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Pathology

# Histomorphological Changes and Cytopathological Co-Relation of Tubo-Ovarian Mass

**Dr. Brinda S. Chandibhamar[1*], Dr. Shamim S. Sheikh[2]**
[1]Resident doctor, Department of Pathology, Shree M. P Shah medical college, Jamnagar-361008, Gujarat, India
[2]Associate professor, Department of pathology, Shree M. P. Shah medical college, Jamnagar-361008, Gujarat, India

**Original Research Article**

***Corresponding author**
*Dr. Brinda S. Chandibhamar*

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**Abstract:** The ovarian tumours manifest with wide spectrums of clinical, morphological, and histopathological features. Cytological examination of ovarian masses is an efficient diagnostic modality for diagnosing ovarian tumors prior to surgery. The main aim of this study was to access the sensitivity, specificity, and accuracy of FNAC in diagnosing ovarian masses. Total 100 patients with ovarian masses were examined and correlation of cytology was made with histopathology in all cases. Cytology of peritoneal/ ovarian fluids was also included in the study. Out of 100 cases, 10 cases were inconclusive due to inadequate sampling and these were considered as cytological false negative for the respective lesions. From 28 non neoplastic lesions, 26 were truly diagnosed on cytology, 2 cases were false positive and 2 cases were false negative. From 48 cases of benign lesions, 40 cases were truly diagnosed, 3 cases were false positive and 8 cases were false negative. 2 cases of borderline tumors were diagnosed as benign on cytology. From 22 malignant cases, 19 cases were truly diagnosed, 3 cases were false negative and no false positive case was found on cytology. Hence, overall sensitivity, specificity and accuracy for cytological diagnosis were 87.52%, 97.15%, 94% respectively. USG guided FNAC seems to be relatively safe, simple, fast and cost effective procedure. In addition, this procedure may be useful in deciding management guidelines prior to any surgical interventions.
**Keywords:** FNAC, ovarian tumors, ultrasonography, cytology, histology.

## INTRODUCTION

Ovaries are paired pelvic female reproductive organ, frequently encountered by neoplastic lesions either benign or malignant. Ovarian cancers account for about 6% of all cancers in females [1].

The ovary is the third most common site of primary malignancy in female genital tract after cervix and endometrium accounting for 30% of all cancers of female genital tract [2]. The complex anatomy of ovary and its peculiar physiology within the constant cyclical changes from puberty to menopause give rise to number of cell types each of which is capable of giving rise to tumors[3]. This morphological diversity of ovarian tumors poses many challenges in diagnosis for both gynaecologists and pathologists.

Screening for ovarian epithelial cancer are improved by various diagnostic modalities, Doppler color flow ultrasonography and transvaginal ultrasonography, measurement of tumor markers such as Serum HCG, serum CA125, serum alpha – fetoprotein, placental alkaline phosphatase and lactate dehydrogenase, ovarian cancer antigen OVX 1 and CA15-3 and numerous, however their accessibility to the practicing gynaecologist for rural based poor population remains very limited even today [4].

Fine needle aspiration cytology (FNAC) under ultrasonography (USG) or CT guidance can be regarded as the investigation of choice for diagnosis of abdominal masses in the early stages of disease [5].

This study is aimed with assessment of role of image guided FNAC in diagnosis of ovarian neoplasms; diagnosis on cytological examination were correlated with histopathological diagnosis.

Geier and Strecker [6] have suggested that FNAC should be used for (1) recurrent and metastatic tumors (2), suspected benign ovarian cysts and (3) when the patient's condition is unsuitable for laparotomy.

## MATERIALS AND METHODS

Cytological smears and histopathological specimens received in respective cytopathology and histopathology section of the pathology department over a period of two years (September 2014 to October 2016) are included in the study. Patient's age, clinical presentation, detailed clinical history, radiological findings and other investigations were noted.

After clinical work up, the patients were subject to abdominal / pelvic ultrasonography or computed tomography guided FNAC. The mass is localized and aspiration performed using 22 or 23 gauge needle attached to 10 ml syringe.

