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OVARIAN CYSTS (A HISTOPATHOLOGICAL STUDY)

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ABSTRACT

Background: Ovarian cysts are the most common cause of enlarged ovaries.The diagnosis of an ovarian cyst causes considerable anxiety for women because of fear of malignancy fortunately the majority of them are benign

Objective: To provide a clinicopathological assessment of ovarian cyst, and focus on the frequency, location, clinical presentation, histopathological and gross appearance of each type and investigate the presence of mucin in different types of ovarian cysts.

Materials and methods: A review of 756 ovarian cysts, representing all the referred cases to Teaching Laboratories of Medical City Teaching Hospital, in period from January 2000 to August 2005, these cases were divided into two major groups: non neoplastic cysts (464 cases) and neoplastic (292 cases) and each group was subdivided according to histologic types. Special stains of mucin including PAS (periodic acid Schiffs) stain and AB (Alcian blue) stain PH 2.5 were applied to a group of these cysts randomly selected.

Results: The age of patients range from 11-78 years, the predominant age group was 20-29 years, 427 (56.48%) were on the right side, 271 (35.84%) were on the left side, 58 (7.67%) were bilateral. The commonest presenting symptoms were both the incidental in 286 (37.83%) and pain in 283 (37.43%); the cysts were mainly obtained from cystectomy operation in 636 (48.01%), and total abdominal hysterectomy and bilateral salpingo-oopherectomyoperations in 328 (43.38%). Gross appearance of each type was studied. Regarding histochemistry results: the*serous*cysts: **benign**, 7 were positive for neutral mucin, 10 for acidic mucin, **borderline**: 2 were positive for acidic and neutral mucin, **malignant** cysts: 6 were positive for acidic and neutral mucin.The*mucinous*cysts: **benign** all were positive for neutral mucin, 18 were positive for acidic mucin, the **borderline** was positive for both acidic and neutral mucin, **malignant** cysts 9 were positive for neutral mucin and 8 for acidic mucin. *Teratoma*: 4 positive for neutral mucin and 2 for acidic mucin, *endometroid* tumor and *granulosa* cell tumor were positive for both types of mucin. *Follicular* cysts: 12 weak positive for neutral mucin, all cases negative for acidic mucin. *Corpus luteal* cysts: 14 were positive for neutral mucin and all were negative for acidic mucin.

Conclusion: These findings suggested that non neoplastic cysts are the most common types of ovarian cysts, and among these the most common are the functional cysts including corpus luteal and follicular cysts. Teratoma and serous cysts are the most common neoplastic cysts followed by mucinous cysts. Most ovarian cysts are found on the right side, complementary study of mucin secretion in ovarian cysts appears to be helpful in histological classification of the cysts.

Ovary is an important progeny production organ that consists of multipotentmesenchymal cells and totipotent sex cells. Because of its histological characteristics, almost any type of tumor can occur within it. One of the most common causes of ovarian enlargement is the ovarian cyst, which can broadly divided into non-neoplastic and neoplastic cysts.[1,2,3]

Non neoplastic ovarian cysts include: follicular, corpus luteum, theca lutein ,polycystic ovary, inclusion cyst, developmental cyst, cyst of Rete ovarii, epidermoidcyst, inflammatory cyst, ovarian endometriosis.[2,4,5,6]

There are numerous types of ovarian tumors, about 80% are benign and mostly occur in young women, the malignant tumors mostly occur in older women between 40-65 years.[3]

Most of ovarian cysts are asymptomatic and it spontaneously disappear, it can cause pressure symptoms when it is large like pelvic pain, frequency …..etc. It can be diagnosed by ultrasound. When the patient had clear, simple ovarian cyst, she requires no treatment, especially when the cyst below 5 cm in diameter, usually it is followed up by several ultrasound. There is good supportive evidence that even with more than 10 cm ovarian cyst, it can be monitored by ultrasound and it is safe to be under observation.[7,8,9,10]

In this study clinicopathological assessment of the ovarian cyst is done focusing on their frequency, site, clinical presentation, gross and histological criteria.The pattern of mucin distribution in different cysts was studied.

