

Imprint Cytology in Diagnosing Various Ovarian Lesions: A Retrospective Study in a Tertiary Care Hospital in Visakhapatnam

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Abstract

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Background: Ovarian neoplasms pose a significant health risk for women, often due to their late detection. Swift and accurate diagnosis can be a game-changer. Cytological methods, like imprint cytology, provide a quick, affordable way to diagnose these tumors during surgery. This can greatly influence surgical decisions and even help preserve fertility in younger patients.

Materials and Methods: We conducted a retrospective study on 96 cases of ovarian tumors over a span of two years. During surgery, imprint cytology was performed, and the results were later compared with the final histopathological diagnoses. We measured the diagnostic accuracy, sensitivity, and specificity of this cytological technique.

Results: Out of the 96 cases, 90 were benign, one was borderline, and five were malignant. The cytological analysis showed an impressive 95% diagnostic accuracy, with sensitivity at 90% and specificity at 94%. There was a notable correlation between positive cytological findings, such as capsular invasion, and tumor type, especially in serous carcinomas. Imprint cytology was not only effective at identifying malignant cells, but also provided more details on tumor architecture.

Conclusion: Cytological evaluation is a reliable, swift, and cost-effective method for diagnosing ovarian tumors during surgery. It aligns well with histopathological findings, helping to accurately classify tumors and guide surgical interventions. Using cytological techniques can reduce the need for extensive surgeries and improve patient outcomes.

Keywords:

Imprint smear, ovarian neoplasms, cytological analysis, histopathology, intraoperative diagnosis

Introduction

Ovarian tumors are a diverse group of growths that affect a substantial number of women worldwide, ranging from benign cysts to aggressive cancers. One of the biggest challenges in treating ovarian cancer is diagnosing it early. Many cases are detected at advanced stages, largely because symptoms are often vague and the ovaries are located deep in the abdomen [1]. Given these diagnostic challenges, there is a dire need for methods that can quickly and accurately distinguish between benign and malignant ovarian tumors, allowing doctors to make real-time decisions during surgery [2].

Imprint cytology has emerged as a potential solution. This technique involves pressing a fresh tissue sample onto a glass slide to

create an imprint, which is then stained and examined under a microscope [3]. Initially used for diagnosing other types of cancers, such as in the breast, thyroid, and lymph nodes, imprint cytology has shown comparable accuracy to traditional histopathology in these areas [4]. The hope is that imprint cytology can provide similar benefits in ovarian tumor diagnosis, allowing doctors to determine the type and severity of a tumor right in the operating room, rather than waiting for more time-consuming lab results [5].

Research into imprint cytology for ovarian tumors suggests that it can be fast, cost-effective, and accurate, sometimes even matching the results of frozen section analysis, which is the current standard for intraoperative diagnoses [6]. However, ovarian tumors are diverse, and their cells can sometimes look similar under a microscope, creating a need for more detailed studies to refine this method further.

This study aims to evaluate how well imprint cytology works in diagnosing ovarian tumors. By comparing the cytology results with traditional histopathology, we hope to better understand its accuracy and determine whether it can become a reliable, rapid diagnostic tool for ovarian tumors, ultimately helping improve patient care during surgery.

Materials and Methods

A retrospective diagnostic analytical study was performed from June 2022 to July 2024, for a period of two years, at Gayatri Vidya Parishad Institute of Health Care and Medical Technology, Visakhapatnam, Andhra Pradesh. The study included all samples of solid and cystic ovarian masses operated in gynecology surgery. Cases with insufficient cellularity in touch imprints and emergency operations for ovarian masses were excluded from the study. Freshly resected lesions were cut, and tissue was obtained from representative areas of both solid and cystic components. Cytology samples were collected from various parts of tumors exhibiting different gross morphologies. Tissue samples were either firmly touched or cut and pressed onto clean, dry, leveled frosted glass slides. Wet smears were immediately fixed in 95% ethanol or 80% isopropyl alcohol and were stained with rapid Hematoxylin and Eosin. The rapid Hematoxylin and Eosin (H&E) staining procedure was undertaken with precision and care. Initially, the slides were stained with Harris hematoxylin for approximately 30 seconds, after which they were rinsed thoroughly in running tap water. The slides were then immersed in a lithium carbonate solution for bluing and rinsed again. For the counterstaining step, 1% eosin was applied for 20 seconds to enhance the visibility of cytoplasmic components. The slides were then mounted with a medium such as Permount, resulting in a vibrant presentation of blue-stained nuclei and pink-stained cytoplasmic components.

