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*Corresponding Author: Shahad Alaa Jabbar
Email: shahad.alaa21001a@comed.uobaghdad.edu.iq

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Histopathological Spectrum of Ovarian Lesions Among Iraqi Women

Shahad Alaa Jabbar[1*], Shams Sabah Kadhim[1], Sara Sattar Salman[1], Ameer Dhaher Humaidi[2]

[1] Family and Community Medicine (Epidemiology), Baghdad College Of Medicine, University Of Baghdad. Baghdad, Iraq.
[2] Department of pathology - Baghdad College of Medicine-University of Baghdad. Baghdad, Iraq.

Abstract

Ovarian cystic lesions are a prevalent issue in clinical practice and amongst women of all ages worldwide, encapsulating a multitude of entities ranging from benign functional cysts to complex neoplasms.

In Iraq, ovarian cancers are notably significant, ranking as the fifth most common cancer amongst females according to the Iraqi Cancer Registry of 2022. This study is a retrospective observational study that included 209 samples obtained in the period from 2021-2024, all are female patients between the ages of 10 to 65 years, who were diagnosed with an ovarian mass and who underwent cystectomy or total abdominal hysterectomy with bilateral salpingooophorectomy. We analyzed the prevalence of ovarian cysts and tumors in Iraqi female population and how each type of lesion correlate with the age of the patient and the size and site of the lesion using SPSS statistics 26. serous cystadenoma was the most common diagnosis in this study, accounting for 33% of cases, followed by teratoma (17%) and follicular cysts (15%). the majority of participants in this study were aged 40–49 years. most lesions in this study were unilateral, with 41% located on the right side, 39% on the left, and 5% bilateral. Benign lesions accounted for 94% of cases in this study, with malignant tumors representing 5% of cases.

Significant associations were found between diagnosis and size and diagnosis and laterality. Larger tumors (>5 cm) were mostly neoplastic, with high grade serous adenocarcinomas comprising the majority of malignant cases.

Keywords: Histopathology, Ovarian Cysts, Neoplastic, None neoplastic

Introduction

Background and Epidemiology

The paired ovaries are crucial organs when it comes to fertility and regulation of reproductive activity in women, chiefly by controlling the development of the dominant follicle and producing two essential hormones namely estrogen and progesterone (1).

Ovarian cystic lesions are a prevalent issue in clinical practice and amongst women of all ages worldwide, encapsulating a multitude of entities ranging from benign functional cysts to complex neoplasms. These lesions can present as an incidental finding during a surgical operation and imaging or show variable manifestations including pelvic mass, abdominal pain, vaginal bleeding or hormonal imbalances (2). A pronounced variation also exists in their histopathological characteristics, and potential for malignancy, which complicates their management and requires a thorough understanding of their nature (3). In Iraq, ovarian cancers are notably significant, ranking as the fifth most common cancer amongst females according to the Iraqi Cancer Registry of 2022 (4).

This highlights the critical need for comprehensive studies on the histopathological spectrum of ovarian cystic lesions to improve clinical sequelae and promote patients' quality of life.

Functional Cysts

Functional or physiological cysts, as the name implies, are a variation of the normal physiology of the ovary during the menstrual cycle. As part of the normal physiology, the mature follicle ruptures to release the egg leading to ovulation, however, if such follicle fails to rupture it forms what is known as a follicular cyst (5).

Follicular cysts are under hormonal stimulation and thus continue to grow becoming in some cases as large as 18 cm, highlighting the potential for significant clinical impact even among benign lesions (6). When a Graafian follicle or follicular cyst bleeds, a complex hemorrhagic ovarian cyst (HOC) is formed (7).

