ORIGINAL ARTICLE

HISTOPATHOLOGICAL SPECTRUM OF OVARIAN EPITHELIAL TUMOURS: A CROSS-SECTIONAL STUDY

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Background: Ovarian cancer (OC) poses a significant health burden, ranking 8th in women's cancers globally. Ovarian epithelial cancers (OEC) can present in a number of histopathologically distinct benign and malignant patterns. This study aims to assess the histopaythological characteristics of ovarian epithelial tumours in our local setting. **Methods:** This retrospective cross-sectional study, conducted at Ayub Medical College, Abbottabad, from Jan 2022 to Dec 2023, included 111 patients with histopathologically confirmed ovarian epithelial lesions. All biopsy records of OC during the study periods were retrieved and assessed for histopathological diagnosis. Confirmed cases of OEC were re-examined and included in the study. Records of patients' associated demographic data were obtained from HMIS of Ayub Teaching Hospital. Data were analysed on SPSS-27. **Results:** The mean age at diagnosis was 53.44±10.52 years, with the majority (73, 65.8%) being multipara and having unilateral lesions. Serous cystadenoma emerged as the most prevalent (42, 37.8%) benign tumour, while serous carcinoma dominated (22, 19.8%) malignant cases. Family history emerged as a significant factor, with 60.5% of malignant cases having a positive family history (p<0.001). Stratification by age at diagnosis, menarche, and menopause revealed no statistically significant difference between benign and malignant lesions in all strata. **Conclusions:** Serous cystadenoma is the most common benign tumour while serous carcinoma is the most common ovarian epithelial malignancy in Hazara division. The predominance of serous cystadenoma and serous carcinoma underscores the need for further exploration of familial risk factors.

Keywords: Ovarian Cancer, Ovarian Epithelial Cancers, Histopathology, Benign, Malignant

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INTRODUCTION

Ovarian cancer (OC) ranks as the 8th most common cancer among women globally, with over 313,000 new cases reported in 2020. It accounts for significant morbidity and mortality, with a 5-year survival rate of only 48.6%.[1,2] This dire prognosis is compounded by the fact that nearly 58% of ovarian cancer cases are diagnosed at advanced stages, where the 5-year survival rate plummets to 30.2%, compared to 92.6% for early-stage localized disease.[3] Despite its lower incidence compared to breast cancer, OC exhibits a mortality rate that is three times higher, earning it the notorious label of a 'silent killer' due to its insidious growth, lack of effective screening tools, and nonspecific symptoms.[4,5]

Histologically, ovarian cancers are broadly classified into epithelial, germ cell, and stromal tumours, with ovarian epithelial cancers constituting approximately 80% of all cases.[6] This group is further stratified into high-grade serous, low-grade serous (borderline), mucinous, endometrioid, and clear cell tumours, with high-grade serous carcinoma accounting for nearly 75% of ovarian epithelial cancers.[7] These tumours typically present at advanced stages, underscoring their clinical significance.

The clinical presentation of ovarian cancer is often subtle, characterized by nonspecific symptoms such as persistent pelvic discomfort, bloating, early satiety, and abdominal distension. These vague symptoms frequently result in delayed diagnosis and poor outcome.[8] Risk factors for ovarian cancer include non-modifiable and modifiable factors. Non-modifiable factors such as advanced age, a positive family history of ovarian or breast cancer, and genetic mutations like BRCA1 and BRCA2 significantly increase the risk.[9] Reproductive factors like early menarche, nulliparity, and late menopause also contribute to the risk of OC.[10] Modifiable factors, including obesity, smoking, sedentary lifestyles, and hormone therapy, provide opportunities for targeted preventive measures.[11]

Understanding the histopathological spectrum of ovarian epithelial tumours is crucial for improving diagnostic precision, identifying high-risk populations, and developing effective prevention strategies. This study aims to bridge the gap in existing literature by exploring the demographic, clinical, and histopathological characteristics of ovarian epithelial tumours in a local population.

METHODOLOGY

This cross-sectional study was conducted from Jan 2022 to Dec 2023 at the Department of Pathology Ayub Medical College, Abbottabad. The sample size comprised of 111 patients, calculated using the Open-

Epi online sample size calculator taking a confidence level of 95%, a desired precision of 8% and an estimated prevalence of malignant ovarian epithelial cancers of 23.6%.[12] Consecutive sampling was used. Inclusion criteria involved patients with histo-pathological diagnosis of either benign or malignant ovarian epithelial lesion. Exclusion criteria included patients who could not be traced for obtaining relevant history. The study was conducted after approval of the Ethics Committee of AMTI Abbottabad. Data collection involved obtaining informed consent from the patients/ attendants and collection of demographic information from patients using a proforma. Biopsy samples, fixed in 10% formalin, were prepared at the Pathology Department of Ayub Medical College Abbottabad. Sections of 4 µm thickness were cut, and stained with H&E stains for assessment under light microscope.

