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Original Article

Histopathological profile of ovarian tumors at a tertiary care center of Nepal

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ABSTRACT

Background: Ovarian tumors encompass a diverse group of neoplasms, including both benign and malignant forms with distinct clinical and histological features. In Nepal, ovarian cancer was the 10th most common cancer in 2022, with 643 new cases, representing 2.9% of all newly diagnosed cancers. Histopathological examination remains the definitive method for identifying and classifying ovarian tumors into benign, borderline, and malignant categories. This study aimed to determine the histopathological patterns of ovarian masses and examine their association with serum tumor markers.

Materials and Methods: This is a cross-sectional descriptive study conducted over 2 years in the Department of Pathology at Paropakar Maternity and Women's Hospital, Thapathali, Kathmandu, which included 319 patients who underwent ovarian biopsies. Histopathological examination was performed post-surgery and the descriptive evaluation of various histopathological subtype were conducted.

Results: Among 319 cases of ovarian specimens, the majority of ovarian masses were benign, 292 cases (91.54%), malignant tumors, 21 cases (6.58%), and borderline tumors, 6 cases (1.88%). Mean age of patients presenting with benign tumors was 32 years, while it was 33 years for malignant tumors, and 51 years for borderline tumors.

Conclusions: The majority of ovarian tumors are benign, with germ cell tumors, particulartly mature cystic teratomas being the most frequent histopathological subtype. Histopathological examination remains the definite gold standard for tumor classification.

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INTRODUCTION

Ovarian tumors include a complex and heterogeneous group of neoplasms, including both benign and malignant lesions with distinct histological and clinical characteristics.[1,2] Although ovarian cancer has no defining symptoms, many women report issues like bloating, pelvic or abdominal pain, trouble eating, or urinary changes. The challenge is that these signs are often ignored until the cancer has already been diagnosed.[3]

Cancer is a major global health concern, responsible for approximately 10 million deaths in 2020, equivalent to

about one in every six deaths worldwide.[4] According to the GLOBOCAN (2022), the 5-year prevalence of ovarian cancer in Asia was 504,953 cases, accounting for 54.3 % of global 5-year prevalent cases as of the 2022 estimates. An estimated 22,008 new cases and 14,704 deaths were reported in Nepal (2022).[5] Ovarian cancers have the poorest prognosis among gynaecological malignancies, primarily because they are often diagnosed at an advanced stage. Early-stage ovarian cancer is usually asymptomatic, making timely detection challenging.[6] In Nepal, ovarian cancer ranked 10th among all cancers (2022); there were 643 new cases, accounting for 2.9% of all new cancer diagnoses, with a cumulative risk of 0.44%. The disease accounted for 452 deaths (3.1%), with a cumulative risk of 0.36%. The five-year prevalence of ovarian cancer was 1,588 cases (9.8 per 100,000 population), reflecting a significant burden on women's health in the country.[5]

Histopathological evaluation remains the definitive method for characterizing ovarian tumors, enabling classification into benign, borderline, and malignant subtypes.[7] Serum tumor markers like Beta-hCG, AFP, and CEA aid in tailored therapeutic decision-making.[8] The study aimed to find the histopathological profiles of ovarian masses received at a tertiary care center in Nepal.

MATERIALS & METHODS

This was a cross-sectional descriptive study carried out at Paropakar Maternity and Women's Hospital, Thapathali, Kathmandu, Nepal, using retrospectively collected data of ovarian specimens submitted to the pathology department from 14 April 2019 to 13 April 2021 after obtaining ethical approval from the Institutional Review Committee of the same institute (Ref. No. 62/421). Serum tumor markers like CA-125, alpha fetoprotein (AFP), and Beta-hCG levels were measured pre-operatively. The normal cut-off value of CA-125 was 35U/ml, AFP was 9ng/ml, and Beta hCG was <10. All cases of ovarian mass biopsies submitted to the pathology department were included in the study, and biopsies with inadequate tissue for a definite opinion were excluded. This study aimed to provide insight into the different histopathological patterns of ovarian masses.

The collected biopsy specimens were processed following standard histopathological protocols. Tissues were fixed in 10% formalin overnight, followed by an additional two hours in each of two stations in the tissue processor. Dehydration was performed using graded alcohols of increasing concentration (70%, 80%, 90%, and absolute alcohol) for 1.5 hours in each station, followed by clearing in xylene for two hours in two stations. The tissues were then impregnated with paraffin at 60–65°C for two hours in each of two stations and subsequently embedded in paraffin blocks. After solidification, the blocks were removed from the base plates and sectioned.

