Original Article

Clinicopathological Spectrum of Ovarian Tumors: A 5-Year Experience in a Tertiary Health Care Center

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ABSTRACT

Background: Ovarian tumors are a heterogeneous group of neoplasm of epithelial, stromal, and germ cell origin. Even in a single class of tumor, there exists inherent heterogeneity with biological behavior ranging from benign to the highly aggressive malignant tumor. The management of the patient also depends on the histological type of the tumor. These facts fascinated and prompted us to undertake the present study. **Aim:** To analyze the modes of presentation and various histopathological patterns of ovarian tumor. **Materials and Methods:** It was a retrospective observational study. The study was conducted in Department of Pathology, B. J. Medical College Pune, India from July 2006 to June 2011. All the histopathology slides of ovarian tumors during the study period were retrieved and reviewed along with the patient's demographics, clinical features, and gross findings. Data thus collected were analyzed. **Results:** A total of 226 cases of ovarian tumors out of 1098 cases of female genital cancers were studied. Age ranged from 12 to 80 years. The surface epithelial tumors were the most common ovarian tumor constituting 163 cases (72.1%), followed by germ cell tumors 45 cases (19.9%). The most common complaint in the present study was pain in the abdomen (115 cases, 50.9%) irrespective of the nature of the ovarian tumor. Bilaterality was common in malignant tumors (66.7%, 16/24). Right and left side was almost equally affected among unilateral tumors. The size of the tumor varied from 3 to 32 cm. **Conclusions:** By knowing clinical data, sonography findings, and gross features, we can narrow our differential diagnosis and reach to the final microscopic diagnosis in most of the cases in very cost-effective manner.

KEY WORDS: Germ cell tumor, ovarian tumor, surface epithelial tumors

INTRODUCTION

Ovarian cancer accounts for about 3% of all cancers in women. According to the surveillance epidemiology and end results data, ovarian tumors represent about 27% of all female genital cancers and account for 52% of deaths caused by female genital cancers.[1] The increased risk of ovarian cancer particularly of surface epithelial tumors (SETs) is associated with use of hormone replacement therapy (HRT),[2] tobacco consumption,[3] family history of ovarian cancer and breast cancer,[4] and mutation of BRCA1 and/or BRCA2.[4] The protective factors are the use of oral contraceptive pills (OCPs) and multiparity not only in the general population but also significantly reduces the risk in BRCA1/BRCA2 carriers.[5]

Of all the gynecological cancers, ovarian tumors represent the greatest challenge to clinicians because it is very difficult to diagnose it in early stage due to its nonspecific symptoms and even asymptomatic nature in many cases. On the other hand, ovarian tumors at an advanced stage are easy to diagnose but associated with poor prognosis despite advances in surgery, chemotherapy, and more recently, targeted therapy. Ovarian tumors are also a

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constant source of confusion to the pathologists because of the wide spectrum of clinical and morphological features. Further, certain nonneoplastic lesions of ovary frequently form a pelvic mass and often associated with abnormal hormonal manifestations, thus potentially mimicking ovarian neoplasm.

Most ovarian tumors cannot be confidently distinguished from one another on the basis of their clinical or gross characteristics alone, although it provides important diagnostic clues in formulating a differential diagnosis. One of the most important clinical features is the age of the patient.[2] The laterality also provides a clue to their nature, for example, tumors in the sex cord stromal category are almost always confined to single ovary while most of the metastatic tumors are bilateral. Gross features also help in differential diagnosis and represent the integral behavior of tumor, like most benign tumors of epithelial category are cystic, on the other hand, the finding of solid element and papillary projections make malignancy more likely. Nevertheless, accurate diagnosis primarily depends on the wide range of microscopic features they exhibit.[6]

Determination of various histological patterns of ovarian tumors is also very important for management of the patient, as the diagnosis and prognosis of ovarian tumors depend upon its histological type. Thus, we conducted the study to analyze the frequency and clinicopathological spectrum of ovarian tumors.