A corpus luteum cyst is defined as persistent growth of the corpus luteum for months after ovulation despite no fertilization leading to fluid buildup (8). Functional cysts are also considered the most common type of ovarian cysts developing in female fetuses due to stimulation by maternal hormones transplacentally (9). Endometriomas, occurring in approximately 17 to 44% of women with endometriosis, can vary greatly in size, ranging from small, densely fibrotic cysts measuring 1-3 cm to large cysts over 20 cm with varying levels of fibrosis (10). These lesions, often called "chocolate cysts" due to the thick, dark brown fluid they contain, are believed to form either from the invasion or metaplasia of functional cysts by endometriotic tissue or from ovarian surface

endometriosis that bleeds into the ovarian cortex (11).

Functional cysts commonly resolve without treatment, however, occasionally due to the asymptomatic nature and the diagnostic delay these cysts can present with complications such as rupture or torsion, mandating medical or surgical intervention (8).

Another important category is cortical inclusion cysts (CICs), which have linked to the development of epithelial ovarian carcinomas, particularly high-grade serous carcinomas (HGSCs). These cysts are believed to arise from the invagination of ovarian surface epithelium, which undergoes metaplasia and potentially neoplastic transformation (12).

Neoplastic Cysts

Neoplastic cysts, on the other hand, can be either benign, borderline, or malignant and arise from a genetic mutation leading to uncontrolled cell growth. According to the WHO classification 2020 (13). Ovarian tumors, either benign or malignant, are grouped into various categories:

surface epithelial tumors, germ cell tumors, sex cord-stromal tumors, metastatic tumors, and other miscellaneous types. Surface epithelial neoplasms are particularly significant as they represent about two-thirds of all primary ovarian neoplasms and nearly 90% of malignant ovarian tumors (13). They include entities such as serous and mucinous cystadenomas and adenocarcinomas as well as brenner tumors which are rare (14).

Serous cystadenomas are the most common type of epithelial ovarian tumors and they are particularly recognised by their potential to become malignant if left untreated (15).

Mucinous cystadenomas, which are sometimes associated with dermoid cysts or Brenner tumors, are notable for their large size and the presence of KRAS mutations in a significant proportion of cases (16).

Germ tumors notably include teratomas, derived from the Greek word "teras" meaning monster, due to their varied morphological appearance often containing skin and hair, teeth, bones on gross examination. They can be mature and benign accounting for 20% of ovarian germ cell tumors, with only 1% having immature malignant components (17). Ovarian teratomas are the most frequently occurring ovarian tumors in the paediatric age group (18). Other germ cell tumors include dysgerminoma, endoderml sinus tumor and choriocarcinoma.

Sex cord stromal tumors are those associated with estrogen or androgen production including granulosa cell tumors and sertoli leydig tumors, respectively (19). Another subtype is fibroma which can be associated with meigs syndrome (20).

Metastatic ovarian are most commonly secondary to gastric carcinoma and often given the name krukenberg tumor only if it is proved to be a signet cell adenocarcinoma (21).

Ovarian Carcinoma

Ovarian carcinomas are grouped into 2 types based on their behavior. Type 1 tumors are mostly low-grade with the exception of clear cell tumors, slowgrowing, and diagnosed early, with a good prognosis. In contrast, Type

2 tumors are high-grade, aggressive, and often identified at advanced stages. They grow rapidly, show high chromosomal instability, and frequently involve Tp53 mutations (22).

The etiology of ovarian cancer is not completely understood, nonetheless, studies have shown that the potential for malignancy increases with advancing age,

making "age" a critical factor in the diagnosis and management of ovarian malignancy (23).

In regard to the size of the lesion, larger sizes (>7cm) prompts further follow up and investigation but it doesn't correlate independently with the risk of malignancy (23).

Certain types of ovarian neoplasms, such as high-grade serous carcinoma (HGSC), are highly aggressive and it was found that 70% display KRAS mutations (24).

Furthermore, serous tumors including cystadenoma, adenofibroma, and surface papilloma exhibited pathogenic variants of BRCA1 or BRCA2 (on chromosome 17q21.31, 13q13.1 respectively), so patients with positive family history of cancer especially breast and ovarian are regarded at increased risk (25).