The smears were evaluated for cellularity, arrangement of epithelial cells, cellular features of malignancy, necrosis, and background. All benign and borderline lesions were reported as negative for malignancy, while malignant lesions were reported as positive. Histopathological diagnosis served as the gold standard for statistical evaluation. Surgical resection specimens were fixed in 10% formalin and processed routinely. Histopathological diagnosis of paraffin-embedded tissue sections was performed using H&E staining and compared with imprint cytology results. Ovarian tumor histopathological diagnoses followed the WHO classification. The results were statistically evaluated for sensitivity, specificity, positive predictive value, and overall diagnostic accuracy. Data analysis was conducted using Microsoft Excel 2021.

Results

The present study consisted of 95 cases. The age range is 16–70 years. The peak age where most of the cases were seen was 26–35 years, consisting of a total of 29 cases. A simplified classification of ovarian tumors along with the spectrum of ovarian lesions

in the current study is provided below [Table 1]. Among the total histopathological diagnoses, 89 cases were benign, one was borderline, and five were malignant [Table 2]. Cytological diagnosis was 91.56% accurate for benign tumors, 28.57% accurate for borderline tumors, and 100% accuracy was recorded for malignant tumors. A 12.6% discordant rate in cytological diagnosis was observed in our study, accounting for a total of 12 cases out of 95 [Table 3]. Due to the limitations of cytology and the adequacy of smears, five borderline tumors, two seromucinous tumors, one cystadenofibroma, one mixed epithelial tumor, and one struma ovarii (a monodermal tumor) were all diagnosed as benign serous tumors in cytological smears, while two seromucinous tumors were diagnosed as benign mucinous tumors.

Table 1: Descriptive table of current ovarian tumor classification and spectrum of ovarian lesions in the present study

Ovarian tumor classification	Ovarian lesions in the present study
Serous tumour	Serous tumour
- Benign	- Benign
- Borderline	- Borderline
- Malignant	- Malignant
Mucinous	Mucinous
- Benign	- Benign
- Borderline	- Malignant
- Malignant	
Endometrioid carcinoma	Endometrioid tumor
Teratoma	Teratoma
- Benign	- Mature
- Malignant	
Undifferentiated carcinoma	Cystadenofibroma
Granulosa cell tumor	- Serous
Metastatic	- Seromucinous
Others	Mixed epithelial tumor, Struma ovarii, Squamous cell carcinoma

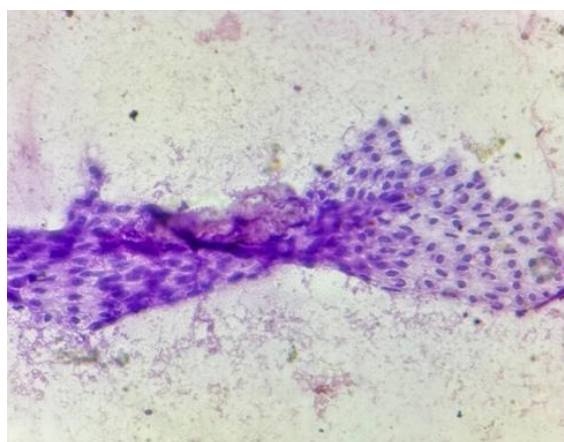
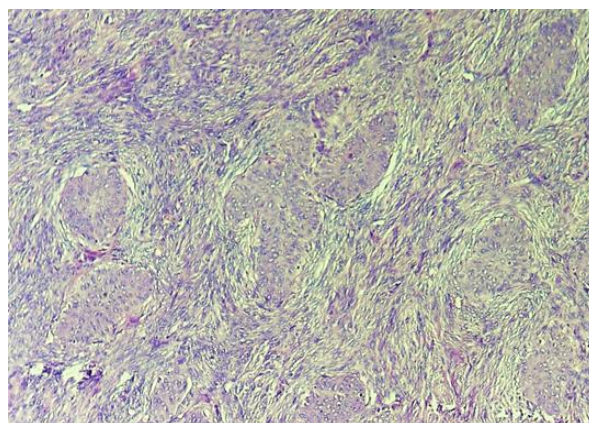
Table 2: Frequency of various ovarian tumors diagnosed in imprint and histopathology

