Original Research Article

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A prospective study of cytopathological analysis of peritoneal washings among patients of ovarian neoplasms and correlation with histopathological parameters

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Abstract:

Background: Ovarian neoplasms are the sixth most common malignancy (30%) reported around the globe. In Indian women, its incidence comes after cervical cancer. Early detection by cytopathological studies may reduce the high mortality rates of ovarian neoplasms. **Material & Methods:** The present prospective observational study was conducted at the department of pathology of our tertiary care hospital. The sample of peritoneal washings was collected from patients who were clinically diagnosed with ovarian tumors, which later on proved by histopathology and presenting with an abdominal lump or a mass along with concomitant ascites. **Results:** Out of the total 84% samples of benign tumors, 80% were true negative on cytology and 4% were false positive. Among them 23 patients had serous cystadenomas, mucinous cystadenomas were found in 8 patients, dermoid cysts were present in 6 patients and fibromas were present in 2 patients. There was only one case of mucinous cystadenoma with Brenner tumor. Among the two false-positive samples, one was of tubercular salpingo-oophoritis and another was a sample of non-specific chronic salpingo-oophoritis. Out of the total 16% cases of malignant tumors, the most common were serous cystadenocarcinomas, which were found among 2 patients. We also found two cases of Krukenberg tumors, along with one patient of mucinous cystadenocarcinomas and endometrioid carcinoma of ovaries respectively. **Conclusion:** The peritoneal washings cytopathology for detecting the ovarian neoplasms is highly specific (96.7%) and highly sensitive (88.8%) with a positive predictive value of 89.8% and a negative predictive value of 97.1%. The accuracy of peritoneal washings cytopathology was found to be 95.7%.

Keywords: Ovarian neoplasm, peritoneal washings cytopathology, benign tumors.

INTRODUCTION:

Ovarian neoplasms are the sixth most common malignancy (30%) reported around the globe. It is reported to be on the fourth position on deaths due to cancers in the USA among women of all ages. In Indian women, its incidence comes after cervical cancer. In the majority of cases (90%) the etiology is sporadic with the mean age of diagnosis being 60±5 years **(1).** Symptoms are generally nonspecific which is responsible for high mortality. Early detection by cytopathological studies may reduce the high mortality rates of ovarian neoplasms. The peritoneal washings and ascetic fluid in ovarian cancer are thick, cloudy, and exudative because of higher protein contents **(2).**

Ovarian neoplasms are among the commonest cause of high mortality and morbidity among the other malignancies all

around the globe. However, with advancements in medical science and research, the mortality rates had shown declining trends in the past decades **(3).** Near about, in ninety percent of cases, the cytology of peritoneal washings and ascetic fluid is benign and nonmalignant. Mostly carcinoma of the gastrointestinal and genitourinary system is responsible for malignant cytopathology of peritoneal washings and ascetic fluid **(4)**. The majority of cancers of epithelial origin have an exophytic growth for example in carcinoma of the ovary, the ovarian surface is in the direct contact of the peritoneal cavity. Hence they usually disseminate via the trans-coelomic spread and seedling in the peritoneal cavity by tumor cells producing the ascites and responsible for malignant cytopathology of peritoneal washings **(5).**
Since the multifactorial pathology includes lymphatic drainage obstruction, increased vascular permeability, and the osmotic difference leads to accumulation of ascetic fluid. Hence peritoneal washings and ascetic fluid is a specific prognostic marker for ovarian carcinoma and present in almost every case since the five-year survival rates are very lower and it is 94.6% for the Ist stage and 28.2% for the IIIrd stage **(6).** The present study aimed to study the cytopathological details of peritoneal washings in the diagnosis of ovarian neoplasms, and also to evaluate and assess the false positive and false negative results for determining the accuracy and validity of peritoneal fluid cytology in relation to the histopathological variant of ovarian neoplasms.

MATERIALS & METHODS

The present prospective observational study was conducted at the department of pathology of our tertiary care hospital. A total number of 50 peritoneal cytology samples were included in the study by simple random sampling over a period of two years. The sample of peritoneal washings was collected from patients who were clinically diagnosed with ovarian tumors, which later on proved by histopathology and presenting with an abdominal lump or a mass along with concomitant ascites. Clearance from Institutional Ethics Committee was taken before the start of the study. Cytological results of ascitic peritoneal washings sample and samples of effusion from peritoneal cavity were examined thoroughly microscopically. After the centrifugation process sediments were used for preparing the slide smears, which were fixed by isopropyl alcohol for about one hour and then stained with Haematoxylin and Eosin stain. Data were entered in the MS office 2010 spreadsheet and Epi Info v7. Data analysis was carried out using SPSS v22. Qualitative data were expressed as a percentage (%) and Pearson's chi-square test was used to find out statistical differences between the study groups and sensitivity, specificity, positive predictive value, and negative predictive value were calculated. If the expected cell count was < 5 in more than 20% of the cells then Fisher's exact test was used. All tests were done at an alpha (level significance) of 5%; which means a significant association was present if the p-value was less than 0.05.