For tissue sectioning, paraffin blocks were trimmed and cut into 4–5 µm thick sections using a rotary microtome. Sections were floated on a preheated water bath at 50°C and mounted onto albumin-coated glass slides, which were dried on a hot plate to remove excess wax. The slides were then subjected to hematoxylin and eosin (H&E) and Giemsa staining. Briefly, slides were dewaxed in xylene (three stations, 2 minutes each), rehydrated through descending alcohol grades (absolute, 90%, 70%, 2 minutes each), and stained with Harris's hematoxylin for 10 minutes. Sections were rinsed in tap water, differentiated in 1% acid alcohol for 10–30 seconds, and rinsed again. Counterstaining was performed with aqueous eosin Y for 2 minutes, followed by rinsing in tap water. Finally, the sections were dehydrated through ascending alcohols (70%, 90%, absolute, 2 minutes each), cleared in two xylene baths, and mounted with DPX before cover-slipping. The prepared slides were then examined under light microscopy were examined by consultant pathologist and classified using WHO classification system of ovarian tumors (5th Edition). Data entry and analysis were done using SPSS version 24.

RESULTS

Among 319 cases of ovarian specimens, the majority of the ovarian masses were benign, accounting for 292 (91.54%) specimens. Malignant tumors were identified in 21 (6.58%) cases, while borderline tumors were observed in 6 (1.88%) cases. The mean age group for benign tumors was 32.34 ± 10.82 years, while those with malignant tumors had a slightly higher mean age of 33.48 ± 13.23 years, and the mean age group for borderline tumors was 51.00 ± 8.20 years.

Among benign tumors, germ cell tumors were the most common, accounting for 132 (45.20%) cases, followed by surface epithelial tumors, 83 (28.42%). Mature cystic teratoma was observed in 130 (44.52%) cases. In case of malignant ovarian tumors, surface epithelial malignancies were the most frequent, 9 (42.86%) cases, followed by germ cell malignancies, 8 (38.09%) cases. Serous carcinoma was the most frequent malignant tumor, with high-grade serous carcinoma 4 (19.05%) occurring more commonly than low-grade serous carcinoma 2 (9.52%). Mucinous carcinoma was seen in 3 cases (14.29%), while immature teratoma was seen in 6 cases (28.57%), and adult-type granulosa cell tumor was observed in 2 cases (9.52%). All borderline tumors observed in the study were mucinous borderline tumors 6 (100%) (Table 1).

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Table 1: Distribution of various histopathological diagnoses of ovarian tumors

		Types of tumors	n (%)
Benign	Surface Epithelial Tumors	Serous cystadenoma	54 (18.49)
		Mucinous cystadenoma	23 (7.88)
		Serous cystadenofibroma	4 (1.37)
		Benign Brenner tumor	2 (0.68)
	Germ Cell Tumors	Mature cystic teratoma	130 (44.52)
		Cystic struma ovarii	2 (0.68)
	Sex Cord Stromal Tumors	Fibroma	2 (0.68)
	Other Benign condition	Endometriotic cyst	37 (12.67)
		Corpus luteal cyst	17 (5.82)
		Endometriosis	7 (2.40)
		Follicular cyst	6 (2.05)
		Ectopic pregnancy	6 (2.05)
		Tuberculosis	1 (0.34)
		Cystic follicle	1 (0.34)
Malignant	Surface Epithelial Tumors	Serous carcinoma	
		Low-grade	2 (9.52)
		High grade	4 (19.05)
		Mucinous carcinoma	3 (14.29)
	Germ Cell Tumors	Dysgerminoma	2 (9.52)
		Immature teratoma	6 (28.57)
	Sex Cord Stromal Tumors	Granulosa cell tumor, adult type	2 (9.52)
	Metastatic Tumors	Metastatic carcinoma	2 (9.52)
Borderline		Mucinous borderline tumor	6 (100)
		Total	319

The right and left ovary was affected in 131 (44.86%) and 128 (43.84%) of benign cases, respectively, and 14 (66.67%) and 5 (23.81%) of malignant cases, respectively. Bilateral ovaries were involved in 23 (7.88%) of benign cases and 2 (9.52%) of malignant cases.

