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Clinicopathological, Epidemiologic Characteristics and Treatment Outcomes of Ovarian Cancer Patients at NCI, Cairo University

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Abstract

Ovarian cancer is the fifth most common type of cancer and the most common cause of death among women with gynecological malignancies.

Aim: The aim of this retrospective study was to present the epidemiological, pathological, clinical characteristics, treatment outcomes, survival and time to progression of ovarian cancer patients in NCI, Cairo University.

Methods: We reviewed the files of all patients presented at NCI from January 2007 till December 2010 with the diagnosis of ovarian cancer.

Results: The study included 265 patients. The median age for all patients was 48 years, 51% of them were premenopausal. Only 4.5% of the patients had a positive family history. Stage III and IV were seen in 58.1%. Epithelial ovarian cancer (EOC) constituted 81.9% of the cases, germ cell 13.6%, sex cord 3.8% and 0.8% for lymphoma. Surgery was the initial treatment in about 90% of cases. Paclitaxel-carboplatin was the first-line chemotherapy in about 78.8%, with a response rate to first-line chemotherapy reaching 55.3%. This percentage reached 58% after second-line chemotherapy, which was 88.4% platinum-based. Five-year disease free survival was 57%. Progression-free survival after the first line was 8 months only. Five years Overall survival (OS) for all patients was 85%.

Conclusion: The age incidence of ovarian cancer in our patients is 10 years younger than that seen in Western countries. EOC constituted the majority among all ovarian cancer cases, followed by Germ cell tumor. The progression free survival (PFS) is lower than that seen in literature.

Keywords: *Ovarian Cancer; Cairo University; Clinicopathological; Middle East Cancer Consortium*

Introduction

Ovarian cancer accounts for approximately 3% of cancers in women. While it is the 10th most common cancer among women, ovarian cancer is the fifth leading cause of cancer related death among women and is the deadliest of gynecologic cancers. Mortality rates are slightly higher for Caucasian women compared to African-American women. In 2012, there were an estimated 22,280 new diagnoses and an estimated 15,500 deaths from this neoplasm in the United States, less than 40% of women with ovarian cancer were cured [1].

Malignant ovarian tumors include epithelial ovarian cancer, germ cell tumors in addition to other less common tumors of low malignant potential. Epithelial ovarian cancer (EOC) is by far the commonest among different malignant ovarian tumors and the most common cause of death arising from a female pelvic malignancy [2].

Most "more than 90%" ovarian cancers are classified as epithelial and are believed to arise from the surface epithelium of the ovary. However, some evidence suggests that the Fallopian tube could also be the source of some ovarian cancers [3].

Ovarian cancer is primarily a disease of postmenopausal women, with the large majority of cases occurring in women between 50 and 75 years old. The disease is more common in industrialized nations, with the exception of Japan. In the United States, females have a 1.4% to 2.5% (1 out of 40-60 women) lifetime chance of developing ovarian cancer [4].

In NCI, Cairo University, tumors of the female genital system represented 4.70% of total malignancy. A total of 135 cases of ovarian malignant tumors, accounting for 29.22% of female genital tract malignancies and 1.37% of total malignancy, are presented during the years 2003-2004 [5].

Surgery is the main line of treatment in most of the cases of epithelial ovarian cancer (EOC), with adjuvant chemotherapy recommended for patients with stage IC and follow up. In locally advanced and metastatic EOC, either primary surgery or neoadjuvant chemotherapy followed by surgery is a reasonable [6].

Numerous combination chemotherapy regimens have been shown to produce responses in patients with ovarian cancer. Since the mid-1990s, a chemotherapy combination consisting of the combination of paclitaxel and a platinum compound has been accepted as the standard of care. Most recent research has focused on further optimization of these regimens to maximize clinical benefit while minimizing toxicity and investigations into alternative taxanes (e.g., docetaxel), other novel agents, and new treatment schedules are ongoing [7].

Aim of Work

A retrospective study aimed to present the clinicopathological characteristics, treatment modalities and the outcomes of different types of ovarian cancer in NCI, Cairo University, Egypt, during the years 2007-2010.