The most common genetic change in high-grade serous ovarian cancer (HGSOC) is a mutation of TP53 gene. The effects of TP53 hotspot mutations on HGSOC patient outcomes and possibly TP53 function vary. Therefore, the state of specific TP53 abnormalities may affect how well a patient responds to treatment and the choice of treatment (26). Current screening strategy focus on U/S in conjunction with CA-125 measurements of high risk groups. Ongoing research is being carried in this area to improve sensitivity and specificity of screening protocols (27).

Aim of the study

This study seeks to analyze the prevalence of the different types of ovarian masses in Iraqi female population and how each type correlate with the age of the patient, size and site of the lesion. In doing so, Build upon and enrich the existing body of research.

1. Provide insight about factors related to the development and progression of the both benign and malignant lesions with the intention of creating the basis for further research.
2. Encourage action to improve diagnostic strategies aiming at early detection of ovarian cancer.

Materials &Methods

Study Design

This study was carried out as a retrospective observational study with data gathered from archived documents in the pathology department of Fatima Al-Zahraa Maternity Hospital, AL-Elwea Maternity Hospital and The National Centre of Educational Laboratories.

Sample size: 209 samples were obtained in the period from 2022-2024

Inclusion criteria: Any female patient of any age group who were diagnosed with an ovarian mass and who underwent cystectomy or total abdominal hysterectomy with bilateral salpingo-oophorectomy.

Exclusion criteria: Non-ovarian masses, abscess and polycystic ovarian lesions, patients with missing data about age and those who were conservatively managed were excluded. For the purpose of this study, the data about histopathologcal diagnosis, patient's age, and type of lesion, site and size were retrieved.

All patient data were kept confidential. Data was analyzed using SPSS statistics 26.

Results

Histopathological Diagnosis:

Serous cystadenoma were the most common diagnosis among participants (68 cases, 33%) followed by teratoma (36 cases 17%) with the least found diagnosis being transitional cell carcinoma (1 case, <1%) and fibroma (3 cases, 1%) as illustrated in Figure 1. A percentage of 68% of the lesions were neoplastic, while 32% were none neoplastic, as shown in Table 1.

Age of participants: In this study, most of the participants were aged 40-49 (56, 27%) years followed by those aged between 20-29 years (45, 22%), with patients ages 60-69 were the less reported age group (2, 1%) as shown in Figure 2.

Type of lesion:

Relation between type of lesion and age:

The results showed that tumors were distributed about equally every ten years from 20-29 years to 50-59 years, also non-neoplastic masses were distributed equally every ten years despite it were more among those aged 40-49 years (30%), as shown in Table 2. No significant association was found between type of lesion and age (P value = 0.484> 0.05).

Table 1: Type of lesion

Type of lesion	Frequency	Percent
Neoplastic	144	68%
None neoplastic	65	32%
Total	209	100%

