Histomorphological Spectrum of Ovarian Lesions in a Tertiary Care Institute in Gujarat with Special Emphasis on Ovarian Tumors

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Abstract

Introduction: Ovarian cancer is the third most common cancer among women of India. Microscopic examination is the gold standard for diagnosing ovarian tumors and plays an important role in determining prognosis.

Purpose: The aim of the study is to assess the frequency of non-neoplastic and neoplastic lesions in ovarian specimens and biopsies and to study the histomorphological spectrum, gross features, and age distribution of the ovarian tumors.

Materials and Methods: The present study was an observational retrospective study conducted over a period of 1 year (February 2019–January 2020) in the Department of Pathology in a Tertiary Care Hospital in South Gujarat. A total of cases (8 ovarian biopsies and 82 ovarian specimens) were analyzed. Tumors were classified according to the WHO classification 2014.

Results: Of 90 cases, eight were of non-neoplastic lesions, 13 were tumor-like lesions, and nine neoplastic lesions. Among neoplastic lesions, 43 cases (62.3%) were benign, 3 (4.4%) were borderline, while 23 (33.3%) cases were malignant. Histopathologically, surface epithelial tumors (76.7%) were the most common subtype followed by germ cell tumors (13.3%) and then sex cord tumors (10%). Malignant surface epithelial tumors constitute 78.2% of the total malignant ovarian tumors. The most common neoplastic lesion was serous cystadenoma. 30–39 years age group was the most common age group overall in ovarian tumors. Benign tumors were most common in the 30–39 years age group, while malignant tumors were most common in the 60–69 years age group. Bilaterality was seen in 10 (16.4%) of 61 gross specimens of ovarian tumors.

Conclusion: The frequency of malignant ovarian tumors was higher in our institute. Accurate histopathological diagnosis is essential for management and determining prognosis.

Key words: Germ cell tumor, Histopathology, Ovarian tumors, Serous carcinoma

INTRODUCTION

The ovaries are paired organs on either side of the uterus close to the lateral pelvic wall. A wide spectrum of pathological conditions – non-neoplastic and neoplastic can be seen in the ovary in routine surgical pathology.[1] Primary ovarian tumors can arise from any of the three cell types in the normal ovary: The multipotent surface (coelomic) epithelium, the totipotent germ cells, and the sex cord-stromal cells. Surface epithelial tumors constitute the large majority of ovarian neoplasms and, their malignant forms, account for almost 90% of ovarian cancers. Germ cell and sex cord-stromal cell tumors are comparatively less common; although they account for 20–30% of ovarian tumors, they are collectively responsible for <10% of ovarian malignancies.[2]

Ovarian cancer is the 7th most common cancer and 8th most common cause of death from cancer in women in the world.[3] National Cancer Registry Programme (NCRP) at Bengaluru, India states that Ovarian cancer is the third most common cancer among Indian women after breast and cervix cancer and constitutes about 6% of total cancer cases among the Indian women.[4]
Ovarian cancers are called “silent killer” as the majority (70%) of women with ovarian cancers have already developed extra ovarian spread at the time of diagnosis. This is due to the fact that ovarian cancers are generally asymptomatic or have vague and nonspecific symptoms. Histopathological examination remains the gold standard for diagnosing ovarian tumors, according to NCRP of India. Most ovarian tumors cannot be differentiated from one another on the basis of clinical or gross characteristics alone. They, however, provide salient pointers which aid in diagnosis; hence, a clinician and pathologist have to work in collaboration to come to a final diagnosis.

Ovarian epithelial cancers must be differentiated from benign tumors, functional cysts, and other benign lesions such as endometriosis, pelvic inflammatory disease, or pedunculated uterine leiomyomata which mimic ovarian cancer. Histological subtyping of ovarian epithelial cancers is important as they differ in their mean age of presentation, 5-year survival, molecular abnormalities, association with familial syndromes, and sensitivity to chemotherapy and other treatment modalities.

According to NCRP of India on the status of ovarian cancers in India (2012–2014), the majority (50%) of the cases occurred between 45 and 65 years of age. Only 5% of the total cases were reported before the age of 25 years. Furthermore, more than 20% of the cases were reported beyond the age of 65 years. Hence, age is an extremely important clinical parameter relating to tumor behavior.

Most of the germ cell tumors are seen in children. Benign surface epithelial tumors occur mostly in young women between the ages of 20 and 45 years, while borderline tumors occur at slightly older ages. Malignant tumors are more common in older women between the ages of 45 and 65 years.