On the basis of distinct pathologic and clinical features, ovarian cancer can be separated into three distinct histologic subtypes: Epithelial tumors, Germ cell tumors and Sex cord stromal tumors. The vast majority of ovarian cancers are epithelial in origin. Fallopian tube carcinomas and extra-ovarian primary peritoneal carcinomas are much less common, but their biology and clinical characteristics are markedly similar to those of epithelial ovarian carcinomas [8].

Ovarian epithelial tumors are heterogeneous and primarily classified according to cell type into serous, mucinous, endometrioid and clear cell subtypes. According to the WHO classification (Table 1) [9], tumors in each of these categories are further subdivided into benign, borderline (intermediate) and carcinoma forms, which are associated with different prognoses. This is done according to the amount of epithelial cell proliferation, the degree of nuclear atypia and the presence or absence of stromal invasion [8].

	Mean	Median	Number (%)
Age	44.9 ± 14.4	48	265 (100%)
1-1o years	--	--	2 (0.8%)
11-20 years	--	--	21 (7.9%)
21-30 years	--	--	23 (8.6%)
31-40 years	--	--	26 (10%)
41-50 years	--	--	90 (34%)
51-60 years	--	--	82 (31%)
61-70 years	--	--	16 (6%)

71-85 years	--	--	5 (1.7%)
Menopausal Status			
Premenopausal	--	--	125 (51%)
Postmenopausal	--	--	119 (48.6)
Primary amenorrhea	--	--	1 (0.4%)
Marital Status			
Single	--	--	35 (13.2%)
Married	--	--	230 (86.8%)
Parital Status			
Nulliparity			47 (17.7%)
Single			35 (13.2%)
Married			12 (4.5%)
Multiparity			218 (82.3%)
One or two child			55 (20.8%)
More than two child			163 (61.5%)
Family History			
Negative			253 (95.5%)
Positive			12 (4.5%)
Presenting Complains			
Abdominal pain			17 (6.4%)
Abdominal mass			3 (1.1%)
Mixed complains			245 (92.5%)

Table 1: *Patient's Characteristics.*

The majority of cases of ovarian cancer are of epithelial origin (~90%).

Currently, however, based on light microscopy and molecular genetics, epithelial ovarian carcinoma is subdivided into five main subtypes (in descending order of frequency):

1. High-grade serous carcinomas (HGSC)
2. Clear cell carcinomas (CC)
3. Endometrioid carcinomas (EC)
4. Mucinous carcinomas (MC)
5. Low-grade serous carcinomas (LGSC)

These five subtypes account for 98% of ovarian carcinomas and can be reproducibly diagnosed. They are inherently different diseases, as indicated by differences in epidemiological and genetic risk factors, precursor lesions, patterns of spread and molecular events during oncogenesis, response to chemotherapy and outcome.

With progress towards subtype-specific management of ovarian carcinoma, accurate subtype assignment by surgical pathologists is becoming increasingly important [10].

Methods

This study was a retrospective study. This study included all the patients diagnosed with ovarian cancer that were treated at National Cancer Institute (NCI), Cairo University, Egypt, between January 2007 and December 2010.

The following information were extracted from the patient medical files: Age at diagnosis, Menopausal status, Marital status and Number of children, Presenting symptoms, Laboratory investigations (Liver function, kidney function, complete blood count and tumor markers), Tumor histological type, Tumor FIGO stage and Degree of differentiation, Treatment modalities, Type of surgery, Chemotherapy regimens received (Adjuvant, neoadjuvant or palliative), Chemotherapy responsiveness or resistance, disease recurrence and disease-free period and patients survival.

Primary endpoint was overall survival, calculated from the date of diagnosis till the date of death or last follow-up. Secondary endpoint was response rate according to WHO. Disease free survival was calculated from the date of surgery or end of chemotherapy till the date of recurrence or last follow-up, if no evident recurrence. Progression free survival "1" (PFS1) was calculated for patients who underwent non-curative surgery and progressed after the end of chemotherapy. Progression free survival"2" (PFS2) was calculated for patients who experienced recurrence after curative surgery and adjuvant chemotherapy and received second line of chemotherapy then progression happened, PFS2 was calculated from date of beginning of second line of chemotherapy till progression.