Raised CA-125 was observed in both benign and malignant cases, but was proportionally much higher in malignant cases, with 6 (28.57%) out of 21 showing elevated levels compared to 9 (3.08%) out of 292 in benign lesions. Elevated AFP and Beta-hCG were observed only in malignant cases 4 (19.05%) each (Table 2).

Table 2: Distribution of cases of raised serum tumor markers in benign and malignant tumors (n= 319).

	Benign (n= 292)	Malignant (n= 21)	Borderline (n= 6)
Increased CA-125	9 (3.08)	6 (28.57)	-
Increased AFP	-	4 (19.05)	-
Increased Beta-hCG	-	4 (19.05)	-

Four cases of high-grade serous carcinoma and two cases of low-grade serous carcinoma showed elevated serum CA-125, ranging from 85 to 700U/mL. Nine cases of benign tumors showed increased serum CA-125 and they were five cases of endometriotic cyst, three cases of endometriosis, and one case of fibroma. Among the malignant ovarian tumors with elevated AFP and Beta-hCG levels, granulosa cell tumor, adult type was identified in two cases, with AFP levels of 105 ng/mL and 90 ng/mL, and corresponding Beta-hCG levels of 99 and 129, respectively. Dysgerminoma was also observed in two cases, with AFP levels 35 and 88 ng/mL, while Beta-hCG levels were 77 to 102.

DISCUSSION

Early, non-invasive detection of ovarian cancer can be achieved through radiological imaging as well as biochemical markers. Serum biomarkers play an important role in the diagnosis of ovarian cancer. Among them, CA-125 is the most widely recognized marker; however, its clinical utility is limited by relatively low sensitivity and specificity.[9] Other biomarkers are more specific for certain ovarian tumor types, such as CEA for mucinous tumors, LDH for dysgerminomas and mixed germ cell tumors, α-fetoprotein for embryonal cell tumors and yolk sac tumors, Beta-hCG for choriocarcinomas, inhibin B for granulosa cell tumors, and HE4 (human epididymis protein 4).[10-12]

In our study, out of 319 ovarian specimens, most tumors were benign, comprising 292 cases (91.54%), whereas malignant tumors were seen in 21 cases (6.58%) and

borderline tumors in 6 cases (1.88%). Another study by Mehra et al. reported that most ovarian tumors were benign (69%), while malignant tumors accounted for 24.5% of cases, and borderline tumors represented 5.4% of the total of 110 cases.[13] Gupta et al. reported that among 96 ovarian tumor cases, the majority were benign (72.9%), while borderline tumors accounted for 4.1% and malignant tumors for 22.9%. Histologically, surface epithelial tumors were the most common (48.8%), followed by germ cell tumors (23.9%), sex cord stromal tumors (8.3%), and metastatic tumors (2.0%).[14] In the study done by Maheshwari et al., surface epithelial tumors (SET) accounted for 65.7% of all ovarian tumors, with benign tumors comprising the majority (182 cases, 71.9%).[15] Among epithelial ovarian tumors, serous tumors were the most common, observed in 87 cases (43.5%), followed by mucinous tumors in 60 cases (30%) and Brenner tumors in 5 cases (2.5%) in a study done by Sampurna K et al.[16]

High-grade serous cystadenocarcinoma was the most frequent malignant ovarian tumor, accounting for 9% of cases, followed by low-grade serous cystadenocarcinoma, which comprised 4.5% of malignant tumors in a study done by Mehra et al.,[13] which was the same as that of our study, where high-grade serous carcinoma was seen in 4 (19.05%) and low-grade serous carcinoma was seen in 2 (9.52%). Dysgerminomas were the most common malignant germ cell tumors of the ovary, accounting for about 45% of all malignant germ cell tumors in the study conducted by McSweeney et al., whereas in our study, it was observed in 2 cases (9.52%).[17] Among non-neoplastic ovarian lesions, solitary follicular cysts were the most common, observed in 56 cases (74.66%), followed by corpus luteal cysts in 15 cases (20%), in a study done by Kanthikar et al., while in our study, the most common non-neoplastic ovarian lesion was an endometriotic cyst, seen in 37 cases (12.67%).[18] Patel et al. reported that the majority of ovarian tumors were unilateral (89.5%), with a slight predominance on the left side, accounting for 49.4% of cases.[19]