MATERIALS AND METHODS

This case series cover 5-year period from July 2006 to June 2011. Before conducting the study, we have taken approval from Institutional Ethics Committee B. J. Medical College and Sassoon General Hospital, Pune and have taken informed consent from patients. We performed a retrospective analysis of all patients diagnosed with ovarian tumors during this period. Nonneoplastic lesions of ovary were excluded from the study. Clinical data (age, site, clinical features, and tumor markers level) and gross findings were obtained from the histopathology record section of the institute, and hematoxylin and eosin-stained slides were retrieved and reviewed. Where necessary, blocks were recut, stained, and reviewed. All the cases of ovarian tumors were classified according to the World Health Organization classification of tumors 2003.[7] Data collected were analyzed.

RESULTS

Of 1098 cases of female genital tract cancers, 226 cases of ovarian cancers (20.6%) were diagnosed. In our study, we found possible causal/risk factor in only 26 cases. The 3 patients are nulligravida presented with primary infertility, 12 patients have history of tobacco chewing, 4 patients have family history of breast and/or ovarian carcinoma in first degree relatives, and seven postmenopausal women have taken HRT for at least 6 months. Although OCPs are believed to the protective for ovarian carcinoma, but in our study, we found total 24 cases of ovarian carcinoma, 18 cases belongs to the SETs and 6 cases to the sex cord-stromal category have taken OCPs during her life for at least 6 months.

The most common histological type was SETs in our study. Distribution of ovarian neoplasm according to histological type listed in Table 1. Benign tumors were the most common accounting for 61.1% (138 cases/226 cases). Among these, mucinous cystadenoma (42 cases/138 cases, 30.4%) was the most common. A total 16 cases (7.1%) of borderline category and 72 cases (31.9%) of malignant ovarian tumors out of total 226 cases were diagnosed. The peak incidence of ovarian tumors was seen in the third and fifth decades accounting for 22.6% (51 cases/226 cases) and 26.5% (60/226), respectively. Germ cell tumors were common in the age group 11–30 years with total 26 cases [Table 2]. One case of metastatic tumor (Krukenberg tumor) was observed in very young female, 27-year-old, with primary gastric cancer [Figure 1].

Of 226 cases, the most common presenting complaint was pain in abdomen (115 cases, 50.9%) followed by the lump

Table 1: Frequency of main histological types of ovarian tumors

Type	Number of cases	Percentage
Surface epithelial tumors	163	72.1
Germ cell tumors	45	19.2
Sex cord stromal tumors	16	7.1
Metastatic	02	0.9

Table 2: Age-wise distribution of ovarian tumors

Types of tumor	Age (in years)						
	1-10	11-20	21-30	31-40	41-50	51-60	>60
Benign serous tumor (*n*=53)	0	1	12	19	13	4	4
Borderline serous tumor (*n*=2)	0	0	1	0	1	0	0
Malignant serous tumor (*n*=31)	0	0	0	1	10	9	11
Benign mucinous tumor (*n*=42)	0	1	15	8	12	2	4
Borderline mucinous tumor (*n*=14)	0	0	1	4	5	2	2
Malignant mucinous tumor (*n*=16)	0	1	0	0	9	4	2
Clear cell carcinoma (*n*=1)	0	0	0	0	1	0	0
Endometrioid carcinoma (*n*=3)	0	0	0	0	3	0	0
Benign Brenner tumor (*n*=1)	0	0	0	0	0	1	0
Dysgerminoma (*n*=3)	0	0	2	1	0	0	0
Mature cystic teratoma (*n*=34)	0	1	16	12	2	2	1
Struma ovarii (*n*=1)	0	0	0	0	1	0	0
Immature teratoma (*n*=1)	0	1	0	0	0	0	0
Yolk sac tumor (*n*=3)	0	3	0	0	0	0	0
Mixed germ cell tumor (*n*=3)	0	1	2	0	0	0	0
Granulosa cell tumor (*n*=9)	0	0	0	1	3	3	2
Fibroma (*n*=5)	0	0	1	1	0	2	1
Sertoli-Leydig cell tumor (*n*=1)	0	0	0	1	0	0	0
Steroid cell tumor (*n*=1)	0	1	0	0	0	0	0
Krukenberg tumor (*n*=2)	0	0	1	0	0	0	1
Total	0	10	51	48	60	29	28

