

Comparative Study between Results of Pre- and Intraoperative Cytological Examination of Ascetic Fluid in Patients with Ovarian Cancer

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ABSTRACT

Background: Ovarian cancer (OC) is a common cause of death, most of the cases are diagnosed in late stages.

Aim: To compare preoperative and intraoperative examinations of ascetic fluid cytology in patients with OC.

Patients and methods: The study included 200 patients with suspicious adnexal masses with ascites, preoperative vs intraoperative aspiration of ascitic fluid followed by preparation and cytological examination searching for malignant cells.

Results: Among the 200 patients with suspicious adnexal mass with the presence of ascitic fluids, presence of malignant cells was present in 63 cases in the preoperative arm and was present in 96 cases in the intraoperative arm.

Conclusion: The detection of malignant cells in ascitic fluid is crucial in OC staging and diagnosis, intraoperative is more sensitive than preoperative cytological examination.

Keywords: Ascites, Ascitic fluid examination, Cytology, Malignant cells, Ovarian cancer.

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INTRODUCTION

Ovarian cancer (OC) is the fifth most common cause of cancer death and remains the leading cause of gynecological death.¹

These poor outcomes are directly related to the fact that a large majority, almost 75% of OCs, are diagnosed at an advanced stage (III/IV) when transperitoneal, hematogenous, and lymphatic dissemination have already occurred.²

In general, effective therapy in OC patients can achieve 90% when the tumor is still confined to the ovary; unfortunately, only 25% of OC can be diagnosed before it exacerbates.³

Despite the modern management, the introduction of improved surgical techniques, combination chemotherapy, and targeted therapies, the overall survival rates for these patients have not been significantly improved, with 70% of all OC patients succumbing to it within 5 years.⁴

The high mortality rate from ovarian malignancy is due to late diagnosis because of the absence of symptoms in the early stage of the disease.⁵

Cytology has not been used properly in the diagnosis of OC. This may be due to (A) ultrasound and CT scans being accurate tools in detecting malignancy and omental or peritoneal deposits, (B) cytology alone could not differentiate tumor subtypes, (C) cytology may disseminate malignant cells in the peritoneal cavity, (D) lack of experience in interpretation of cytology results, and (E) it may delay optimal surgical procedure.⁵

However, there are certain situations where cytology plays an important role such as (A) in differentiating malignant from non-malignant ovarian tumors, (B) in diagnosing recurrence, (C) in OC diagnosis in the unfit patient for surgical intervention, (D) in advanced metastatic OC, (E) unusual sites for recurrence or

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metastasis, (F) ascitic or pleural fluid cytology for detection of malignant cells, and (G) peritoneal washings at the time of surgery to detect peritoneal deposits.⁵

There is a relationship between OC stages and the prognosis. Patients with advanced stages have a low 5-year survival rate, while patients diagnosed with OC confined to the ovary often require less aggressive surgical treatment and have a better 5-year survival rate.⁶

The presence of malignant cells in the peritoneal cavity is a very important prognostic factor in patients with OCs. So, the peritoneal fluid examination is a routine step in OC management. presence of malignant cells in ascitic fluid is more sensitive than peritoneal wash in the diagnosis of OC.⁵

Malignant ascites are present in 10% of patients with ascites.⁷

Ascites may be exudative and transudative. Transudates make up 90% of ascitic fluids and they are caused by conditions of non-malignant etiology. This fluid is clear, with a small number of cells

and a low level of albumin. An exudate is usually malignant, and cloudy, with a greater number of cells and a higher level of proteins than transudate.⁸

The pathogenesis of malignant ascites is multifactorial and the most important pathogenetic mechanisms include increased vascular permeability, lymphatic drainage obstruction, increased difference in hydrostatic pressure, and reduced difference in oncotic pressure. 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.⁸

Aim

The aim of this research is to compare preoperative and intraoperative examination of ascetic fluid cytology in patients with OC.

PATIENTS AND METHODS

This prospective study was carried out on 200 patients with suspicious adnexal masses, the study was performed at the Gyne–Oncology unit, El Shatby Maternity University Hospital after signing a written consent. During the period from October 2017 to November 2020.

Inclusion Criteria

- Suspicious adnexal mass (bilateral, mixed cystic, and solid; presence of papillae; abnormal Doppler study).
- Presence of ascites.
- Fit for surgery.
- Acceptance to participate in this research.