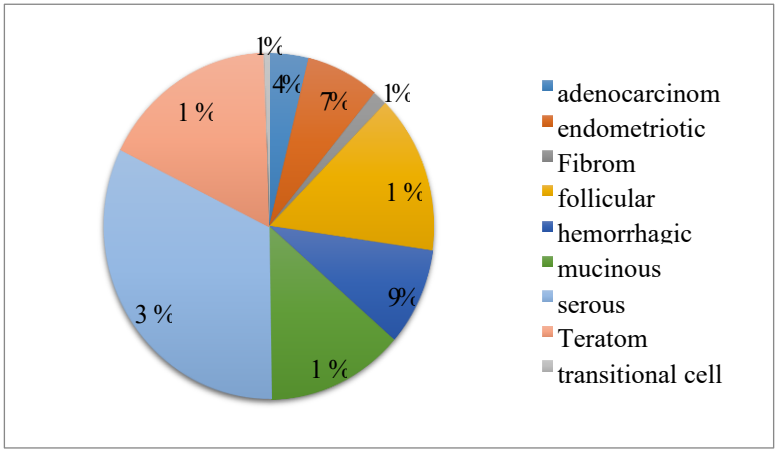

Figure 1: Histopatholoical diagnosis

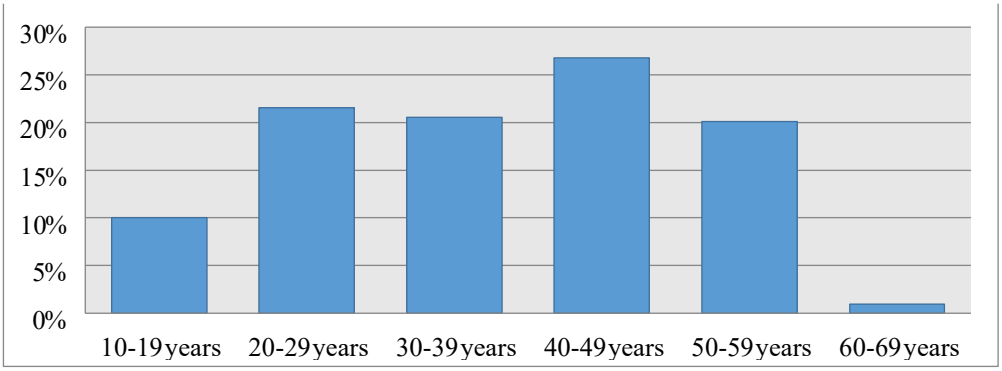

Figure 2: Age of participant

Table 2: Relation between type of lesion and age

	Age							Total
	10-19 years	20-29 years		30-39 years	40-49 years	50-59 years	60-69 years	
Type	neoplastic	Freq.	13	25	23	25	21	2	109
		%	12%	23%	21%	23%	19%	2%	100%
	nonneoplastic	Freq.	8	20	20	31	21	0	100
		%	8%	20%	20%	31%	21%	0%	100%
Total	21	45		43	56	42	2	209
Chi square	4.473							
p value	0.484							
Association	Not significant							

Relation between age and diagnosis:

Serous cystadenomas and follicular cyst were most commonly among those aged 40-49 years, while teratoma and mucinous cystadenomas were most common among aged between 20-29 years, accordingly no significant association was found between age and diagnosis. As shown in Table 3.

Size of the lesion:T

he results showed that 38% (80 cases) of the lesions were 2-5 cm in size and about the same percent was of size more than 5 cm, as shown in Figure 3.

Relation between type of lesion and size:

Majority of tumors are more than 5 cm in size (55%) while majority of none neoplastic lesions were 2-5 cm in size (47%), as shown in Table 4. A significant association was found between type of lesion and size (P value = 0.001< 0.05).

Table 3: Relation between age and diagnosis

Diagnosis	Age						Total
	10-19 years	20-29 years	30-39 years	40-49 years	50-59 years	60-69 years	
adenocarcinoma	0	0	1	3	4	0	8
endometriotic cyst	0	5	5	3	2	0	15
Fibroma	0	0	1	1	1	0	3
follicular cyst	2	8	5	12	4	0	31
hemorrhagic cyst	4	5	3	4	3	0	19
mucinous cystadenoma	2	9	5	7	5	0	28
serous cystadenoma	8	6	13	22	17	2	68
Teratoma	5	12	10	3	6	0	36
transitional cell carcinoma	0	0	0	1	0	0	1
Total	21	45	43	56	42	2	209
Chi square	43.25						
P value	0.335						
Association	**Not significant**						