II MATERIALS AND METHODS:

Materials:

A retrospective study of 756 cases of ovarian cysts representing all cases of ovarian cysts referred to teaching laboratories of medical city teaching hospital in the period from January 2000 to August 2005.

The collected specimens were either of cystectomy, total abdominal hysterectomy with bilateral or unilateral salpingo-oopherectomy, wedge resection or ovarian tissue in association with cystectomy.

Methods:

For histochemical staining method we used Hematoxylin and eosin, periodic acid Schiff with or without diastase to demonstrate mucin and differentiate it from glycogen which stained strongly positive with periodic acid Schiff only,Alcian blue PH 2.5.

Statistical analysis was performed using statistical package social science (spss) version 11. Computer software in addition to Microsoft excel xp. Student test and chi square test X2 were used to evaluate the probability of data using < 0.05 as a significant value.

Results:

Patients distribution according to years (in period equal approximately to six years) are shown in table 1 below.

Table 1: Distribution of ovarian cysts in years (2000-2005)

Type of ovarian cysts	years												total	
	2000		2001		2002		2003		2004		2005			
	No	%	No	%	No	%	No	%	No	%	No	%	No	%
Non-neoplastic														
- follicular	50	25	36	18	34	17	25	12.5	38	19	17	8.5	200	26.4
- corpus luteal	37	18.2	30	14.8	37	18.2	31	15.3	43	21.2	25	12.3	203	26.8
- inclusion	6	20	4	13.3	5	16.7	6	20	4	13.3	5	16.7	30	3.96
- chocolate	2	15.4	1	7.7	5	38.4	3	23.1	1	7.7	1	7.7	13	1.71
- Para-ovarian	10	55.5	5	27.8	-	-	-	-	3	16.7	-	-	18	2.38
Neoplastic														
Serous cysts:														
Benign	24	23.1	10	9.61	18	17.3	12	11.53	25	24.03	15	14.42	104	13.75
Borderline	1	33.3	-	-	-	-	-	-	1	33.3	1	33.3	3	0.39
Malignant	1	14.2	2	28.5	2	28.5	1	14.2	-	-	1	14.2	7	0.92
Mucinous cysts:														
Benign	16	33.3	5	10.4	7	14.5	8	16.7	6	12.5	6	12.5	48	6.34
Borderline	1	100	-	-	-	-	-	-	-	-	-	-	1	100
Malignant	3	30	2	20	1	10	2	20	2	20	-	-	10	1.32
Miscellaneous														
Teratoma	23	20	24	20.8	24	20.8	21	18.26	16	13.91	7	3.47	115	15.21
Endometroid T	-	-	-	-	-	-	1	50	-	-	1	50	2	0.26
Yolk sac T	-	-	-	-	-	-	-	-	1	100	-	-	1	0.132
GranulosacellT	-	-	-	-	-	-	1	100	-	-	-	-	1	0.132
Total	174	23.01	119	15.7	133	17.59	111	14.68	140	18.51	79	10.44	756	100

