

Clinical and Histopathological Features of Ovarian Cancer in Rizgary Hospital/Erbil City from 2014 to 2017

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Abstract

Background: Ovarian cancer is a heterogeneous disease with variations in clinical behavior and outcome. It is a group of many subtypes with distinct biological features that lead to differences in response to treatments, recurrence rates, and survival. **Objective:** The aim of the study is to describe the epidemiology of the diagnosed cases of ovarian cancer from 2014 to 2017 in Erbil, Iraq. **Materials and Methods:** This is a retrospective study, 100 ovarian cancer cases were reviewed from Rizgary Oncology Center in Erbil. Then, we compared histological types with age groups of the study as premenopausal and postmenopausal, stage of the disease, grade, and with side of tumor. Furthermore, this study includes the most important risk factors that may affect the incidence of ovarian cancer which includes menarche age, age of menopause, and with obesity. **Results:** The result showed that ovarian cancer occurs in old age groups with a percentage of 64%. The most common type is epithelial ovarian cancer with subtype papillary serous adenocarcinoma in 56%, with all types, the most affected site is the right one in a percent of 57%. Grade 3 is the dominant one at presentation in a percent of 49%. About staging at the time of diagnosis, Stage 4 presented in a percent of 58%, and 16% of patients were obese. **Conclusion:** Most common type of cancer is epithelial type of papillary serous cystadenocarcinoma histology that occur in old patients and presented in advanced stage at the time of diagnosis with poor differentiation, and the most effective treatment is total abdominal hysterectomy + bilateral salpingo-oophorectomy followed by adjuvant platinum-based chemotherapy.

Keywords: Adenocarcinoma, incidence, ovarian cancer, risk factors

INTRODUCTION

Ovarian cancer accounts for more than deaths than all other gynecologic malignancies combined. Worldwide each year, $\geq 225,000$ women are diagnosed, and 140,000 women die from the disease.^[1] However, there are no effective screening tests for ovarian cancer and few notable early symptoms. As a result, two-thirds of patients have advanced disease when they are diagnosed.^[2,3] Aggressive debulking surgery, followed by platinum-based chemotherapy, usually results in clinical remission. However, up to 80% of these women will develop a relapse that eventually leads to disease progression and death.^[4]

Risk factors for epithelial ovarian cancer are: null parity, early menarche, late menopause, white race, increasing age, family history, personal history of breast cancer, ethnic background (European Jewish, Icelandic, and Hungarian), postmenopausal hormone therapy, and Pelvic Inflammatory Disease (PID). Genetic screening for ovarian cancer can be done to any patient with a personal history of epithelial ovarian cancer or breast cancer in certain circumstances or from family

history because 90% of ovarian cancer result from germline mutation in the BRCA1 or BRCA2 genes.^[5] In high-risk women, screening can be done by BRCA1 or BRCA2 carriers, CA125, and transvaginal sonography with pelvic examination. In general population, routine screening for women at average risk is not recommended. Unlike, a significant proportion of epithelial ovarian carcinomas (EOCs), malignant germ cell tumors are not generally considered heritable, although rare familial cases are reported.^[6] Malignant germ cell tumors are the most common ovarian malignancies diagnosed during childhood and adolescence, although only 1% of all ovarian cancer develop in these age groups.^[7,8] At age 20, however, the incidence of EOC begins to rise and exceeds that of germ cell tumors. For sex cord tumors, they originate from the ovarian

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matrix, and they have the potential for hormone production in an average of 90%. Individual with these tumors typically present with signs and symptoms of estrogen or androgen excess. Surgical resection is the primary treatment, although recurrent disease poorly responds to treatment.^[9,10]

The aim of this study was to show the epidemiology of ovarian cancer who had been diagnosed at Rizgary Teaching Hospital in Erbil city, Iraq.