in abdomen (66 cases, 29.2%) irrespective of the nature of the tumor. Ascites, anorexia, and weight loss were more commonly observed in borderline and malignant tumors. Menstrual irregularities, excessive bleeding, and postmenopausal bleeding were the presenting complaints in the 27 cases (11.9%). Totally, 16 cases of ovarian tumors were incidentally found all were benign; the most common finding in these was serous cystadenoma (8 cases). None of the malignant tumor was diagnosed incidentally. Totally 3 cases, one of serous cystadenoma, one of mucinous cystadenoma, and one of well-differentiated Sertoli-Leydig cell tumor was presented with acute abdomen. We also found 1 case of steroid cell tumor with typical symptoms of virilization.

Cancer antigen (CA) 125 value was available in total 27 cases of SETs. Of 22 malignant tumors, 20 cases showed CA 125 value >35 U/ml, whereas 3 cases out of 5 benign tumors also showed more value than cut-off of 35 U/ml indicating CA 125 as sensitive marker (sensitivity 90.9%) preoperatively but not specific (40%). Diagnostic accuracy was 81.5% (analysis had done using SPSS inc; Chicago 17.0 version software). Alpha fetoprotein (AFP) level was available only in 3 cases of germ cell tumors, 2 cases of yolk sac tumor (YST), and 1 case of mixed germ cell tumor, having values 960 ng/ml, 920 ng/ml, and 840 ng/ml, respectively.

The most common surgical specimen in benign and borderline ovarian tumors was cystectomy constituting 57.3% (79/138) and 43.8% (7/16), respectively, whereas in malignant ovarian tumors, the most common surgical specimen was transabdominal hysterectomy with bilateral salpingo-oophorectomy (TAH + BSO) with or without omentum constituting 80.6% (58/72).

Size range was 3–32 cm in the present study. The largest tumor in our study was borderline mucinous cystadenoma sized 32 cm found. Size-wise distribution of various ovarian tumors is listed in Table 3.

On gross inspection, totally 115 cases out of 138 cases of benign tumors and all 16 cases of borderline tumors were cystic in consistency, whereas in malignant tumors, most of the tumors showed (47 cases out of 72 cases) partly cystic and partly solid consistency. All cases of fibroma (5 cases), endometrioid carcinoma (3 cases), dysgerminoma (3 cases) [Figure 2], YST (3 cases) [Figure 3], metastatic tumors (2 cases), Brenner tumor (1 case), and steroid cell tumor (1 case) were completely solid in consistency. Within cystic tumors, serous tumors showed mainly uniloculated cyst (44 cases out of 55 cases) whereas in mucinous tumors, multiloculation was common finding (45 out of 56 cases). In 29 cases, where omentum was received, 5 cases of serous cystadenocarcinoma and

Table 3: Size wise distribution of ovarian tumors

Types of tumor	Size (in cm)			
	1-10	11-20	21-30	>30
Benign serous tumor (*n*=53)	35	13	5	0
Borderline serous tumor (*n*=2)	2	0	0	0
Malignant serous tumor (*n*=31)	20	10	1	0
Benign mucinous tumor (*n*=42)	17	23	2	0
Borderline mucinous tumor (*n*=14)	3	7	3	1
Malignant mucinous tumor (*n*=16)	5	7	4	0
Clear cell carcinoma (*n*=1)	1	0	0	0
Endometrioid carcinoma (*n*=3)	2	1	0	0
Benign Brenner tumor (*n*=1)	1	0	0	0
Dysgerminoma (*n*=3)	1	2	0	0
Mature cystic teratoma (*n*=34)	28	6	0	0
Struma ovarii (*n*=1)	1	0	0	0
Immature teratoma (*n*=1)	1	0	0	0
Yolk sac tumor (*n*=3)	1	1	1	0
Mixed germ cell tumor (*n*=3)	0	2	1	0
Granulosa cell tumor (*n*=9)	3	6	0	0
Fibroma (*n*=5)	3	2	0	0
Sertoli-Leydig cell tumor (*n*=1)	0	0	0	1
Steroid cell tumor (*n*=1)	0	1	0	0
Krukenberg tumor (*n*=2)	2	0	0	0
Total	126	81	17	2