Tumor stage and laterality may also give a clue to their nature. While sex cord-stromal tumors are predominantly unilateral, bilaterality is more commonly seen in tumors metastasized to the ovary and in serous carcinomas. Important risk factors for ovarian cancer include nulliparity, family history, and germline mutations in certain tumor suppressor genes.

The WHO classification of ovarian tumors is primarily morphologic and based on the cytologic features of the tumor cells. The findings of recent molecular studies, for the most part, support this morphology-based classification system and also demonstrate that it accurately reflects both histogenesis and the underlying molecular abnormalities of the different ovarian tumor subtypes.

The aim of this study is to assess the frequency of non-neoplastic and neoplastic lesions in ovarian specimens and biopsies and to study the histomorphological spectrum, gross features, and age distribution of the ovarian tumors.

**MATERIALS AND METHODS**

- **Study design** – This study was an observational study (retrospective)
- **Study location** – The study was conducted in the department in a tertiary care hospital in South Gujarat
- **Study duration** – The study duration was 1 year (February 1, 2019–January 30, 2020)
- **Sample size** – The sample size was 90.

**Inclusion Criteria**

Ovarian biopsies and all ovarian specimens with histopathologically proven non-neoplastic and neoplastic lesion received as either as a solitary specimen or part of total abdominal hysterectomies or cystectomies.

**Exclusion Criteria**

The following criteria were excluded from the study:
1. Normal ovaries
2. Specimen of post-chemotherapy ovaries.

The present study was an observational retrospective study (February 2019–January 2020) conducted in the Department Of Pathology in a Tertiary Care Hospital in South Gujarat. A total of eight ovarian biopsies and 82 ovarian specimens with histopathologically proven non-neoplastic or neoplastic lesions received either as a solitary specimen or as part of total abdominal hysterectomy specimens or cystectomy specimens were studied. The normal ovaries and specimens of post-chemotherapy ovaries were excluded from the study.

A detailed patient history, clinical examination findings, radiological findings, and other relevant laboratory findings were noted from the histopathological requisition form sent alongside the specimen. The excised ovarian specimens and biopsies were fixed in 10% neutral buffered formalin. The tumors were weighed and measured. Thorough gross examination was done scrutinizing the outer surface and on-cut surface diligently looking for a cyst, its locularity, type of cystic fluid, any solid area, papillary projections, and hemorrhage and necrosis. From cysts, up to three sections of 3 mm were taken and from solid tumors, one section for each centimeter was taken, especially from areas of papillary appearance and any unusual area (hemorrhagic, calcified, or necrotic area). Associated tissue pieces were also examined and grossed.

Tissue processing was done as per standard procedure and paraffin-embedded blocks were made. Tissue sections of
5 µ thick were cut using a rotary microtome and stained by hematoxylin and eosin followed by microscopic examination. Special stains such as reticulin and Periodic Acid Schiff (PAS) and immunohistochemistry were performed whenever required. The tumor-like and neoplastic lesions were classified according to the 2014 WHO classification of ovarian tumors.

RESULTS

Our department received a total of 90 ovarian cases which included eight ovarian biopsies and 82 ovarian specimens either as solitary specimens or cystectomies or as part of hysterectomies with unilateral or bilateral salpingectomies over a period of 1 year (February 2019–January 2020), of which non-neoplastic and neoplastic lesions were identified. Of 90 cases (specimens and biopsies), eight were of non-neoplastic lesions, 13 were tumor-like lesions, and 69 were neoplastic lesions.

Among non-neoplastic lesions, five cases were of hemorrhagic cyst secondary to torsion and three cases were of endometriosis. All of them belonged to the 30–50 years age group.

Among 13 cases of tumor-like lesions, eight were luteal cysts and five were follicular cysts. They were seen within 20–59 years of age group and showed maximum incidence in 40–49 years age group.

Among neoplastic lesions, 43 cases (62.3%) cases were benign, three (4.4%) were borderline, while 23 (33.3%) cases were malignant [Figure 1].

Histopathologically, surface epithelial tumors (53 cases; 77%) were the most common subtype followed by germ cell tumors (9 cases; 13.04%) and then sex cord tumors (7 cases; 10.4%) [Figure1]. The most common neoplastic lesion as well most common benign tumor was serous cystadenoma. Serous carcinoma was the most common malignant tumor. The most common germ cell tumor and the second most common benign tumor was mature cystic teratoma. The most common sex cord-stromal tumor was fibroma [Table 1].

