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CLINICOPATHOLOGICAL ASSESSMENT OF OVARIAN MALIGNANCIES IN A SAMPLE OF IRAQI PATIENTS IN BAGHDAD DISCRETE

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ABSTRACT

Introduction: Ovarian cancer is one of the leading causes of mortality in women, and is the fifth most prevalent cancer in Iraqi women, it's classified as epithelial tumors, representing almost 90% of cases, mesenchymal tumors, mixed epithelial and mesenchymal tumors, sex cord stromal tumors representing (2%) of cases, germ cell tumors representing (3%) of cases, miscellaneous tumors and tumor-like lesions. The risk of developing ovarian cancer increases with age. Symptoms may include pelvic pain or tender- ness, swollen abdomen, nausea or dysphagia, changes in bowel habits (constipation), and irregular vag- inal bleeding. To assess the histopathological diagnosis of malignant ovarian tumors in a group of Iraqi female patients in Baghdad discrete in correlation with various clinicopathological parameters (Age, Clinical presentation, Gross morphology, Histopathological type and Tumor grade, and pathological stage). **Methods**: Study including analysis of 70 female patients with ovarian malignancies from Teach- ing Laboratories of al Emamain al kadhimain medical city (AS) and Baghdad Medical City from January 2018 to December 2022. The data were collected from patient archived pathological report, collected samples were formalin fixed paraffin embedded blocks and hematoxylin and eosin-stained slides, new sections from each block were taken, stained with hematoxylin and eosin. The data were statistically analyzed using appropriate statistical techniques (SPSS) version 26 measuring mean, standard deviation, frequency, percentage, and the association relationships were investigated using yates CHI square test, P value of <0.05 was considered statistically significant. **Results:** The patients' age ranged from 9-76 years with a mean of 44.81 years ± 15.16 SD. Most were at age group ≤ 50 years, the most common histopathological type was high grade serous adenocarcinoma in 24.28, that is to say the epithelial tumors were the most frequent (54.27%). Most cases presented with abdominal pain (31.43%) and least frequent presentation was weight loss (1.43%), most tumors presented as mass (55.71%) unilateral (61.43%) and right sided (53.49%), tumor size ranged from 3.5-20cm with a mean of (11.59 ± 4.16 SD). As for grading, most were in grade III (44.28%). And half the cases were stage III (50%). **Conclusion**: The most common histopathological type was high grade serous adenocarcinoma, which means the epithelial tumors were the most frequent Most malignant tumors of the ovary in patients are of large size and present at ad- vanced stage and higher nuclear grade, this is due to late presentation of patients after disease progres- sion.

KEYWORDS: Clinicopathological, Assessment, Ovary, Tumors, Sample, Iraqi, Patients, Cancer.

INTRODUCTION

Ovarian cancer is one of the leading causes of mortality in women.[1] Ovarian cancer is the fifth most prevalent cancer in Iraqi women. The WHO (world health organization) classified ovarian tu- mors in 2020 as follow:[2,3]

Epithelial tumors which includes Serous tumors, Mucinous tumors, Endometrioid tumors, Clear cell tumors, Seromucous tumors, Brenner tu- mors and Other carcinomas including Meso- nephric-like adenocarcinoma, Undifferentiated and dedifferentiated carcinoma, Carcinosarcoma and Mixed carcinoma and then Mesenchymal tu- mors and Mixed epithelial and mesenchymal tu- mors And Sex cord stromal tumors and Germ cell tumors, Miscellaneous tumors and finally Tumor- like lesions.[3]

Epithelial ovarian cancer presents as bloating, abdominal distension or discomfort, pressure ef- fects on the bladder

and rectum, constipation, vaginal bleeding, indigestion and acid reflux, shortness of breath, tiredness, weight loss, and early satiety. The patient may feel an abdominal mass.[4]

Sex cord stromal tumors induce hyper andro- genicity may present with virilization signs (e.g., hirsutism), whereas tumor subtypes associated with abnormal estrogen production may present with hypoestrogenic (e.g., isosexual precocity in children, abnormal uterine bleeding, endome- trial hyperplasia, and carcinoma).[5]

