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EVALUATION OF CYTOLOGICAL ANALYSIS OF ASCITIC FLUID IN OVARIAN CARCINOMA

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ABSTRACT

Background: Ovarian carcinoma is among the commonest cause of high mortality and morbidity among the cancerous causes all around the globe. However, with advancement in medical science and research the mortality rates had shown declining trends in the past decades. **Materials and methods:** Ovarian carcinoma is among the commonest cause of high mortality and morbidity among the cancerous causes all around the globe. However, with advancement in medical science and research the mortality rates had shown declining trends in the past decades. **Results:** 62.2% patients had serous cystadenomas, mucinous cystadenomas was found in 19.5% of the cases, dermoid cysts were present in 12.2% of patients and fibromas present in 2.4% of the cases. There was only one sample of mucinous cystadenoma with Brenner tumor. Among the two false positive samples, one was of tubercular salpingo-oophoritis and another was sample of non-specific chronic salpingo-oophoritis. out of the malignant tumors, most common were serous cystadenocarcinomas, which was found among 50% of the cases. We found three cases of Krukenberg tumors, along with two- two cases of mucinous cystadenocarcinomas and endometrioid carcinoma of ovaries respectively. In the present study we found two false negative cases one was of yolk sac tumor and second case was of teratoma with squamous cell carcinoma. **Conclusion:** The ascitic fluid cytology for detecting the ovarian carcinoma is a highly specific (97.6%) and highly sensitive (88.9%) with the positive predictive value of 88.9% and negative predictive value of 97.6%. The accuracy of ascitic fluid cytology was found to be 96%.

Keywords: Ascites, Ovarian carcinoma, Peritoneal fluid cytology.

INTRODUCTION

Ovarian carcinoma is among the commonest cause of high mortality and morbidity among the cancerous causes all around the globe. However, with advancement in medical science and research the mortality rates had shown declining trends in the past decades **(1)**. Ascites is defined as when free fluid in accumulated in large amount inside the abdomen and which is not absorbed effectively. Near about in ninety percent of cases the cytology of ascetic fluid is benign and non malignant. Mostly carcinoma of gastrointestinal and genitourinary system is responsible for

malignant cytopathology of ascetic fluid **(2)**. The majority of cancers of epithelial origin have an exophytic growth for example in carcinoma of 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 peritoneal cavity by tumor cells produce the ascites **(3)**.

Ovarian carcinoma is the sixth most common cancer (30%) reported in 2004 around the globe. It is on fourth position on deaths due to cancers in USA among women of all ages. In Indian women, it comes after the cervical cancer. In majority of cases (90%) the etiology is sporadic with the mean age of diagnosis is 60±5 years **(4)**. Symptoms are nonspecific which responsible for high mortality. Early detection by cytopathological studies may reduce the high mortality rates of ovarian carcinoma. The ascetic fluid in ovarian cancer is thick, cloudy and exudative because of higher protein contents **(5)**. Since the multifactorial pathology which includes lymphatic drainage obstruction, increased vascular permeability and the osmotic difference leads to accumulation of ascetic fluid. Ascetic fluid is a specific prognostic marker for ovarian carcinoma and present in almost each 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 aim of the present study was to study the cytopathlogical details of ascitic fluid in the diagnosis of ovarian carcinoma, and also to evaluate and assess the false positive and false negative results for determine the accuracy and validity of peritoneal fluid cytology in relation to the histopathological variant of ovarian carcinoma.

MATERIALS & METHODS

The present retrospective observational study was conducted at department of pathology of our tertiary care hospital. A total number of 100 peritoneal cytology samples were included in study by simple random sampling over a period of two years. The sample of ascetic fluid collected from patients who were presenting with an abdominal lump or a mass along with concomitant ascites and also clinically diagnosed with ovarian tumors, which later on proved by histopathology. Clearance from Institutional Ethics Committee was taken before start of study. Cytological results of ascitic fluid sample and samples of effusion from peritoneal cavity were examined thorough microscopically. After 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 spread sheet and Epi Info v7. Data analysis was carried out using SPSS v22. Qualitative data was expressed as 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 alpha (level significance) of 5%; means a significant association present if p value was less than 0.05.

RESULTS

In the present study, we studied 100 ascitic fluid samples and data was recorded. Majority of samples from the patients were of among the age group of 21-40 years. Majority of samples in present study showed benign nature of ovarian tumor in 82% of samples. Approximately all the

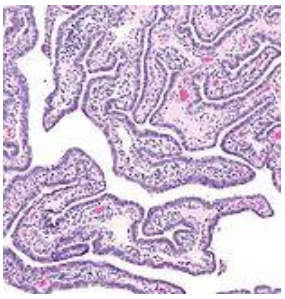
samples of malignant histopathology were of the above forty years of age, except the one sample of yolk sac tumor which was present in less than forty year of patient. Ascitic fluid cytopathological study was done for all the histopathological variants of study samples. Out of the total 82 samples of benign tumors, 80 were true negative on ascitic fluid cytology and 2 were false positive. Among them 62.2% patients had serous cystadenomas, mucinous cystadenomas was found in 19.5% of the cases, dermoid cysts were present in 12.2% of patients and fibromas present in 2.4% of the cases. There was only one sample of mucinous cystadenoma with Brenner tumor. Among the two false positive samples, one was of tubercular salpingo-oophoritis and another was sample of non-specific chronic salpingo-oophoritis. (Table 1)