Peritoneal / ovarian fluids are received for evaluations of tubo ovarian masses are included in the study. Fluids are process by using cyto centrifuge machine.

Smears are fixed in 95% alcohol and stained with Pap or H & E stain. Specimens sent to the histopathology section are fixed, processed, stained and reported.

Descriptive statistics were used to determine correlation between cytological and histological findings. Sensitivity and specificity for the cytological diagnoses were calculated using the histological confirmation as the gold standard.

## OBSERVATIONS AND RESULTS

During the period of two years, 100 cases of ovarian lesions were evaluated by cyto- pathological smears and followed by histopathological sections.

Out of 100 cases, USG guided FNA was performed in 78 cases, peritoneal & ovarian fluids were received in 15cases & 7cases respectively.

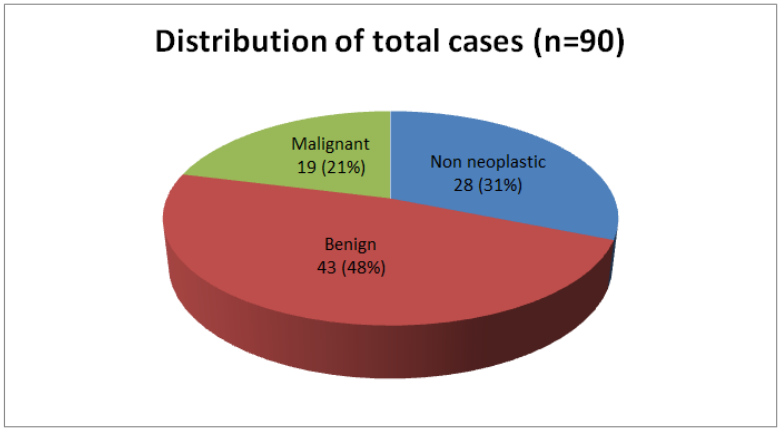


**Fig-1: Distribution of total cases based on cyto-pathological diagnosis**

Amongst these 100 cases, evaluated by cyto-pathologically, 10 cases were inconclusive due to inadequate sampling. Out of 90 cases where cytological diagnosis given, 28(31%) cases were non-neoplastic, 43 (48%) cases were benign neoplastic and the rest 19 (21%) cases diagnosed as malignant lesions (fig.1).

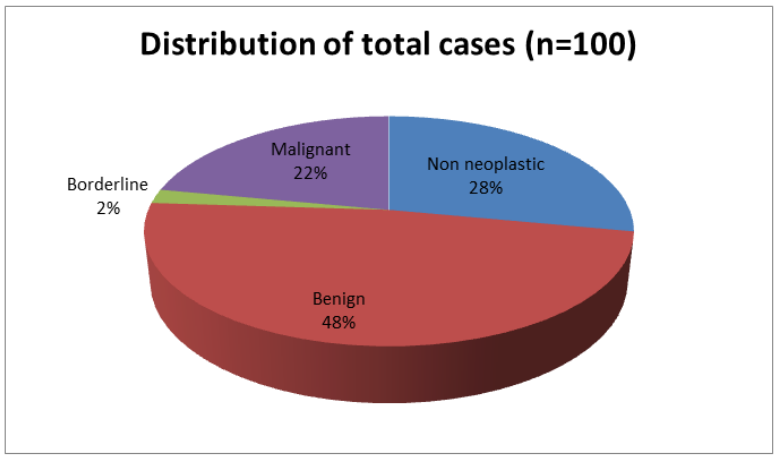


**Fig-2: Distribution total cases based on histo-pathological diagnosis**

These 100 cases were followed by histo-pathological examination, where diagnosis given as non-neoplastic in 28 (28%) cases, benign in 48(48%) cases, borderline in 2 (2%) cases and malignant in 22 (22%) cases (fig.2)

