovarian tumors including histologic type, grade, tumor size, capsular invasion, and omental metastasis, using chi-square test. A p value of <0.05 was considered as statistically significant.

**Results:** Out of the 30 cases of ovarian tumors involved in the study, twenty-five cases were surface epithelial tumors, two sex-cord stromal tumors, one germ cell tumor, one primary ovarian lymphoma and one metastatic carcinoma. Capsular invasion was seen in 56.3 % of the cases, and omental metastasis in 46.6 % of the cases. A significant positive correlation was seen between positive peritoneal cytology and capsular invasion and omental metastasis with a p value of <0.001.

**Conclusions:** Peritoneal fluid cytology is an indicator of peritoneal metastasis. Positive cytology also correlates with capsular invasion and histologic type in ovarian tumors. Therefore, it should always be used as an adjunctive tool in the surgical management of ovarian tumors.

**Keywords:** Ascitic fluid cytology, Capsular invasion, Ovarian cancer, Omental metastasis

### INTRODUCTION

Ascites is a large amount of fluid accumulated in the abdomen. Under normal conditions, several litres of peritoneal fluid are produced daily, and it is not accumulated but effectively absorbed.

It is believed that the pathogenesis of malignant ascites is multifactorial and that the most important pathogenetic mechanisms include increased vascular permeability, lymphatic drainage obstruction, increased difference in hydrostatic pressure and reduced difference in oncotic

pressure.<sup>1</sup> Ascites is the most common complaint of patients with ovarian carcinoma. In 54% of patients with peritoneal carcinomatosis, ascites was the first detectable sign of malignancy.<sup>2</sup>

More than two-thirds of patients that present to us in the hospital have grades III and IV of the disease. Survival rate in advanced stages (III and IV) is 5-20%.<sup>3</sup> The presence of neoplastic cells in peritoneal washings reflects intraperitoneal spread of the neoplastic process beyond the primary organ site. When this occurs, it often correlates with a poor prognosis in a variety of tumors;

one important exception is positive washings in patients with borderline ovarian tumors.

Ovarian neoplasms are detected late in the disease course when it is significantly enlarged in size to cause abdominal distention and distress. Analysis of peritoneal fluid cytology serves as a useful predictor of ovarian surface involvement and peritoneal metastasis in ovarian cancers.<sup>4,5</sup>

On the other hand, omental and peritoneal spread of ovarian cancers has a huge impact on prognosis and upstages prognostic morbidity. Analysis of ascitic fluid and peritoneal washing cytology serves as a useful predictor of ovarian surface involvement and peritoneal metastasis in ovarian cancers.<sup>4</sup>

Early detection of microscopic disease in ovarian cancer may reduce the mortality rate of this disease by enabling an earlier diagnosis of primary recurrent ovarian cancer. Staging of ovarian cancer is mainly surgical. The pelvic peritoneal wash was introduced as a formal procedure by Keetel and Elkins in 1950 with the stated objective of detecting early spread in patients undergoing surgery for suspected malignancy.<sup>6</sup>

The purpose of present study was to find out the rate of positivism of malignant cells in ascitic fluid and to correlate peritoneal cytology with various histologic features of ovarian malignancies in our set-up.

**METHODS**

It was a retrospective study. A total of 30 cases of ovarian neoplasms were included in the study that underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy and omental and lymph node sampling during a period of 3 years 2015 till Aug 2017 at Gandhi Medical College and Hamidia Hospital, Bhopal. Any free abdominal fluid was aspirated before surgery or at the time of surgery.

Cytological findings of ascitic fluid and peritoneal cavity effusion were sampled and examined microscopically in the Department of Pathology, after cytopspin following which the sediments were collected, used for preparing smears on slides, fixed in isopropyl alcohol for one hour and stained with Haematoxylin and Eosin.

Histology techniques were followed for histopathology specimens of cases. Results of peritoneal cytology were correlated with various histologic features of ovarian tumors including histologic type, grade, tumor size, capsular invasion, and omental metastasis, using chi-square test. All results were statistically processed, tabulated and calculated using SPSS 8.0 so as to obtain the sensitivity, specificity, positive predictive value and negative predictive value. A p value of <0.05 was considered as statistically significant.

**RESULTS**

The mean age was 48.9 years (±13) and range was 30 to 85 years. Out of the thirty cases of ovarian tumors involved in the study, twenty-five cases were of Malignant ovarian neoplasm and rest five were borderline. Out of the thirty cases of ovarian tumors involved in the study, twenty-five cases were surface epithelial tumors, two sex-cord stromal tumors, one germ cell tumor, one primary ovarian lymphoma and one metastatic carcinoma. Overall sensitivity and specificity in malignant ovarian carcinoma were 88% and 82% respectively.

**Table 1: Distribution according to histopathological diagnosis.**

Type of ovarian tumour	No. of total cases =30	Percent
Borderline serous	1	3.3%
Borderline mucinous	4	13.3%
<b>Malignant</b>		
Epithelial tumours	Serous	13 43.3%
	Mucinous	04 13.3%
	Endometroid	2 6.6%
	Clear cell	1 3.3%
Sex cord stromal tumour (Granulosa cell tumour)	2	6.6%
Germ cell tumour	Dysgerminoma	1 3.3%
	Yolk sac tumour	0 0%
Lymphoma	1	3.3%
Metastatic mucinous adenocarcinoma	1	3.3%

The mean tumor size was 12cm.