Distribution of Surface Epithelial Tumors

Of 53 cases of surface epithelial tumors, 35 (66%) cases were serous tumors, 16 cases (30.2%) were of mucinous tumors, and two cases (3.8%) were of endometrioid histotype.

Alternatively, surface epithelial tumors can also be classified into benign (32 cases; 60.4%), borderline (3 cases; 5.6%), and

Table 1: Histomorphological spectrum of ovarian tumors as per WHO classification 2016

<table>
<thead>
<tr>
<th>Nature</th>
<th>Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface epithelial tumors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. Serous</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serous cystadenoma</td>
<td>18</td>
<td>35</td>
</tr>
<tr>
<td>Serous cystadenofibroma</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Serous borderline tumor</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Serous carcinoma</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>B. Mucinous</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mucinous cystadenoma</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Mucinous borderline tumor</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Mucinous carcinoma</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>C. Endometrioid tumors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endometrioid carcinoma</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Germ cell tumors</td>
<td>9</td>
<td>13.03 %</td>
</tr>
<tr>
<td>Mature cystic teratoma</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Dysgerminoma</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Sex cord-stromal tumors</td>
<td></td>
<td>10%</td>
</tr>
<tr>
<td>Adult granulosa tumor</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Fibroma</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Sex cord-stromal tumor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>with annular tubules</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>along with foci of granulosa and Sertoli cell tumor</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Sclerosing stromal tumor</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
malignant (18 cases; 34%). Malignant surface epithelial tumors constitute 78.2% (17 of 22 cases) of the total ovarian cancers.

Among 35 cases of serous histology, 20 were benign, 1 case borderline, and 14 cases malignant. In the case of mucinous tumors, 12 were benign, two borderline, and two were malignant. Both cases of endometrioid type were malignant.

**Distribution of Germ Cell Tumors**

Among nine cases of germ cell tumors, most cases (eight cases; 88.9%) were mature cystic teratoma, while one case (11.1) was dysgerminoma [Figure 2].

**Distribution of Sex Cord Tumors**

Adult granulosa cell tumor [Figure 3] was the most common sex cord-stromal tumor followed by fibroma (2 cases) [Figure 4]. One case of the sclerosing stromal tumor and one case of sex cord-stromal tumor with annular tubules along with foci of granular and Sertoli cell tumors [Figure 5] were also seen.

**Age Distribution of Ovarian Tumors**

The youngest patient was 5 years old and the oldest case belonged to an 82-year female.

Among 69 cases of ovarian tumors, most cases belonged to 30–39 years age group followed by 60–69 year age group benign tumors were most common in 30–39 years age group and gradually showed a decrease in later age groups. On the other hand, malignant tumors were most common in the 60–69 years age group [Figure 6].

Germ cell tumors were the only neoplastic lesions found below 20 years age group. Surface epithelial tumors were seen after 20 years of age and showed a bimodal peak at 30–39 years age group and 60–69 years age group due to the high incidence of benign and malignant tumors in these decades, respectively.

Sex cord-stromal tumors were mostly found in 20–59 years of age group and only one case was seen after 60 years of
age (most cases of sex cord-stromal tumors were seen in 40–59 years age group.

**Gross Features of Ovarian Tumors**

Of 61 gross specimens of ovarian tumors, the majority were cystic (40 cases; 65.6%), while 17 cases (27.8%) were solid mixed with cystic and four cases (6.6%) were pure solid. Among the 40 cystic specimens, most cases (37 cases; 92.5%) were benign, while two cases were malignant and one case was borderline.

Among epithelial tumors, 29 (90.6%) of 32 benign tumors were cystic, while only three cases (9.4%) were cystic mixed with solid. Among 11 cases of malignant tumors, nine cases (81.8%) were cystic mixed with solid and one case (9.1%) was pure solid while only one case (9.1%) of low-grade serous carcinoma was pure cystic. Among two cases of borderline epithelial tumors, one was pure cystic, while one case was cystic with solid.

