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# Histopathological Study of Ovarian Tumors at a Tertiary Care Hospital of Central Nepal

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## ABSTRACT

**Background:** Ovarian tumors are histogenetically varied and complex tumors spanning all age groups. They account for 30% of all gynaecologic cancers. Malignant tumors carry a high mortality due to their late detection and ineffective screening programs. Current study aims at finding association between age at presentation and size of tumor with behavior of tumors and also association between category of tumor and age at presentation. **Methods:** This Hospital record based cross-sectional (historical) study was carried out on 158 cases of ovarian tumors received in Department of Pathology, College of Medical Sciences and Teaching Hospital during a time period of five and a half years from January 2012 to June 2017. **Results:** Age of the patients ranged from 12 to 88 years with maximum cases 96 (60.8%) in 20-40 years age group. The mean±SD of age was 36.6±14.4 years. Majority of the cases 137 (86.7%) were benign. Sixteen (10.1%) cases were malignant and 5 (3.2%) cases were borderline. Majority of both benign and malignant cases were seen in 20–40 years age group. Size of the tumors ranged from 2-30 cm with mean±SD of 9.9±5.0 cm and maximum 93 (58.9%) cases in the size range of 5-10 cm. Majority of both benign and malignant tumors were in the size range of 5–10 cm. There was no association of age at presentation and size of tumor with behavior of tumor ($p > 0.05$). Sevety five (47.5%) cases were germ cell tumors, 72 (45.6%) cases were surface epithelial-stromal tumors, 9 (5.7%) cases were sex cord-stromal tumors, 1 (0.6%) was bilateral with surface epithelial tumor in right ovary and germ cell tumor in left ovary and 1 (0.6%) case was soft tissue tumor not specific to ovary. Majority of cases of germ cell tumors were seen below 40 years age whereas significant proportion of surface epithelial-stromal tumors was seen after 40 years with significant association between category and age at presentation ($p < 0.05$). Most common histopathological diagnosis overall was dermoid cyst in 43.7% cases. **Conclusions:** Benign ovarian tumors were more common than malignant ones. Malignancy was seen in all age groups and in any size tumor. Surface epithelial-stromal tumors and germ cell tumors were roughly equal in frequency with slight predominance of latter. Germ cell tumors were common in younger whereas surface epithelial-stromal tumors were more common in older individuals. Histopathological examination in any ovarian tumor at any age with any size is mandatory.

**Keywords**: benign; borderline; germ cell; histopathology; malignant; ovarian tumor; surface epithelial-stromal; sex cord-stromal.

## INTRODUCTION

Ovary is an important organ as it is concerned with the production of progeny.[1] Most common types of lesions encountered in the ovary include functional or benign cysts and tumors.[2] Neoplastic conditions form a complicating and baffling subject in the history of oncology because of the varied histogenetic background.[3]

Worldwide, ovarian cancer ranks twenty and fifteenth cause of cancer mortality overall in both sexes and is eighth cause of cancer mortality in females. In Nepal, it ranks second after cervical cancer out of cancers of genital tract, sixth common cancer overall and is seventh leading cause of cancer mortality in females.[4] Ovarian tumors accounts for 16.7% of total gynaecological visits in Nepal according to one study.[5]

Overall they fall into benign, borderline, and malignant categories. About 80% are benign, and these occur mostly in young women between the ages of 20 and 45 years. Borderline tumors occur at slightly older ages. Malignant tumors are more common in older women, between the ages of 45 and 65 years.[2] Only 3% of ovarian carcinoma develops in patients younger than 20 years of age.[6] Ovarian tumors behave in diverse way and generally escape detection due to small size and

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location within the peritoneal cavity, resulting in minimal local irritation or interference with the vital structures with vague presentation.[7] Inaccessibility of the ovaries for screening, complex nature with widely differing clinicopathological features, unpredictable behavior and prognosis poses a challenge to both gynaecologist and pathologist.[8]

This study was carried out to study the histopathologic spectrum of ovarian tumors in College of Medical Sciences and Teaching Hospital and see their frequency and age distribution and also to check association between age at presentation and size of tumor with behavior of tumors and also association between category of tumor and age at presentation.