The risk of developing ovarian cancer increases with age, with more than half of all cases in the UK in those aged 65 and over. A higher risk of de- veloping ovarian cancer is associated with[8] BRCA genes or those linked to Lynch syndrome (MLHL, MSH2, MSH6, PMS2, and EPCAM), his- tory of breast cancer or bowel cancer, history of radiotherapy treatment for a previous cancer., endometriosis and diabetes mellitus. Early men- arche or late menopause, have never used any hormonal contraception, such as the pill or an implant, are taking hormone replacement ther- apy (HRT), are overweight or smoke.[6]

Tests and procedures used to diagnose ovarian cancer include:[7] Pelvic exam, Imaging tests, such as ultrasound or CT scans of your abdomen and pelvis, Blood tests might include organ func- tion tests and tumor markers that indicate ovar- ian cancer. For example, a cancer antigen (CA) 125. Or Surgery for removal of ovarian lesion for histopathology and immunohistochemistry and finally Genetic testing to look for gene changes that increase the risk of ovarian cancer. If there is inherited mutation in the DNA helps making de- cisions about the treatment plan.[7]

To assess the histopathological diagnosis of malignant ovarian tumors in a group of Iraqi female patients in Baghdad discrete in correlation with various clinicopathological parameters (Age, Clinical presentation, Gross morphology, Histopathologi- cal type, tumor grade and pathological stage).

METHODS

Study design: A cross-sectional study was con- ducted from January 2018 to December 2023, in- volving a retrospective analysis of 70 female pa- tients with ovarian malignant tumors. The sam- ples were collected from the Teaching Labora- tory of Al-Imamain Al-Kadhimain Medical City, and Baghdad Medical City. Histopathological re- ports and slides were reexamined and reviewed retrospectively. Clinical parameters such as (De- mographic analysis (name and age). Clinical presentation, Gross morphology, Histopathologi- cal type and tumor grade, Pathological stage) were extracted from patient admission case sheets and pathology reports.

The practical work included

1. Collection of 70 histopathological reports and slides from from total abdominal hysterectomy with bilateral oophorectomy and from cystec- tomy samples and oophorectomy samples spec- imens.

2. Slide inspection and re-evaluation by the study's supervising pathologist at the College of Medicine/Al-Nahrain University Pathology De- partment. The study lasted one year, from Janu- ary 2023 to January 2024.

Inclusion Criteria: Female patients of all ages with malignant ovarian tumors including meta- static tumors.

Exclusion criteria: Missing Data.

Tissue sectioning: Tissue sections were cut to 4-micrometer thickness with a rotary microtome for microscopic examination. The tissue was flat- tened in a warm water bath before placing it on a glass microscope slide.

Staining: Routine Hematoxylin and Eosin Stain was applied following a standard procedure of deparaffinization, hydration, staining, differenti- ation, rinsing, counterstaining, dehydration, clearing, and mounting.

Image Capture: H&E-stained slides were exam- ined using a light microscope (Leica, Germany) at 10x and 40x magnifications to identify histo- pathological features. Photomicrographs were taken with an iPhone 11 [12 MP wide-angle cam- era, f/1.8 aperture].

Statistical methods: Collected data were ana- lyzed using SPSS version 26. Data were plotted as bar charts and pie charts for better visualiza- tion. Contingency tables and Chi-squared tests were used to assess the correlation between in- vestigated variables, with p-values less than 0.05 considered statistically significant.

RESULTS

A total number of 70 female patients were in- cluded in the study sample. The age of the stud- ied sample ranged from 9-76 years with a mean of 44.81 years ± 15.16 SD). More than half of the study's sample were ≤ 50 years (57.14%), as il- lustrated in table (4.1)

Table 4.1: Study sample according to age.

Age	frequency	Percentage
≤ 50 years	40	57.14%
> 50 years	30	42.86%
Total	70	100

The most common tumor was serous adenocar- cinoma seen in 28 cases (40%) of the total sam- ple of which 17 cases (24.28%) were high grade serous carcinoma and 11 cases (15.71%) were low grade serous carcinoma (Epithelial tumor group). As in table (4.2) and (4.3).

Table 4.2: Study sample according to main histo-pathological group.

