**Original Research Article**

# Role of Imprint cytology in rapid diagnosis of ovarian neoplasms with histopathology correlation

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## Abstract

**Background:** Imprint cytology plays a major role in rapid intraoperative diagnosis of lesions similar to frozen sections. Besides its speed and simplicity, it also provides excellent cellular details. Although histopathology is considered to be gold standard in diagnosis of ovarian neoplasms, yet the delay involved may at times affect the course of treatment. The optimal management of benign and malignant ovarian neoplasms is different especially in patients who want to retain fertility. This calls for a rapid intraoperative diagnosis which will decide further management.

**Aim and objectives:** To study the imprint cytology of ovarian neoplasms and compare with histopathology findings, to establish the reliability of imprint smears in intraoperative diagnosis by statistical evaluation.

**Material and methods:** The present study was done at MNJ Institute of Oncology, Hyderabad, a tertiary care center for period of one and half years i.e. from January 2017 to June 2018. The study was done on 40 fresh unfixed ovarian specimens sent for imprint cytology. Multiple imprint smears was taken from fresh resected masses after detailed gross examination. The findings were noted and compared to subsequent histopathology sections.

**Results:** In the present study, out of 40 cases, 21 (52.5%) were benign, 9(22.5%) were borderline, 10(25%) were malignant based on imprint cytology smears. On histopathology sections, 22 (55%) were benign, 1(2.5%) was borderline and 17(42.5%) were malignant. The overall accuracy was 87.5% on imprint smears.

**Conclusion:** Imprint cytology is an excellent, simple, inexpensive, useful diagnostic tool in intraoperative diagnosis of ovarian neoplasms. This forms an important step in intraoperative decision-making for better management.

## Key words

Imprint cytology, Ovarian neoplasms, Intraoperative.

## Introduction

Imprint cytology is an intraoperative diagnostic technique introduced by Dudgeon and Patrick in 1927 [1]. It was a major breakthrough in the field of rapid tissue diagnosis. Despite its speed, simplicity and excellent cellular details, imprint cytology is not utilized to its fullest extent in many centers. This technique avoids freezing artefact giving it an edge over frozen section analysis.

Ovarian tumors are the seventh most common cancer in women worldwide and have shown increase in incidence rates over the years. Ovarian tumors are a diverse group comprising benign and malignant tumors of epithelial, stromal and germ cell origin. Though, ovarian masses could be approached by ultrasound-guided aspiration or tru-cut biopsy, there are controversial views regarding their safety [2].

Imprint cytology offers a simple, rapid, inexpensive technique with good preservation of cellular details [3]. It has an advantage of taking multiple representative samples and preservation of tissue. Hence, imprint cytology is increasingly used in ovarian tumors to provide provisional diagnosis compared to frozen section and guide the extent of surgery. In the present study the findings of imprint cytology were compared to histopathology. An attempt was made to evaluate the reasons in cases where the findings did not correlate.

## Aim and objectives

- To study the imprint cytology of ovarian lesions compare it with their histopathology.
- To establish validity and reliability of imprint cytology.
- To evaluate the statistical parameters of imprint cytology in diagnosing ovarian lesions.

## Materials and methods

The present study was done at MNJ Institute of oncology, Hyderabad, a tertiary care center for period of one and half years i.e. from January 2017 to June 2018. The study was done on 40 fresh unfixed ovarian specimens sent for imprint cytology. The lesions were cut and gross features were noted. Serial cuts were given wherever necessary and surface was mopped dry of fluid and blood. Imprints were taken by firmly touching clean and dry glass slides on the representative areas with different gross morphology. Undue pressure and lateral movements were avoided while taking imprints. Slides were immediately fixed in 90% isopropyl alcohol for 5 minutes. Staining was done by rapid hematoxylin and eosin staining method. These imprint smears were reported within 15-20 minutes of receiving the fresh specimen. Later, all specimens were fixed in 10% buffered formalin. Histopathology diagnosis of paraffin-embedded tissue was done and compared to results on imprint smears. Histopathology diagnosis was considered as the gold standard for statistical evaluation. The results were statistically evaluated for sensitivity, specificity, positive predictive value and overall accuracy of diagnosis.