Statistical Analysis

Descriptive statistics was used to describe different clinicopathological characteristic of age, histopathology, stage, grade distribution, symptoms, treatment categories, response to treatment. Survival analysis was done using the Kaplan-Meyer method. Comparison between two survival curves will be done using log–rank test. P-value < 0.05 will be considered significant.

IRB Approval

The study started after the approval of the IRB. Data collection and presentation were anonymous and both privacy and confidentiality were protected to the maximum possible standards.

Results

This is a retrospective study in the National Cancer Institute (NCI), Cairo University implemented in the period from 1st January 2007–31st December 2010, where it included 265 cases that were found in the registry during this period.

Patient's Characteristics

A total of 265 patients diagnosed and treated at the NCI over the specified period (2007-2010), the median age was 48 years (range 8-85) with the majority (>72%) of cases diagnosed in women over 40 years old. The majority of patients were in the age group between 41-60 years. More than half of the cases were premenopausal. Regarding the marital status, most of them were married (87%) at the time of the development of the disease.

Family history was positive in 12 patients only, who represent 4.5% of all patients (Figure 5) (Table 1).

Nulliparity was encountered in about 18% of the patients, while 218 patients (82%) have at least one child. The majority of the patients (92%) presented with a complaint of abdominal mass, abdominal pain or vaginal bleeding (Table 1).

With regards to the laboratory results, CA125 was evaluated in 261 cases with mean result of 916.4 and a range of 1.0-19860.0. CA125 was done irrespective of type of pathology, but it was elevated mainly in epithelial ovarian carcinoma, especially serous adenocarcinoma subtype. CA125 was elevated in 216 cases (82.7%) while it was normal in 45 cases. CEA was done in 59 cases with mean 32.2 (range 0.4-530.0). We observed that CEA was high in all cases with mucinous adenocarcinoma subtype. AFP and BHCG were done in about 48 cases and were elevated in 28 cases only (58.4%) in germ cell tumor and sex cord tumor. LDH was elevated especially in lymphoma cases.