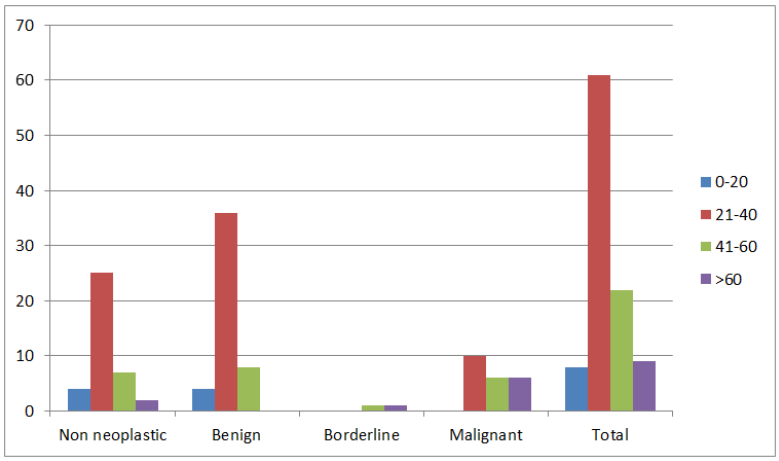


**Fig-3: Age wise distribution of ovarian lesions (Various age groups in years)**

The average age of women is 37.34 years. All over most common age group for ovarian lesions is 21-40 years (61 cases) (fig.3).

Amongst 100 cases, highest 22 cases of benign mucinous cystadenoma shows bilateral involvement of ovary (table.2). All over uni-lateral involvement was observed more frequently (in 76 cases) then bilateral involvement (in 24 cases) (fig.4).

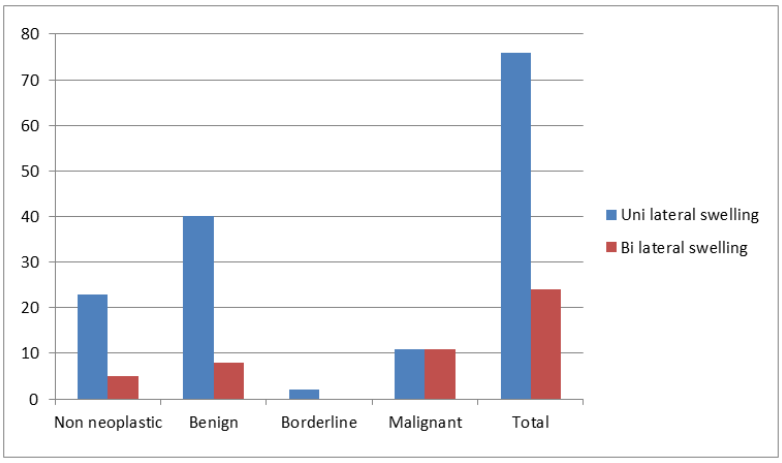


**Fig-4: Unilateral or bilateral involvement of ovarian lesions**

The most commonly ovarian lesions were presented as cystic swelling (in 51 cases) followed by solid-cystic swelling (in 42 cases) and least frequently presented as an only solid swelling (in 7 cases) (fig.5).

When characteristic cyto-morphological findings were appreciated, the specific diagnosis could be offered on cytology.

The diagnosis of haemorrhagic cyst (endometriotic cyst) was offered on cytology when sheets of epithelial cells and spindle (stromal) cells were seen against haemorrhagic background containing hemosiderin laden macrophages (fig.6).