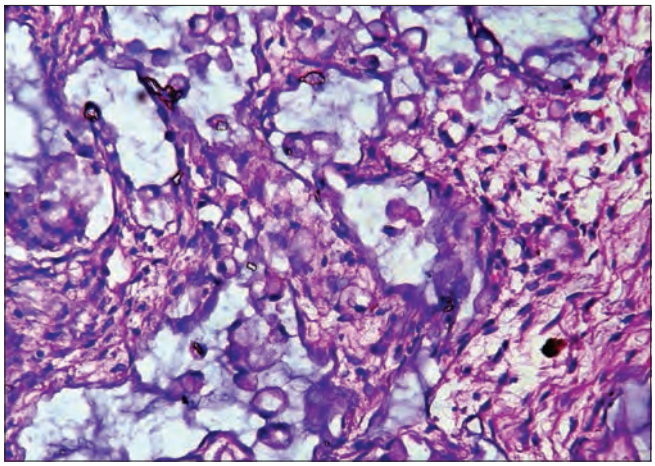

Figure 1: Photomicrograph of Krukenberg tumor showing signet ring cells within the pools of mucin (H and E, ×400)

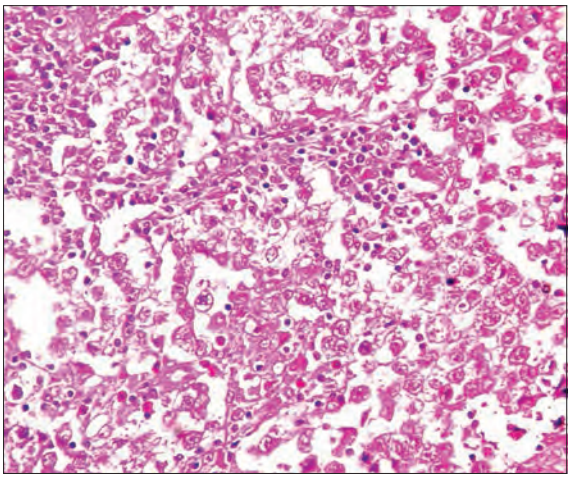

Figure 2: Photomicrograph of dysgerminoma showing lobules of round to polygonal cell with clear cytoplasm, round nuclei, and prominent nucleoli separated by fibrous septa infiltrated by lymphocytes (H and E, ×400)

3 cases of mucinous cystadenocarcinoma showed tumor deposits.

Special stain periodic-acid Schiff (PAS) was done in all cases of mucinous tumors to confirm intracellular mucin and in YST to confirm the presence of hyaline globules which are PAS positive.

DISCUSSION

Frequency of ovarian tumors in total surgical pathology specimens (21,256) in this study was 1.1% (226 cases), similar to Saxsena *et al*.[8] Among female genital tract malignancies, ovarian cancer constituted 20.6% next to the cancer of the cervix (61.2%), comparable to the study of Dhakal and Pradhan[9] from Nepal who reported 85.2% of cervical cancers and 6.4% of ovarian cancers in total gynecological cancers. Data were different from cancer statistics 2009 report by Jemal *et al*.[1] where the ovarian tumor was the leading cancer of female genital tract. This difference is may be due to the poor socioeconomic status, poor hygiene, and environmental factors in developing countries causing more cases of cervical cancer.