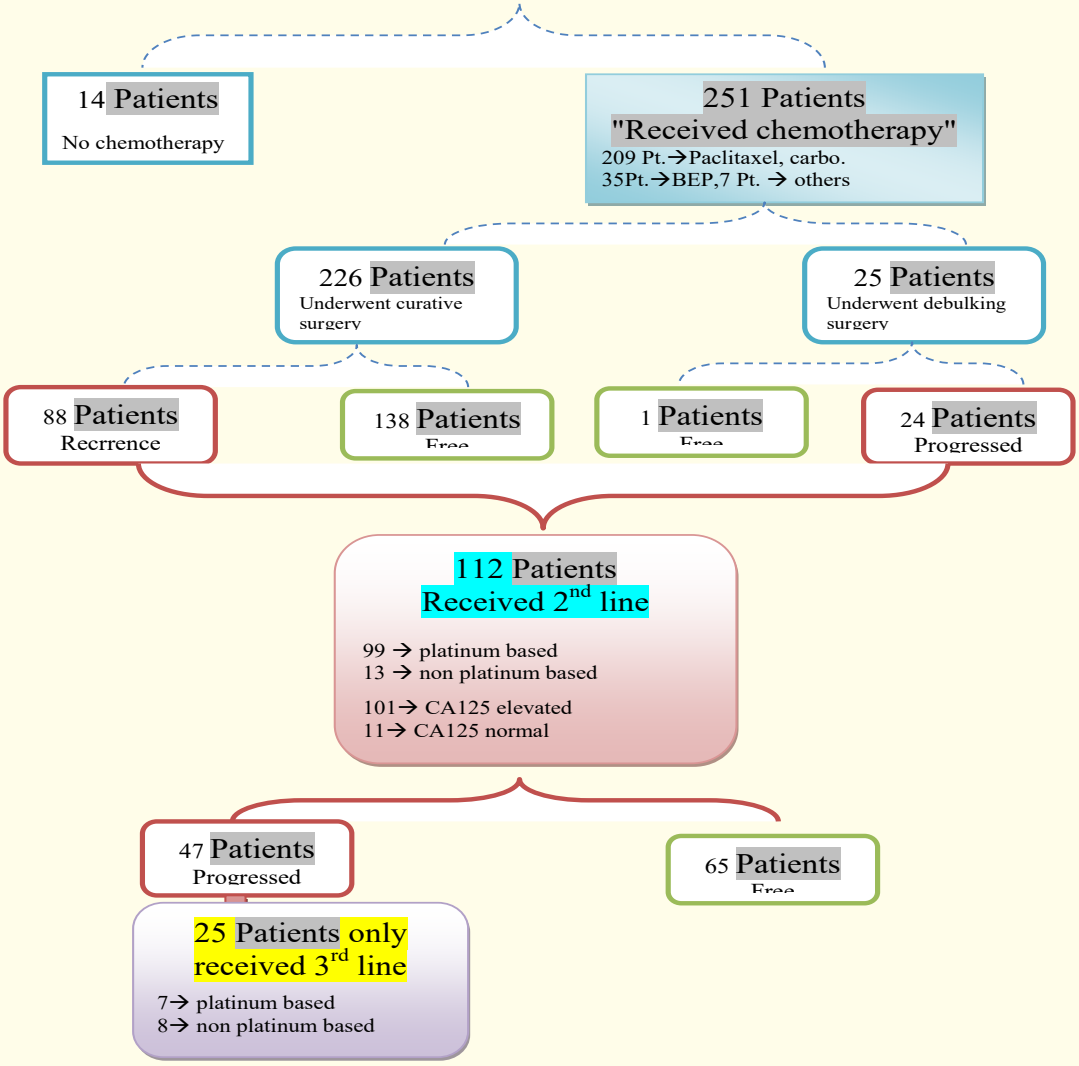


Figure 5: *Summary of Treatment, Recurrence and Progression in Studied Group.*

Bilateral ovarian cancer was found in 118 cases which comprised 44.5% of all cases (Table 2).

Histopathological grade II was present in majority of the cases which was about 139 cases (52.5%), grade I was present in 28%, while 52 cases had grade III disease (Table 2).

Stage I, according to FIGO staging, was the commonest presented in our study in non-epithelial ovarian cancer (NEOC) as 46 cases were stage I and II which represent 95.9%, while 65 cases only of EOC presented with stage I and II, which represent 30% of all EOC. Stage III and IV was the commonest presentation in EOC as about 70% of cases presented with stage III or IV, while only 2 cases of NEOC presented with stage III which represent 4.1%. Overall, stage I and II represented 41.9% while stage II and IV represented 58.1% (Table 2).

	Number	Percentage
Site		
Bilateral	118	44.5%
Right	93	35.0%
Left	54	20.5%
Histopathological Grade		
Grade I	74	27.9%
Grade II	139	52.5%
Grade III	52	19.6%
FIGO Staging		
Stage I	73	27.5%
EOC	30	13.9%
NEOC	43	89.6%
Stage II	38	14.4%
EOC	35	16.1%
NEOC	3	6.3%
Stage III	114	43.0%
EOC	112	51.6%
NEOC	2	4.1%
Stage IV	40	15.1%
EOC	40	18.4%
NEOC	0	0%

Figure 2: *Tum or Characteristics.*

Of the total group, 217 records (81.9%) were for epithelial ovarian cancer, 36 records (13.6%) were for germ cell tumor, 10 records (3.8%) were for sex cord tumor, and lastly 2 records were for Burkitt's lymphoma which was equal to 0.7% (Figure 1) (Table 2).

The epithelial ovarian cancer was the commonest type among all groups which was presented by 82%. Serous adenocarcinoma was the commonest subtype of EOC which was presented by 198 cases or about 91% of all EOC. Mucinous type was in the second place, presented by 12 cases which meant 5.5% of all EOC. Only 2 cases presented with clear cell type. Other types such as endometrioid, undifferentiated and unclassified type were presented by 5 cases only from all 217 cases (Figure 2) (Table 2).

Germ cell tumor (GCT) was the second pathological type of our study. Dysgerminoma as first subtype of GCT was presented by 50% of cases, 25% for yolk sac tumor, 19.4 % for teratoma and 5.6% for mixed germ cell tumor. Embryonal type was presented by 2 cases only of all 36 cases, one case for each type (Figure 3). Other pathological types of ovarian cancer like sex cord tumor, were presented by only 10 cases out of 265 cases, representing 3.8%. Burkitt's lymphoma was diagnosed in 2 cases only (Table 2).