P value = 0.95 NS $x^2 = 1.07$ **(between neoplastic and non neoplastic cysts)**

P value = 0.05 S $x^2 = 17.81$ **(among the neoplastic cysts)**

Patients' distribution according to their age are shown in table 2 below

Table 2: Age distribution in years

Type of ovarian cysts	Age in years													
	10-19		20-29		30-39		40-49		50-59		60-69		70-79	
	No	%	No	%	No	%	No	%	No	%	No	%	No	%
Non-neoplastic														
- follicular	22	11	40	20	39	19.5	72	36	22	11	5	2.5	-	-
- corpus luteal	23	11.33	61	30.1	46	22.66	48	23.64	25	12.31	-	-	-	-
- inclusion	1	3.33	2	6.66	9	30	14	46.66	4	13.3	-	-	-	-
- chocolate	-	-	1	7.69	10	76.92	2	15.38	-	-	-	-	-	-
- Para-ovarian	-	-	8	44.4	-	-	8	44.44	2	11.11	-	-	-	-
Neoplastic														
Serous cysts:														
Benign	6	5.76	19	18.3	45	43.26	21	20.19	7	6.73	4	3.84	2	1.92
Borderline	-	-	-	-	-	-	1	33.3	1	33.3	1	33.3	-	-
Malignant	-	-	-	-	3	42.85	2	28.57	1	14.28	1	14.28	-	-
Mucinous cysts:														
Benign	1	2.08	9	18.7	24	50.01	7	14.58	4	8.33	2	4.16	-	-
Borderline	-	-	-	-	-	-	1	100	-	-	-	-	-	-
Malignant	-	-	-	-	6	60	1	10	1	10	2	20	-	-
Miscellaneous														
Teratoma	13	11.3	74	64.3	19	16.52	6	5.21	-	-	3	2.6	-	-
Endometroid T	-	-	-	-	1	50	-	-	1	50	-	-	-	-
Yolk sac T	-	-	1	100	-	-	-	-	-	-	-	-	-	-
GranulosacellT	-	-	-	-	-	-	1	100	-	-	-	-	-	-
Total	66	8.73	215	28.4	202	26.71	184	24.33	69	9.12	18	2.38	2	0.26

P value = o.ooooo1 S X^2 = 55.36 (between neoplastic and non neoplastic cysts)
P value = 0.000001 S X^2 = 102.97 (among neoplastic cysts)

Right sided ovarian cysts were 427 (56.48%) while 271 (35.84%) on the left side, bilateral ovarian cyst were seen in 58 (7.67%).
The commonest presenting symptoms were incidental in 286 (37.83%), pain in 283 (37.43%), while the least common were infertility 17 (2.24%) and vaginal bleeding in 17 (2.24%) of cases.
The cysts were mainly obtained from cystectomy in 363 (48.01%) and total abdominal hysterectomy with bilateral salpingo-oopherectomy in 328 (43.38%), oophorectomy in 36 (4.76%) and ovarian biopsy or wedge resection in 29 (3.83%) cases. Among the cases of cystectomy the highest number were for corpus luteal cyst and teratoma 93 cases for each, while among the cases of total abdominal hysterectomy with salpingo-oopherectomy the follicular cysts were forming the highest number in 120 cases.

The gross appearance of the ovarian cyst are shown in table 3 below

TABLE 3: Gross appearance of the ovarian cysts

Type of ovarian cysts	Gross appearance								Total	
	Outer surface		Inner surface		Locularity		Fluid content			
	No	%	No	%	No	%	No	%	No	%
Non-neoplastic - follicular	Smooth 200	100	Smooth 200	100	Unilocu 180 Multilo 20	90 10	Straw100 Clear80 Hemor20	50 40 10	200	26.4
- corpus luteal	Smooth 203	100	Corrug 185 Smooth 18	91 9	Unilocu 173 Multilo 30	85 15	Straw 116 Thick gel 15 hemor 72	57 5 38	203	26.8
- inclusion	Smooth 29 Rough 1	97 3	Rough 29 Smooth 1	97 3	Unilocu 29 Multilo 1	97 3	Watery 15 Straw13 Hemor2	50 13 7	30	3.96
- chocolate	Rough 12 Smooth 1	92 8	Rough 13	100	Unilocu 12 Multilo 1	90 10	Hemorrhagic 13	100	13	1.71
- Para-ovarian	Smooth 18	100	Smooth 18	100	Unilocu 18	100	Watery 18	100	18	2.38
Neoplastic Serous cysts: Benign	Smooth 104	100	Papill. 62 Smooth 42	59.6 40.4	Unilocu 83 Multilo11 Bilocul10	79.8 10.6 9.6	Hemorrhagic 62 Straw42	59.6 40.4	104	13.75
Borderline	Smooth 3	100	Papill. 2 Smooth 1	66.7 33.3	Uniloc1 Multi.2	33.3 66.7	Watery1 Hemor1 Thick mucoid1 Watery1	-	3	0.39
Malignant	Smooth 5 Rough 2	71 29	Smooth 2 Rough 2	29 71	Multil.6 Unilocu1	85.7 14.3	Watery5 Hemor1 Turbid1	71 15 14	7	0.92
Mucinous cysts: Benign	Smooth 48	100	Smooth 48	100	Multil. 4 Unilocu 40 Bilocul 4	8.3 83.4 8.3	Thick 44 Watery 4	91.7 8.3	48	6.34
Borderline	Smooth 1	100	Rough 1	100	Multilo 1	100	Thick gel. 1	100	1	100
Malignant	Smooth 8 Rough 2	80 20	Papill. 8 Smooth 2	80 20	Multilo 8 Unilocu 2	80 20	Watery6 Hemor1 Mucoid3	60 10 30	10	1.32
Miscellaneous Teratoma	Smooth 115	100	Rough 98 Smooth 17	85.2 14.8	Unilocu 69 Multilo 40 Bilocul 6	60 35 5	Pasty 58 Straw 29 hemorr 28	50.4 25.2 24.4	115	15.21
Endometroid T	Smooth 2	100	Smooth 2	100	Multilo 2	100	Hemor 2	100	2	0.26
Yolk sac T	Smooth 1	100	Smooth 1	100	Multilo 1	100	Watery 1	100	1	0.132
GranulosacellT	Smooth 1	100	Smooth 1	100	Multilo 1	100	Straw 1	100	1	0.132