## Results

A total number of 40 ovarian tumors sent to Department of Pathology were studied. Out of these 40 cases, 21 (52.5%) were benign, 9(22.5%) were borderline, 10(25%) were malignant based on imprint cytology smears. On histopathology sections, 22 (55%) were benign,

1(2.5%) was borderline and 17(42.5%) were malignant (**Table – 1**).

**Table - 1:** Distribution of ovarian neoplasms based on imprint cytology and histopathology report.

| | **Imprint smears** | **Histopathology** |
|---|---|---|
| **Benign** | 21 (52.5%) | 22(55%) |
| **Borderline** | 9 (22.5%) | 1 (2.5%) |
| **Malignant** | 10 (25%) | 17 (42.5%) |

**Table - 2:** Imprint cytology and histopathology correlation of ovarian neoplasms.

| | **Imprint smears** | **Histopathology** |
|---|---|---|
| Serous tumors | | |
| Benign | 14 | 13 |
| Borderline | 7 | 0 |
| Malignant | 8 | 14 |
| Mucinous | | |
| Benign | 6 | 8 |
| Borderline | 2 | 1 |
| Malignant | 0 | 0 |
| Chocolate cyst | 1 | 1 |
| Germ cell tumor | 2 | 2 (dysgerminoma) |
| Sex cord stromal tumor/granulosa cell tumor | 0 | 1 |

**Table - 3:** Statistical parameters.

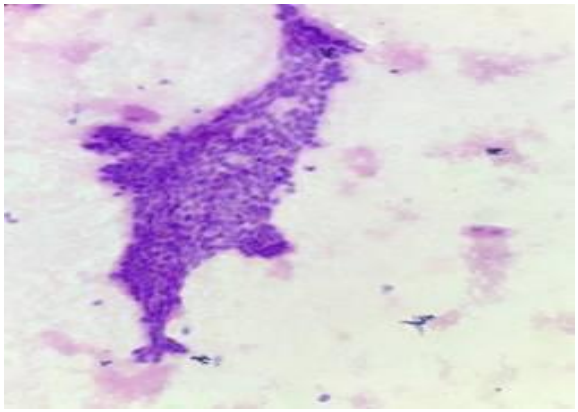
| **Histopathology** | **Positive** | **Negative** | **Total** |
|---|---|---|---|
| **Imprint smears** | | | |
| Positive | 16(TP) | 3(FP) | 19 |
| Negative | 2(FN) | 19(TN) | 21 |
| Total | 18 | 22 | 40 |

(TP - True positive; FN - False negative; FP - False positive; TN- True negative.)

Out of the 40 ovarian neoplasms 29 were serous tumors, 8 were mucinous, 1 was chocolate cyst and 2 were germ cell tumors, on imprint smears. On histopathology, 27 were serous, 9 were mucinous, 1 was chocolate cyst, 2 were diagnosed as dysgerminoma, 1 was diagnosed as granulosa cell tumor (**Table – 2**).

10 cases which were malignant on imprint correlated with histopathology. Out of 21 cases which were benign on imprint, 19 correlated with histopathology (**Figures - 1, 2, 3)** and 2 cases were diagnosed as malignant. Out of 9 cases which were diagnosed as borderline on imprint, one correlated, 3 were labelled as benign and 5 turned out to be malignant.

**Figures – 1, 2:** Imprint smears with aggregates of epithelial cells of columnar shape with bland nucleus. Background shows muinous material with few macrophages.