**Laterality**

Ten cases (16%) (four benign and six malignant), of 61 ovarian specimens were bilateral. About 9% of benign tumors were bilateral, while 37.5% of malignant tumors were bilateral. Eight of 10 cases of bilateral tumors were surface epithelial type (three cases serous carcinoma [Figure 7], two cases benign serous tumors, and one case each of mucinous and endometrioid carcinoma) while only two cases were of germ cell origin (one case of dysgerminoma and mature cystic teratoma each). Bilaterality was not seen in any case of sex cord tumors.

Among unilateral ovarian tumors, the majority of tumors were right side (62%) in comparison to compared to the left side (37%).

Twelve of 16 specimens of ovarian malignant tumors had FIGO Stage 1, while two cases were Stage 2 and two cases were Stage 3.
Role of Special Stains and Immunohistochemistry

Special stains such as reticulin and PAS stain were utilized for the diagnosis of adult granulosa tumor and mucinous tumor. Immunohistochemistry played a key role in the final diagnosis of tumors. WT1 was used for diagnosing serous tumors [Figure 8] and tp53 was used for differentiating between low grade and high-grade serous carcinoma. Endometrioid carcinoma was diagnosed as well as distinguished from secondary tumors with the help of ER, PR, vimentin positivity, and CK20 and CDX2 negativity. Dysgerminoma was identified with the help of PLAP, CD-117 positivity, and EMA negativity. Non-Hodgkin’s lymphoma was concluded after LCA and CD20 positivity and CK, vimentin, EMA, CEA, CD117 negativity. Sex cord-stromal tumor with annular tubules along with foci of adult granulosa tumor and Sertoli cell tumor showed CD99, CK positivity and S-100, chromogranin, EMA, PLAP, vimentin, and CK7 negativity.

DISCUSSION

In the current study, 82 ovarian specimens and eight ovarian biopsies were studied extensively. Ninety cases were classified into non-neoplastic lesions (8), tumor-like lesions (13), and neoplastic lesions (69 cases).

Non-neoplastic lesions (endometriosis and hemorrhagic cyst secondary to torsion) and tumor-like lesions were more common in the reproductive age group of 30–50 years in concordance with their functional nature. Luteal cysts were slightly more common than a follicular cyst.

Of 69 neoplastic lesions, 43 cases (62.3%) were benign, 3 (4.4%) were borderline, while 23 cases (33.3%) were malignant. Our findings are consistent with the study done by Panchonia et al.[8] The percentage of malignant tumors is much higher in the present study as compared to studies done by Phukan et al.,[9] Sawant et al.[10], and Itha and Veeragandham,[11] as our institution being a tertiary care hospital receive a referral of a large number of malignant tumors from peripheral centers [Table 2].

Surface epithelial tumors (53 cases; 76.7%) were the most common subtype followed by germ cell tumors (9 cases; 13.03%) and then sex cord tumors (7 cases; 10%). Overall malignant surface epithelial tumors constitute 78.2% of the total malignant ovarian tumors [Table 3].

Table 2: Comparative analysis of ovarian tumors based on the nature of tumors

<table>
<thead>
<tr>
<th>Name of study</th>
<th>Benign cases (%)</th>
<th>Borderline cases (%)</th>
<th>Malignant cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present study</td>
<td>62.3</td>
<td>4.4</td>
<td>33.3</td>
</tr>
<tr>
<td>Panchonia et al.</td>
<td>58</td>
<td>4</td>
<td>38</td>
</tr>
<tr>
<td>Phukan et al.</td>
<td>75</td>
<td>3.6</td>
<td>21.4</td>
</tr>
<tr>
<td>Sawant and Mahajan[9]</td>
<td>75.7</td>
<td>6.1</td>
<td>18.2</td>
</tr>
<tr>
<td>Garg et al.</td>
<td>81</td>
<td>1.2</td>
<td>17.6</td>
</tr>
<tr>
<td>Sharma and Bharadwa[12]</td>
<td>86.6</td>
<td>3.6</td>
<td>9.8</td>
</tr>
<tr>
<td>Mohan et al.[14]</td>
<td>82.2</td>
<td>5.2</td>
<td>12.5</td>
</tr>
<tr>
<td>Patel et al.</td>
<td>93</td>
<td>1.2</td>
<td>6.2</td>
</tr>
</tbody>
</table>