Malignant cells originating from the ovarian mesothelium showing nuclear stratification, hyperchromatic pleomorphic nuclei along with atypical mitotic figures, and infiltrating into the ovarian stroma with stromal reaction were considered malignant ovarian epithelial tumours. Benign lesions demonstrated well-differentiated epithelial cells with orderly growth patterns, lack of significant cellular atypia (uniform nuclei with minimal nuclear enlargement, hyperchromasia, or irregularity), and well-defined capsule.[7] The microscopic examination was carried by two consultant clinical histopahologists having at least five years of post-fellowship experience. After discussion the final diagnoses were reported.

Data was analysed on SPSS-27. Descriptive statistics, including Mean±SD for continuous variables and frequency and percentages for categorical variables were calculated. Chi-square and student's *t*-test were applied to determine the correlation between the presence of a benign or malignant lesion and the studied parameters like age, ages at menarche and menopause, laterality and parity, and $p \leq 0.05$ was considered statistically significant.

RESULTS

Table-1 illustrates the demographic and clinical characteristics of study participants presented in the form of either Mean±SD or frequencies and percentages. The mean age of the patients at the time of diagnosis was 53.44±10.52 years. Majority (73, 65.8%) of patients were multipara, had unilateral lesion 102 (91.9%), while 23 (20.7%) patients had a positive family history of female genital system malignancy and 73 (65.8%) cases had benign lesions.

Table-2 shows the frequency of the various benign and malignant lesions with which our patients were diagnosed. Patients were diagnosed with various lesions but serous cyst adenoma (benign tumour) was encountered in 42 (37.8%) cases, followed by serous carcinoma (malignant tumour) diagnosed in 22 (19.80%) cases and mucinous cyst adenoma (benign tumour) diagnosed in 18 (16.2%) cases.

Table-3 displays the categorical characteristics stratified by lesion histopathologic type, aiding in understanding lesion malignancy factors. None of the benign lesions had a positive family history, while 23 (60.5%) of malignant lesions did ($p<0.001$). Laterality of lesion and parity distribution showed no significant differences between benign and malignant cases ($p=0.953$) and ($p=0.767$) respectively.

Table-4 displays the cross-tabulation of continuous characteristics—age at diagnosis, age at menarche, and age at menopause—stratified by lesion type (benign *vs* malignant). No statistically significant differences were observed for these characteristics between patients with benign and malignant lesions, ($p>0.05$).

Table-1: Demographics and clinical characteristics of the study population

Characteristics	Mean±SD	
Age (Years)	53.44±10.52	
Age at Menarche (Years)	11.88±0.75	
Age at Menopause (Years)	48.76±3.54	
Laterality of lesion	**N**	**%**
Unilateral	102	91.9
Bilateral	9	8.1
Parity Status		
Nulliparous	14	12.6
Parity (1–3)	24	21.6
Multipara	73	65.8
Family history of female genital system malignancy		
Positive	23	20.7
Negative	88	78.3
Histopathologic type of lesion		
Benign	73	65.8
Malignant	38	34.2

Table-2: Frequency of benign and malignant lesions in our patients

Lesion	Frequency	Percentage
Serous Cyst-adenoma	42	37.80
Mucinous Cyst-adenoma	18	16.20
Serous Cyst-adenofibroma	7	6.30
Endometriotic Cysts	4	3.60
Benign Brenner's tumour	2	1.80
Serous Carcinoma	22	19.80
Mucinous Carcinoma	9	8.10
Endometrioid Carcinoma	5	4.50
Clear Cell Ca	2	1.80

Table-3: Cross-tabulation of categorical characteristics

Variable		Benign (n=73)	Malignant (n=38)	*p*
Laterality	Unilateral	67 (91.8%)	35 (92.1%)	0.953
	Bilateral	6 (8.2%)	3 (7.9%)	
Family history of female genital system malignancy	Positive	0 (00%)	23 (60.5%)	<0.001
	Negative	73 (100%)	15 (39.5%)	
Parity	Nulliparous	8 (10.9%)	6 (15.8%)	0.767
	Parity (1–3)	16 (21.9%)	8 (21.1%)	
	Multipara	49 (67.1%)	24 (63.1%)	

Table-4: Cross-tabulation of continuous characteristics

	Lesion type	N	Mean±SD	*p*
Age	**Benign**	73	53.18±10.218	0.717
	Malignant	38	53.95±11.213	
Menarche	**Benign**	73	11.8493±0.75776	0.515
	Malignant	38	11.9474±0.73328	
Menopause	**Benign**	55	48.5818±3.25287	0.523
	Malignant	30	49.1000±4.06287	

DISCUSSION

We investigated the histopathological spectrum of ovarian epithelial tumours among women who presented with suspected ovarian lesions. Our findings are largely consistent with previously published literature, although there may be slight variations depending on regional factors. The findings provide valuable insights into the patient characteristics, distribution of tumour types, and potential associations with clinic-pathological factors.