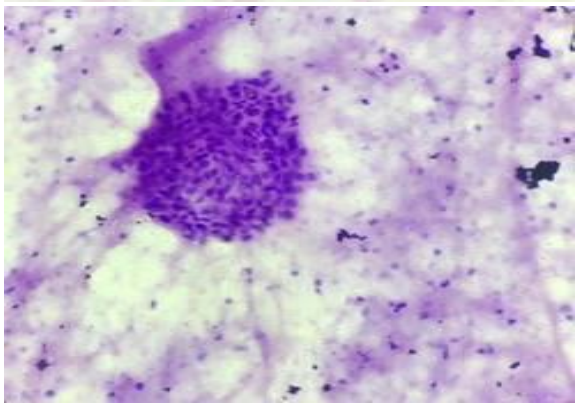
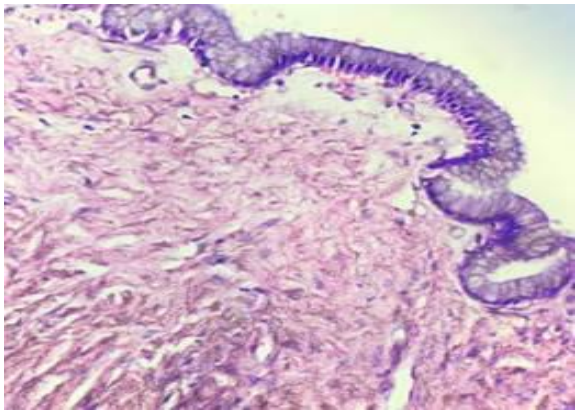


**Figure - 3:** HP section of mucinous cystadenoma.



One Mucinous cystadenoma and 2 cases of serous cystadenoma were incorrectly reported as

borderline tumors on imprint smears. 4 cases of serous carcinoma were diagnosed as borderline on imprint smears and one case which were diagnosed as borderline serous tumor on imprint turned to be granulosa cell tumor on histopathology. 2 cases of serous carcinomas were reported as benign serous cysts on imprint. 2 cases reported as germ cell tumor on imprint correlated with histopathology and reported as dysgerminoma **(Figures - 4, 5, 6).**

**Figures – 4, 5:** Imprint smears shows dis cohesive cells with marked nuclear pleomorphism, pale to clear cytoplasm. Background shows few lymphocytes.

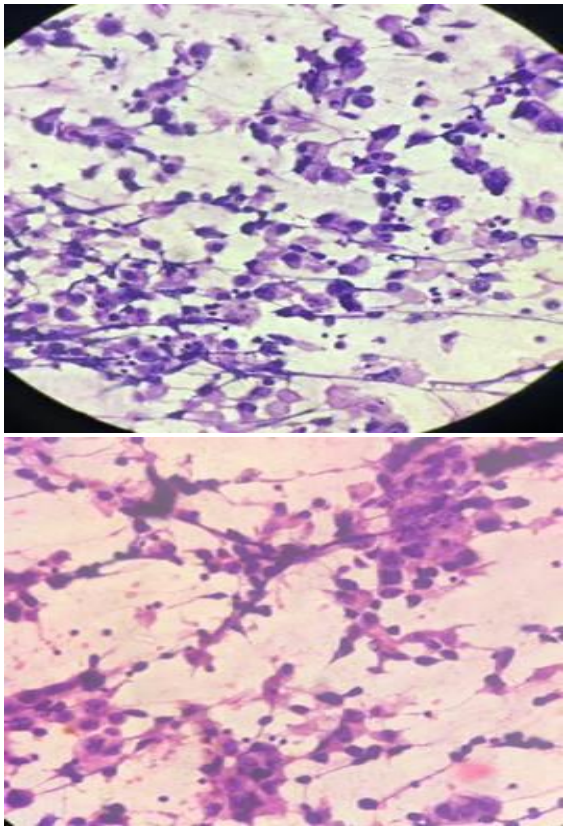
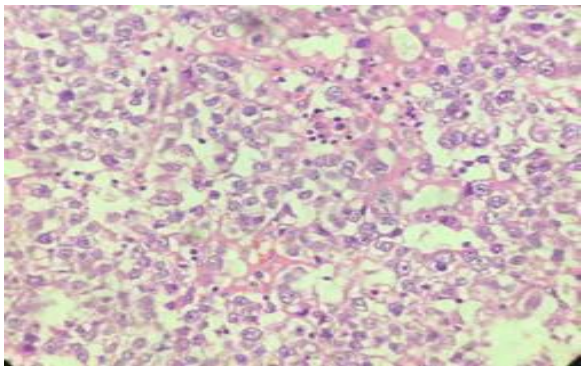