Ovarian neoplasm	Histopathology	Imprint cytology
Serous tumour		
- Benign	55	64
- Borderline	7	2
- Malignant	1	1
Mucinous		
- Benign	10	13
- Borderline	0	0
- Malignant	1	1
Endometrioid tumor		
- Benign	0	0
- Borderline	0	0
- Malignant	2	2
Teratoma		
- Mature	7	7
- Immature	0	0
Cystadenofibroma		
- Serous	5	4
- Mucinous	0	0
Seromucinous	4	0
Mixed epithelial tumor	1	0
Struma ovarii	1	0
Squamous cell carcinoma	1	1
Total	95	95

Table 3: Correlation between imprint smear and histopathology of various ovarian tumors

Total cases n=95	Histological diagnosis n=95	Accurate cytological diagnosis n=83	Incorrect cytological diagnosis n=12
Benign	83 (87.36%)	76 (91.56%)	7 (5.8%)
Borderline	7 (7.36%)	2 (28.57%)	5 (71.42%)
Malignant	5 (5.26%)	5 (100%)	0 (0%)
total	100%	87.37%	12.63%

In our study, five cases of serous cystadenomas were associated with torsion and two cases with bilaterality [Fig. 1]. Among ten cases of mucinous cystadenomas, one was associated with torsion and one with mature cystic teratoma. There were seven cases of benign cystic teratomas. Apart from these, three others were associated with squamous cell carcinoma, mucinous cystadenoma, and one endometrioid carcinoma among the two. Only one mixed epithelial tumor was noted in our study, which showed both the features of Brenner and mucinous tumor [Fig. 2].

**Figure 1: H&E 10x : Imprints of serous cystadenoma showing sheets of benign epithelial cells.****Figure 2: H&E 10x : Epithelial cell nests in a mixed epithelial tumor consisting features of both brenner and mucinous components**

In the present study, there was some amount of discordance due to the limitations of cytological study. A total of 12 cases were discordant between the cytological and histopathological diagnoses. Five cases of borderline tumors diagnosed on histopathology

were given as benign serous tumors in their cytological reports. One case each of serous cystadenofibroma, mixed epithelial tumor, and struma ovarii were also diagnosed as benign serous tumors in their cytology reports. Seromucinous tumors, having both the morphological and histological features of serous and mucinous components, can be challenging for an accurate cytological report. In this study, a total of four cases of seromucinous tumors were observed; two were diagnosed as benign serous tumors and two as benign mucinous tumors. While most of the mismatched cases were benign or borderline (accounting for seven and five cases, respectively), none of them were malignant [Table 4].

