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ORIGINAL ARTICLE

Morphological and histopathological spectrum of ovarian lesions diagnosed at a tertiary care center in Karachi, Pakistan

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ABSTRACT

Objectives: To determine the clinicopathological spectrum and histopathological patterns of ovarian lesions and assess their distribution across different age groups among patients presenting to a tertiary care diagnostic center.

Methods: This descriptive cross-sectional study was conducted at Department of Histopathology, Dow Diagnostic Research and Reference Laboratory, Dow University of Health Sciences, Karachi, Pakistan, over 14 months following institutional ethical approval. A total of 222 ovarian specimens were examined histopathologically and classified according to World Health Organization classification. Clinical, gross morphological, and histopathological findings were recorded. Associations between lesion type, histological subtype, and age groups were analyzed using Fisher's exact test.

Results: Of the 222 patients, 124 (55.9%) aged 21-40 years. Majority (n=200) presented with unilateral lesions. Non-neoplastic lesions predominated (58.6%), followed by benign (35.1%), malignant (3.6%), and borderline neoplasms (2.7%). Follicular cysts (25.7%) and simple ovarian cysts (13.1%) were the most common non-neoplastic lesions, whereas serous cystadenoma (17.1%) and mucinous cystadenoma (6.3%) were the predominant benign neoplasms. Surface epithelial tumors constituted the largest neoplastic category (32.9%), followed by sex cord-stromal tumors (5.0%). Most patients presented with abdominal pain or abdominal mass. No significant association was observed between age group and lesion type (p=0.882), histological subtype (p=0.273), or surface epithelial tumor subtype (p=0.537).

Conclusion: Non-neoplastic ovarian lesions were more frequent than neoplastic lesions, with follicular cysts and serous cystadenoma representing the predominant non-neoplastic and neoplastic diagnoses, respectively. Ovarian lesions occurred across all age groups without significant differences in their histopathological distribution. Histopathological examination remains essential for accurate diagnosis and classification.

Keywords: Ovarian Diseases (MeSH); Neoplasms (MeSH); Ovarian Neoplasms (MeSH); Ovarian Cysts (MeSH); Pathology (MeSH); Histological Techniques (MeSH); Immunohistochemistry (MeSH); Neoplasm Grading (MeSH); Mixed Tumor, Malignant (MeSH); Age Distribution (MeSH). Diagnostic Techniques and Procedures (MeSH).

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INTRODUCTION

Ovarian lesions comprise a broad and heterogeneous spectrum of conditions, ranging from non-neoplastic cysts to benign, borderline, and malignant tumors, with diverse morphological and histopathological patterns.[1] Among gynecological malignancies, ovarian cancer remains one of the most fatal cancers, mainly because of its insidious onset, asymptomatic progression, and frequent diagnosis at an advanced stage. Globally, ovarian cancer ranks as the eighth most common cancer among women and accounted for approximately 3.7% of all female cancers and 4.7% of cancer-related deaths in 2020.[2,3] Recent global estimates reported 313,959 new cases of ovarian cancer worldwide in 2020, with an incidence rate of 6.6 per 100,000 women.[4] Similarly, in 2019, more than 294,000 cases and 198,000 deaths were documented, under-scoring its considerable global disease burden.[5] Although ovarian cancer is less common than several other female malignancies, it is associated with disproportionately high mortality, largely due to delayed detection. According to the 2020 World Health Organization classification, ovarian tumors are histopathologically categorized into epithelial, germ cell, and sex cord-stromal tumors. Epithelial tumors constitute nearly 70% of ovarian tumors and represent the most frequent subtype.[6]

Age distribution has an important influence on the occurrence and biological behavior of ovarian lesions. Evidence consistently shows that benign ovarian lesions are more frequent among younger women, particularly those in the reproductive age group,[7] whereas malignant tumors are more commonly encountered in postmenopausal women.[8] Recent institutional studies have reported that most ovarian tumors are benign, accounting for approximately 65–82% of cases, while malignant tumors constitute about 14–30% and borderline tumors around 2–5%, with broadly comparable findings across tertiary care centers in South Asia.[6,9] Surface epithelial tumors remain the most common histological subtype, comprising nearly 60-70% of ovarian

tumors, followed by germ cell tumors at 20-30% and sex cord-stromal tumors at 3-8%.10 In addition, global epidemiological data indicate that the highest incidence and mortality of ovarian cancer occur among women aged 50-69 years, with increasing rates observed in aging populations and in certain geographic regions.[5]