**Figure - 6:** HP section of Dysgerminoma.



**Figures – 7, 8:** Imprint smears showing papillary fragments, nuclear overcrowding and mild nuclear atypia.

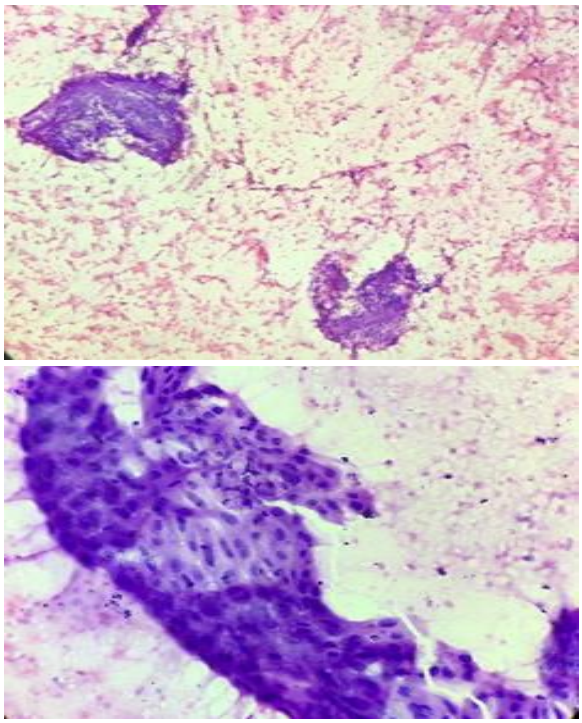
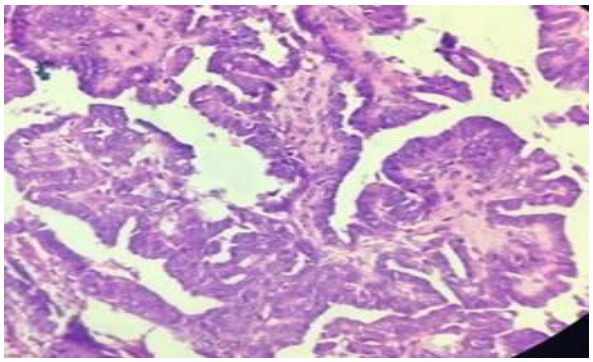


**Figure - 9:** HP section of Papillary serous cystadenocarcinoma.



For statistical purposes, all malignant and borderline ovarian tumors were taken as a positive control and all benign lesions were taken as a negative control. Cytology and histology-positive cases were labeled true positive (TP), histology-positive and cytology-negative cases were labeled as false negative (FN), histology and cytology-negative cases were labeled as true negative (TN), and histology-negative and cytology-positive cases were labeled as false positive (FP). Sensitivity, specificity, and diagnostic accuracy were calculated using descriptive statistics (**Table – 3**).