Regarding surgical management, total abdominal hysterectomy with bilateral salpingoophorectomy (TAH BSO) plus omentectomy with lymph nodes excision and peritoneal sampling, which is called the classical operation of ovarian cancer, was the main line of surgery in our study. About 75% of cases underwent classical operation, while only 16% (42 cases) took the chance of preservation of fertility and underwent unilateral oophorectomy (fertility preserving operation). All cases with aggressive disease underwent debulking surgery, which represent 9.4% of all cases (Table 3).

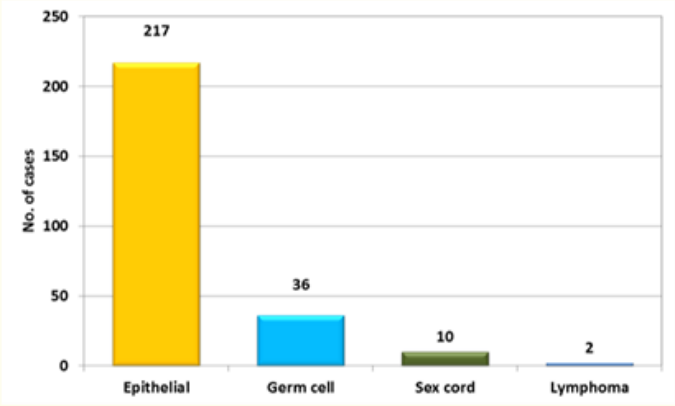


Figure 1: *Pathological Classification of the Studied Group.*

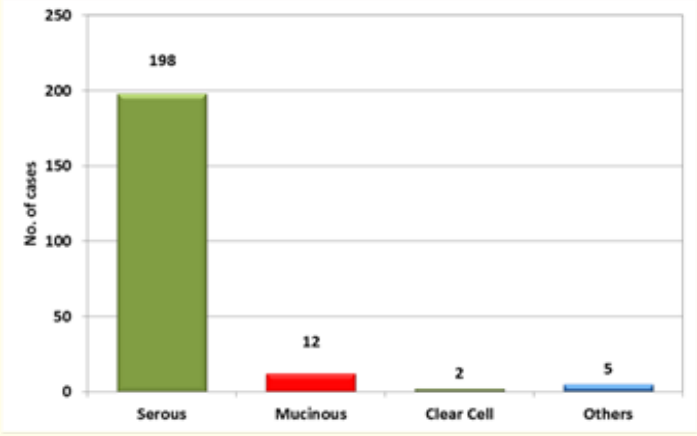


Figure 2: *Pathological Types of the Epithelial Tumors.*

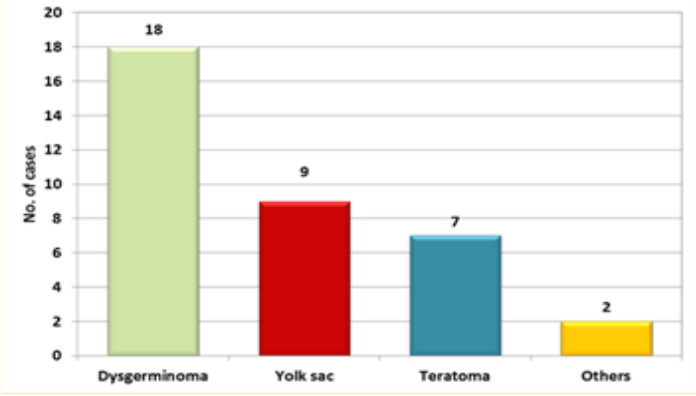


Figure 3: *Pathological Types of the Germ Cell Tumors.*

	Median	Minimum	Maximum	Number	Percentage
Type of surgery					
Proper surgery				198	74.7%
Fertility preserving				42	15.8%
Debulking				25	9.5%
Type of chemotherapy					
Neoadjuvant				13	4.9%
Adjuvant				224	84.5%
Palliative				14	5.3%
No chemotherapy				14	5.3%
Chemotherapy protocol 1st line(251 case)					
Paclitaxel, carbo				209	83.3%
BEP				35	14.0%
Others				7	2.7%
Number of cycles of 1st line					
1-4 cycles				22	8.8%
6				226	90.0%
8				3	1.2%
Recurrence"226 case"					
Yes				88	38.9%
No				138	61.1%
Progression"25 case"					
Yes				24	96.0%
No				1	4.0%
CA125 before 2nd line					
Elevated	2050	120	10356	101	82.9%
Normal	8	1	20	11	17.1%
Time of recurrence					
< 6 months				13	11.6%
> 6 months				99	88.4%
Chemotherapy protocol 2nd line"112 case"					
Platinum based				99	88.4%
Non platinum based				13	11.6%