## METHODS

This Hospital record based cross-sectional (historical) study was carried out in Department of Pathology, College of Medical Sciences and Teaching Hospital. Ethical approval from the Institutional Review Committee was obtained. 158 consecutive cases of ovarian tumors found in cystectomy, ovariotomy, oophorectomy, salpingo-oophorectomy, total abdominal hysterectomy with bilateral or unilateral salpingo-oophorectomy specimens received in the Histopathology section of Department of Pathology of College of Medical Sciences and Teaching Hospital during a time period of five and a half years from January 2012 to June 2017 were included in the study. Inflammatory, non-neoplastic, gestational and developmental disorders were excluded. All the cases of ovarian tumors received in the study period were reviewed. Tumors were classified using WHO classification (4th edition).[9]

Data was initially entered in MS-Excel, refined and finally analyzed by SPSS 16.0. Variables like age of presentation, laterality of involvement, size, surface involvement, consistency, histopathological diagnosis, category and behavior were analyzed. In cases of bilateral tumors, mean size of both right and left tumor was calculated. Association between behavior of tumors and age was tested using Likelihood Ratio. Associations between size and behavior of tumor and age at presentation and category of tumors were tested using one way ANOVA test. Level of significance was considered as 5%. Independent variables were considered as category and behavior of ovarian tumors and dependent variables were considered as age at presentation and size of tumor.

## RESULTS

Total 158 cases of ovarian tumors were received in the study period. Age of the patients ranged from 12 to 88 years with maximum cases 96 (60.8%) in 20 – 40 years age group. The mean±SD of age was 36.6±14.4 years. Eighty-five (53.8%) cases involved right ovary, 60 (38.0%) cases involved left ovary and 13 (8.2%) cases were bilateral.

Majority of the cases 137 (86.7%) were benign. Sixteen (10.1%) cases were malignant and 5 (3.2%) cases were borderline tumors. Maximum number of both benign and malignant cases, 86 (54.4%) and 7 (4.4%) cases respectively, were seen in 20 – 40 years age group. Majority of both benign and malignant tumors were in the size range of 5 – 10 cm. There was no significant association between age at presentation and size of tumor with behavior of tumors (Tables 1, 2).

**Table 1. Behavior of ovarian tumors in different age groups.**

| Age group (years) | Behavior | | | Total |
|---|---|---|---|---|
| | Benign | Borderline | Malignant | |
| < 20 | 10 | 0 | 3 | 13 |
| 20 – 40 | 86 | 3 | 7 | 96 |
| 41 – 60 | 33 | 2 | 2 | 37 |
| > 60 | 8 | 0 | 4 | 12 |
| Total (n=158) | 137 | 5 | 16 | 158 |

Likelihood Ratio=20.010, p=0.067

**Table 2. Association between size and behavior of tumor.**

| Behavior | Mean size (cm) | SD (cm) | 95% Confidence Interval for Mean | | *P-Value |
|---|---|---|---|---|---|
| | | | Lower Bound | Upper Bound | |
| Benign | 9.5 | 4.7 | 8.7 | 10.3 | |
| Borderline | 13.8 | 8.0 | 3.8 | 23.8 | |
| Malignant | 11.9 | 5.9 | 8.7 | 15.1 | 0.064 |

* Using one way ANOVA

Surface involvement was present in only 4 (2.5%) cases seen in all malignant cases. Consistency was mostly cystic in 139 (88.0%) cases, solid in 8 (5.0%) cases and both solid and cystic in 11 (7.0%) cases. Out of 137 benign tumors, 134/137 (97.8%) were cystic and 3/137 (2.2%) were solid.

All 5 borderline cases were cystic. Out of 16 malignant tumors, 11/16 (68.7%) were solid and cystic and 5/16 (31.3%) were entirely solid.

Seventy-five (47.5%) cases were germ cell tumors, 72 (45.6%) cases were surface epithelial-stromal tumors, 9 (5.7%) cases were sex cord-stromal tumors, 1 (0.6%) was bilateral with surface epithelial tumor (mucinous cystadenoma) in right ovary and germ cell tumor (mature cystic teratoma) in left ovary and 1 (0.6%) case was soft tissue tumor not specific to ovary (lymphangioma). Majority of cases of germ cell tumors 62/74 (83.8%) were seen below 40 years age whereas 33/72 (45.8%) of surface epithelial-stromal tumors were seen after 40 years (Table 3).