**Figure - 10:** Imprint smears with papillary fragments, cells show marked pleomorphism.

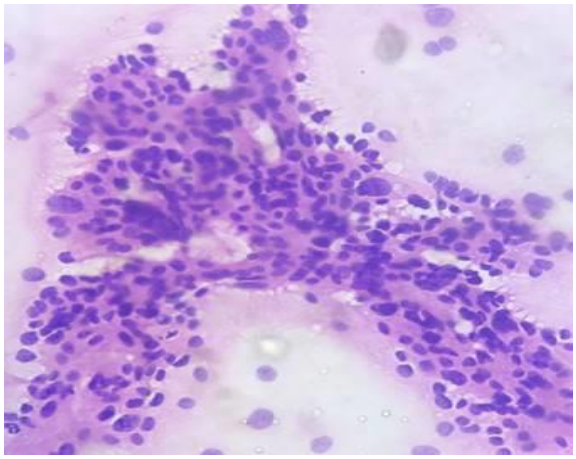
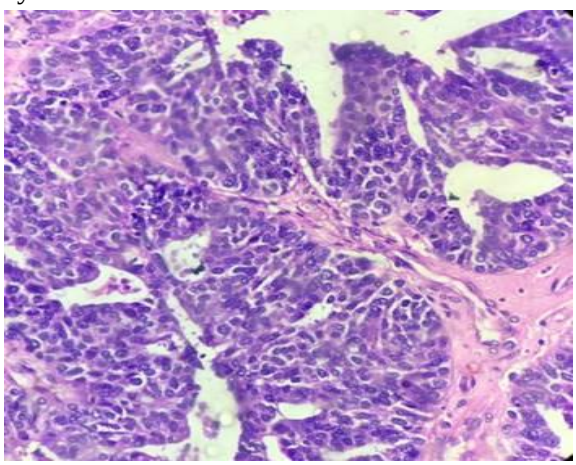


**Figure - 11:** HP section of Papillary serous cystadenocarcinoma.

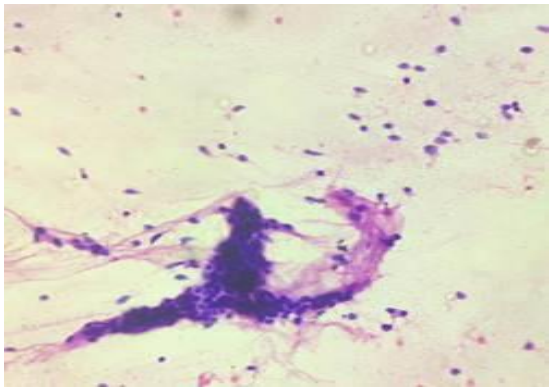


In our study, sensitivity was 88.89%, specificity was 86.36%, positive predictive value was 84.21%, and overall accuracy was 87.5%.

## Discussion

Intra-operative diagnostic cytology is finding increasing use in the present day when the patient care and management has become very individualized [4]. The various methods include frozen section, imprint smear cytology and scrape cytology. The use of FNAC in preoperative and intra-operative diagnosis of ovarian lesions is controversial because of fear of spillage of tumor contents into peritoneal cavity and secondary implantation [5]. Capsule rupture leading to upstaging of the tumor and lack of representative sample especially in cystic lesion are other drawbacks [6]. Imprint smears are simple, rapid with good cellular details and also different sites of the tumour can be assessed [7]. Imprint smears have been reported to have comparable diagnostic accuracy to frozen sections which requires expensive equipment and skilled technical expertise [8].

**Figures – 12, 13:** Imprint smears show cell aggregates with nuclear crowding and mild nuclear atypia.



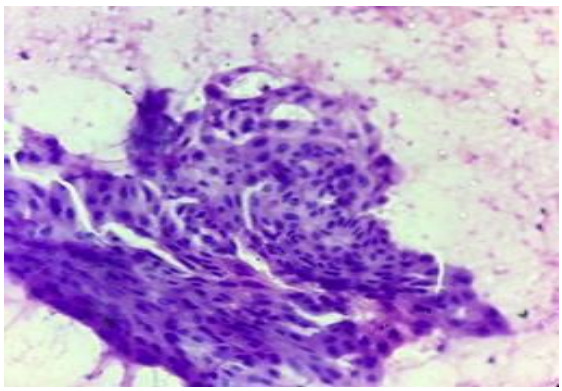
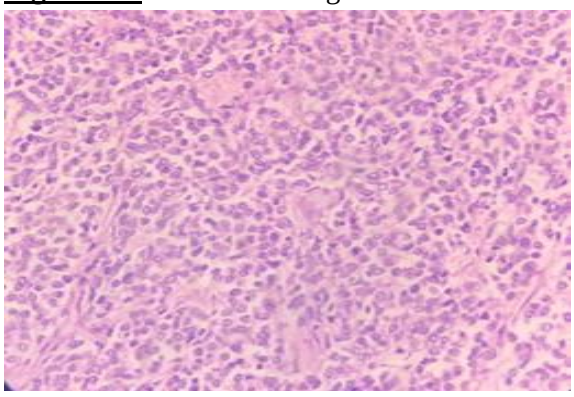