Number of cycles of 2nd line					
1-4 cycles				28	25%
6 cycles				80	71.4%
8 cycles				4	3.6%
Progression after 2nd line					
Yes				47	42.0%
No				65	58.0%
Time of progression					
< 6 m				20	42.5%
> 6m				27	57.5%
Chemotherapy protocol 3rd line"25 case"					
Platinum based				17	68.0%
Non platinum based				8	32.0%
Number of cycles of 3rd line					
1-4 cycles				17	68.0%
6 cycles				7	28.0%
8 cycles				1	4.0%

Table 3: *Treatment Options.*

Regarding medical management, 224 cases were treated with adjuvant chemotherapy, while 14 cases only were low-grade with early stage and they were let go without any line of treatment after their operation, just follow-up only. Patients who were treated by neoadjuvant, adjuvant, palliative and no chemotherapy just follow-up consisted of 4.9%, 84.5%, 5.3% and 5.3% respectively (Figure 4) (Table 3).

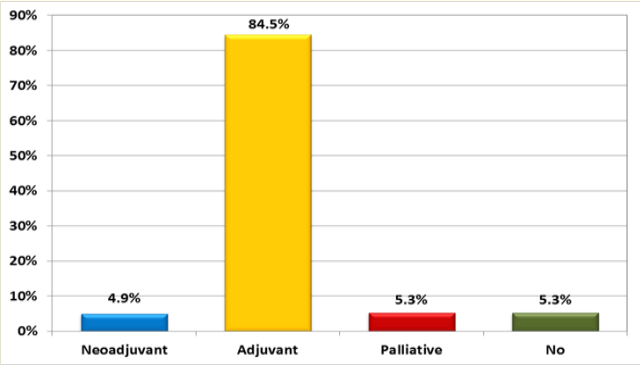


Figure 4 : *Type of Chemotherapy.*

Paclitaxel and carboplatin was the main line of treatment among the group as 209 cases were treated by this line as 1st line chemotherapy, especially those who were diagnosed as epithelial ovarian cancer. On the other hand, patients who were diagnosed as germ cell tumor or sex cord tumor were treated by Bleomycin, Etopside and Platinol (BEP) as 1st line of treatment and they were represented by 35 cases. Most of the patients received 6 cycles chemotherapy regardless of the type of chemotherapy as about 226 cases received 6 cycles of their chemotherapy protocols (Table 3).

With regards to the recurrence for those who underwent curative surgery, 88 cases (39%) developed recurrent ovarian cancer while 138 cases continued on regular follow-up without evidence of recurrence. For patients who underwent debulking surgery, 96% of them progressed after the end of chemotherapy, while only one case did not report for progression, either the case lost follow-up or was kept free (Table 3).

Among the cases that developed either recurrence or progression, CA125 was elevated in 101 cases while only 11 cases were in the normal value of CA125 (Table 3).

Regarding 2nd line chemotherapy, it was platinum based chemotherapy in 88.4% of all cases, while 11.6% only received non-platinum based chemotherapy. The total number of chemotherapy cycles in 2nd line was mainly 6 cycles as 72 cases received 6 cycles of their chemotherapy protocols regardless of the type of chemotherapy (Table 3).

There were a total of 112 patients who received 2nd line chemotherapy 47 (42%) of them progressed after the end of 2nd line chemotherapy, 25 patients received 3rd line chemotherapy as progression occurred, 68% of them were platinum sensitive and received platinum based chemotherapy and 8 cases were resistant to platinum so they received non-platinum based chemotherapy (Table 3).

Survival Data

Disease Free Survival

DFS for the whole group of patients at 1, 3 and 5 years was 92%, 63% and 57% respectively (Figure 6).