Mucinous pattern in ovarian cyst are shown in table 4 below

Table 4: Mucin pattern in ovarian cysts.

Diagnosis	No. of cases	PAS stain (neutral mucin)				AB stain (acidic mucin)			
		3	2	1	0	3	2	1	0
Serous tumors	30								
Adenoma	20		1	6	13		2	8	**10**
Borderline	3		1	1	1			2	**1**
Carcinoma	7		2	4	1		1	5	**1**
Mucinous tumors	31								
Adenoma	20	17	3			10	5	3	**2**
Borderline	1		1					1	
Carcinoma	10		6	3	1		5	3	**2**
Follicular cysts	20		2	10	8				**20**
Corpus luteal cysts	20		3	11	6		3		**20**
Teratoma	20		2	2	16			2	**18**
Endometroid carcinoma	2		2					2	
Granulosa tumor	**1**			**1**				**1**	

Benign serous cyst constitute about 13.75% of all cases. Benign mucinous cyst constitute about 6.35% of cases.

III. DISCUSSION:

In the present study **56.48%** of ovarian cysts were found on the right side, **35.84%** of cases were on the left side, and **7.67%** cases were bilateral, comparatively similar results were reported by other authors; **Al-Saadi et al, 1988** [11] found 38% of cases on the right ovary, 35% of cases on the left ovary, and 17% were bilateral. While **AbulAlah et al 2004** [12] found 56% of ovarian cysts on the right side, 32% of cases on the left side, and 12% of cases were bilateral**.**

Regarding the clinical presentations, in the present study; **incidental presentation** and **pain** were the commonest presentations accounting for **37.85%**, and **37.43%** of cases respectively. While pain was the commonest presenting symptom in other study [11], and abdominal enlargement due to a cystic or solid mass was the most common presenting symptoms in both benign and malignant ovarian cysts as pointed by **AbulAlah et al 2004** [12].

Regarding ovarian carcinoma; **Goff et al 2000** [13] stated that 95% of the females were symptomatic, 77% with abdominal symptoms (abdominal bloating and pain), 70% with gastrointestinal symptoms, 50% with constitutional symptoms, 34% with urinary symptoms, 20% with pelvic symptoms.

Fitch et al 1999 [14] stated that 9% of Canadian women were asymptomatic prior to diagnosis of ovarian carcinoma. **Olson et al 2001** [15] found that 93% of patients with ovarian cancer reported at least one symptom; in which abdominal symptoms were constant and not intermittent (fullness, pressure, and bloating).

In the present study most of the ovarian cysts specimens were presented as **cystectomy operation** 48% of the cases, no previous Iraqi study was done regarding the type of operation.

In our study the incidence of neoplastic ovarian cysts was 38.62%, and the non neoplastic cysts was 61.38%, **Al-Saadi et al 1988** [11] found the frequency of benign and malignant ovarian tumors and cysts 78% and 22% respectively. These figures compare reasonably well with those ratio reported by others [3], about 70%-85% benign and 15-31% malignant depending on the reporting centers, bearing in mind that our study did not include all ovarian tumors, the study was restricted to those tumors with cystic nature, excluding the solid tumors.