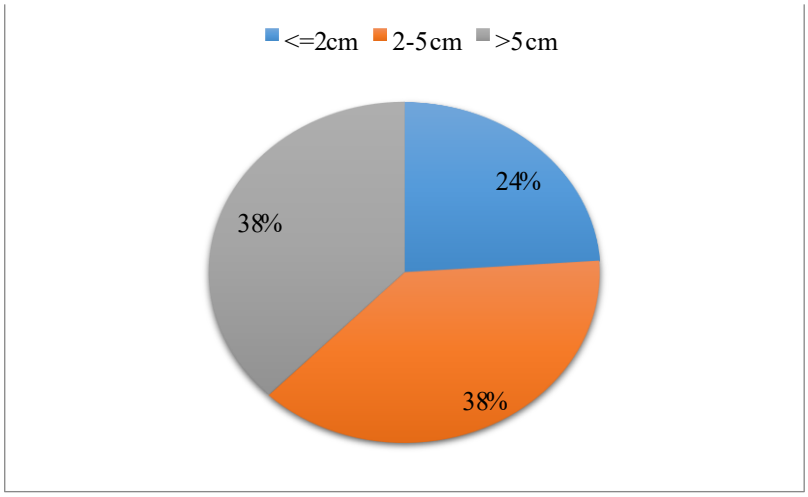

Figure 3: size of the lesion

Table 4: Relation between type of lesion and size

		Freq. & %	Size			Total
			<=2 cm	2-5 cm	>5 cm	
Type	neoplastic	Freq.	17	33	60	109
		%	16%	30%	55%	100%
	nonneoplastic	Freq.	33	47	19	100
		%	33%	47%	19%	100%
Total			50	80	79	209
Chi square			48.466			
P value			0.001			
Association			Significant			

Side of lesion:

Table 5 shows that 41% (86 cases) of the patients their lesion was on the right-side while 39% (82 cases) of them was on the left side and 5% (10 cases) were bilateral. As demonstrated in Figure 4.

Relation between type and lesion side:

In this study about 45% (49 cases) of tumors were on the left side and 36% (39 cases) were on the right side while 47% (47 cases) on non-neoplastic lesions were on the right

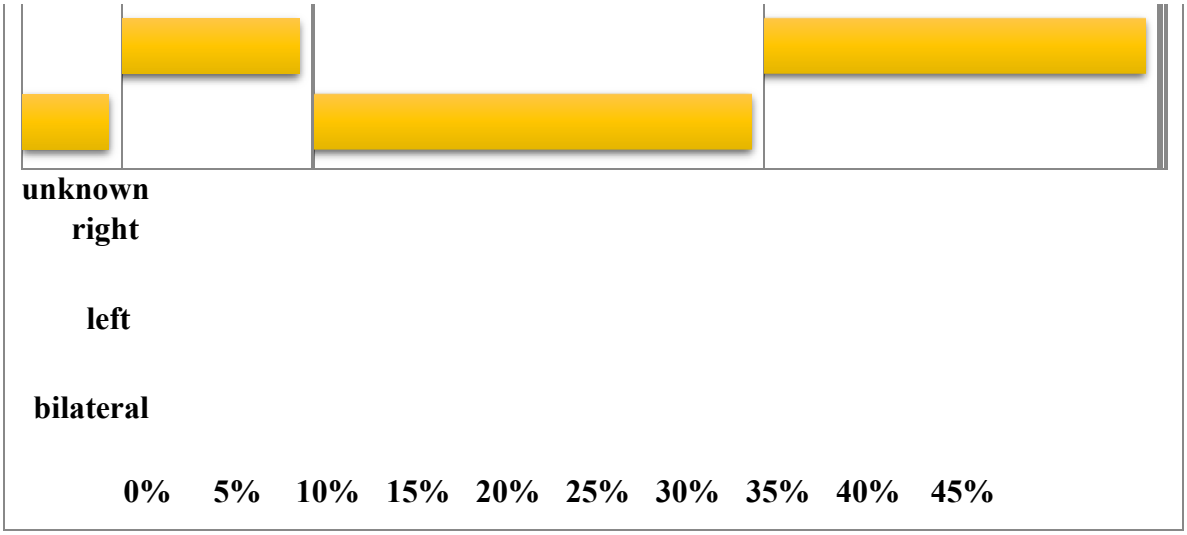

Figure 4: Side of the lesion

side and 33% of it were on the left side, as shown in Table5. Accordingly, no significant association was found between type and side of lesion (P value 0.117).