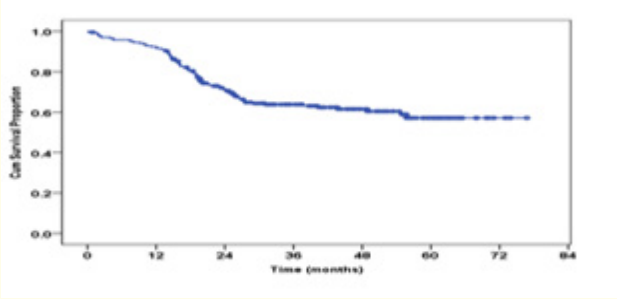


Figure 6: *Disease free survival Results of the whole study group.*

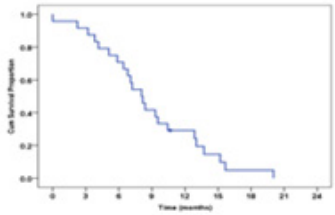
Progression Free Survival "1"

PFS was calculated for patients who underwent non-curative surgery and progressed after the end of chemotherapy. Median PFS was 8.0 months only, one year PFS consisted of 24.3% of all cases and two years PFS was 0.0% as all patients progressed before 2 years (Figure 6).

Progression Free Survival "2"

PFS2 was calculated for those who underwent curative surgery then received adjuvant chemotherapy, after which recurrence occurred and they received 2nd line of chemotherapy, then progression happened. PFS2 was calculated from the date of beginning the 2nd line of chemotherapy till progression occurred. Also, PFS2 was calculated for patients with residual disease after the end of 1st line. After one year, about 58.6% of the cases progressed (Figure 7).

PFS of the whole study group.



PFS "2" of the whole study group (2nd line)

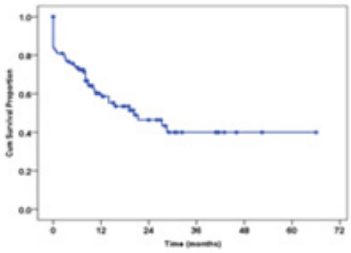


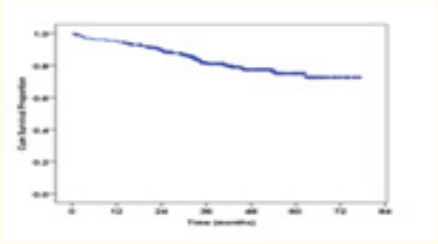
Figure 7: *Progression free survival of the whole study group.*

Overall Survival

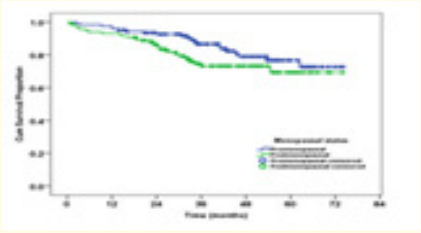
OS for all patients at 1, 3 and 5 years was 95%, 90% and 85% respectively.

Median OS of all patients wasn't reached because 20% only of the whole group died, while the rest were either free or lost to follow-up (Figure 8).

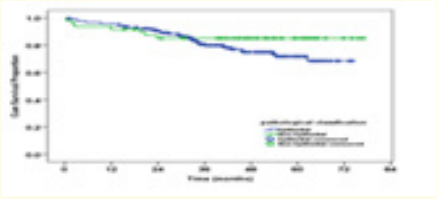
OS of whole study group



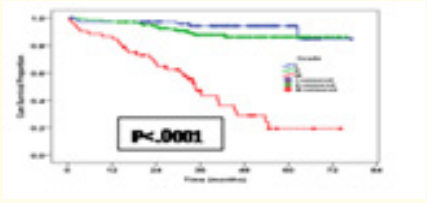
OS in relation to menopausal status



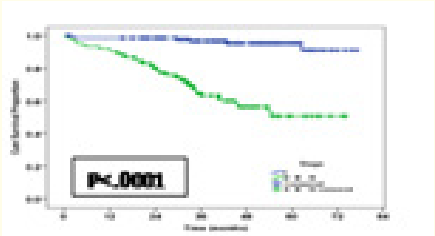
OS in relation to pathological classification



OS in relation to histopathological grade



Survival in relation to stage



OS in relation to type of surgery

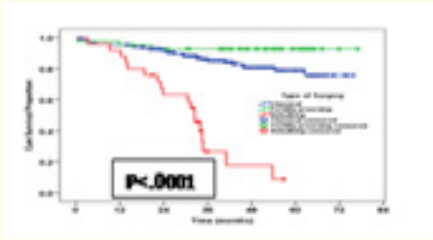


Figure 8*: Overall survival Results.*

Comparing between pre and post menopausal status and its effect on OS, we find that 23 cases who died were premenopausal while 30 cases were postmenopausal, with borderline significant difference P= 0.078.