Table 4: Unmatched imprint smear diagnosis

Imprint smear diagnosis	Histopathology diagnosis	Number
Benign serous tumor	Borderline serous tumor	5
Benign serous tumor	Serous cystadenofibroma	1
Benign serous tumor	Seromucinous tumor	2
Benign mucinous tumor	Seromucinous tumor	2
Benign serous tumor	Mixed epithelial tumor	1
Benign serous tumor	Struma ovarii	1

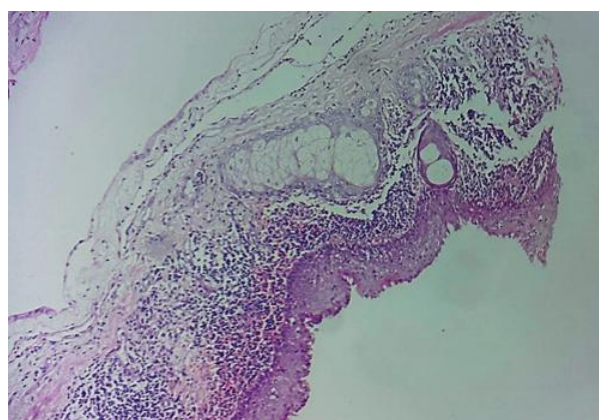


Figure 3: H&E 10x : Ovarian cyst wall of teratoma with residual stroma and adjacent sebaceous glands and squamous epithelium

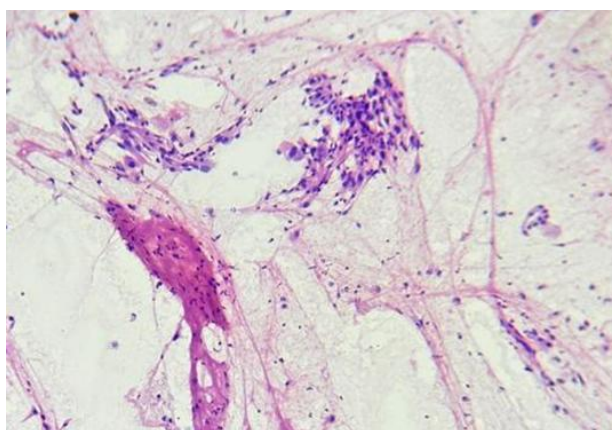


Figure 4: H&E 10x : Imprints of adenocarcinoma comprising of clusters of cells showing marked nuclear and cytoplasmic pleomorphism.

Discussion

Imprint cytology is a valuable diagnostic tool that provides information on the morphological patterns of both benign and malignant lesions, despite the limitations. It has many advantages over frozen section study, including its rapid intraoperative diagnosis, cost-effectiveness, high accuracy, and simple technique, which makes it a key diagnostic procedure [7]. Although this study deals with imprint cytology and its pros and cons, on a thoughtful note, it is highly significant to discuss the same in detail for frozen section technique. For ovarian tumors, the frozen section method has a number of benefits and drawbacks depending on several factors. Its main advantage is that it allows for quick intraoperative diagnosis in 15 to 30 minutes, which facilitates prompt surgical decision-making. Examples of these decisions include deciding whether to perform a hysterectomy or a cystectomy, or the extent of staging. This can save money by avoiding the need for follow-up surgeries, but it comes with a high upfront cost because it requires specialized equipment (cryostats) and skilled personnel, which makes it less feasible in environments with limited resources, unlike imprint cytology, which is relatively cheaper and requires minimal expertise. The method aids in tumor staging by detecting larger metastatic deposits and evaluating invasion, where imprint cytology clearly lacks the advantage. However, its sensitivity for isolated tumor cells or micrometastases is still low, and artifacts and shallow section depth can make it difficult to evaluate invasive features like stromal or capsular invasion, which could compromise staging accuracy. Although frozen sections are a great tool for directing intraoperative care, tissue quality, technical expertise, and resource availability all affect how reliable they are. All things considered, it is a helpful tool for prompt diagnosis and customized surgical procedures; however, its sensitivity limitations, resource needs, and interpretive difficulties call for careful and situation-specific use.

In our study, the sensitivity and specificity of the cytological technique were 87.37% and 88%, respectively, which were in concordance with the studies done by Nagai et al. and Shikha Agarwal et al. [8,9]. The overall accuracy was 87.68%, which showed similar results to the study done by Aparjita Samaddar et al. [10], which demonstrated 90.91% accuracy.