**Table 3. Different categories of ovarian tumors in different age groups.**

| Category | Age group | | | | Total |
|---|---|---|---|---|---|
| | <20 | 20 – 40 | 41 – 60 | >60 | |
| Surface epithelial stromal Tumors | 2 | 37 | 26 | 7 | 72 |
| Germ cell tumors | 10 | 52 | 9 | 4 | 75 |
| Sex cord stromal tumors | 1 | 5 | 2 | 1 | 9 |
| Unclassified* | 0 | 1 | 0 | 0 | 1 |
| Soft tissue tumor | 0 | 1 | 0 | 0 | 1 |
| **Total** | 13 | 96 | 37 | 12 | 158 |

*Surface epithelial-stromal tumor in right ovary and germ cell tumor in left ovary

Including only the three major categories of surface epithelial-stromal, germ cell and sex cord-stromal tumors, association between category of ovarian tumor and age of presentation was tested using one way ANOVA test. There was significant association between the major categories tested and age at presentation as p value < 0.05 (Table 4).

**Table 4. Association between category of ovarian tumor and age of presentation.**

| Category* | Mean age (yrs) | SD (yrs) | 95% Confidence Interval for Mean | | P value ** |
|---|---|---|---|---|---|
| | | | Lower Bound | Upper Bound | |
| Surface epithelial stromal | 40.6 | 14.3 | 37.2 | 43.9 | 0.003 |
| Germ cell | 32.5 | 13.6 | 29.4 | 35.6 | |
| Sex cord stromal | 37.6 | 17.2 | 24.4 | 50.7 | |

*'Unclassified' and 'Soft tissue tumor' categories were excluded.
**Using one way ANOVA test

Out of 72 (45.6%) cases of surface epithelial-stromal tumors, 63/72 (87.5%) were benign, 5/72 (6.9%) were borderline and 4/72 (5.5%) were malignant. Out of 75 (46.8%) cases of germ cell tumors, 69/75 (92.0%) were benign and 6/75 (8.0%) were malignant. Out of 9 (5.7%) cases of sex cord-stromal tumors, 6/9 (66.7%) were malignant and only 3/9 (33.3%) cases were benign.

The final histopathological diagnoses made in 72 (45.6%) cases of surface epithelial-stromal tumors were serous cystadenoma in 46/72 (63.9%) cases, mucinous cystadenoma in 16/72 (22.2%) cases, combined seromucinous cystadenoma in 1/72 (1.4%) case, borderline mucinous tumor in 4/72 (5.5%) cases (Figure 1), borderline serous tumor in 1/72 (1.4%) case, high grade serous adenocarcinoma in 3/72 (4.2%) cases and transitional cell carcinoma, non-Brenner type in 1/72 (1.4%) case (Figure 2).

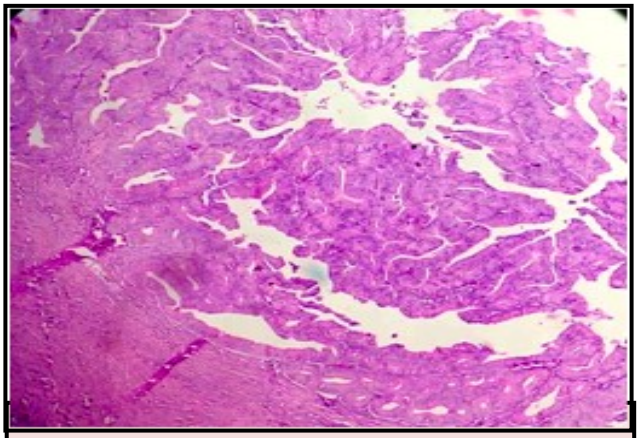

**Figure 1. Photomicrograph showing borderline mucinous tumor, endocervical type with complex papillary arrangement (H and E X100).**

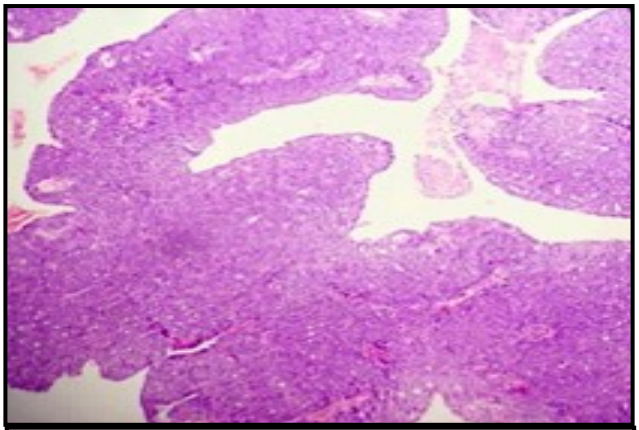

**Figure 2. Photomicrograph showing transitional cell carcinoma, non Brenner type (H and E X100).**

Out of 75 (47.5%) cases of germ cell tumors, 69/75 (92.0%) were mature cystic teratomas or simply dermoid cysts, 3/75 (4.0%) cases were dysgerminomas, 1/75 (1.3%) case was yolk sac