Table 3: Comparative studies of the histomorphological pattern of ovarian tumors

<table>
<thead>
<tr>
<th>Name of study</th>
<th>Surface epithelial tumors (%)</th>
<th>Germ cell tumor (%)</th>
<th>Sex cord-stromal tumors (%)</th>
<th>Others (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present study</td>
<td>76.7</td>
<td>13.03</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Patel et al.[15]</td>
<td>77.7</td>
<td>18.5</td>
<td>3.8</td>
<td>0</td>
</tr>
<tr>
<td>Garg et al.[12]</td>
<td>70.6</td>
<td>18.8</td>
<td>7</td>
<td>2.4%</td>
</tr>
<tr>
<td>Pilli et al.[16]</td>
<td>70.9</td>
<td>21.2</td>
<td>6.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Phukan et al.[8]</td>
<td>66.7</td>
<td>23.8</td>
<td>7.2</td>
<td>2.4</td>
</tr>
<tr>
<td>Mohan et al.[14]</td>
<td>66.66</td>
<td>23.95</td>
<td>7.29 2.4</td>
<td>2.4</td>
</tr>
</tbody>
</table>
Among 43 cases of surface epithelial tumors, serous tumors (66%) were the most subtype followed by mucinous type (30.2%). Endometrioid tumors (3.8%) were relatively infrequent. This is consistent with Garg et al.\cite{6} Itha and Veeragandham,\cite{7} Phukan et al.,\cite{8} Modi et al.,\cite{9} and Dutta et al.\cite{10} [Table 4].

Serous tumors were 57.1% benign 2.9% borderline and 40% malignant.\cite{11} Mucinous tumors were 75% benign, 12.5% borderline, and 12.5% malignant. Both cases of endometrioid tumors were malignant.

Hence, while both serous and mucinous tumors were more commonly benign. In contrast, endometrioid tumors were predominantly malignant. This is consistent with studies done by Phukan et al.,\cite{8} and Modi et al.\cite{9}

The most common neoplastic lesion was serous cystadenoma. This is consistent with studies done by Devi et al.,\cite{12} Panchonia et al.,\cite{8} and Sharma and Bharadwaj.\cite{13} Serous carcinoma was the most common malignant lesion in our study, consistent with studies done by Modi et al.\cite{17}

Among 69 cases of ovarian tumors, most cases belonged to 31–40 years age group. This consistent with studies done by Patel et al.,\cite{14} Devi et al.,\cite{12} Garg et al.,\cite{12} and Pilli et al.\cite{16} However, 40–49 years of age group was more commonly affected followed by 30–39 years age group in Mohan et al.\cite{17} and Srinivasan et al.\cite{19}

Of 61 specimens of ovarian tumors, the majority are cystic (65.5%) followed by cystic with solid (27.8%) and pure solid (6.6%). Most benign tumors were cystic (86%), while the majority of malignant tumors were cystic mixed with solid (75%). This is concordant with studies done by Phukan et al., Patel et al., Itha and Veeragandham, and Mohan et al. [Table 5].

Ovarian tumors are known for their bilaterality. Bilaterality was seen in 10 (16.4%) of 61 gross specimens of ovarian tumors and more commonly seen in malignant tumors. This correlates with the higher pathological grading. Bilateral involvement often depends on the histological subtype of ovarian tumors. Bilaterality was most frequently seen in surface epithelial tumors and specifically in serous carcinomas (3 of 5 cases). Bilaterality in other studies was by 11% (Panchonia et al.,\cite{8}) and 22% (Itha and Veeragandham\cite{11}).

Among unilateral lesions, neoplastic lesions were more common on the right side. This is consistent with studies done by Panchonia et al.,\cite{8} (52%).

**CONCLUSION**

Ovarian tumors are a heterogeneous group of tumors and this diversity creates challenges in timely diagnosis and management. An accurate diagnosis primarily relies on histomorphological examination which remains the gold standard with the support of ancillary studies such as special stains and immunohistochemistry. Clinical parameters such as age, laterality, and stage are additional factors which guide the overall management and prognosis of these neoplasms.

The ovarian neoplasms in our institute represented a wide histomorphological spectrum. The frequency of the distribution of neoplasms was similar to the reports in the literature. However, the incidence of malignant tumors was higher in our setup, as our institute is a tertiary care center. It is concluded from our study that the majority of ovarian tumors are benign. Surface epithelial tumors are the most common histological subtype of ovarian tumors.

The observations of our study and their assessment will provide valuable insight of distribution pattern of ovarian neoplasms in western India. Early diagnosis plays a critical role in decreasing morbidity as well as mortality among these patients.
ACKNOWLEDGMENTS

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