MATERIALS AND METHODS

Study design

This retrospective study had been approved by Scientific Counsel of Medical Specialization/Kurdistan Board for Medical Specialties. The study was conducted at Rizgary Teaching Hospital at Oncology Department in Erbil city, Kurdistan region, Iraq, for the period from 2014 to 2017.

Study groups

All patients with different age at presentation that diagnosed as any type of ovarian cancer in Rizgary Oncology Department during this time period were identified through their file medical records to assess whether patients met the study inclusion criteria.

Participants (inclusion and exclusion criteria)

Inclusion criteria included all ages from birth and after the menopausal period that visit Rizgary Hospital/Oncology Department. They also included all patients who diagnosed as ovarian cancer including all histopathological types with all grades and stages that related to epithelial ovarian tumor, germ cell tumors, and sex cord tumors. Exclusion criteria included none exclusion criteria.

Data collected

Data collected including age, menopausal state, body surface area (BSA), histopathological types, stage, grade, and side of tumor.

Study protocol

This is a retrospective study of 100 ovarian cancer patients who had the disease between (2014 and 2017) in Rizgary Oncology Center in Erbil. The data of this study were retrospectively retrieved from archived patient's case material at the registry unit. Eligible patients included all female patients who have been diagnosed previously as a case of ovarian cancer, operated or received adjuvant chemotherapy. For the study, a written official permission had been obtained from Rizgary Oncology Center as the main center for collecting study samples. All the files were reviewed to provide the following data on each patient: histopathology, imaging reports, data, and treatment protocols. Regarding histopathology subtypes, grades and staging of the disease of almost all the patients were taking from their pathology reports. For the other information taken from case files, treatment protocols (which had been received by the patients), were taken directly from the patient's case files. The results were compared with published international data.

Statistical analysis

Data had been recorded on a specially designed questionnaire. Statistical analysis began by entering the data in the computer using the Microsoft Excel program. The statistical calculations were performed using a Statistical Package for the Social Sciences Version 21 (SPSS, IBM Company, Chicago, USA). The results were analyzed using frequency distribution, *t*-test and Chi-square tests. $P < 0.05$ were considered as statistically significant.

RESULTS

This study conducted at Rizgary Oncology Center in Erbil city, the data of 100 ovarian cancer cases were reviewed retrospectively between (2014 and 2017). The results are shown as tables and figures.

Table 1 shows that the descriptive data of participants in the study which include age distribution with the menopausal state that includes premenopause, perimenopause, and menopause. Last descriptive data are body surface area that divided into normal and obese categories.

Table 2 shows the age distribution that includes the mean age at the diagnosis of ovarian cancer and the mean age of menarche and menopause.

Figure 1 shows the age distribution according to the study groups ranging from <15 years, 15–49 years, and ≥50-year-old. The largest group is the third group that participates in the study.

Figure 2 shows the menopausal state that includes premenopause, perimenopause, and menopause with the largest participants included in the menopausal group.

Regarding the BSA that divided in this study into normal and obese, the results found that the largest group is the normal

Table 1: Descriptive data of participants in the study

Variable	Category	n (%)
Age groups (years)	<15	1
	15–49	35
	≥50	64
Menopausal status	Premenopause	21
	Perimenopause	14
	Menopause	65
Body surface area	Normal	84
	Obese	16
Total		100

Table 2: Age distribution among the patients of the study

Variable	Minimum	Maximum	Mean	SD
Age	14	88	52.59	14.93
Age of menarche	8	15	11.45	1.81
Age of menopause	48	55	50.89	1.85

SD: Standard deviation

group that participates in the study with BSA <2 in a percent 84%, and just 16% with BSA 2 or more.

Table 3 shows the histopathological type from the data that collected during the study with the most histopathological type is the papillary serous cystadenocarcinoma.

Table 4 shows the side of the tumor either the left, right, or bilateral with the most frequent side is the right side tumor.

Table 5 shows the grading of the tumor either Grade 1, 2, or 3 and according to the study data, Grade 3 was the more documented on at the time of presentation and Grade 2 in the second line and finally Grade 1.