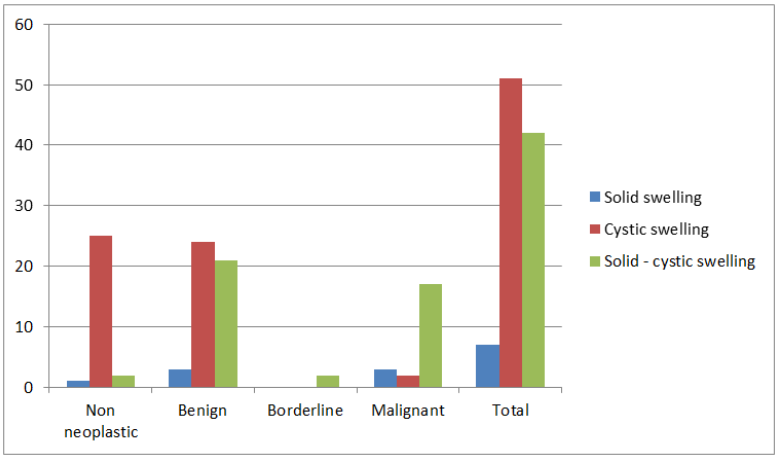


**Fig-5: Gross presentation of ovarian lesions**

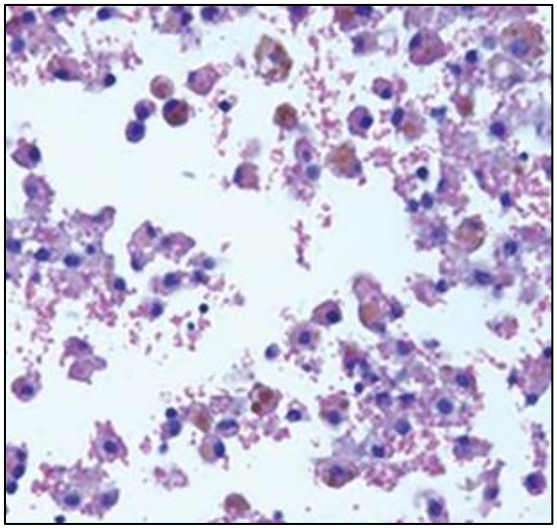

**Fig-6: Haemorrhagic cyst**

Serous cystadenomas on FNA yielded straw coloured fluid. Smears showed small few papillary fragments with bland nuclei and cyst macrophages. (fig.7). Benign mucinous neoplasms showed small clusters and isolated columnar epithelial cells with basally placed nuclei against a mucinous background (fig.8).

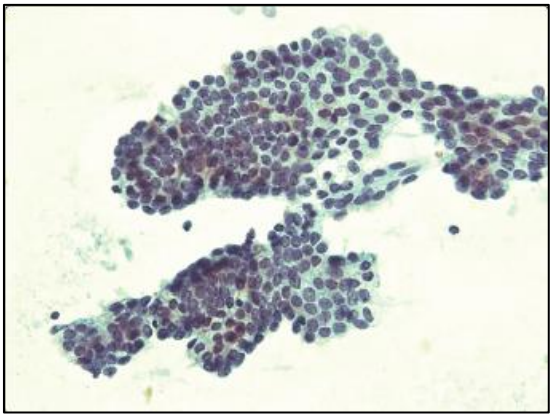

**Fig-7: Benign serous cystadenoma**

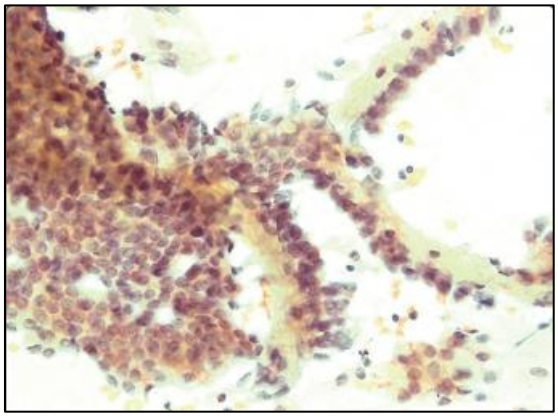

**Fig-8: Benign mucinous cystadenoma**

Aspirates from benign cystic teratoma showed mature squamous epithelial cells, degenerated cells, few glandular like epithelium and occasionally hair shaft in dirty background (fig.9) whereas fibroma-thecoma showed a few tight clusters of benign plump spindle cells(fig.10).