However, the histopathological spectrum of ovarian lesions shows considerable geographic variation. A study from Saudi Arabia conducted between 2016 and 2020 reported benign tumors in 64.4% of cases, malignant tumors in 29.4%, and borderline tumors in 6.2%, with the highest frequency observed in the 41-50 year age group. Similarly, recent WHO-based analyses from 2020 to 2024 have shown that benign lesions account for approximately 69% of ovarian lesions, while malignancies increase markedly after the age of 50 years, with notable variation in histological subtypes across different age groups.[6,12] Another study involving more than 250 cases also demonstrated that benign tumors are more common among younger women, particularly those aged 21–40 years, whereas malignant tumors increase significantly after the fifth decade of life. Epithelial tumors remain the predominant histological category across most age groups.[13] Collectively, these findings indicate that the pattern of ovarian lesions is not uniform across populations. Both tumor type and age distribution vary considerably between regions, highlighting the importance of conducting region-specific histopathological studies.

Despite advances in classification systems and diagnostic techniques, region-specific data on the relationship between patients' age and the morphological and histopathological features of ovarian lesions remain limited. Many available studies focus mainly on neoplastic lesions or do not adequately integrate demographic variables with histopathological findings. This restricts a clear understanding of local disease patterns, which is important for early diagnosis, risk stratification, and appropriate clinical management.

Therefore, the present study was conducted to determine the morphological and histopathological spectrum of ovarian lesions and to assess their frequency in relation to patients' age. By addressing this evidence gap, the study aimed to generate population-specific data that may improve diagnostic accuracy and support more effective, age-oriented clinical decision-making.

METHODS

This descriptive cross-sectional study was conducted in the Department of Histopathology, Dow Diagnostic Research and Reference Laboratory (DDRRL), Dow University of Health Sciences (DUHS), Karachi, Pakistan, over a period of 14 months. The study was initiated after approval from the Institutional Review Board of DUHS (Reference No. IRB-2727/DUHS/Approval/2022/1108; dated: November 14, 2022).

The sample size was calculated using the Epi Info sample size calculator. A minimum sample size of 222 was estimated, based on a 95% confidence interval, 3% margin of error and a previously reported frequency of hemorrhagic cysts of 5.5%.[14]

All ovarian lesion specimens reported at DDRRL were obtained from the Histopathology Department, DUHS. Patient consent was obtained through telephone contact. Surgical specimens included resected ovarian masses, tubo-ovarian masses, cystectomy specimens, ovarian biopsy specimens, and hysterectomy with salpingooophorectomy specimens. All specimens were received in 10% buffered formalin for fixation.

Relevant clinical information was recorded for each patient, including presenting symptoms, examination findings, and ultrasonographic findings, as documented in the histopathology requisition forms.

Each specimen was assigned a unique identification number. Gross examination was performed to assess the size, external appearance, consistency, and cut surface of the specimen. Representative tissue sections, approximately 1.5×1 cm in size, were taken from relevant areas. The tissues were processed through routine histopathological techniques, including dehydration in alcohol, paraffin wax embedding, sectioning into 3-5 µm thick sections, and staining with hematoxylin and eosin.

Histopathological slides were examined by the researcher and reviewed by a consultant histopathologist. The microscopic findings were correlated with the available clinical history, examination findings, and ultrasonographic features. Ovarian lesions were categorized according to the World Health Organization (WHO) classification. Neoplastic ovarian tumors were further classified into three major groups: surface epithelial tumors (SET), sex cord-stromal tumors (SCST), and germ cell tumors (GCT). Surface epithelial tumors were subcategorized into serous cystadenoma, serous cystadenocar-cinoma, serous borderline tumor, mucinous cystadenoma, mucinous borderline tumor, mucinous cystadenocarcinoma, Brenner borderline tumor, and endometrioid carcinoma. Sex cord-stromal tumors included the fibroma-thecoma group, while germ cell tumors included yolk sac tumor, dysgerminoma, mature cystic teratoma, and immature teratoma.[11]

Data were systematically entered into Microsoft Excel and analyzed using SPSS version 26. Continuous variables were presented as mean±standard deviation or median with interquartile range, depending on data distribution. Categorical variables were summarized as frequencies and percentages. Associations between categorical variables, including lesion type, histological subtype, and age groups, were assessed using the chi-square test or Fisher's exact test, where appropriate. A p-value of <0.05 was considered statistically significant.