All patients were subjected to the following processes:

- Full history and clinical examination.
- Optimal radiological study.
- Tumor markers.
- Preoperative assessment.
- Ascetic fluid aspiration: Transabdominal or transvaginal (in cases with minimal ascites) ultrasound-guided needle gauge number 18 to aspirate ascetic fluid from 100 to 200 mL, after immediate sedimentation for 10 minutes at a velocity of 2000/minute, the cell-free supernatant remains in the chamber after centrifugation and removed by careful aspiration, then dried and stained. Preparation and interpretation were done by pathologists.
- In the same sitting in the operating theater, laparotomy was done for suspicious adnexal masses and after anterior abdominal wall incision, aspiration of ascetic fluid using a wide pore syringe to obtain from 100 to 200 mL of ascetic fluid to be prepared with the same method and the same person.

Interpretation of both samples was done, and a comparison between them was done. Correlation between final histopathological findings and results of cytology also were done.

The cytology report should state that malignant cells are either absent (no malignant cells identified) or present (positive for malignant cells).

Statistical Analysis

The data was collected and entered into the personal computer. Statistical analysis was done using statistical package for social sciences (SPSS) software, version 20.

This study is a prospective study; sample size is estimated according to statistical rules and data are normally distributed.

The statistical tests used were as follows: Arithmetic mean and standard deviation; for categorized parameters, Chi-square test was used, while for two groups, *t*-test was used for parametric data. The level of significance was 0.05.

RESULTS

The presence of ascites in patients with suspicious adnexal mass is a common finding and it is very important to diagnose the presence of malignant cells in this ascitic fluid.

In our study, 70% of patients were postmenopausal and the range of age was between 43 and 78 years.

The presence of malignant cells in the ascitic fluid was tested by the following two methods: Preoperative aspiration under ultrasound guidance (transvaginal ultrasound was performed on 7 cases and 193 cases by transabdominal ultrasound) and intraoperative aspiration of the ascitic fluid sample by using wide pore syringe.

Preoperative aspiration of ascetic fluid shows the presence of malignant cells in 63 cases while intraoperative aspiration shows 96 cases with malignant cells (31.5 and 48%, respectively) (Table 1).

Serous cystadenocarcinoma was the most common histopathological subtype followed by mucinous cystadenocarcinoma. Endometrioid adenocarcinoma was present in 18 cases only (Table 2).

Table 1: Comparison between the two methods regarding the presence of malignant cells

	Preoperative sampling		Intraoperative sampling	
	Number	%	Number	%
Positive	63	31.5	96	48.0
Negative	137	68.5	104	52.0
Total	200	100.0	200	100.0
$\chi^2 = 11.4$ $p = 0.00079$				

Table 2: Correlation between preoperative and intraoperative positive cytological examination of ascitic fluid and histopathological subtypes

Histopathological subtype	Number of cases	Preoperative positive	Preoperative negative	Intraoperative positive	Intraoperative negative	χ^2	p-value
Serous adenocarcinoma	74	21	53	33	41	4.19	0.040*
Mucinous adenocarcinoma	49	19	30	27	22	2.62	0.105
Endometrioid adenocarcinoma	18	7	11	12	6	3.18	0.045*
Metastatic OC	23	10	13	16	7	3.44	0.040*
Others	36	6	30	8	28	0.354	0.551
Total	200	63	137	96	104		

*Significance of *p*-value < 0.05

Table 3: Sensitivity, specificity, and accuracy of preoperative aspiration cytology in different subtypes in relation to intraoperative cytology as a gold standard

Preoperative cytology	Intraoperative cytology		Total number	Sensitivity	Specificity	Accuracy
	Positive	Negative				
Serous adenocarcinoma						
Positive	20	1	21	60.6	97.6	81.1
Negative	13	40	53			
Total	33	41	74			
Mucinous adenocarcinoma						
Positive	19	0	19	70.4	100.0	83.5
Negative	8	22	30			
Total	27	22	49			
Endometrioid adenocarcinoma						
Positive	6	1	7	50.0	83.3	61.1
Negative	6	5	11			
Total	12	6	18			
Metastatic OC						
Positive	10	6	16	100.0	53.8	73.9
Negative	0	7	7			
Total	10	13	23			
Others						
Positive	4	4	8	66.7	86.7	83.3
Negative	2	26	28			
Total	6	30	36			

Preoperative aspiration and cytological examinations were more sensitive in metastatic OC than others and more specific and accurate in mucinous adenocarcinoma than others (Table 3).

After the final histopathological diagnosis after surgical treatment, we found 12 cases with benign ovarian tumors; all of them were suspicious before surgery and all of them were associated with ascetic, pre- and intraoperative cytological examinations were negative in all patients.

So, cytological examination is considered a good negative test.

Of the 12 cases; 4 cases were with fibroma, 3 cases were with mature cystic teratoma, 2 cases were tubo-ovarian abscesses, and 3 cases were with borderline serous ovarian tumors.