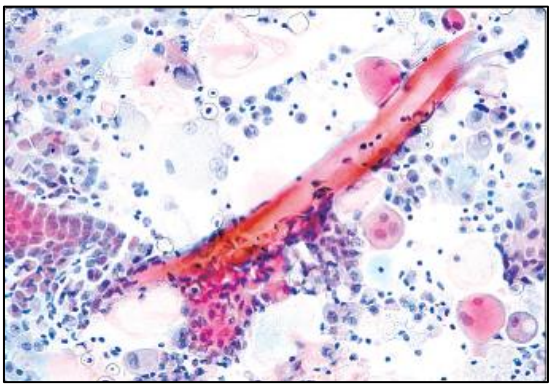

**Fig-9: Mature cystic teratoma**

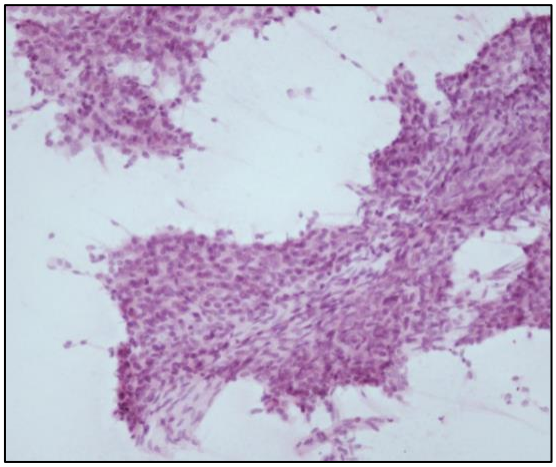

**Fig-10: Fibroma- thecoma**

Papillary serous cystadenocarcinoma showed papillary fragments comprised of tumor cells with hyperchromatic nuclei and a high nuclear- cytoplasmic ratio (fig.11).

Granulosa cell tumor showed uniformly small round nuclei with microfollicle formation and nuclear grooves (fig12).