RESULTS

Table 1 summarizes the clinicpathological characteristics of 222 patients with ovarian lesions. Most patients were aged 21-40 years (124, 55.9%). Lesions were almost equally distributed between the right (101, 45.5%) and left (99, 44.6%) sides, with bilateral involvement in 22 cases (9.9%). Most patients were married

Table I: Clinico-pathological characteristics of the study population

Characteristics		Frequency (n=222)	Percentage
Age (years)	≤20	30	13.5
	21-40	124	55.9
	41-60	42	18.9
	>60	26	11.7
Laterality	Right	101	45.5
	Left	99	44.6
	Bilateral	22	9.9
Marital Status	Unmarried	16	7.2
	Married-Nulliparous	39	17.6
	Married-Parous	167	75.2
Lesion Consistency	Cystic	97	43.7
	Solid	94	42.3
	Cystic and Solid	31	14.0
Clinical Presentation	Abdominal Pain	57	25.7
	Abdominal Mass	56	25.2
	Menstrual Irregularities	24	10.8
	Abdominal Pain + Mass	31	14.0
	Abdominal Pain + Menstrual Irregularities	39	17.6
	Post-Menopausal Bleeding	25	11.3
Lesion Type	Non-Neoplastic	130	58.6
	Neoplastic, Benign	78	35.1
	Neoplastic, Borderline	6	2.7
	Neoplastic, Malignant	8	3.6
Histological Subtype	Epithelial Tumor	73	32.9
	Sex Cord-Stromal Tumors	11	5.0
	Germ Cell Tumors	8	3.6

Table II: Distribution of ovarian lesion according to histopathological diagnosis

Type of Lesion			Frequency (n=222)	Percentage
Non-Neoplastic Lesion [n= 130 (58.6%)]		Endometriosis	12	5.4
		Follicular Cyst	57	25.7
		Corpus Luteal Cyst	20	9.0
		Simple Ovarian Cyst	29	13.1
		Hemorrhagic Cyst	12	5.4
Neoplastic lesion [n= 92 (41.4%)]	Surface Epithelial Tumors	SC	38	17.1
		SBT	3	1.4
		SCAC	4	1.8
		MC	14	6.3
		MBT	3	1.4
		MCAC	4	1.8
		BBT	5	2.3
		EC	2	0.9
	Sex Cord-Stromal Tumors	Fibroma- Thecoma Group	6	2.7
	Germ Cell Tumors	Dysgerminoma	3	1.4
		YST	3	1.4
		MCT	4	1.8
		IT	3	1.4

Note: SC: Serous Cystadenoma; SBT: Serous Borderline Tumor; SCAC: Serous Cystadenocarcinoma; MC: Mucinous Cystadenoma; MBT: Mucinous Borderline Tumor; MCAC: Mucinous Cystadenocarcinoma; BBT: Brenner Borderline Tumor; EC: Endometrioid Carcinoma; YST: Yolk Sac Tumor; MCT: Mature Cystic Teratoma; IT: Immature Teratoma.