Main tumor group	Frequency	Percentage
Epithelial tu-mors	38	54.275%
Sex cord stromal tu-mors	13	18.56%
Metastatic adenocarci-noma	10	14.285%
Germ cell tumors	9	12.845%
total	70	100%

Table 4.3: Histopathological diagnosis of ovarian tumors in this study.

Tumor type	Frequency	Percentage
High grade se- rous carcinoma	17	24.28
Low grade se- rous carcinoma	11	15.71
Metastatic ade-nocarcinoma	10	14.285
Adult Granulosa cell tumor	8	11.43
Mucinous ade-nocarcinoma	4	5.71
Immature tera-toma	4	5.71
Yolk sac tumors	3	4.285
Endometroid carcinoma	3	4.285
Sertoli Leydig cell tumor	2	2.85
Clear cell carci-noma	2	2.85
Juvenile Granu-losa cell tumor	2	2.85
Dysgerminoma	2	2.85
Malignant mixed mullerian tumor	1	1.43
Sex cord stromal tumors NOS	1	1.43
Total	70	100%

Abdominal pain was the most common (22 cases) (31.43%), the least common was weight loss in one case (1.43%), Of 70 patients, 39 tu- mors (55.71%) presented as solid mass, 21 tu- mors (30%) presented as cyst, and 10 tumors (14.28%) presented as mixed cystic and solid mass. 27 tumors (38.57%) were bilateral, 43 tu- mors (61.43%) were unilateral, of which 23 (53.49%) were in the right ovary and 19 (44.19%) on the left ovary, The tumor size ranged from 3.5-20.0 cm with a mean of (11.59 ± 4.16 SD). Most tumors were ≥10 cm (61.4%). Regarding 60 ma- lignant primary tumors (The study sample after exclusion of metastatic tumors), the majority were in stage III (50%). Followed by Stage I then stage II, as for grading, out of 70 cases most were in grade III (44.28%), grade I (37.14%), grade II (18.57%).

A statistically significant association was de- tected between histopathology and clinical presentation (P value = 0.041); as shown in table (4.4) and between histopathology and affected side (P value < 0.001); more on the right side as shown in table (4.5) between histopathology and pathological grade (P value = 0.003); as shown in table (4.6).

DISCUSSION

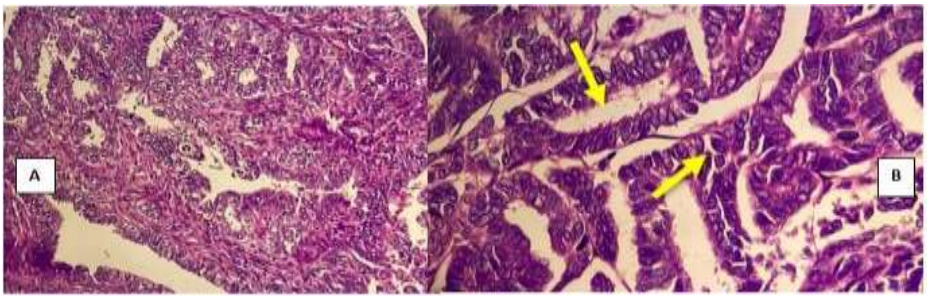

Figure 1: Section of high-grade serous carcinoma of the ovary show neoplastic epithelial formation with glandular, cystic and papillary formation, with high grade nuclear features (pleomorphism is well estab- lished – yellow arrow) (H&E) A(X10) B (X40).

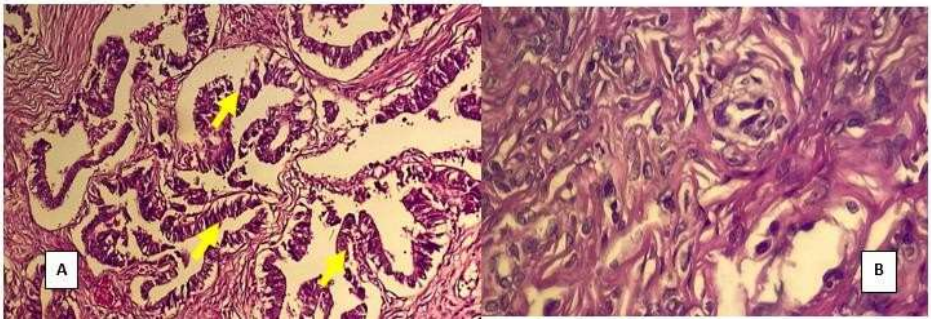

Figure 2: Section of Low-grade serous carcinoma show true papillae formation (Yellow arrows), complex proliferation of malignant serous type lining. (H&E) A(10X) B(40X).