Table 6 shows the staging of ovarian cancer at the time of presentation distributed according to the International Federation of Gynecology and Obstetrics staging to Stage 1, 2, 3, and 4. The most frequent stage at presentation in the oncology department is Stage 4 of ovarian cancer.

Table 7 shows that patients divided according to menopausal state as premenopausal and postmenopausal and compared with histopathological types, grade, and stage with the most common is papillary serous cystadenocarcinoma more frequent with Grade 3 and Stage 4 in postmenopausal patients.

Table 8 shows that we divided the patients into two groups according to their BSA as normal with BSA <2, and obese patients with BSA 2 or more, compared with histopathological types, grade, and stage, with the more common is papillary serous cystadenocarcinoma in obese patients, and Grade 3 and Stage 4 more common in normal group.

Table 9 shows the relation of histopathology with the grading of the cancer at the time of presentation for all type of the histopathology. *P* value was 0.007 which is a statistically significant value.

Table 10 shows the relationship between the histopathological subtypes of ovarian carcinoma with stage. For papillary, endometrioid, and mucinous adenocarcinoma. Majority

Table 3: The histopathological types diagnosed from patients with ovarian cancer collected during the study

Histopathological type	Frequency (%)
Papillary serous cystadenocarcinoma	56 (56.0)
Endometrioid carcinoma	13 (13.0)
Granulosa cell tumor	10 (10.0)
Other types	9 (9.0)
Mucinous adenocarcinoma	3 (3.0)
Dysgerminoma	3 (3.0)
Teratoma	3 (3.0)
Leydig cell tumor	3 (3.0)
Total	100 (100.0)

Table 4: Side of the tumors among patients with ovarian cancer

Side of tumor	Frequency (%)
Right side	57 (57.0)
Left side	27 (27.0)
Bilateral	16 (16.0)
Total	100 (100.0)

Table 5: Grading of the tumors among patients with ovarian cancer

Grade	Frequency (%)
1	15 (15.0)
2	36 (36.0)
3	49 (49.0)
Total	100 (100.0)

Table 6: The staging of ovarian cancer at time of presentation

Stage	Frequency (%)
1	21 (21.0)
2	5 (5.0)
3	16 (16.0)
4	58 (58.0)
Total	100 (100.0)