tumor (Figure 3), 1/75 (1.3%) case was immature teratoma (Figure 4) and 1/75 (1.3%) had malignant transformation in dermoid cyst into squamous cell carcinoma.

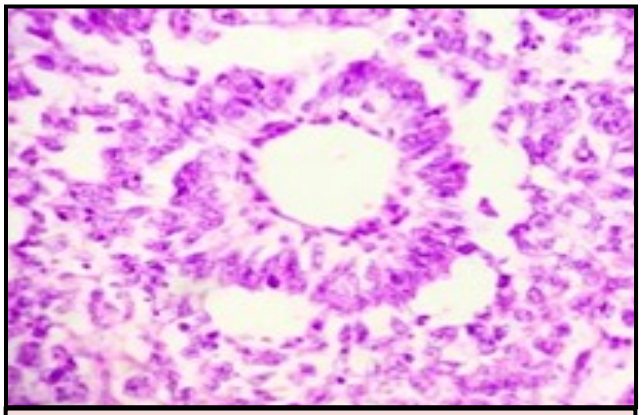

**Figure 3. Photomicrograph showing Schiller-Duval body in yolk sac tumor (H and E X400).**

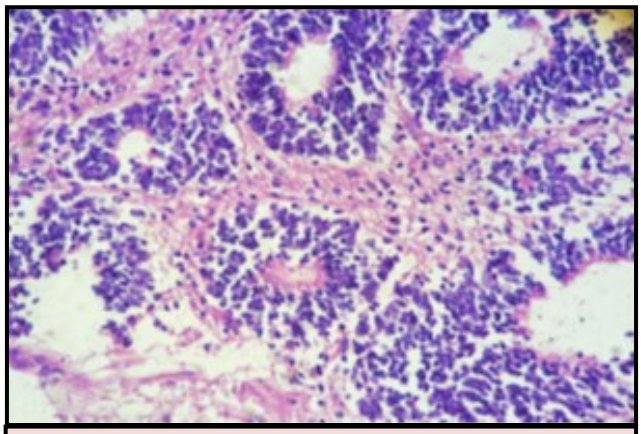

**Figure 4. Photomicrograph showing immature neuroepithelium in immature teratoma (H and E X100).**

Out of 9 (5.7%) cases of sex cord-stromal tumors, 3/9 (33.3%) cases were fibromas, 3/9 (33.3%) cases were granulosa cell tumor, adult type (Figure 5), 2/9 (22.2%) were steroid cell tumors,

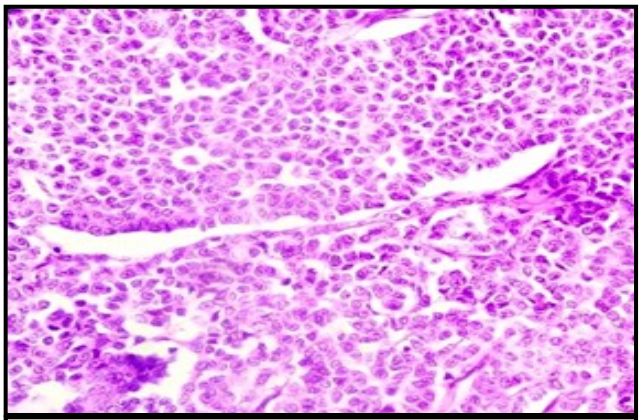

**Figure 5. Photomicrograph showing Call-Exner bodies in granulosa cell tumor (H and E X400).**

NOS (Figure 6), and 1/9 (11.1%) case was Sertoli Leydig cell tumor.