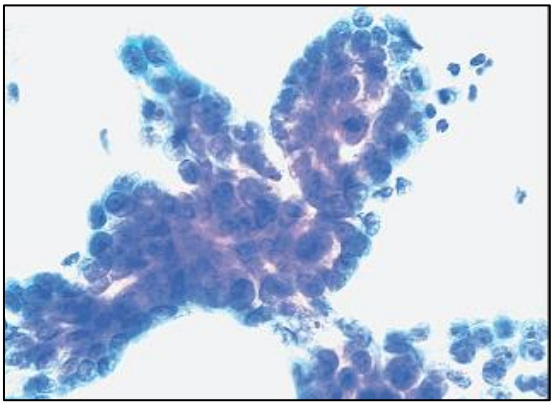

**Fig-11: Papillary serous cystadenocarcinoma**

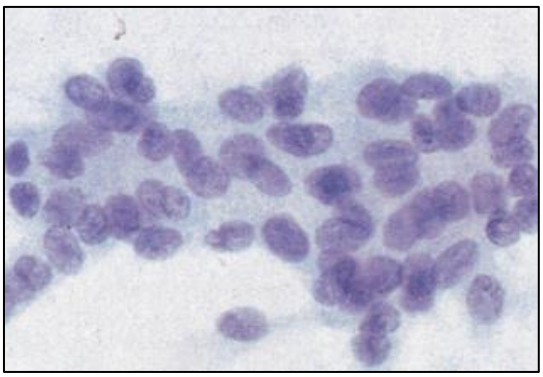

**Fig-12: Granulosa cell tumor**

**Table-1: Comparison between cyto-pathological and histo-pathological diagnosis of ovarian lesions**

| Sr. no | Histo-pathological diagnosis | Cyto-pathological correct diagnosis | False positive cases | False negative cases |
|---|---|---|---|---|
| | **NON NEOPLASTIC LESIONS** | | | |
| 1. | Simple ovarian cyst/ simple mucinous cyst/ simple serous cyst (n=12) | 11 | - | 1 |
| 2. | Lutenized cyst (n=2) | 2 | - | - |
| 3. | Haemorrhagic cyst (n=12) | 11 | 2 | 1 |
| 4. | Xanthogranulomatous oophoritis (n=2) | 2 | - | - |
| | Total (n=28) | 26 | 2 | 2 |
| | **NEOPLASTIC- BENIGN LESIONS** | | | |
| 5. | Benign serous cystadenoma (n=12) | 10 | 3 | 2 |
| 6. | Benign mucinous cystadenoma (n=22) | 18 | - | 4 |
| 7. | Mature teratoma (n=11) | 9 | - | 2 |
| 8. | Fibroma – thecoma (n=3) | 3 | - | - |
| | Total (n=48) | 40 | 3 | 8 |
| | **NEOPLASTIC- BORDERLINE TUMORS** | | | |
| 9. | Borderline serous epithelial tumor (n=2) | - | - | 2 |
| | Total (n=2) | - | - | 2 |
| | **NEOPLASTIC- MALIGNANT** | | | |
| 10. | Serous cystadenocarcinoma (n=12) | 10 | - | 2 |
| 11. | Serous cystadenocarcinoma with omental deposition (n=4) | 3 | - | 1 |
| 12. | Granulosa cell tumor (n=4) | 4 | - | - |
| 13. | Endometrioid carcinoma (n=2) | 2 | - | - |
| | Total (n=22) | 19 | - | 3 |

Chi- square test was performed to correlate between cyto- pathological and histo- pathological diagnosis and was highly significant ($p < 0.0001$).

**Table-2: Category wise analysis of discordant cases**

| Histo- pathological diagnosis | Cyto- pathological diagnosis | | | | | |
|---|---|---|---|---|---|---|
| | Inconclusive | Non- neoplastic | Benign | Borderline | Malignant | Total |
| Inconclusive | - | - | - | - | - | - |
| Non- neoplastic | 2 | 26 | - | - | - | 28 |
| Benign | 6 | 2 | 40 | - | - | 48 |
| Borderline | - | - | 2 | - | - | 2 |
| Malignant | 2 | - | 1 | - | 19 | 22 |
| Total | 10 | 28 | 43 | - | 19 | 100 |

Chi- square test = 165.909
p value <0.0001

Cytological evaluation of 100 cases revealed inconclusive diagnosis in 10 cases. From these 10 cases; 1 case of simple serous ovarian cyst, 1- haemorrhagic cyst, 1- benign serous cystadenoma, 3- benign mucinous cystadenoma, 2- mature teratoma, 2- serous cystadenocarcinoma were diagnosed histologically. These inconclusive diagnoses were considered as false negative for their respective lesions (Table1).

**Table-3: Category wise statistical analysis of cyto- pathological diagnosis**

| Category | Sensitivity | Specificity | Positive predictive value | Negative predictive value | Accuracy |
|---|---|---|---|---|---|
| Non- neoplastic | 92.86% | 97.22% | 92.86% | 97.22% | 96% |
| Benign | 83.33% | 94.23% | 93.02% | 85.96% | 89% |
| Malignant | 86.36% | 100% | 100% | 96.30% | 97% |
| Overall cytology | 87.52% | 97.15% | 95.29% | 93.16% | 94% |

Above statistical data suggest that overall diagnostic sensitivity was higher for non- neoplastic lesions as compare to neoplastic lesions while specificity is highest (100%) in malignant cases.

## DISCUSSION

Advancement of the radiologic guidance technique has contributed to the higher accuracy of FNAC in recent years [7]. Gynaecologists are concerned about the safety of this procedure and the consequent upstaging of ovarian cancers. Zanetta *et al*. [8] reported fewer complications in a study of aspiration of 838 ovarian cysts. They concluded that FNAC can decrease the need for surgery in many women with ovarian cysts.