The mean age of our study participants at diagnosis was 53.44 years, aligning with the range reported in previous studies (49–57 years).[13–16] The majority of patients were multiparous (65.8%), similar to observations in other studies. For instance, a study conducted in India reported a mean age of 53 years for patients with ovarian neoplasms, while another study from Saudi Arabia found that the highest frequency of ovarian neoplasms occurred in women aged 40–65 years.[13,14] Additionally, a study from India reported that benign ovarian tumours were diagnosed mostly in patients between 20–40 years of age.[15] Regarding the prevalence of unilateral lesions (91.9%), this finding corroborate well with published literature. For example, a study from Saudi Arabia found that 63.2% of ovarian neoplasms were unilateral, while another study from India reported that only about 17% of cases involved bilateral lesions.[13,14]

Serous cystadenoma was the most frequently diagnosed benign tumour (37.8%), followed by mucinous cystadenoma (16.2%). This aligns with the established prevalence of these benign tumour types in ovarian epithelial tumours. Serous carcinoma was the most common malignant tumour (19.8%), consistent with its well-documented dominance among ovarian malignancies.

Serous cystadenoma is the most frequently diagnosed benign tumour, typically making up around 37–47% of benign ovarian tumours.[13,17] Serous carcinoma, specifically high-grade serous carcinoma, is the most dominant form of ovarian malignancy, representing nearly 70% of cases.[15,17] Furthermore, a study on the histopathological patterns of ovarian neoplasms in different age groups found that high-grade serous carcinoma 42 (19.8%) was the most common histological type among malignant cases while among the benign lesions, 73 (34.4%) were serous cyst-adenomas cases.[14] A study on the global incidence and temporal trends of OC by histologic subtype observed a consistent highest incidence of serous carcinoma among all, with 45% global incidence rate.[18] This global incidence rate of the malignant tumours is followed by mucinous carcinomas (13%), endometrioid carcinomas (13%), and clear cell carcinomas (6%).[18] They also reported that deviation from the general global trends of the incidence rates of the OC was most prominent in the Asian region where they have a relatively higher proportions of endometrioid, clear cell and mucinous carcinomas.

A notable finding in our study was the positive family history of female genital system malignancy in 20.7% of patients, which is higher than the prevalence reported in some studies (5–10%).[14,16] This finding warrants further investigation in larger cohorts to determine if it represents a regional trend or is attributable to other factors. However, it is well-established understanding that family history of ovarian and breast cancer is linked to an increased risk of ovarian cancer.[4,15,] This is said to be due to the BRCA-1 and BRCA-2 mutations associated with female genital malignancies especially breast, ovarian and endometrial cancers.[5] Our study identified a statistically significant association between family history and tumour malignancy. Patients with malignant lesions were significantly more likely to have a positive family history compared to those with benign lesions ($p<0.001$). Studies have shown that patients with malignant lesions are significantly more likely to have a positive family history compared to those with benign lesions.[19,20] For example, a large study from Nature Scientific Reports explored familial associations of histology-specific ovarian cancer with other cancers and found that the relative risk of ovarian cancer was 2.42 in families with one ovarian cancer patient and it reached 11.36 with two affected individuals.[16] Another study from Nature Communications demonstrated that family history of breast cancer showed a dose-response on ovarian cancer risk.[19] This finding underscores the potential role of family history as a risk factor for ovarian cancer, highlighting the importance of family history assessment in clinical practice. However, we did not observe any significant associations between laterality, parity, age at diagnosis, age at menarche, or age at menopause and tumour malignancy. Further research with larger sample sizes and diverse populations is needed to elucidate these potential relationships more definitively.

LIMITATIONS

Our study has limitations inherent to its cross-sectional design, precluding the establishment of causal relationships between observed factors and tumour malignancy. The sample size was moderate, potentially limiting the generalization of findings.

CONCLUSION

Our study contributes to the existing knowledge on the histopathological spectrum of ovarian epithelial tumours by characterizing patient demographics, tumour distribution, and clinicopathological associations in a Pakistani population. There is predominance of serous cystadenoma among benign tumours and serous carcinoma among malignant tumours, and potential significance of family history as a risk factor. Further research is warranted to explore the observed associations and gain deeper understanding of the factors influencing ovarian tumour development and progression in diverse populations.

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SMK: Concept, Study design, Literature search, Approval of the final manuscript
MT: Literature search, Critical review
SN: Concept, Study design
SMM: Data collection, analysis and interpretation
AR: Data collection, analysis and interpretation, Critical review and write-up
FJ: Data collection, analysis and interpretation, write-up of the manuscript

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