**Figure 6. Gross photograph showing steroid cell tumor with yellowish cut surface.**

One (0.6%) case had mucinous cystadenoma in right ovary and dermoid cyst in left ovary and 1 (0.6%) case was diagnosed as lymphangioma (Figure 7). Most common histopathological diagnosis overall was dermoid cyst in 69/158 (43.7%) cases (Tables 5, 6).

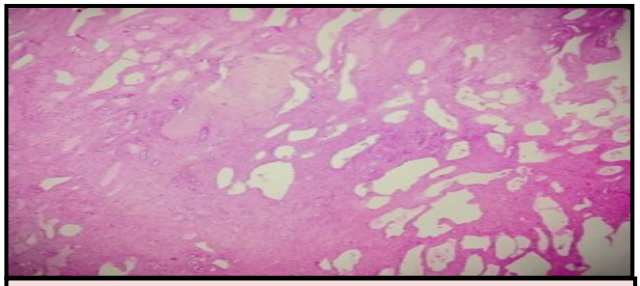

**Figure 7. Photomicrograph showing dilated lymphatic spaces in lymphangioma (H and E X40).**

**Table 5. Distribution of benign, borderline and malignant cases in one or both ovaries.**

| Diagnosis | Unilateral | Bilateral | Total |
|---|---|---|---|
| **Benign tumors (n=137)** | | | |
| Serous cystadenoma | 44 | 2 | 46 |
| Mucinous cystadenoma | 15 | 1 | 16 |
| Seromucinous cystadenoma | 1 | 0 | 1 |
| Dermoid cyst | 64 | 5 | 69 |
| Fibroma | 2 | 1 | 3 |
| Unclassified* | 0 | 1 | 1 |
| Lymphangioma | 1 | 0 | 1 |
| **Borderline tumors (n=5)** | | | |
| Borderline mucinous tumor | 4 | 0 | 4 |
| Borderline serous tumor | 0 | 1 | 1 |
| **Malignant (n=16)** | | | |
| Serous adenocarcinoma | 1 | 2 | 3 |
| Transitional cell carcinoma, non Brenner type | 1 | 0 | 1 |
| Dysgerminoma | 3 | 0 | 3 |
| Immature teratoma | 1 | 0 | 1 |
| Dermoid cyst transforming into scc | 1 | 0 | 1 |
| Yolk sac tumor | 1 | 0 | 1 |
| Granulosa cell tumor, adult type | 3 | 0 | 3 |
| Steroid cell tumor, NOS | 2 | 0 | 2 |
| Sertoli-Leydig cell tumor | 1 | 0 | 1 |
| **Total** | **145** | **13** | **158** |

*Surface epithelial-stromal tumor in right ovary and germ cell tumor in left ovary

**Table 6. Distribution of histopathological diagnoses in various age groups.**

| Diagnosis | Age group | | | | Total |
|---|---|---|---|---|---|
| | <20 | 21-40 | 41-60 | > 60 | |
| **Benign tumors (n=137)** | | | | | |
| Serous cystadenoma | 2 | 26 | 14 | 4 | 46 |
| Mucinous cystadenoma | 0 | 8 | 8 | 0 | 16 |
| Seromucinous cystadenoma | 0 | 0 | 0 | 1 | 1 |
| Dermoid cyst | 8 | 49 | 9 | 3 | 69 |
| Fibroma | 0 | 1 | 2 | 0 | 3 |
| Unclassified* | 0 | 1 | 0 | 0 | 1 |
| Lymphangioma | 0 | 1 | 0 | 0 | 1 |
| **Borderline tumors (n=5)** | | | | | |
| Borderline mucinous tumor | 0 | 2 | 2 | 0 | 4 |
| Borderline serous tumor | 0 | 1 | 0 | 0 | 1 |
| **Malignant (n=16)** | | | | | |
| Serous adenocarcinoma | 0 | 0 | 1 | 2 | 3 |
| Transitional cell carcinoma, non Brenner type | 0 | 0 | 0 | 1 | 1 |
| Dysgerminoma | 1 | 2 | 0 | 0 | 3 |
| Immature teratoma | 1 | 0 | 0 | 0 | 1 |
| Dermoid cyst transforming into scc | 0 | 0 | 0 | 1 | 1 |
| Yolk sac tumor | 0 | 1 | 0 | 0 | 1 |
| Granulosa cell tumor, adult type | 0 | 2 | 0 | 1 | 3 |
| Steroid cell tumor, NOS | 1 | 1 | 0 | 0 | 2 |
| Sertoli-Leydig cell tumor | 0 | 1 | 0 | 0 | 1 |
| **Total** | 13 | 96 | 37 | 12 | 158 |