SETs of the ovary were the commonly encountered tumors in the study of Pilli *et al*.[10] and Gupta *et al*.[11] comparable to our study. For many years, it was assumed that the serous tumors are arising from ovarian surface epithelium (OSE) which is the part of the pelvic peritoneum overlies the ovary and lines the epithelial inclusion cyst. But in recent years, a new hypothesis of tubal fimbrial origin for serous carcinoma was given by many authors. Piek *et al*.[12] found the dysplastic (termed as tubal intraepithelial carcinoma [TIC]) and hyperplastic lesions on fimbriae of 11 out of 12 prophylactic salpingo-oophorectomy specimens removed from BRCA mutations carriers, and showed increased proliferation and over-expression of p53 similar to the high grade serous ovarian tumors which also showed p53 mutation. This hypothesis later supported by many authors.[13,14] The controversy whether the serous carcinomas arise from the tubal fimbriae or the OSE is still ongoing because none of the study concluded 100% positivity in favor of either the fimbrial or the OSE hypothesis. Therefore, dual model for serous tumors carcinogenesis should be followed. In our study, we found 31 cases of serous carcinomas but only one section of tube from the fimbrial end was given, and we did not found any TICs or hyperplastic lesion. This may be due to the limited section from the tube was taken.

The preponderance of benign tumors in our study was also similar to Pilli *et al*.[10] and Gupta *et al*.[11] The frequency of borderline tumors in the present study was higher than the Ahmad *et al*.,[15] Pilli *et al*.,[10] and Koonings *et al*.[16] Reason for these may be more sections taken from mucinous tumors as they show geographic variability with admixture of benign, borderline, and overtly malignant components in the same tumor, and we found >10% focus of borderline tumor to labeled them as borderline tumors.

In the present study, benign tumors were more common in the 21–40 years of age group and malignant tumors were more common after the 40 years of age, similar to Vora and Bhargav.[17] They also reported almost similar age range. The incidence of germ cell tumors in the first two decades was 60% in our study which was comparable to Ahmad *et al*.[15] and Pilli *et al*.[10] Mature cystic teratoma [Figures 4 and 5] has wider age distribution with a peak incidence in the third and fourth decade, finding was similar with others.[10,15,16] In accordance with Kooning *et al*.[16] and Pilli *et al*.,[10] the proportion of mature cystic teratomas were decreased in the present study with the advancement in age. The age range in sex cord stromal tumors was 20–65 years with median 51 years in the present study as compared to Haroon *et al*.[18] who reported the median age 45 years.

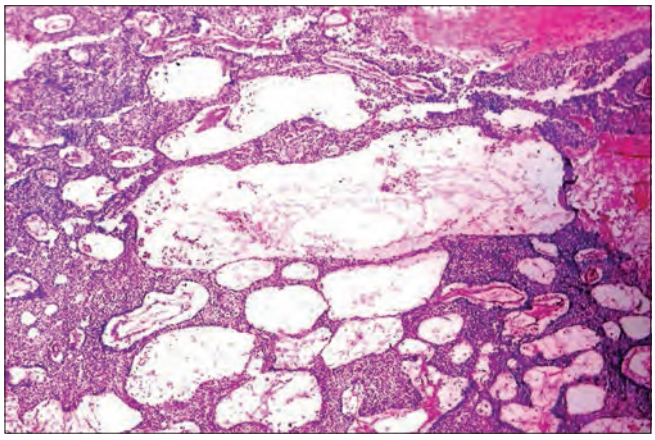

Figure 3: Photomicrograph showing cystic and reticular pattern in yolk sac tumor (H and E, ×100)

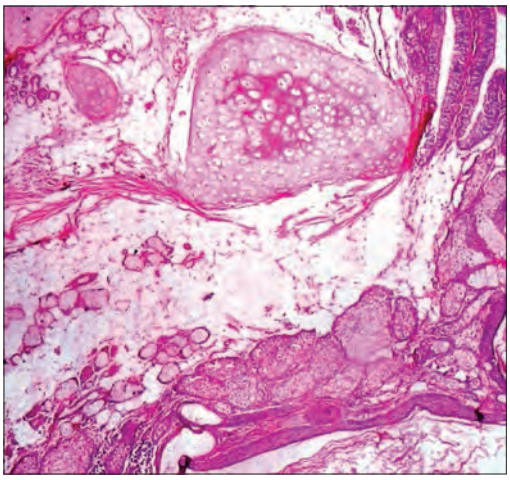

Figure 4: Photomicrograph of mature cystic teratoma showing skin, sebaceous glands, cartilage, intestinal villi, and mucous glands (H and E, ×40)