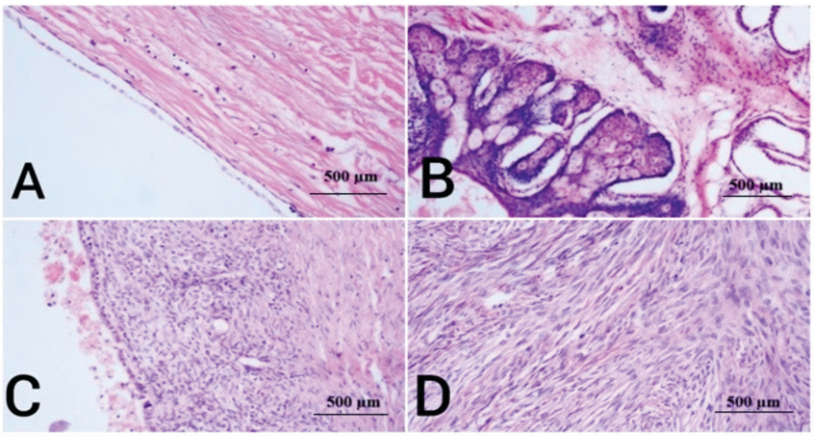

Figure 1: H&E-stained photomicrographs of ovarian lesions at 400× magnification. **(A)** Serous cystadenoma (SC) showing a cyst wall lined by a single layer of flat to columnar epithelium. **(B)** Mature cystic teratoma (MT) showing skin with adnexal structures including sebaceous glands and neural tissue. **(C)** Endometriosis shows endometrial glands and stroma with hemosiderin-laden macrophages. **(D)** Fibroma showing spindle-shaped cells arranged in a storiform pattern with hyperchromatic nuclei and inconspicuous nucleoli. Scale bar: 500 μm]. Staining: Hematoxylin and Eosin (H&E).

and parous (167, 75.2%). Cystic (97, 43.7%) and solid lesions (94, 42.3%) were comparable, while 31 (14.0%) were mixed. The most common presentations were abdominal pain (57, 25.7%) and abdominal mass (56, 25.7%). Non-neoplastic lesions predominated (130, 58.6%), followed by benign (78, 35.1%), malignant (8, 3.6%), and borderline tumors (6, 2.7%). Histologically, non-neoplastic lesions (130, 58.6%) and epithelial tumors (73, 32.9%) were most common.

Table II shows that non-neoplastic lesions constituted the majority of cases, with follicular cysts (57, 25.7%) and simple ovarian cysts (29, 13.1%) being the most common. Among neoplastic lesions, serous cystadenoma (38, 17.1%) and mucinous cystade-

Table III: Distribution of ovarian lesions and histological subtypes across age groups

Lesions		Age (years)				p-value*
		≤20	21-40	41-60	>60	
Lesion type	Non-Neoplastic	17	78	21	14	0.882
	Neoplastic, Benign	11	38	18	11	
	Neoplastic, Borderline	1	4	1	0	
	Neoplastic, Malignant	1	4	2	1	
Histological Subtype	Epithelial Tumor	11	37	17	8	0.273
	SCST	1	3	3	4	
	GCT	1	6	1	0	
	Non-Neoplastic Lesion	17	78	21	14	
Non-Neoplastic Lesion	Endometriosis	1	4	4	3	0.537
	Follicular Cyst	6	34	12	5	
	Corpus Luteal Cyst	2	15	1	2	
	Simple Ovarian Cyst	5	18	3	3	
	Hemorrhagic Cyst	3	7	1	1	
Surface Epithelial Tumors	SC	4	21	9	4	
	SBT	0	2	1	0	
	SCAC	0	2	1	1	
	MC	4	6	3	1	
	MBT	1	2	0	0	
	MCAC	1	1	1	1	
	BBT	0	2	2	1	
	EC	1	1	0	0	
Sex Cord-Stromal Tumors	Fibroma-Thecoma Group	1	1	1	3	
Germ Cell Tumors	Dysgerminoma	0	3	0	0	
	YST	0	0	2	1	
	MCT	1	2	1	0	
	IT	0	3	0	0	

Note: *Fisher exact test; SC: Serous Cystadenoma; SBT: Serous Borderline Tumor; SCAC: Serous Cystadenocarcinoma; MC:Mucinous Cystadenoma; MBT: Mucinous Borderline Tumor; MCAC: Mucinous Cystadenocarcinoma; BBT: Brenner Borderline Tumor; EC: Endometrioid Carcinoma; YST: Yolk Sac Tumor; MCT: Mature Cystic Teratoma; IT: Immature Teratoma

noma (14, 6.3%) were the predominant subtypes (Figure 1).

The analysis of ovarian lesions across different age groups is presented in Table III, showing no statistically significant associations. Age was not significantly associated with lesion type (p=0.882), histological subtype (p=0.273), or SET subtypes (p=0.537). Overall, non-neoplastic lesions were most common across all age groups, followed by benign neoplasms, while borderline and malignant lesions were infrequent. Among neoplastic lesions, SET were the most frequent, followed by SCST and GCT.