**Figure - 14:** HP section of granulosa cell tumor.



Out of 40 ovarian neoplasms studied, total of 31 cases correlated with histopathology findings. The 9 cases which did not correlate were mostly borderline cases on imprint cytology, 4 of them were carcinomas (**Figures - 7, 8, 9**), reason may

be due to the inability to sample the representative area which may be because of huge size of the tumor [9]. The other reasons may be interpretative errors in well differentiated carcinomas which cannot be differentiated cytologically and also evaluation of stromal invasion is may not be possible in cytology. In 3 cases, borderline tumors were labelled as one benign mucinous and two serous cystadenomas on histopathology. This may be due to the presence of focal mild nuclear atypia and epithelial crowding on imprint smears. In one case cytology revealed cohesive sheets of mucin-secreting columnar cells with moderate degree of cell overlapping with moderate nuclear atypia. On histopathology stratification with mild atypia was seen and reported as borderline mucinous tumor. A case of granulosa cell tumor was solid and cystic filled with serous material grossly. Imprint smears were hypocellular and showed cells with mild nuclear atypia and pleomorphism giving the impression of borderline tumor of epithelial type possibly serous (**Figures - 12, 13, 14**).

All 8 cases reported as serous adenocarcinoma on imprint cytology correlated with histopathology. Smears were highly cellular with cells showing high N:C ratio, nuclear pleomorphism in a necrotic background, papillary fragments were also seen in some cases (**Figures – 10, 11**). Germ cell tumors could be correctly diagnosed on imprint smears by classical cytomorphological features. Smears were highly cellular with diffuse arrangement of cells with abundant pale cytoplasm and large nuclei and atypical mitosis. Background had few mature lymphocytes (**Figures - 4, 5, 6**).

In our study, sensitivity was 88.89%, specificity was 86.36%, positive predictive value was 84.21%, and overall accuracy was 87.5%. This was comparable to various studies regarding imprint cytology of ovarian neoplasm. Chhanda Das, et al. (2014) in her study on cytohistological correlation of ovarian tumors, the sensitivity was 94%, specificity 74%, positive predictive value was 63% diagnostic accuracy 78% [10]. Sangita Bohora, et al. (2018) had a sensitivity, specificity, positive predictive value, diagnostic accuracy of 88.88%, 96%, 96%, 92.3% respectively in their study on Intraoperative cytology of ovarian neoplasms [11]. Dey Soumit, et al. had sensitivity 96.2%, specificity 75%, and diagnostic accuracy 83.3% [12]. These studies were comparable to the present study. In the study of imprint cytology of ovarian neoplasms done by Kar Tushar, et al. [13] (2005), the sensitivity and specificity were 93% and 92% respectively.

## Conclusion

Imprint cytology is an excellent useful diagnostic tool in intra-operative diagnosis of ovarian neoplasms. It is simple, inexpensive technique which does not require any sophisticated equipment. It gives rapid (10-15 minutes), reliable diagnosis for planning further surgical management. This is more so in young patients who require conservative surgery in order to preserve fertility. Imprint smears may not be very reliable in epithelial borderline tumors as they were difficult to distinguish from both benign and malignant epithelial tumors due to overlapping cytological features and stromal invasion cannot be assessed. The accuracy of imprint cytology can be further improved by taking extensive sections of specimen and taking multiple imprints from different representative areas. It is comparable to frozen section in terms of reliability and at times better as it avoids freezing artefact. Hence, it can be used conveniently as a substitute for frozen section especially in developing countries.

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