**Table 2: Histopathologic features of ovarian tumors.**

	Frequency	Omental metastasis	Capsular invasion
Serous tumour	14	00 (0%)	00 (0%)
Borderline	01	9 (69.2%)	10 (77%)
Malignant	13		
Mucinous	08	00 (0%)	00 (0%)
Borderline	04	02 (50%)	02 (50%)
Malignant	04		
Endometroid Ca	02	01 (50%)	01 (50%)
Clear cell carcinoma	01	00 (0%)	00 (0%)
Granulosa cell tumour	02	00 (00%)	01 (50%)
Dysgerminoma	01	00 (0%)	00 (0%)
NonHodgkin Lymphoma	01	01 (100%)	01 (100%)
Metastatic (Krukenberg)	01	01 (100%)	01 (100%)

Capsular invasion was seen in (n=16)56.3 % of tumors and omental metastasis in (n=14) 46.6 % of all tumors. In our study, there were 5 borderline tumours (one serous and 4 mucinous), all showed negative cytology as well as no omental metastasis or capsular invasion.

Out of 30 cases, (25 malignant) peritoneal cytology was positive in 14 cases only (46.6 %). Ascitic fluid cytology in most cases of serous adenocarcinoma showed moderate to abundant cellularity which was easily identifiable as malignant and as papillary in type. Peritoneal cytology in cases of mucinous cystadenocarcinoma showed variable cellularity. Cells were present in sheets, singly scattered, focally showing honey comb pattern and picket fencing. Cytoplasm was often well defined, with prominent vacuolization. Mucin

was present intracellularly as well extracellularly. One case was diagnosed as metastatic adenocarcinoma.

The cytology revealed highly cellular smear with a mildly hemorrhagic background. Mainly dispersed cells with focal acinar pattern and intracytoplasmic mucin were present.

Table 1 shows that serous tumours were most common among all.

Table 2 shows that in surface epithelial tumours, serous carcinoma had a significantly higher frequency of positive peritoneal cytology (69.2%) as compared to mucinous (50%) and endometrioid (50%).

**Table 3: Correlation of peritoneal cytology with histological subtype of tumor.**

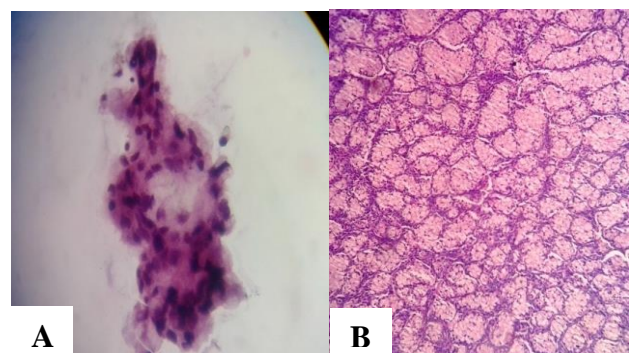
Peritoneal cytology	Positive		Negative		P value
	+ve Number	+ve Percentage	- ve Number	- ve Percentage	
Serous carcinoma (13)	09	69.2	04	30.7	0.009
Borderline serous tumour (1)	00	00	01	100	
Mucinous carcinoma (4)	02	50	02	50	
Borderline mucinous tumour (4)	00	00	04	100	
Clear cell carcinoma (1)	00	00	01	100	
Endometrioid carcinoma (2)	01	50	00	00	
Granulosa cell (2)	00	00	02	100	
Dysgerminoma (1)	00	00	01	100	
Lymphoma (1)	01	100	00	00	
Metastatic carcinoma (1)	01	100	00	00	
Total	14 (46%)				

**Table 4: Correlation of peritoneal cytology with capsular invasion.**

Peritoneal cytology	Frequency	Capsular invasion Present	Capsular invasion Absent
Positive	46.6% (14)	100% (14)	0% (0)
Negative	53.4% (16)	12.5% (2)	87.5% (14)
Total	30	16	16

**Table 5: Correlation of peritoneal cytology with omental metastasis.**

Peritoneal cytology	Frequency	Omental metastasis Present	Omental metastasis Absent
Positive	46.6% (14)	92.8% (13)	7.1% (1)
Negative	53.4% (16)	6 % (1)	94% (15)
Total	30	14	14