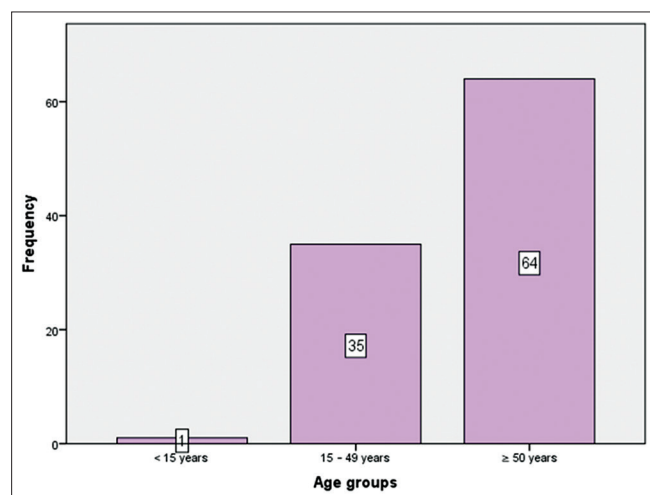


Figure 1: Age distribution according to the study groups

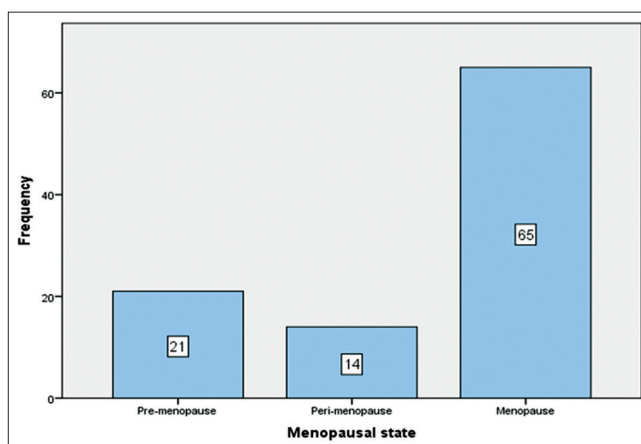


Figure 2: The menopausal state of the participants

Table 7: Distribution of patients according to menopausal state

Variables	Categories	Menopausal status		P
		Premenopause	Postmenopause	
Histopathology	Papillary serous cystadenocarcinoma	13 (36.1)	43 (67.2)	0.04
	Endometrioid carcinoma	7 (19.4)	6 (9.4)	
	Granulosa cell tumor	5 (13.9)	5 (7.8)	
	Other types	6 (16.7)	3 (4.7)	
	Mucinous adenocarcinoma	0 (0.0)	3 (4.7)	
	Dysgerminoma	1 (2.8)	2 (3.1)	
	Teratoma	2 (5.6)	1 (1.6)	
	Leydig cell tumor	2 (5.6)	1 (1.6)	
Grade	1	8 (22.2)	7 (10.9)	0.27
	2	13 (36.1)	23 (35.9)	
	3	15 (41.7)	34 (53.1)	
Stage	1	15 (41.7)	6 (9.4)	0.002
	2	1 (2.8)	4 (6.3)	
	3	5 (13.9)	11 (17.2)	
	4	15 (41.7)	43 (67.2)	
Total	n (%)	36 (100)	64 (100)	

Table 8: Distribution of patients according to the body surface area

Variables	Categories	Body surface area		P
		Normal	Obese	
Histopathology	Papillary serous cystadenocarcinoma	46 (54.8)	10 (62.5)	0.77
	Endometrioid carcinoma	11 (13.1)	2 (12.5)	
	Granulosa cell tumor	7 (8.3)	3 (18.8)	
	Other types	8 (9.5)	1 (6.3)	
	Mucinous adenocarcinoma	3 (3.6)	0 (0.0)	
	Dysgerminoma	3 (3.6)	0 (0.0)	
	Teratoma	3 (3.6)	0 (0.0)	
	Leydig cell tumor	3 (3.6)	0 (0.0)	
Grade	1	11 (13.1)	4 (25.0)	0.47
	2	31 (36.9)	5 (31.3)	
	3	42 (50.0)	7 (43.8)	
Stage	1	20 (23.8)	1 (6.3)	0.37
	2	4 (4.8)	1 (6.3)	
	3	14 (16.7)	2 (12.5)	
	4	46 (54.8)	12 (75.0)	
Total	n (%)	84 (100)	16 (100)	

Table 9: Relation of histopathology with the grading of the cancer

Histopathology	Grade			Total
	1	2	3	
Papillary serous cystadenocarcinoma	4 (26.7)	20 (55.6)	32 (65.3)	56 (56.0)
Endometrioid carcinoma	0 (0.0)	8 (22.2)	5 (10.2)	13 (13.0)
Granulosa cell tumor	5 (33.3)	1 (2.8)	4 (8.2)	10 (10.0)
Other types	3 (20.0)	2 (5.6)	4 (8.2)	9 (9.0)
Mucinous adenocarcinoma	0 (0.0)	2 (5.6)	1 (2.0)	3 (3.0)
Dysgerminoma	2 (13.3)	1 (2.8)	0 (0.0)	3 (3.0)
Teratoma	1 (6.7)	1 (2.8)	1 (2.0)	3 (3.0)
Leydig cell tumor	0 (0.0)	1 (2.8)	2 (4.1)	3 (3.0)
Total	15 (100.0)	36 (100.0)	49 (100.0)	100 (100.0)

P: 0.007

Table 10: Histopathological types of ovarian carcinoma with the staging of the tumor