Table 4.4: Association between histopathology and clinical presentation.

Variable	Clinical presentation						Total	p- value
	Abdominal pain	Abdominal distension	Pelvic mass	Vaginal bleeding	Weight loss	Bloating		
High Grade Serous adenocarcinoma	5	7	2	0	0	3	17	0.041
	29.4%	41.2%	11.8%	0.0%	0.0%	17.6%	100.0%	
Low Grade Serous adenocarcinoma	4	2	2	0	0	3	11	
	36.4%	18.2%	18.2%	0.0%	0.0%	27.3%	100.0%	
Metastatic adenocarcinoma	5	2	1	1	1	0	10	
	50.0%	20.0%	10.0%	10.0%	10.0%	0.0%	100.0%	
Adult Granulosa cell tumor	0	1	2	5	0	0	8	
	0.0%	12.5%	25.0%	62.5%	0.0%	0.0%	100.0%	
Mucinous adenocarcinoma	2	1	0	0	0	1	4	
	50.0%	25.0%	0.0%	0.0%	0.0%	25.0%	100.0%	
Immature teratoma	1	2	1	0	0	0	4	
	25.0%	50.0%	25.0%	0.0%	0.0%	0.0%	100.0%	
Yolk sac tumor	1	2	0	0	0	0	3	
	33.3%	66.7%	0.0%	0.0%	0.0%	0.0%	100.0%	
Endometrioid carcinoma	2	1	0	0	0	0	3	
	66.7%	33.3%	0.0%	0.0%	0.0%	0.0%	100.0%	
Sertoli Leydig cell tu-mor	1	0	1	0	0	0	2	
	50.0%	0.0%	50.0%	0.0%	0.0%	0.0%	100.0%	
Clear cell carcinoma	1	0	1	0	0	0	2	
	50.0%	0.0%	50.0%	0.0%	0.0%	0.0%	100.0%	
Juvenile Granulosa cell tumor	0	0	2	0	0	0	2	
	0.0%	0.0%	100.0%	0.0%	0.0%	0.0%	100.0%	
Dysgerminoma	1	1	0	0	0	0	2	
	50.0%	50.0%	0.0%	0.0%	0.0%	0.0%	100.0%	
Malignant mixed mullerian tumor	0	0	0	1	0	0	1	
	0.0%	0.0%	0.0%	100.0%	0.0%	0.0%	100.0%	
Sex cord stromal tumor NOS	0	0	1	0	0	0	1	
	0.0%	0.0%	100.0%	0.0%	0.0%	0.0%	100.0%	
Total	22	19	13	7	1	8	70	
	31.4%	27.1%	18.6%	10.0%	1.4%	11.4%	100.0%	

Table 4.5: Association between histopathology and affected side.

Variable	Affected side			Total	P-Value
	Right side	Left side	Bilateral		
High Grade Serous adenocarcinoma	2	1	14	17	< 0.001
	11.8%	5.9%	82.3%	100.0%	
Low Grade Serous Carcinoma	2	4	5	11	
	18,2%	36.4%	45.4%	100.0%	
Metastatic adenocarcinoma	1	0	9	10	
	10.0%	0.0%	90.0%	100.0%	
Adult Granulosa cell tumor	5	3	0	8	