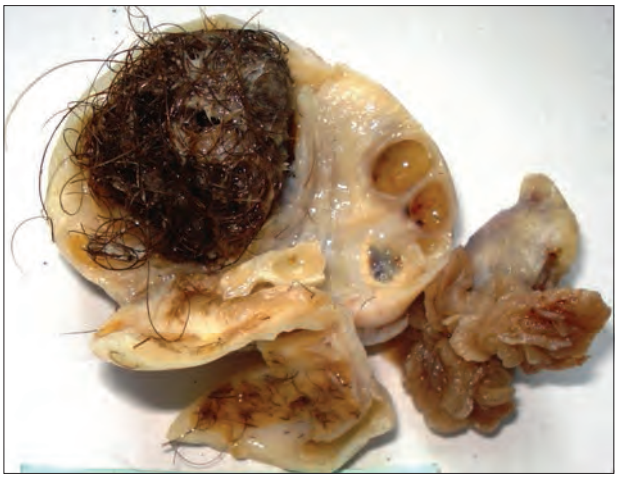

Figure 5: Gross photograph of mature cystic teratoma showing hair tufts with hard cartilaginous area

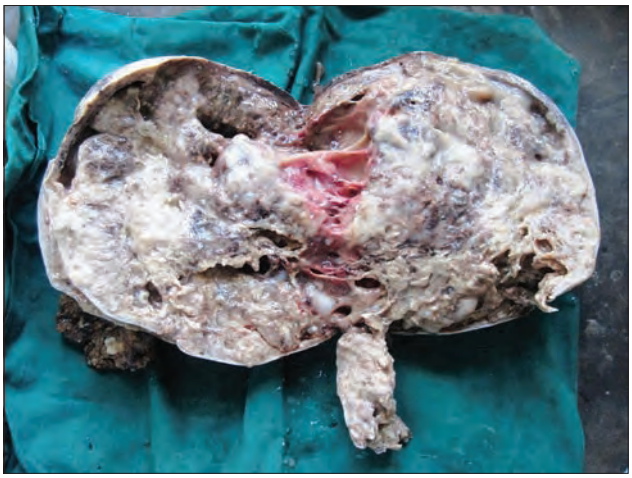

Figure 6: Gross photograph of serous cystadenocarcinoma showing grayish white cut surface with areas of hemorrhages and necrosis

Granulosa cell tumor (GCT) was common after the 40 years of age, Lee *et al*.[19] also found that >90% of GCTs occur after the age of 30 years in the multicenter analysis of 113 cases of GCT.

Irrespective of the nature of ovarian tumors, the most common presenting complaint in the present study was pain in abdomen followed by a lump in abdomen in contrast to other studies[10,17] which reported lump in abdomen as chief complaint followed by pain in the abdomen. This difference in symptomatology may be due to the increased awareness to get early medical advice and due to the availability of imaging techniques nowadays. Results by Wasim *et al*.[20] from Pakistan were similar. In accordance to Bhuvanesh and Logambal[21] and Pilli *et al*.,[10] ascites, anorexia, and weight loss were commonly associated with malignant tumors. Frequency of menstrual disorders was lower in our study as compared to others.[17,21]

For preoperative assessment of the inherent nature of ovarian tumors, CA 125 using >35 U/ml cut-off was not much helpful due to less specificity in the present study. Vasilev *et al*.[22] and Medeiros *et al*.[23] reported better specificity using same cut-off and concluded that CA 125 was a useful preoperative test for predicting the benign or malignant nature of ovarian masses. The reason for the difference could be the smaller sample size of the present study as compared to the large review study of them. The AFP level was elevated in all 3 malignant germ cell tumors, and it was nearer to 1000 ng/ml; the finding was similar to the Kawai *et al*.[24]