RESULTS

In the present study, we studied 50 peritoneal washings samples, and data was recorded. The majority of samples from the patients were among the age group of 40-50 years. The majority of samples in the present study showed the benign nature of ovarian tumors in 84% of samples. In the present

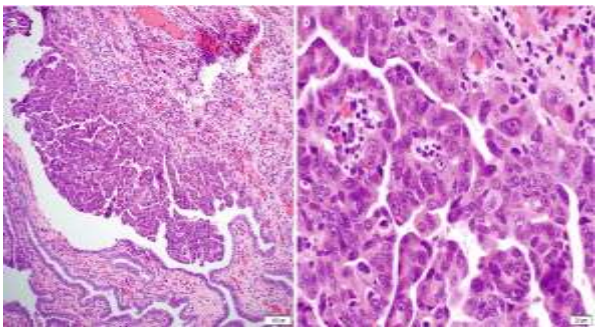
study, all the samples of malignant histopathology were of above forty years of age. Peritoneal washings cytopathological study was done for all the histopathological variants of study samples. Out of the total 84% samples of benign tumors, 80% were true negative on cytology and 4% were false positive. Among them 23 patients had serous cystadenomas, mucinous cystadenomas were found in 8 patients, dermoid cysts were present in 6 patients, and fibromas were present in 2 patients. There was only one case of mucinous cystadenoma with Brenner tumor. Among the two false-positive samples, one was of tubercular salpingo-oophoritis and another was a sample of non-specific chronic salpingo-oophoritis. (Table 1)

Table 1: Distribution and cytological evaluation of benign ovarian tumors [N=42 (84%)]

Histopathological examination	Ascitic fluid cytology results	No. of cases
Serous cystadenomas	Negative	23
Mucinous cystadenomas	Negative	8
Dermoid cysts	Negative	6
Fibroma /Fibrothecoma	Negative	2
Mucinous cystadenoma with Brenner tumor	Negative	1
Tuberculous salpingo-oophoritis	False-positive	1
Non –specific chronic salpingo-oophoritis	False positive	1

In the present study during the Peritoneal washings cytopathological evaluation, several inflammatory cells and reactive mesothelial cells were observed and diagnosed as for adenocarcinoma and reported positive for malignancy, hence this was the reason for the two false-positive cases. Although these two samples of ovarian masses were actually had inflammatory pathology, they were still included in the present study, to focus and enlighten the fact that differentiating reactive mesothelial cells can be mistaken with adenocarcinoma presentation in cytopathology. (Fig 1 and Fig 2).

Fig 1: Fig 2: showing cytopathology of salpingo-oophoritis and adenocarcinoma



In the present study out of the total 16% cases of malignant tumors, the most common were serous cystadenocarcinomas, which was found among 2 patients. We also found two cases of Krukenberg tumors, along with one patient of mucinous cystadenocarcinomas and endometrioid carcinoma of ovaries respectively.

All these 8 patients were true positive and showed positive results on cytological evaluation for malignant cells. In the present study, we found two false-negative cases one was of yolk sac tumor and the second case was of teratoma with squamous cell carcinoma. (Table 2)

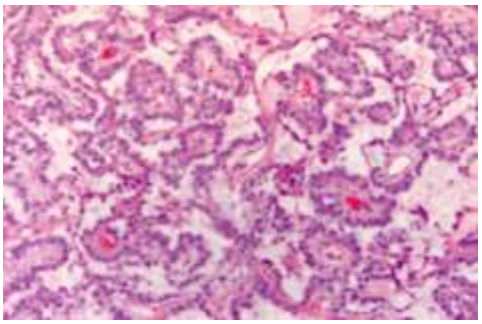
Table 2: Distribution and cytological evaluation of benign ovarian tumors [N=8 (16%)]

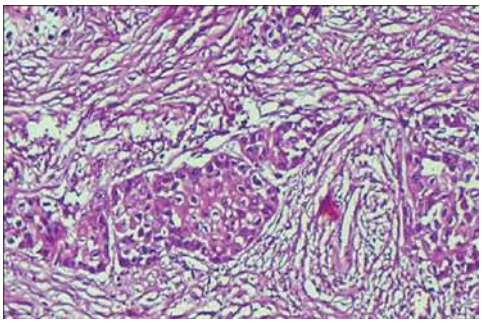
Histopathological examination	Ascitic fluid cytology results	No. of cases (%)
Papillary serous cystadenocarcinoma	Positive	2
Krukenberg tumors	Positive	2
Mucinous cystadenocarcinoma	Positive	1
Endometrioid carcinoma	Positive	1
Yolk sac tumor	False negative	1
Teratoma with SCC	False negative	1