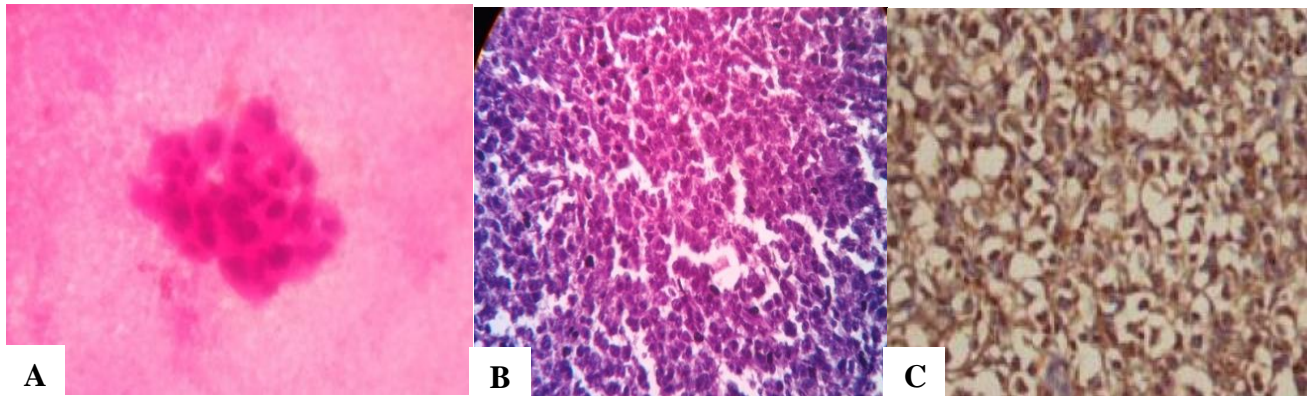


**Figure 1: (A): Positive peritoneal cytology in metastatic signet-ring adenocarcinoma, (B): Hematoxylin and Eosin stain section of Metastatic ovarian adenocarcinoma.**

There were two cases of endometrioid carcinoma out of which one was falsely diagnosed as serous carcinoma in cytology and other case was reported as negative for malignant cell.

A significant positive correlation was seen between positive peritoneal cytology with omental metastasis and capsular invasion with a p value of <0.001.

In present study, 14 cases had positive cytological findings and 13 of the positive showed omental metastasis. Out of the 16, cytological negative; one case showed omental metastasis.



**Figure 2: Primary ovarian lymphoma (A): Smears positive for malignant cells, (B): Section shows sheets of monomorphic small round blue tumor cells with indistinct cytoplasmic border, large darkly stained nuclei showing abnormal mitosis, (C): Immunohistochemistry marker: CD 45 was positive (negative for cytokeratin) .**

## DISCUSSION

Ascitic fluid and peritoneal washing cytology is a useful indicator of ovarian surface involvement and peritoneal dissemination by ovarian tumors. It may identify subclinical peritoneal spread and thus provide valuable staging and prognostic information.<sup>7</sup> For the same reason, peritoneal washing cytology was implemented in ovarian cancer guidelines and is routinely performed in ovarian cancer surgeries. In 1976; FIGO incorporated it into staging protocols. The majority of epithelial cancers has an exophytic growth on ovarian surface that provide them a direct contact with peritoneal cavity. They typically disseminate by trans-coelomic spread and peritoneal seeding by tumor cells produce ascites. Early detection of microscopic disease in ovarian cancer may reduce the mortality rate of this disease by enabling an earlier diagnosis of primary recurrent ovarian cancer.

Cytology detection rates of abdominal spread in ovarian cancers vary in different studies. Fadare et al, reported 25% and Rubin et al, reported 30% detection rate, while Colgan et al, revealed 50% detection rate.<sup>8-10</sup> As much as 90% positive cytology detection rate has also been reported in a study.<sup>11</sup> This can be due to the inclusion of ascitic fluid along with peritoneal washings, as ascitic fluid has a much higher rate of detecting malignant cells.

The main cytological characteristics of malignant ascites are increased number of leukocytes and positive cytology for the presence of malignant cells. A positive cytological finding represents an important predictive factor in prognosis and recurrence.

In present study observation, serous carcinomas (n = 9 out of 13) were most common ovarian neoplasm to involve abdominal cavity as represented by positive peritoneal cytology. Fifty percent of endometrioid carcinoma (n=1 out of 2), 50% mucinous carcinoma (n=2 out of 4), 100% of primary ovarian lymphoma (n= 1) showed positive cytology. Borderline ovarian tumours (both serous and mucinous) were negative for peritoneal cytology. Fadare et al, reported 71.4% of serous carcinoma (n = 57), 55 % of endometrioid carcinoma (n=30), 20% of clear cell carcinoma (n= 19), and 50 % of mucinous carcinoma (n= 13) showing positive peritoneal cytology.<sup>8</sup> Similar study by Rubin et al, analyzed 96 cases of ovarian tumors of which 29 cases showed positive peritoneal washing cytology.<sup>9</sup>

## CONCLUSION

The results of present study indicate that ascitic fluid cytology is a highly specific and sensitive test in malignant ovarian tumors, especially in advanced stages of malignancy with which most of studied patients present in authors' hospital.

In conclusion, ascitic fluid cytology and positive peritoneal washing cytology is a useful prognostic factor in ovarian tumors. It greatly aids in supporting the diagnosis, in predicting the prognosis and chance of recurrence of the tumor, that in turn helps in proper management and treatment of the patients. In addition to being an indicator of peritoneal metastasis, positive cytology also correlates with capsular invasion in ovarian tumors.

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