DISCUSSION

The present study highlights the broad clinicopathological spectrum of ovarian lesions encountered at a tertiary care referral laboratory. Non-neoplastic lesions predominated, followed by benign neoplasms, whereas malignant and borderline tumors were relatively uncommon. Follicular cysts and serous cystadenoma were the most frequent non-neoplastic and neoplastic lesions, respectively. Most patients belonged to the reproductive age group (21–40 years), although no significant age-related differences were observed in the histopathological distribution of lesions. These findings reflect the heterogeneous nature of ovarian lesions, which exhibit diverse morphological and histopathological characteristics and variable biological behavior. Given the nonspecific clinical presentation and limitations of preoperative diagnosis, histopathological examination remains the gold standard for accurate diagnosis, classification, and appropriate clinical management.

The present study demonstrated that non-neoplastic ovarian lesions predominated, followed by benign neoplasms, whereas malignant and borderline tumors were relatively uncommon. These findings are broadly consistent with previous histopathological studies reporting that benign and non-neoplastic lesions constitute the majority of ovarian pathology. Naik SN, et al.,[15] in a 10-year study, similarly reported that most ovarian neoplasms were benign (84%), with malignant tumors accounting for only 14.2%. They also identified surface epithelial tumors as the predominant neoplastic category and serous cystadenoma as the most common benign tumor. Likewise, a five-year institutional study from India reported that non-neoplastic lesions comprised 44% of all ovarian lesions, with follicular cysts representing nearly half of these cases, further supporting the predominance of functional cysts in routine ovarian pathology.[16]

The predominance of surface epithelial tumors (SET) observed in the present study is consistent with previous national and international reports. In a Pakistani series of 390 ovarian neoplasms, SET accounted for 63.1% of tumors, followed by germ cell tumors (29.5%) and sex cord-stromal tumors (6.9%).[9] Similar studies have likewise reported that SET constitute approximately 60-70% of ovarian neoplasms, confirming their predominance across diverse populations.[17,18]

Among epithelial tumors, serous cystadenoma was the most frequent subtype, followed by mucinous cystadenoma. These findings agree with previous studies identifying serous cystadenoma as the commonest benign ovarian neoplasm.[12,15,19] For example, Naik SN et al.[15] reported that serous cystadenoma comprised 47.1% of benign ovarian tumors, followed by mucinous tumors (18.4%), demonstrating a comparable histopathological pattern.

Germ cell tumors (GCT) and sex cord-stromal tumors (SCST) were relatively uncommon in the present study. This finding is consistent with previous reports showing that GCT constitute approximately 10-15% of ovarian neoplasms, while SCST account for 5-8%, with GCT occurring more frequently in younger women.[20,21]

No significant association was observed between age and lesion type or histopathological subtype. Similar findings have been reported in several hospital-based studies, where benign and non-neoplastic lesions were distributed across a wide age range despite an increasing frequency of malignant tumors with advancing age.[22] Likewise, Mehra P et al.[6] and Patel N et al.[23] found that although epithelial tumors were more common in older women, the overall association between age and histological subtype was not statistically significant. These findings suggest that, while certain ovarian lesions exhibit age-related trends, age alone may not reliably predict the histopathological pattern of ovarian lesions.

Limitations of the study

This study has several limitations. Its single-center design may limit the generalizability of the findings. Histopathological diagnosis was based solely on hematoxylin and eosin-stained sections, as immunohistochemistry was not routinely performed, which may have affected the characterization of selected lesions. In addition, inter-observer agreement and blinded slide review were not assessed, introducing the potential for observer bias. Finally, the sample size was calculated using the prevalence of hemorrhagic cysts, which may not fully represent the heterogeneous spectrum of ovarian lesions. Future multicenter studies incorporating immuno-histochemical evaluation and standardized patho-logical review are warranted to validate these findings.

CONCLUSION

Non-neoplastic ovarian lesions predominated, with epithelial tumors representing the most common neoplastic category. Although most lesions occurred in women of reproductive age, no significant association was observed between age and lesion type or histopathological subtype. These findings emphasize the importance of histopathological evaluation for the accurate diagnosis and classification of ovarian lesions. Further multicenter studies incorporating larger sample sizes and molecular and immunohistochemical analyses are warranted to improve the characterization and diagnosis of ovarian lesions.

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AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

SSR & UB: Conception and study design, acquisition, analysis and interpretation of data, drafting the manuscript, approval of the final version to be published

BS & FD: Acquisition, analysis and interpretation of data, critical review, approval of the final version to be published

SHS & LA: Study design, drafting the manuscript, critical review, approval of the final version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

Authors declared no conflict of interest, whether financial or otherwise, that could influence the integrity, objectivity, or validity of their research work.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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