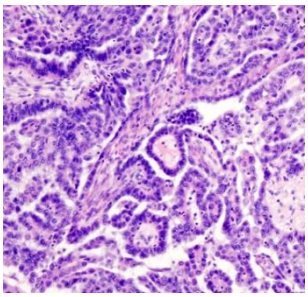
Table 1: Distribution and cytological evaluation of benign ovarian tumors (N=82)

Histopathological examination	Ascitic fluid cytology results	No. of cases (%)
Serous cystadenomas	Negative	51 (62.2%)
Mucinous cystadenomas	Negative	16 (19.5%)
Dermoid cysts	Negative	10 (12.2%)
Fibroma /Fibrothecoma	Negative	2 (2.4%)
Mucinous cystadenoma with Brenner tumor	Negative	1 (1.2%)
Tuberculoussalpingo-oophoritis	False positive	1 (1.2%)
Non –specific chronic salpingo-oophoritis	False positive	1 (1.2%)

In the present study during the ascitic fluid cytological 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, but 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 non-specific chronic salpingo-oophoritis and adenocarcinoma





In the present study out of the total 18 cases with malignant tumors, most common were serous cystadenocarcinomas, which was found among 50% of the cases and accounts for the most common ovarian carcinoma. We also found three cases of Krukenberg tumors, along with two- two cases of mucinous cystadenocarcinomas and endometrioid carcinoma of ovaries respectively. All these 16 cases were true positive and showed positive results on ascitic fluid cytological evaluation for malignant cells. In the present study we found two false negative cases one was of yolk sac tumor and second case was of teratoma with squamous cell carcinoma. (Table 2)

Table 2: Distribution and cytological evaluation of benign ovarian tumors (N=18)

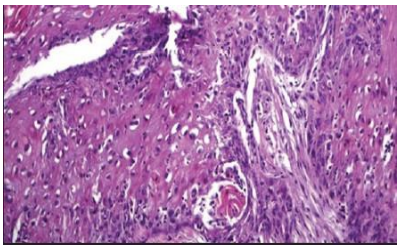
Histopathological examination	Ascitic fluid cytology results	No. of cases (%)
Papillary serous cystadenocarcinoma	Positive	9 (50%)
Krukenberg tumors	Positive	3 (16.7%)
Mucinous cystadenocarcinoma	Positive	2 (11.1%)
Endometrioid carcinoma	Positive	2 (11.1%)
Yolk sac tumor	False negative	1 (5.6%)
Teratoma with SCC	False negative	1 (5.6%)

In the present study on the statistical calculation of ascitic fluid cytology we found 88.9% of sensitivity along with 97.6% of specificity. On the calculation of predictive values we found positive predictive value of 88.9% and negative predictive value of 97.6%. accuracy of ascitic fluid cytology was found to be 96%. (Table 3)

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

	sensitivity	specificity	Positive predictive value	Negative predictive vaue	Accuracy
Ascetic fluid cytology	88.9 %	97.6%	88.9%	97.6%	96%

Fig 3: Showing teratoma with squamous cell carcinoma



DISCUSSION

In the present study, we studied 100 ascitic fluid samples and data was recorded. Majority of samples from the patients were of among the age group of 21-40 years. Majority of samples in present study showed benign nature of ovarian tumor in 82% of samples. Approximately all the samples of malignant histopathology were of the above forty years of age, except the one sample of yolk sac tumor which was present in less than forty year of patient. The main cytopathological findings of malignant ascitic fluid were presence of malignant cells with raised leukocytes. A positive cytopathological results represents an important prognostic factor for remission and recurrence. The main reason for false positive cytopathological findings was 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 nucleus and nucleolus may also contain vacuoles. On the 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)**.

Ascitic fluid cytopathological study was done for all the histopathological variants of study samples. Out of the total 82 samples of benign tumors, 80 were true negative on ascitic fluid cytology and 2 were false positive. Among then 62.2% patients had serous cystadenomas, mucinous cystadenomas was found in 19.5% of the cases, dermoid cysts were present in 12.2% of patients and fibromas present in 2.4% of the cases. There was only one sample of mucinous cystadenoma with Brenner tumor. Among the two false positive samples, one was of tubercular salpingo-oophoritis and another was 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 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, but 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

depends upon staging of the disease and peritoneal inclusion **(10)**.

In the present study out of the total 18 cases with malignant tumors, most common were serous cystadenocarcinomas, which was found among 50% of the cases and accounts for the most common ovarian carcinoma. We also found three cases of Krukenberg tumors, along with two- two cases of mucinous cystadenocarcinomas and endometrioid carcinoma of ovaries respectively. All these 16 cases were true positive and showed positive results on ascitic fluid cytological evaluation for malignant cells. In the present study we found two false negative cases one was of yolk sac tumor and second case was of teratoma with squamous cell carcinoma. A study conducted by Karoo et al reported contrary results to 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 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 ascitic fluid cytology we found 88.9% of sensitivity along with 97.6% of specificity. On the calculation of predictive values we found positive predictive value of 88.9% and negative predictive value of 97.6%. accuracy of ascitic fluid cytology was found to be 96%. 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 a important prognostic factor for treatment outcome and for the follow up. The results of secondary cytology after the complete treatment was also an crucial independent prognostic marker which 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 ascitic fluid cytology for detecting the ovarian carcinoma is a highly specific (97.6%) and highly sensitive (88.9%) with the positive predictive value of 88.9% and negative predictive value of 97.6%. The accuracy of ascitic fluid cytology was found to be 96%. Since the incidence of malignant ovarian tumors is increasing and especially in advancing stages, ascitic fluid cytology can aid in supporting the diagnosis, to knw the optimal effect of surgical treatment and to know the prevalence of recurrence and to estimating the overall survival rate.

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