Regarding the incidence and frequency of non neoplastic cysts; in our study follicular and corpus luteal cysts were the commonest ovarian cysts (26.45% and 26.85% respectively, **Alash 1988** [16] found follicular cyst representing 25.45%, and luteal cysts representing 19%, **Al-Saadi et al 1988** [11] found follicular cysts representing 15%, and corpus luteal cysts representing 9.2%, the percentage of para ovarian cysts and chocolate cysts in our study was comparable to other studies [11, 16]. The age and the gross appearance are in agreement with that previously reported [16].

Regarding the neoplastic ovarian cysts; there are certain broad conclusions regarding the frequency of common epithelial tumors; they constitute about 45% of the whole series [11], in the present study they represent 59.2% of the whole neoplastic cysts.

Benign serous cysts constitute about 13. 75% of all cases,figure (1),while benign mucinous cysts constitute about 6.35%, these were comparable to other results [11,16]; benign serous cysts are reported to be more common than mucinous tumors [11, 12, 16].

Germ cell tumors represent about 15%-20% of all ovarian tumors [2, 4, 3], in this study benign cystic teratoma was relatively common forming about 15.4% of total ovarian cysts. Mature cystic teratoma is the most common

germ cell neoplasm and in some series the most common ovarian neoplasm removed at surgery [17, 18]. It is most common ovarian mass in children [19]. The gross appearances are in agreement with that previously reported [20], figure (2).

Mucin stain: there is secretion of neutral and acidic mucins in different intensities with PAS and AB 2.5 staining methods, but there are no significant differences between the intensity of staining (scores) and grades of epithelial ovarian cysts, this may be due to the fact that most of these cystic tumors secret small and scant amount of mucin except the mucinous cysts with obvious secretion of all types of mucin.

Other studies [12, 21] have used Orcein / AB 2.5 stain for demonstration of sulphatedmucin.

Serous cysts: in the present study the results of mucin staining show that a small amount of mucin of different types are present in the upper part of the epithelial cells and intralumenally in different scoring, these results are similar to that obtained by **Kelmi et al 1978** [22] on serous tumors and cyst, and they suggested that theses mucin secretions were increased with increase malignancy, and also similar to **Garsia-Bunnel et al 1961** [23], in both studies they related mucin secretion with ultrastructural findings.

Mucinous cysts: the presence of mucin is the most conspicuous here, in mucinous cystadenoma neutral and acidic mucinsintracellular and extracellular are seen in different proportions. With increasing malignancy the amount of mucin decreases, i.e. there is negative correlation between PAS & AB PH 2.5 stains and grades of mucinous tumors. Other studies found moderate to strong positive correlation between Orcein / AB PH 2.5 stain and grades of mucinous tumors [12, 21], and they found that the highest score of Orcein stain in mucinous cystadenocarcinoma is different from borderline and benign cysts score, that helps in differentiation between them [21, 23,22].

In **endometroid carcinoma**: moderate amounts of neutral and acidic mucin were found mainly at the luminal border of the cells and intralumenally are seen, however, the special stains of mucin are not helpful to differentiate endomertroid carcinoma from serous and clear cell carcinoma [21, 22].

The presence of mucin in teratoma reflects the nature of elements of teratoma, and the presence of endodermal tissue like gastrointestinal and bronchial epithelium [19].

MC Kay D.J et al 1961 [24] showed that in the ovarian follicles, there was a little amount of glycogen and glycoprotein in the granulosa cells of ova, which increase in corpus luteum; this may explain the mucin results in these functional cysts.

Conclusion and Recommendations:

The most common type of ovarian cyst was shown in this study is non-neoplastic ovarian cyst, serous cyst and benign cystic teratoma are the most common neoplastic cyst. Complementary study of mucin secretion in ovarian cyst appears to be helpful in histological classification of these cysts, but negative cases had not been differentiated whether they were borderline or malignant.

We recommend further detailed clinic pathological and follow up information regarding each type of ovarian cyst as separate entity. Also we recommend using flow cytometry and genetic methods to predict the prognosis for each cyst type and to determine the treatment protocol.