Out of 95 cases, the majority were benign tumors, accounting for 83 (87.36%), similar to the results of the studies done by Ivan et al. and Archana Shivamurthy et al. [11,12], with 80% and 85% cases, respectively. Among all the entities, epithelial tumors constituted the majority of tumors, collectively accounting for 86 (90.5%) of cases, which correlated with the results from the study by Archana Shivamurthy et al. [12]. Ovarian cystadenofibromas in general are rare and account for about 1.7% of all ovarian tumors. Typically, these tumors consist of solid grey-white areas, which can be confused for borderline or even malignant tumors, and obtaining imprints from precise locations can be intimidating (Fig. 3). In our study, we encountered five cases of benign serous cystadenofibromas, among which two of them showed papillary features and one showed discordance with histopathology. The results were similar to those of the study done by Begum M et al. [13]. Among the epithelial tumors, serous cystadenomas were the majority of the entities not only in our study but in many other studies [11,14,15]. Usually, diagnosing these is not challenging, but in a few cases, it might get difficult when associated with ovarian torsion, considering the hemorrhagic elements which sometimes may mask the features of a straightforward diagnosis.

One case of mixed epithelial tumor was noted in this study, which had both the features of Brenner and mucinous tumors. In the imprint, only the mucinous component was retrieved from the cystic part, missing the dual lesion, thereby diagnosing it as a benign mucinous tumor rather than a mixed mucinous and Brenner tumor. Similarly, one case of struma ovarii was also noted, which was misdiagnosed as a benign serous tumor in imprint cytology, which was in concordance with the study done by Reilly Ivan [11].

Limitations in our study ranged from identifying and retrieving the exact site for study to diagnosing malignant epithelial tumors

and tumors with low malignant potential, similar to other cytological studies irrespective of site and organ. While straightforward malignancies and benign tumors have less to no limitations in diagnosing, borderline tumors are strenuous to report. Our study encountered seven cases of borderline serous tumors, of which five cases were inaccurately diagnosed as benign serous tumors. Reporting of borderline cases was limited to observing the benign part only in the imprint, resulting in them being reported as benign serous tumors. The results were similar to many other studies that also highlighted the limitations of diagnosing borderline tumors, namely Aisha Akbar et al. and Aparajita et al. [10,15], which showed five discordant cases.

Malignant tumors, on the contrary, were diagnosed straight away with 100% sensitivity based on their attributes in the cytology slides (Fig. 4). In the present study, two of the malignant tumors were associated with mature cystic teratoma, among which one showed direct transformation to squamous cell carcinoma. Most of the studies done by various research teams culminated in 90–99% sensitivity in diagnosing malignancies. One study by Azami Shiho et al. [5] acquired 90.9%, and Surapan et al. [17] attained 98% sensitivity in the malignancy group.

Conclusion

Imprint cytology provides rapid and efficient results in diagnosing ovarian neoplasms. Although the frozen section technique is more advanced and provides accurate results, its availability and the required expertise are major limitations, whereupon imprint cytology plays an important role. Besides successfully diagnosing benign and malignant tumors without much effort, in the present study, borderline tumors were relatively strenuous to obtain a specific diagnosis straight away. Nevertheless, this technique's utmost significance can be noted in rapid intraoperative diagnosis and differentiation of tumors from benign, malignant, and tumor-like lesions, namely teratomas, papillary serous cystadenocarcinoma, endometrioid carcinoma, and squamous cell carcinoma. So far, that was the only prime challenge cum limitation in the study, making the specificity marginally on the superior side compared to sensitivity.

Abbreviations:

MGG – May-Grunwald Giemsa, PAP – Papanicolaou stain, NHGUC – Negative for High-Grade Urothelial Carcinoma, AUS – Atypical Urothelial Cell, LGUC – Low-grade urothelial neoplasm, HGUC – High-grade urothelial carcinoma, PUNLMP – Papillary urothelial neoplasm of low malignant potential

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