Table 3: Assessment of ascetic fluid cytological evaluation of ovarian tumors (N=100)

	sensitivity	specificity	Positive predictive value	Negative predictive value	Accuracy
Ascetic fluid cytology	88.8%	96.7%	89.8%	97.1%	95.7%

Fig 3: Fig 4: showing cytopathology of yolk sac tumor and teratoma with squamous cell carcinoma





In the present study on the statistical calculation of Peritoneal washings cytopathological evaluation, we found 88.8% of sensitivity along with 96.7% of specificity. On the calculation of predictive values, we found a positive predictive value of 89.8% and a negative predictive value of 97.1%. Accuracy of ascitic fluid cytology was found to be 95.7%. (Table 3)

DISCUSSION

In the present study, we studied 50 peritoneal washings samples, and data was recorded. The majority of samples from the patients were among the age group of 40-50 years. The majority of samples in the present study showed the benign nature of ovarian tumors in 84% of samples. In the present study, all the samples of malignant histopathology were of above forty years of age. Peritoneal washings cytopathological study was done for all the histopathological variants of study samples. The main cytopathological findings were the presence of malignant cells with raised leukocytes. Positive cytopathological results represent an important prognostic factor for remission and recurrence. The main reason for false-

positive cytopathological findings was the interpretation inadequacy of mesothelial cells which were reactively altered **(7).** On cytological evaluation, these cells were arranged in grape-like clusters, enlarged and dense cytoplasm and with rounded cell contours with big nuclei and nucleolus may also contain vacuoles. In contrast, the cytological evaluation of adenocarcinoma shows the high nucleo-cytoplasmic ratio and pleomorphic nuclei with prominent nucleoli and depicts focal acinar and papillary findings **(8).**

Out of the total 84% samples of benign tumors, 80% were true negative on cytology and 4% were false positive. Among them 23 patients had serous cystadenomas, mucinous cystadenomas were found in 8 patients, dermoid cysts were present in 6 patients, and fibromas were present in 2 patients. There was only one case of mucinous cystadenoma with Brenner tumor. Among the two false-positive samples, one was of tubercular salpingo-oophoritis and another was a sample of non-specific chronic salpingo-oophoritis. A study conducted by Oscar L found that on peritoneal cytology false-positive cases were 4.5% and reported that high false-negative cases more than 20% of total patients **(9)**.

In the present study during the ascitic fluid cytological evaluation, several inflammatory cells and reactive mesothelial cells were observed and diagnosed as adenocarcinoma and reported positive for malignancy, hence this was the reason for the two false-positive cases. Although these two samples of ovarian masses were actually had inflammatory pathology, they were still included in the present study, to focus and enlighten the fact that differentiating reactive mesothelial cells can be mistaken with adenocarcinoma presentation in cytopathology. Similar findings were obtained by a study conducted by Runyon et al also reported the false positive and false negative cases with the sensitivity of 97%, which was reported to be dependent upon the staging of the disease and peritoneal inclusion **(10).**

In the present study out of the total 16% cases of malignant tumors, the most common were serous cystadenocarcinomas, which was found among 2 patients. We also found two cases of Krukenberg tumors, along with one patient of mucinous cystadenocarcinomas and endometrioid carcinoma of ovaries respectively. All these 8 patients were true positive and showed positive results on cytological evaluation for malignant cells. In the present study, we found two false-negative cases one was of yolk sac tumor and the second case was of teratoma with squamous cell carcinoma. A study conducted by Karoo et al reported contrary results to the present study in which they found 12% false-negative cases with a sensitivity of 60% and specificity of almost 100% **(11)**. A study conducted by Zuna et al reported that by application of peritoneal cytology they found the specificity of 98.1% and sensitivity of 82.9% in diagnosing intraperitoneal involvement of ovarian carcinoma **(12).**

In the present study on the statistical calculation of Peritoneal washings cytopathological evaluation, we found 88.8% of sensitivity along with 96.7% of specificity. On the calculation of predictive values, we found a positive predictive value of 89.8% and a negative predictive value of 97.1%. accuracy of ascitic fluid cytology was found to be 95.7%. A study conducted by Cheng et al reported that the sensitivity of ascitic fluid cytology was 94% which was higher from the results obtained in the present study **(13).** A study conducted by Sirop S et al reported that the ascitic fluid cytology was an important prognostic factor for treatment outcome and the follow-up.

The results of secondary cytology after the complete treatment was also a crucial independent prognostic marker that was strongly correlated with the optimal effect of surgical treatment and recurrence and the overall survival rate **(14).**

CONCLUSION

We concluded from the present study that the peritoneal washings cytopathology for detecting the ovarian neoplasms is highly specific (96.7%) and highly sensitive (88.8%) with a positive predictive value of 89.8% and a negative predictive value of 97.1%. The accuracy of peritoneal washings cytopathology was found to be 95.7%. Since the incidence of malignant ovarian neoplasms is increasing and especially in advancing stages, peritoneal washings cytopathology can aid in supporting the diagnosis and aid in improving the outcome and overall survival rate.

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