Histopathology	Stage				Total
	1	2	3	4	
Papillary serous cystadenocarcinoma	1 (4.8)	1 (20.0)	12 (75.0)	42 (72.4)	56 (56.0)
Endometrioid carcinoma	3 (14.3)	1 (20.0)	4 (25.0)	5 (8.6)	13 (13.0)
Granulosa cell tumor	7 (33.3)	1 (20.0)	0 (0.0)	2 (3.4)	10 (10.0)
Other types	4 (19.0)	1 (20.0)	0 (0.0)	4 (6.9)	9 (9.0)
Mucinous adenocarcinoma	0 (0.0)	0 (0.0)	0 (0.0)	3 (5.2)	3 (3.0)
Dysgerminoma	1 (4.8)	1 (20.0)	0 (0.0)	1 (1.7)	3 (3.0)
Teratoma	2 (9.5)	0 (0.0)	0 (0.0)	1 (1.7)	3 (3.0)
Leydig cell tumor	3 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (3.0)
Total	21 (100.0)	5 (100.0)	16 (100.0)	58 (100.0)	100 (100.0)

P: 0.001

of them presented with Stage 4. While for granulosa, dysgerminoma, teratoma, and Leydig cell tumor presented in early-stage cancer. *P* value was 0.001) which is statistically significant, means a correlation between the type of the tumor and staging at presentation.

DISCUSSION

Ovarian cancer is the leading cause of cancer incidence and mortality worldwide. This study describes the magnitude of the problem and summarizes age factor, menarche, menopausal state, and BSA, that may increase and decrease the risk of this lethal disease. These factors have likely impacted the diverse patterns and trends of ovarian cancer incidence and mortality seen across the globe. Most risk factors show substantial heterogeneity across the histopathological types. Additional research is needed to better understand the heterogeneous etiology of this deadly disease with a view to better prevention and early detection strategies.

In this study, the EOC comprised 81% cases, while sex cord tumor comprised 13% and germ cell tumor 6% only. Several authors worldwide reported that histologic subtypes were diagnosed as epithelial ovarian carcinomas (EOCs) in different rates of 60.9%, 71.6%, 80%, and 90% respectively. Age has a strong correlation to ovarian cancer risk and 64% of cases are diagnosed after 50 years of age.^[1-3]

Advancing age increased the possibility of malignant transformation.^[4] Wentzensen *et al* reported that the disease increases from 35 years of age and reaches a peak between the ages of 55 and 64. In their study, the mean age at diagnosis reported varied between 52.2 and 59.5 years.^[5] Other studies reported a median age of 48 years at diagnosis and maximum incidence of 44.3% in the age group of 41–50 years.^[6,7] An epidemiological risk prediction model by Morice *et al* reported a median age of EOC in various countries as 52.4 years.^[8] In our study, the mean age at diagnosis was 52.59 years. Doufekas reported the mean age at diagnosis to be 63 years in the UK.^[9]

In this study, 64% of cases were postmenopausal, 67.2% of them have papillary serous cystadenocarcinoma histology, and 53.1% and 67.2% of them having Grade 3 and Stage 4,

respectively. In Jung *et al.* study, 62.6% of postmenopausal patients had papillary serous cystadenocarcinoma.

Other factors which are related to increased risk include obesity due to an increase in free biologically active estradiol.^[10,11] In this study, 16% of patients were obese, 62.5% of them have papillary serous histology with 43.8% and 75% of them have Grade 3 and Stage 4, respectively, indicating increased risk of carcinoma ovary with obesity. In a study by Catherine M. Olsen, there was increased risk for low-grade invasive serous tumors in obese patients.^[12]

Other factors such as endometriosis (related to endometrioid and clear cell carcinoma), asbestos, and talc exposure, increase the risk of Ovarian cancer.^[13] The protective factors include pregnancy, the use of contraceptive pills, non-steroidal anti-inflammatory drugs, hysterectomy, and salpingo-oophorectomy.^[14,15]