Most of the benign and borderline tumors were unilateral, whereas bilaterality was common in malignant tumors, findings are similar to Pilli *et al*.[10] Among bilateral tumors, the most common tumor was serous cystadenocarcinoma [Figure 6] in the present study as well as in the study by Prabhakar and Maingi.[25] The question of the occurrence of bilateral ovarian carcinomas whether they arise simultaneously as primary tumors or one developed because of metastatic spread from another ovary harboring primary tumor was raised by Pejovic *et al*.[26] and Micci *et al*.[27] In their study, cytogenetic analysis of bilateral tumors has done. They concluded that most of the bilateral tumors showed similar karyotypic pattern suggesting the metastatic spread; although the side carrying the primary tumor could not be identified. The gross and microscopic features suggestive of metastatic spread or both are primary tumors not addressed in any of the studies. However, the presence of peritoneal deposits, surface growth, positive ascitic fluid, and difference in the size of both tumors are suggestive features of metastatic spread to another ovary. Larger tumor can be considered primary and smaller was secondary because it has lesser time for growth. In our study, we found total 24 cases of bilateral ovarian cancer out of 226 cases which constitute 10.6% from these 15 cases belong to malignant SETs category. The size of tumor in right and left side was almost similar in 10 cases ranging from 4 to 15 cm in diameter whereas in 5 cases marked difference in size of both sides which is 8–12 cm. All 5 cases showed omental deposits and positive ascitic fluid cytology for malignant cells. None of the case showed surface growth. We have no facility for a cytogenetic study to prove monoclonality. However, we can assume that among 15 bilateral tumors, only 5 cases were due to metastatic spread from contralateral ovary because of marked variation in size, presence of omental deposits and ascites. But the question arose then why with widespread omental deposits and positive ascitic fluid cytology, the contralateral ovary was normal in unilateral malignant tumors. Hence, more studies should be undertaken to resolve this issue.

Side (right or left) preponderance was not found in the present study whereas Saxsena *et al*.[8] and Pilli *et al*.[10]

found the right side to be more commonly involved. None of the case of sex cord stromal tumor was bilateral in the present study similar to Pilli *et al*.[10] whereas Prabhakar and Maingi[25] found bilaterality in 3 cases of sex cord stromal tumors.

In the present study, the most common specimen (as treatment modality) in malignant tumors was TAH + BSO (with or without omentum) In 80.6% cases. In the study of Randhawa and Lata,[28] it was almost similar (72.5%). Whereas in benign and borderline tumors fertility preserving surgery in the form of cystectomy, unilateral salpingo-oophorectomy and oophorectomy were most commonly attempted.

Grossly, 83.3% benign tumors were cystic; whereas 65.3% malignant tumors were partly cystic and partly solid, and 30.6% were solid in consistency. Data are comparable with Prabhakar and Maingi[25] and Pilli *et al*.[10] Both of the studies did not report the predominantly solid consistency in borderline tumors similar to our study. It can be seen from present study that size is not an important factor in accessing the nature of tumor, as size range in benign, borderline, and malignant tumors were almost similar 3–30 cm, 7–32 cm, and 4–25 cm, respectively.

CONCLUSION

Ovarian tumors exhibited the wide spectrum of clinical and histological features. Ovarian cancers are second most common cancer among all cancers in the female genital tract. SETs were the most common followed by germ cell tumors. Borderline tumors were encountered more in the mucinous category than serous. Anorexia, ascites, and weight loss were associated with malignant tumors. On grossing presence of solid element makes malignancy more likely. The size of the tumor was not related to the nature of the tumor. In the era of immunohistochemistry and molecular pathology, where the diagnosis is based on these, in the institutes with limited resources, these clinicomorphological features are very helpful for diagnosis and proper management of the patients.

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Conflicts of interest

There are no conflicts of interest.

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