*Surface epithelial-stromal tumor in right ovary and germ cell tumor in left ovary

## DISCUSSION

Tumors of ovary represent about 30% of all cancers of female genital system.[9] Ovarian cancer is said to be a silent killer as majority do not have significant symptoms until an advanced stage. The complex anatomy of ovary and its peculiar physiology, the constant cyclical changes from puberty to menopause gives to a number of cell types, each of which is capable of giving rise to complex varieties of tumors.[10]

Ovarian tumor may occur at any age, including infancy and childhood. Incidence rate, however increase with age, with the greatest number of new cases being diagnosed beyond 4th and 5th decade.[11] Age of the patients ranged from 12 to 88 years with mean±SD of age 36.6±14.4 years and maximum cases in 20 – 40 years age group which was similar to studies done by Maharjan in Chitwan, Pradhan et al. and Vaidya et al. in Kathmandu, Mankar et al. and Swamy et al. in India and Ashraf et al. in Pakistan.[12-17]

Majority of the cases 137 (86.7%) were benign, 16 (10.1%) cases were malignant and 5 (3.2%) cases were borderline which was similar to various studies done in Nepal and India.[11-13,16,18,19] However in studies done by Mankar et al. and Narang et al. in India and Ahmad et al. in Pakistan, malignant cases also accounted for significant percentage, 31.1%, 33.5% and 40.81% respectively.[14,20,21]

Maximum number of both benign and malignant cases, 86/137 (62.8%) and 7/16 (43.7%) respectively, were seen in 20 – 40 years age group. Only 6/16 (37.5%) malignant cases were seen after 40 years of age. Common age group for benign tumors was similar, however, age group for malignant tumors was relatively older in other studies.[11,16,20,22,23] Present study emphasizes the need of proper histopathological evaluation of ovarian tumors at all ages due to relative predominance of malignant cases at younger age. However, larger sample size including more number of malignant cases is required.

Size of the tumors ranged from 2–30 cm and maximum 128 (81.0%) cases in the size range of 5 –15 cm which was comparable to finding of Maharjan where size range was from 3 – 28 cm and majority were between 5 – 15 cm.[15] This study did not find any association between size and behavior of ovarian tumor. An interesting observation made by Howarth et al. regarding size was that patients with early stage ovarian cancer had more than twice as large size as those found in advanced disease and early stage ovarian cancer grew locally and did not disseminate, and advanced stage disseminated while the tumor was still relatively small.[24] Majority of benign tumors were cystic whereas all the malignant tumors were either both solid and cystic or entirely solid which was in accordance to findings of Pradhan et al. in Dharan, Nepal and Narang et al. in India.[13,20]

Bilateral tumors were 8.2% in this study which is comparable to finding of Pradhan et al. in Kathmandu and Maharjan in Chitwan where 7.7% and 6.2% cases were bilateral.[15,18] A higher percentage of 22%, 12.3%, 18.6% and 20% cases were bilateral in studies done by Pradhan et al. in Dharan, Kayastha and Pudasiani et al. in

Kathamndu and Swamy et al. in India respectively.[5,13,16,25] Only 2/16 malignant cases were bilateral in present study in contrast to 6/9 in study done by Kayastha, 11/26 in study done by Jha et al. and 15/30 in study done by Swamy et al.[5,16,19] Maharjan found all benign tumors in 8 bilateral cases.[15] Also 5/7 and 11/18 bilateral cases were benign in studies done by Pradhan et al. in Kathamndu and Pradhan et al. in Dharan respectively.[13,18] Most of the studies indicate bilaterality as a risk factor for malignant tumors.[5,19,23] However, this was not supported by present study.