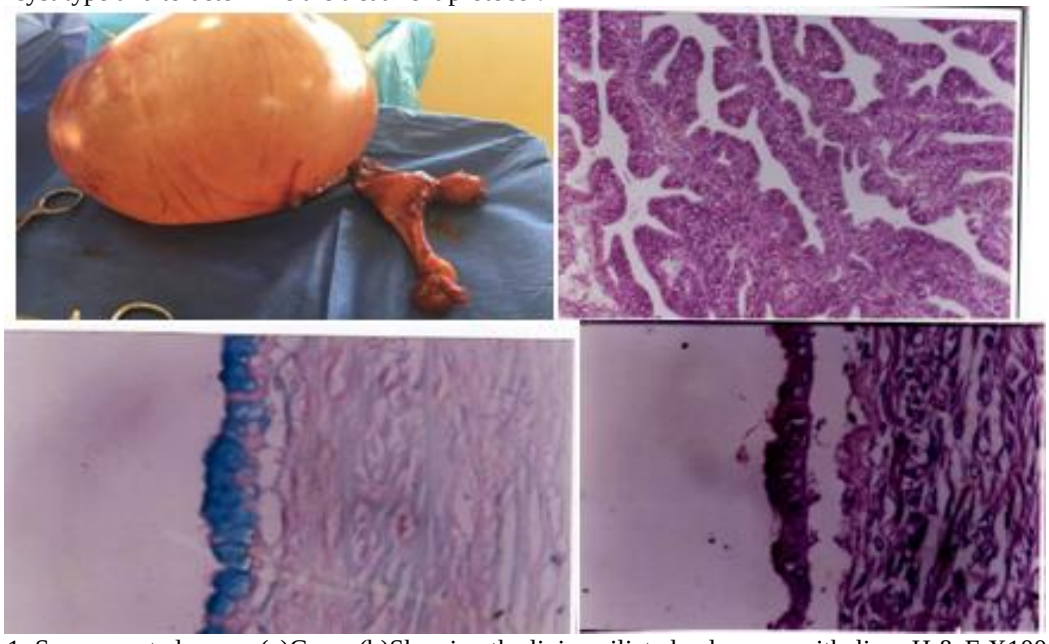

Figure 1: Serous cystadenoma.(a)Gross (b)Showing the lining ciliated columnar epithelium.H & E X100(c)AB stain X 400 (d) PAS stain X 400.

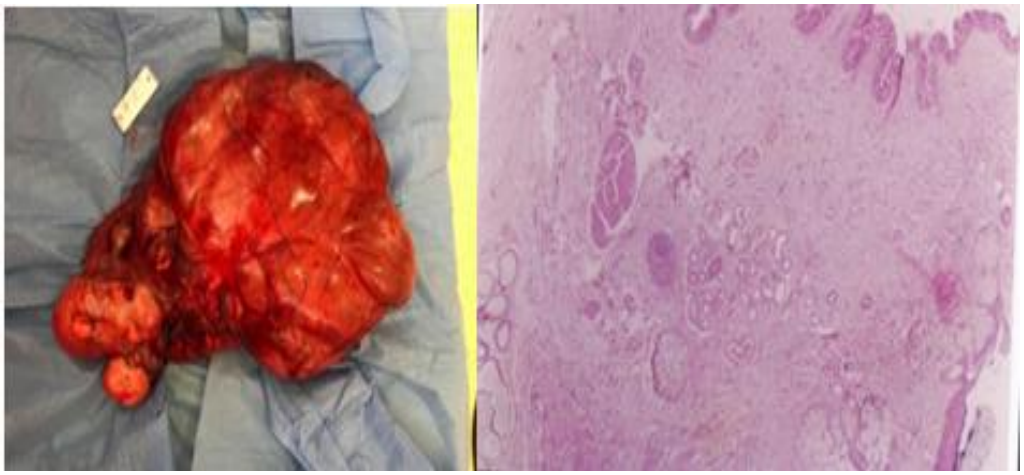

Figure 2: Teratoma. (a) Gross
(b) Mature cystic H & E X 50 Showing the respiratory epithelium, skin with its appendages and neuronal components.

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