DISCUSSION

Diagnosis of OC is not so easy and usually, we proceed to surgical treatment without an accurate diagnosis, presence of malignant cells in ascitic fluid is very helpful in the diagnosis and prognosis of ovarian malignancy.

In our research, we are comparing two methods for cytological diagnosis (pre- and intraoperative).

Intraoperative aspiration of ascetic fluid for cytological examination is more accurate than preoperative diagnosis. This may be due to inadequate interpretation of reactively altered mesothelial cells or the presence of malignant cells in groups or spheres so the diameter of the needle that we aspirate by is different. Also, the bad distribution of cells in the sampled ascetic fluid, bad preparation, or insufficient cell exfoliation, and since cytology is a subjective method, errors may be due to inadequate interpretation of findings.

In our study, sensitivity, specificity, and accuracy of intraoperative cytology versus intraoperative cytology ranged 50–100%, 53.8–100%, and 61.1–83.5%, respectively.

The sensitivity of peritoneal cytology stated in a study by Runyon et al. can be up to 97%, depending on the study, disease stage, and peritoneal inclusion.⁹

In a study performed by Karoo et al.,¹⁰ the sensitivity was 60% because the majority of the patients presented with advanced stage of ovarian carcinoma. Specificity was 100%.

According to a study by Zuna and Behrens,¹¹ the sensitivity of peritoneal cytology was 82.9% and specificity was 98.1% and in a study performed by Cheng et al., the sensitivity of peritoneal fluid cytology was 94%.^{12,13}

CONCLUSION

- Preoperative and intraoperative cytological diagnosis is helpful in the diagnosis of OC.
- Intraoperative cytological diagnosis is more accurate than preoperative.
- Serous adenocarcinoma is more common than other subtypes of OC.

REFERENCES

1. Torre LA, Bray F, Siegel RL, et al. Global cancer statistics, 2012. *CA Cancer J Clin* 2015;65(2):87–108. DOI: 10.3322/caac.21262.
2. Gasparri ML, Savone D, Besharat RA, et al. Circulating tumor cells as trigger to hematogenous spreads and potential biomarkers to predict the prognosis in ovarian cancer. *Tumour Biol* 2016;37(1):71–75. DOI: 10.1007/s13277-015-4299-9.

3. Kolostova K, Matkowski R, Jedryka M, et al. The added value of circulating tumor cells examination in ovarian cancer staging. *Am J Cancer Res* 2015;5(11):3363–3375. PMID: 26807317.
4. Cheng X, Zhang L, Chen Y, et al. Circulating cell-free DNA and circulating tumor cells, the “liquid biopsies” in ovarian cancer. *J Ovarian Res* 2017;10(1):75. DOI: 10.1186/s13048-017-0369-5.
5. Ramljak V, Muhaxhiri MA, Kelčec IB. Cytology in diagnosis of ovarian cancer. *Libri Oncologici* 2015;43(1–3):33–39. PMID: 27281838.
6. Janagam C, Atla B. Study of ascitic fluid cytology in ovarian tumors. *Int J Res Med Sci* 2017;5(12):5227–5231. DOI: 10.18203/2320-6012.ijrms20175382.
7. Sangisetty SL, Miner TJ. Malignant ascites: A review of prognostic factors, pathophysiology and therapeutic measures. *World J Gastrointest Surg* 2012;4(4):87–95. DOI: 10.4240/wjgs.v4.i4.87.
8. Becker G, Galandi D, Blum HE. Malignant ascites: Systematic review and guideline for treatment. *Eur J Cancer* 2006;42:589–597. DOI: 10.1016/j.ejca.2005.11.018.
9. Runyon BA, Hoefs JC, Morgan TR. Ascitic fluid analysis in malignancy-related ascites. *Hepatology* 1988;8(5):1104–1109. DOI: 10.1002/hep.1840080521.
10. Karoo R, Lloyd T, Garccea G. How valuable is ascitic cytology in the detection and management of malinancy. *Postgrad Med J* 2003;79:292–294. DOI: 10.1136/pmj.79.931.292.
11. Zuna RE, Behrens AJ. Peritoneal washing cytology in gynecologic cancers: Long-term follow-up of 355 patients. *J Natl Cancer Inst* 1996;88(14):980–987. DOI: 10.1093/jnci/88.14.980.
12. Cheng L, Wolf NG, Rose PG, et al. Peritoneal washing cytology of ovarian tumors of low malignant potential: Correlation with surface ovarian involvement and peritoneal implants. *Acta Cytol* 1998;42(5):1091–1094. DOI: 10.1159/000332094.
13. Garg R, Singh S, Rani R, et al. A Clinicopathological study of malignant ovarian tumors in India. *J South Asian Feder Menopause Soc* 2014;2(1):9–11. DOI: 10.5005/jp-journals-10032-1024.