	62.5%	37.5%	0.0%	100.0%	
Mucinous adenocarcinoma	3	1	0	4	
	75.0%	25.0%	0.0%	100.0%	
Immature teratoma	3	1	0	4	
	75.0%	25.0%	0.0%	100.0%	
Yolk sac tumor	0	3	0	3	
	0.0%	100.0%	0.0%	100.0%	
Endometrioid carcinoma	1	2	0	3	
	33.3%	66.7%	0.0%	100.0%	
Sertoli Leydig cell tumor	2	0	0	2	
	100.0%	0.0%	0.0%	100.0%	
Clear cell carcinoma	0	2	0	2	
	0.0%	100.0%	0.0%	100.0%	
Juvenile Granulosa cell tumor	0	2	0	2	
	0.0%	100.0%	0.0%	100.0%	
Dysgerminoma	2	0	0	2	
	100.0%	0.0%	0.0%	100.0%	
Malignant mixed mullerian tumor	1	0	0	1	
	100.0%	0.0%	0.0%	100.0%	
Sex cord stromal tumor NOS	1	0	0	1	
	100.0%	0.0%	0.0%	100.0%	
Total	26	17	27	70	
	37.1%	24.3%	38.6%	100.0%	

Table 4.6: Association between histopathology and pathological grade.

Variable	Grade			Total	P-Value
	Low	Intermediate	High		
High Grade Serous adenocarcinoma	0	0	17	17	0.003
	0%	0%	100%	100.0%	
Low Grade Serous Carcinoma	11	0	0	11	
	100%	0%	0%	100.0%	
Adult Granulosa cell tumor	5	3	0	8	
	62.5%	37.5%	0.0%	100.0%	
Mucinous adenocarcinoma	3	1	0	4	
	75.0%	25.0%	0.0%	100.0%	
Immature teratoma	3	1	0	4	
	75.0%	25.0%	0.0%	100.0%	
Yolk sac tumor	0	3	0	3	
	0.0%	100.0%	0.0%	100.0%	
Endometrioid carcinoma	1	2	0	3	
	33.3%	66.7%	0.0%	100.0%	
Sertoli Leydig cell tumor	2	0	0	2	
	100.0%	0.0%	0.0%	100.0%	
Clear cell carcinoma	0	2	0	2	
	0.0%	100.0%	0.0%	100.0%	
Juvenile Granulosa cell tumor	0	2	0	2	
	0.0%	100.0%	0.0%	100.0%	
Dysgerminoma	2	0	0	2	
	100.0%	0.0%	0.0%	100.0%	
Malignant mixed mullerian tumor	1	0	0	1	
	100.0%	0.0%	0.0%	100.0%	
Sex cord stromal tumor NOS	1	0	0	1	0.003
	100.0%	0.0%	0.0%	100.0%	
Total	26	17	27	60	
	37.1%	24.3%	38.6%	100.0%	

DISCUSSION

The most common age at presentation was ≤ 50 years, comprising 57.14% of cases which is paral- lel to Iraqi study done by Mohammed MS et al in Mosul 2022[8] in