**Table-4: Comparative statistical analysis of cytological diagnosis**

| Serial no. | Study | Year | Sensitivity | Specificity |
|---|---|---|---|---|
| 1. | Aysun & Canan | 2005 | 95.1% | 90.4% |
| 2. | Khan *et al*. | 2009 | 79.2% | 90.6% |
| 3. | Cole and co-workers | 2011 | 50% | 100% |
| 4. | Gupta and Rajwanshi | 2012 | 85.7% | 98.0% |
| 5. | Present study | 2016 | 87.52% | 97.15% |

Owing to its complexity and the wide spectrum of diagnoses, cytological analysis of ovarian lesions is a difficult issue. However, differentiation into malignant and benign tumours is possible by the careful evaluation of the cyto architecture and background features [7].

Ganjei & Dickinson correctly diagnosed 9 out of 12 ovarian malignancies by FNAC; cytological examination correctly predicted all benign lesions of the ovary in their study, and they observed a sensitivity of 75% [9]. Wojcik & Selvaggi also reported that the majority of cystic ovarian lesions can be diagnosed accurately; however, they did not correlate FNAC with histology in 53% of their cases [10].

Our observations corroborate closely with those of other investigators, which indicates that FNAC can have appreciable sensitivity, specificity and accuracy in the diagnosis of ovarian masses.

The differences in the reported accuracy of cytological evaluation of ovarian masses may reflect the differences in the technique used to aspirate the lesion (transvaginal, transabdominal, laparoscopic or during laparotomy, with or without image guidance) as well as differences in smear preparation. USG can provide

necessary clues towards the nature of the lesion: anechoic to hypoechoic lesions suggest a benign cyst, while solid cystic lesions with heterogeneous echogenicity indicate malignancy.

FNAC of borderline ovarian lesions was reported by Athanassiadou and Grapsa[11]. It was not possible to separate borderline ovarian lesions from well-differentiated cystadenocarcinomas by FNAC alone [12,13]. Diagnosis of borderline tumors was also not possible in cytology in our series.

One of the major objections for the use of FNAC in cystic ovarian tumors is the high percentage of inadequate samples [14]. Since the exact position of the needle is not always known, the aspirate may represent peritoneal rather than cystic fluid [12]. We found that aspirates from serous cystadenomas and mucinous cystadenomas were often hypocellular and inconclusive.

Several other factors may explain a poor cyto-histopathological correlation. FNAC of an ovary may yield cyst fluid, ovarian cortex, ovarian stroma, or a combination of these structures. Ovarian cyst fluid may have occasional cells only (in a background of fluid) to provide an accurate impression of the lesion. Malignant cells in the ovary may not be uniformly distributed in the organ, and it can often be seen that cytological examination of the peritoneal washings in patients with known ovarian malignancy fails to identify malignant cells [15].

Pelvic masses should be evaluated meticulously by laboratory, radiography and USG tests. Despite the lack of evidence, gynaecologists prefer exploratory laparotomy to FNAC due to the fear of peritoneal seeding from tumour cell spillage. FNAC of solid ovarian SOLs may play a useful role in determining tumour type and formulating management. Moreover, FNAC in patients with benign lesions like endometriosis or inflammatory masses may also lead to the patients being spared unnecessary surgery [9].

Although the potential risk of seeding of an ovarian cancer during FNA has been mentioned in textbooks, only one reference was documented [16-18]. This was a series of 2 cases having a tumour which was believed to have spread due to the FNA performed during laparoscopy [19], while available recent literature remains silent in this regard.

## CONCLUSION

To conclude, image-guided FNAC is a quick, easy, fairly sensitive, specific and cost effective modality for the preoperative diagnosis of malignant as well as benign ovarian masses with minimal morbidity, pending histological confirmation.

Dissemination and seeding of malignant cells during the procedure is not supported by adequate and conclusive literature. Targeted larger trials to address the issue of seeding of malignant cells during the procedure are needed to prove or disprove its debatable role in diagnosis.

Cytological diagnosis should be used as a preoperative diagnosis to guide the management of patients; however histopathology remains the gold standard procedure.

So with healthy communications and discussions for making diagnosis of diseases, a team effort, would help to serve the human race in the best possible way.

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