Tubal ligation was decreased risk by 39%, while hysterectomy was decreased by 50%.^[16] Previous history of breast cancer and radiotherapy treatment also carried the long-term risk of ovarian cancer.^[17] The role of diet, ovulation-inducing agents, ethnicity, and smoking are inconclusive as the findings are contradictory in various studies.^[18] We could not comment on these factors, as ours was retrospective study and need a big detailed study.^[19]

The disease is diagnosed in late stages as there is a delay between the onset of symptoms and diagnosis.^[20] Bristow *et al* reported that 60% of cases were diagnosed in Stage 3 and 4.^[21] In our study, 16% of patients were in Stage 3 and 68% were in Stage 4. In study by Saini *et al.*, 20.8% of cases were in Stage 2, 47.85% in Stage 3, and 16.56% in Stage 4. Other authors reported that 20% cases diagnosed in Stage 2 and 60% in Stage 3, while they found that 80% of patients were in Stage 3/4 at diagnosis.^[22,23]

Determination of histology pattern is useful in diagnosis, treatment, and prognosis in OC.^[23,24] Endometrioid carcinoma is identified at an early stage and being chemosensitive is associated with better prognosis. Clear cell carcinoma when identified at an early stage has a good prognosis, but in the later stage has a worse prognosis in comparison to serous carcinoma, as it is less sensitive to platinum-based chemotherapy. There is

an increase in clear cell carcinoma which is related to increased incidence of endometriosis, while mucinous carcinoma is related to cigarette smoking.^[25,26]

The most common histopathological malignancy in all studies is serous carcinoma. In a percentage of 41.6%, 49.69%, 49.5%, 45%, and 38.3% in Basu, Saini, Se le Kim, Yogambal, and Mondal respectively^[27,28] Doufekas reported serous subtype in one-third cases. Its malignant potential is highest, spread is faster, but the response to chemotherapy is good. In our study, 85.5% of cases were serous carcinoma. Histopathological grading is also related to patient survival. Basu *et al.* reported tumors to be well differentiated in 27%, moderately differentiated in 48%, and poor differentiation in 25% cases; while in our study, only 15% were well differentiated, 36% had moderate differentiation, and 49% poor differentiation.^[29-31]

The standard management consists of surgical staging with optimal cytoreduction followed by a platinum-based chemotherapy as per stage of tumor.^[32] There is an improvement in survival rates in early-stage disease due to advancement in chemotherapy and surgery, but unfortunately, majority of the patients report in late stage.^[33-35]

In our study, we can find out that the most affected side by the tumor is the right side in 57%, the left side in 27%, and finally bilaterally in 16%. In contrast to the results that had been done by the Surveillance Epidemiology and End Results Program which shown that malignant serous tumors were bilateral in 57.5% of cases, mucinous, clear cell, endometrioid, and other epithelial tumors were 21.3%, 13.3%, 26.8%, and 35.6%, respectively.^[36-37]

CONCLUSION

Efforts should be made to detect the disease at an early stage through population education with respect to epidemiological factors. Currently, a major goal of ovarian cancer research is to develop an effective test that can detect the disease at its earliest stages, which would ultimately result in decreased mortality. Increased knowledge of ovarian cancer etiology and pathogenesis would greatly enhance the development of this tool.

Another approach that can improve the diagnosis of ovarian cancer is to educate primary care physician about ovarian cancer and to include it in differential diagnosis in the specific patient population. Further studies are needed to elicit the causative factors responsible for the increase in the incidence of the disease and also their mechanism of action. Most ovarian cancers are environmental in origin and therefore in principle preventable. It is suggested that in low-resource settings such as Iraq, an epidemiological study should be done to find the effect of screening programs using relatively easy available imaging modality (USG) on diagnosis in ovarian cancer-risk age group patients with vague gastric symptoms.

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Conflicts of interest

There are no conflicts of interest.

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