Akakpo et al. reported that the most common tumors were Germ cell tumors (41.9%), occurring at a relatively younger age with a mean age of 30.7 ± 12.7 years, and were predominantly mature teratomas (39.2%).[20] Farag et al. showed that benign ovarian neoplasms (64.4%) were more frequent than malignant (29.4%) and borderline tumors (6.2%) across all age groups, except in women over 60 years.[21] Among ovarian tumors, serous tumors were the most frequent (42.9%), followed by mucinous tumors (25.5%), teratomas (17%), granulosa cell tumors (6.7%), dysgerminomas (2.48%), and endodermal sinus tumors (1.77%).[22] Histopathologically, surface epithelial tumors were the predominant subtype, accounting for 76.7% of ovarian tumors, followed by germ cell tumors (13.3%) and sex cord–stromal tumors (10%). Bilateral involvement was seen in 10 out of 61 gross ovarian specimens (16.4%) as reported in another study.[23]

In this study, raised CA-125 was observed in both benign and malignant cases, but was proportionally much higher in malignant cases, with 6 (28.57%) out of 21 showing elevated levels compared to 9 (3.08%) out of 292 in benign lesions. CA-125 is recognized as an important protein biomarker for assessing treatment effectiveness and monitoring disease progression in patients with ovarian cancer, with its levels correlating with clinical stage and survival outcomes, thereby aiding clinical decision-making.[24] A recent study emphasized the clinical significance of lowering nadir CA-125 levels, showing that patients with levels below 10 U/mL experienced longer progression-free survival (PFS). However, the extent to which maximal surgical effort contributes to achieving these reduced CA-125 levels remains unclear, highlighting the need for further investigation into optimizing treatment strategies.[25]

In our study, increased Beta-hCG was observed only in malignant cases, 4 (19.05%). Nowak-Markwitz et al. demonstrated increased expression and widespread distribution of Beta-hCG in eight cases of ovarian epithelial carcinoma.[26] A study reported markedly increased hCG mRNA and protein expression in epithelial ovarian carcinoma, with significantly higher levels observed in advanced-stage disease. Both elevated hCG expression and the presence of tumor metastasis were shown to be independent predictors of poorer overall survival.[27] A study done by Lenhard M et al. assessed serum hCG levels in ovarian tumor patients and demonstrated hCG positivity in 68% of ovarian cancer tissues, with expression varying across histological subtypes. Tumor stage and grade were found to significantly affect hCG expression, and patients with hCG-positive tumors that were Luteinizing Hormone Receptor positive and Follicle-Stimulating Hormone Receptor negative showed improved five-year survival outcomes in their study.[28]

AFP is a fetal glycoprotein, useful as a tumor marker for the detection of malignancies such as yolk sac tumors, which predominantly occur in young women. It serves as a diagnostic tumor marker for several malignancies, including hepatocellular carcinoma, yolk sac tumors (YST), embryonal carcinoma of the ovary, and certain testicular cancers.[29] In our study, elevated AFP was seen in 4 (19.05%) of malignant ovarian tumors and was not seen in any benign or borderline cases. Elevated AFP levels were observed in 11 out of 17 immature teratoma cases (64.7%), with one patient showing a markedly high value exceeding 1000 ng/ml in a study done by Kawai et al.[30]

The most common mean age group for benign tumors was 32.34 ± 10.82 years, while those with malignant tumors had a slightly higher mean age of 33.48 ± 13.23 years in this study. Similarly, Prakash et al. conducted a study where a total of 52 ovarian tumor patients were included in the study, with a mean age at presentation of 42.69 ± 14.55 years.[31] In our study right and left ovary was affected in 131 (44.86%) and 128 (43.84%) of benign cases, respectively, and 14

(66.67%) and 5 (23.81%) of malignant cases, respectively. A study done by Tailor et al. showed that the right ovary was involved in 47.5% of cases and demonstrated a higher rate of malignancy (16.9%), whereas the left ovary was affected in 40.7% of cases, predominantly by benign tumors (33.9%). Bilateral and borderline ovarian involvement was uncommon.[32]

This study has a few limitations. Being conducted in a single center with a limited sample size may affect the generalizability of the findings.

CONCLUSIONS:

The majority of ovarian masses in this study were benign. Malignant ovarian tumors showed a higher frequency of elevated serum tumor markers compared to benign lesions. These findings highlight the predominance of benign ovarian masses and underscore the importance of histopathological examination as the definitive diagnostic tool.

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