Table 5: Relation between type of lesion and side

		Freq. & %	Site				Total
			bilateral	left	right	unknown	
Type	Neoplastic	Freq.	3	49	39	18	109
		%	3%	45%	36%	17%	100%
	None neoplastic	Freq.	7	33	47	13	100
		%	7%	33%	47%	13%	100%
Total			10	82	86	31	209
Chi square			5.896				
P value			0.117				
Association			Not significant				

Relation between diagnosis and the laterality:

Teratoma and and serous cystadenomas were commonly of the left side (20%, 35% respectively), although serous cystadenoma had quite a similar percentage on the left and right side (35%, 34% respectively). On the other hand, endometriotic cyst was the most common lesion to present bilaterally, as shown in Table 6. A significant association was found between diagnosis and the site (P value = 0.032< 0.05).

Lesion behavior:

In the majority (196 cases, 94%) of the participants the lesion was benign on histopathological examination with only 10 lesions (5%) found to be malignant and 3 cases (1%) were of borderline in nature, as shown Figure 5.

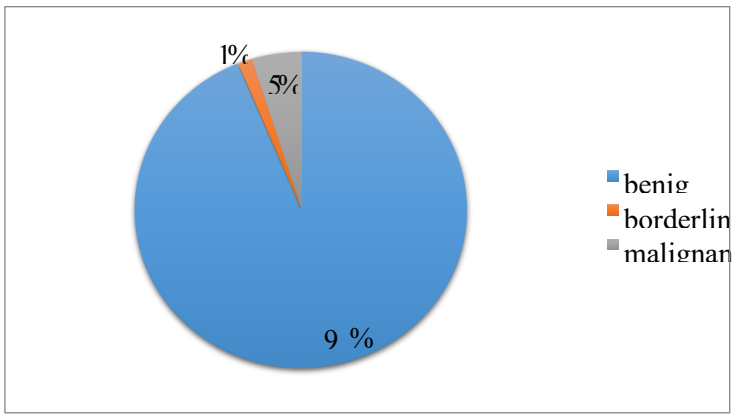

Figure 5: Lesion behavior

Table 6: Relation between diagnosis and the laterality.

		Site								Total
		bilateral		left		right		unknown		
		Freq.	%	Freq.	%	Freq.	%	Freq.	%	
adenocarcinoma		2	20%	1	1%	2	2%	3	10%	8
Diagnosis	endometriotic cyst	3	30%	3	4%	5	6%	4	13%	15
	Fibroma	0	0%	2	2%	0	0%	1	3%	3
	follicular cyst	2	20%	13	16%	10	12%	6	19%	31
	hemorrhagic cyst	0	0%	5	6%	11	13%	3	10%	19
	mucinous cystadenoma	1	10%	12	15%	15	17%	0	0%	28
	serous cystadenoma	1	10%	29	35%	29	34%	9	29%	68
	Teratoma	1	10%	16	20%	14	16%	5	16%	36
	transitional cell carcinoma	0	0%	1	1%	0	0%	0	0%	1
Total		10	100%	82	100%	86	100%	31	100%	209
Chi square		38.277								
P value		0.032								
Association		Significant								

Discussion

This study offers a comprehensive analysis of the histopathological spectrum of ovarian masses among women in Baghdad, with an emphasis on their laterality, size, histological subtypes, and malignancy rates.