Surface epithelial-stromal tumors account for about two-thirds of all primary ovarian tumors, and their malignant form for almost 90% of all ovarian cancers in western world.[26] In the present study, 75 (47.5%) cases were germ cell tumors, 72 (45.6%) cases were surface epithelial-stromal tumors and 9 (5.7%) cases were sex cord-stromal tumors. Surface epithelial-stromal tumors were more common in various studies in Nepal, India and Pakistan ranging from 47–74%.[5,8,11,13-16,19-22,25] However, germ cell tumors were slightly more common in present study which was similar to findings of Vaidya et al. and Pradhan et al. in Kathmandu, Nepal where germ cell tumors were more common and accounted for 51.52% and 53.85% respectively.[12,18] 5.7% cases were sex cord stromal tumors in present study which was higher than findings of Maharjan (2.3%), Jha et al. (3.1%), Agarwal et al. (3.3%) and Naik et al. (3.9%).[8,11,15,19] However, Narang et al. had 10.1% sex cord stromal tumors in their study.[20] Majority of cases of germ cell tumors 62/74 (83.8%) were seen below 40 years age whereas 33/72 (45.8%) of surface epithelial-stromal tumors were seen after 40 years. This corroborated with the findings of Jha et al. where majority of surface epithelial-stromal tumors were seen after 40 years (57.1%) and 72.0% germ cell tumors were seen before 40 years of age. This finding was supported by other studies done by Kayastha, Maharjan and Vaidya et al. in Nepal.[5,12,15]

Out of 137 benign tumors, 46.0% were surface epithelial-stromal tumors, 50.4% were germ cell tumors and 2.2% were sex cord-stromal tumors in present study. Surface epithelial-stromal tumors were more common benign tumors in some studies [5,11,15,19,25] whereas germ cell tumors were more common in others studies.[12,13,18] Dermoid cyst was most common benign tumor comprising 50.4% cases followed by serous cystadenoma in 33.6% cases in present study.

All 5 (3.2%) borderline cases were surface epithelial-stromal tumors. Borderline tumors account for 0.7–3.8% cases in various studies with all epithelial tumors.[8,11-13,15,16,18,20,22]

Out of 16 malignant tumors 37.5% each were germ cell tumors and sex cord-stromal tumors and only 25% were surface epithelial stromal tumors in present study. Malignant surface epithelial tumors were less common than studies conducted by Jha et al., Agarwal et al. and Ahmad et al. where they accounted for 69.2%, 67.8% and 63.5% cases respectively.[11,19,21] In present study, out of 16 malignant cases, 3 (18.7%) cases each were serous adenocarcinoma, dysgerminoma and granulosa cell tumor. In study done by Swamy et al., granulosa cell tumor and endometrioid carcinoma were the most common malignancies.[16] In study done by Maharjan in Chitwan, out of 7 malignant tumors, 3 were dysgerminoma, 2 were yolk sac tumor, 1 was papillary cystadenocarcinoma and 1 was granulosa cell tumor comprising germ cell tumors as most common amongst malignant tumors.[15] However, serous cystadenocarcinoma was the most common observed malignancy in other studies.[8,11,19,21]

One case had bilateral ovarian tumor in which tissue of origin of right and left ovarian tumor was different. This case had dermoid cyst in left ovary and mucinous cystadenoma in right ovary. Naik et al. had observed 3 such cases out of 499 ovarian tumors with different tissue of origins in right and left tumor.[8] However, Maharjan had excluded such cases in her study.[15] There is a provision for classifying mixed ovarian tumor in same ovary.[9] However, two different histological types of ovarian tumors in both ovaries are extremely rare and there are only case reports in existing literature.[27,28] With continuing increase in such cases, an insight into their pathogenesis and classification as a separate entity may be necessary. Interestingly, 1 case of lymphangioma was found in the present study. Lymphangioma is an extremely rare condition of ovary, first described in 1908 with only case reports in ovary in literature. This is a slow growing neoplasm mostly found incidentally on histopathologic examination.[29,30]

## CONCLUSIONS

Ovarian tumors were seen over a wide age range and were more common in reproductive age women. Benign tumors were more common than malignant tumors in all age groups. Though, literature states than malignant tumors are more common in older age group, present study did not

observe so. Malignancy can be observed in any size tumor. Germ cell tumors were the commonest histological type. Surface epithelial-stromal tumors were more common in older age group whereas germ cell tumors were more common at younger age. Benign tumors were more common in bilateral tumors. Some rarities were encountered in present study like two histologically different tumors in right and left ovary in a case of bilateral ovarian tumor and a case of lymphangioma. Histopathological examination in ovarian tumors is the gold standard.

This is a hospital based study. Hence, the results may not reflect upon the entire population. Larger data size for malignant tumors is required. The results are based on Haematoxylin and Eosin stained sections only.

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**Conflict of Interest:** None

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