which 70% of cases age in this range, also this result goes study in India by Sharma et al in 2020[9] in which 74.62% of cases were in this age group. While it disagrees with a study by Paes et al in 2011 in Brazil[10] in which 48.28% of the malignant tumors were in this age group, this difference may be due to different sample size, geographic and environmental fac- tors. Most cases were High grade serous carci- noma (24.28%) followed by low grade serous car- cinoma (15.71%) and then metastatic adenocar- cinoma (14.28%) and according to the main groups Epithelial tumors were seen in 38 case (54.275%) followed by sex cord stromal tumors in 13 case (18.56%) followed by metastatic ade- nocarcinoma in 10 cases (14.285%) and finally germ cell tumors in 9 cases (12.845%). In the study done in Libya by Saad.R et al in 2022[11], epithelial tumors were 51%, germ cell tumors were 28%, sex cord stromal tumors were 16% and metastatic tumors were 5%.[11] This differ- ence can be due to genetic and environmental factors. In the Iraqi study done by Mohammed MS et al in Mosul 2022.[8] Most of cases 72.5% were surface epithelial tumors, followed by germ cell tumors 15% and sex cord stromal tumors 12.5%. the difference could be due to difference in the sample size in the forementioned study (n=40) and not including the metastatic tumors in it. Abdominal pain was the most common (31.43%), followed by abdominal distension (27.41%), and pelvic mass (18.57 %) then bloat- ing (11.43) then vaginal bleeding (10%) and fi- nally weight loss in one case (1.43%). Two cases were mentioned in reports to be associated with ascites, one with endometrioid carcinoma and the other adult granulosa cell tumor type, the latter was also associated with pleural effusion. In a study done by Saeed M. et al in Pakistan 1991[12], abdominal distension was the most common symptom in malignant tumors (70%), followed by abdominal pain (62.5%) followed by weight loss (25%) then vague abdominal com- plaint (17.5%) then postmenopausal bleeding and menstrual irregularities both with percent- age of (7.5%), the differences in results could be due to racial and geographical differences and difference in the number of study sample. In the Iraqi study done by Mohammed MS et al in Mo- sul 2022[8] (42.5%) of cases presented with ab- dominal mass, (35%) with ascites, (12.5%) with abdominal lump, and (10%) as incidental finding, the difference in results may be due to sample size as the forementioned study had only 40 cases. Also, 39 tumors (55.71%) presented as solid mass, 21 tumors (30%) presented as cyst, and 10 tumors (14.28%) presented as mixed solid/cystic. These results are against those of previous studies like the Iraqi study done by Mo- hammed MS et al in Mosul 2022[8] in which Tu- mors with solid/cystic in nature were found in (50%) While (27.5%) were purely cystic and (22.5%) were solid in nature. And the study done by Jain R, et al in India[13] in which solid/cystic was seen in 53.84% followed by Solid in 38.46% and then cystic in 7.69%. The difference in results could be due to difference in sample size and tu- mor type involved in the study. In our study 27 tumors (38.57%) were bilateral, 43 tumors (61.43%) were unilateral, of which 23 (53.49%) were in the right ovary and 19 (44.19%) on the left ovary, this is consistent with the Iraqi study done by Mohammed MS et al in Mosul 2022[8] in which 45% of cases were involved in the right ovary which were slightly more than left ovary 37.5% as result 82.5% of cases were unilateral and 17.5% were bilateral. Also similar was found in the Iraqi study done by Mohamad B.J. et al (2022)[14], in which high frequency was found at right ovary by 63.3%. It is also consistent with the study done in Libya by Saad. R et al in 2022[11], where the majority were unilateral (66%) and the rest of patients presented with bilateral ovarian tumor (34%). The tumor size ranged from 3.5-20.0 cm with a mean of (11.59 ± 4.16 SD). Most tumors were ≥10 cm (61.4%). Which is in agree- ment with those of previous studies like the Iraqi study done by Mohammed MS et al in Mosul 2022[8] in which (57.5%) were more than 10 cm while (42.5%) were <10 cm, while it disagrees with study done by Barla KS. Et al 2023 in India[15] in which the tumor size was less than 10 cm in 58.3% of cases, more than 10 cm in 41.67% of cases. This difference could be due to genetic and racial factors, and early diagnosis in India, while in Iraq most cases come as late diagnosis and large size. In the current study, the majority were in stage III (50%). Followed by Stage I then stage II, as for grading, most were in grade III (44.28%), grade I (37.14%), grade II (18.57%).

These results are consistent with those obtained by the Iraqi study done by Mohammed MS et al in Mosul 2022[8] in which 72.4% of cases were grade III, followed by Grade II in 17.2% and then grade I in 10.3%. And with the study done by Chandra K, et al in India 2019[16] in which stage III was most common followed by stage II and then stage I. However it disagrees with the study done by Mohamad B.J. et al Baghdad 2022[14], in which the most common tumor stage was stage IC with rate of 29.6%, which could be due to dif- ferent sample size and agrees in terms of Grad- ing, as the most common Grade seen was Grade III by 40.7%.[14]

CONCLUSION

1. Ovarian cancer in the present study showed highest frequency at the age group ≤ 50 years. There is no significant association between final diagnosis with age.
2. High grade serous carcinoma as the most fre- quent histological type. and Malignant mixed mullerian tumor and Sex cord stromal tumors NOS were the least common both with a per- centage of 1.85%.
3. In our study in the majority of cases tumor size was ≥ 10 cm. and the majority presented with abdominal pain and only one case presented with weight loss.
4. In this study there was a significant association between histopathological type and the affected size most of the cases were unilateral right sided. And most cases presented as a mass.
5. There is significant association between the histopathological type and the pathological grade, the most frequent is grade III, followed by grade I

and the least frequent is grade II.

6. Half of the cases were stage III, followed by stage I and then stage II, there is no significant association between the histopathological type and the pathological stage.

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