Regarding histopathological diagnosis, serous cystadenoma was the most common diagnosis in this study, accounting for 33% of cases, followed by teratoma (17%) and follicular cysts (15%). This aligns with findings by Batool et al. (2022) (28) and Ibrahimkhil et al. (2022) (29), where serous cystadenomas were the predominant benign tumors. The prominence of follicular cysts over corpus luteum cysts in this study may reflect a higher prevalence of functional cysts in the sampled population, a pattern partially consistent with findings from Zahra (2016) (30) in Qatari women.

As for age Distribution, the majority of participants in this study were aged 40–49 years, followed by the 20–29 age group. This distribution aligns with findings from Sabbagh et al. (2023) (31). where most ovarian masses were diagnosed in women aged 40 and above in Kerbala City. However, Laul et al. (2020) (32) reported a broader age range for benign ovarian masses, with a higher frequency in younger women aged 20–29. These variations emphasize the influence of regional and demographic factors on ovarian mass presentations.

It was also revealed that the size varied significantly, with 38% measuring 2–5 cm and another 38% exceeding 5 cm. larger lesions (>5 cm) were predominantly serous cystadenomas and teratomas, demonstrating a significant correlation between diagnosis and size ($p = 0.001$). These findings are in line with Laul et al. (2020) (32), where benign lesions averaged 5–6 cm and malignant tumors exceeded 7 cm, Such observations underscore the importance of the size as a diagnostic indicator, particularly for distinguishing benign from malignant masses.

Additionally, most lesions in this study were unilateral, with 41% located on the right side, 39% on the left, and 5% bilateral. A significant association between diagnosis and laterality ($p = 0.046$) was observed, with serous cystadenomas frequently presenting unilaterally. This finding aligns with Sabbagh et al. (2023) [31], where right-sided lesions predominated in Kerbala City. Notably, endometriotic cysts were more often bilateral, consistent with findings by Nori et al. (2023) (8) at Kadhimiya Hospital in Baghdad. The regional aspect is critical, as this study, conducted in Baghdad, complements and extends the existing data by capturing different hospital and patient demographics. In regard to malignancy and neoplasia. Benign tumors accounted for 94% of cases in this study, with malignant tumors representing 5%. Serous Adenocarcinomas were the most common malignancy, a pattern consistent with global and regional findings, including those reported by Ibrahimkhil et al. (2022) and Abena et al. (2023) (29-33). These findings reinforces the importance of histopathological examination in guiding clinical management.

Regional Comparisons and Implications

This study complements existing data from Iraq by providing insights from Baghdad, adding to findings from Kerbala (Sabbagh et al.) and Kadhimiya (Nori et al.). The prevalence of benign ovarian cysts in this study mirrors those reported in these regions

and aligns with trends observed in Pakistan and Afghanistan. However, differences in laterality, size, and histological subtypes highlight the potential influence of local environmental, genetic, and healthcare factors.

Limitations and Future Directions

The study is limited to data from 3 centers in Baghdad and may not fully capture variations across Iraq. Future research should explore genetic and molecular risk factors to better understand regional differences in ovarian cyst presentations and improve diagnostic accuracy.

Conclusions

Serous cystadenoma was the most common type (33%), followed by teratoma (17%) and follicular cyst (15%). Significant associations were found between diagnosis and factors such as size and laterality. Larger tumors (>5 cm) were mostly neoplastic, with high grade serous adenocarcinoma comprising the majority of malignant cases. These findings emphasize the importance of early detection and tailored management strategies.

Recommendations

1. Enhanced Screening and Early Diagnosis: It is recommended that healthcare providers in Baghdad implement more widespread screening protocols for ovarian cysts and tumors, focusing on early detection to improve patient outcomes and reduce the risk of malignancy.
2. Targeted Research on Regional Variations: Further studies should investigate the specific histopathological variations of ovarian cysts and tumors in different regions of Iraq, considering potential genetic, environmental, and socio-economic factors.
3. Public Awareness and Education: Efforts should be made to raise awareness among women regarding the importance of regular gynecological check-ups, particularly for those at higher risk of developing ovarian pathologies, to promote early intervention and better health outcomes.

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