Overall survival in relation to pathological type was not significantly different between epithelial or non-epithelial ovarian cancer as P= 0.2 (Figure 8).

The histopathological grade significantly affected the survival curve. We found that there was a highly significant difference between three types, especially between grade I & II on one side and grade III on the other side with P value <0.0001 (Figure 8).

Overall survival was greatly affected by the stage of the tumor with P<0.0001. There were 45 recorded deaths for stage III and IV, while there were 8 recorded deaths only for stage I and II (Figure 8).

The type of surgery had a clear impact on overall survival, the worst effect was with debulking surgery. On the other hand, the fertility preserving operation was the best type of surgery (P<0.001) (Figure 8).

Discussion

Ovarian cancer is the fifth most common type of cancer and the fourth most common cause of cancer deaths in women. The estimated lifetime risk for a woman developing ovarian cancer is about 1 in 54. Ovarian cancer is predominantly a disease of older, postmenopausal women with the majority (>80%) of cases being diagnosed in women over 50 years old [11]. In the Arab world, the frequency of ovarian cancer varies from one country to the other. It accounts for 6.3% in Oman, 5.7% in Bahrain, 5.1% in Jordan, 4.6% in Somalia, 4.2% in Algeria, 4% in Egypt according to NCI registry, 3.6% in Saudi Arabia, 3.5% in Qatar, 3.4% in Tunisia, 3.1% in Kuwait, 2.8% in Lebanon and 1.9% in UAE. Our study included 265 patients diagnosed as ovarian tumors who presented at NCI during the period from January 2007 till December 2010 [12].

The median age for the whole group was 48 years old, age ranged from 8 to 85 years. More than 80% of the patients were over 50 years old with a median age of 63 years old. This age incidence peak is about one and a half decades lower than what is seen in Western populations [13], but it is similar to Alex University [14] as the median age was 48 years also. In the Gharbia population-based cancer registry, the mean age at diagnosis was 47.2 years and the median age was 49 years [15]. In the year 2007, the Middle East Cancer Consortium (MECC) evaluated the incidence of ovarian cancer among four member countries in this consortium, namely Egypt, Israel, Cyprus, and Jordan. Compared to the US SEER database, it was noticed that, while Cypriots, Israeli and US SEER data showed that the highest proportion of patients with ovarian cancer were in the age group from 50 to 69 in Egyptians, Jordanians and Israeli Arabs, the highest age group was below the age of 50 years, which is very close to our results [16].

Also, in our study, premenopausal patients consisted of about 51%, even though it is a disease of post menopause [11].

In our study, positive family history to cancers was present in 4.5% of the patients, without any available data about the type of cancer and degree of relationship. Family history plays a very important role in the development of ovarian cancer although, in a recent study, 44% patients with high-grade serous ovarian cancer and a germline BRCA mutation did not report a family history of cancer [11]. In our study, not one of them underwent BRCA mutation.

The results of our study stand midway between the consistent higher percentages of positive family history in Pakistani studies, but it is similar to the percentage in western data in which only 5-10% of epithelial ovarian cancer cases have strong family histories [17].

In our study, EOC predominates, constituting 81.9% of all ovarian cancer cases. In the Middle East Consortium Study, epithelial ovarian tumors ranged from 77.8% to 93.2% of the cases according to the region, it was the lowest in Egypt (77.8%) followed by Jordan (81%), then Israeli Arabs (84.5%), Cyprus (88.4%), US SEER data (91.8%) and Israel (93.2%) [13].

Among our patients with EOC, 91.2% were serous carcinomas and 5.5% were mucinous carcinomas. In the Middle East Consortium Study, serous carcinomas predominated with percentage ranging between 27.2% and 49.9%, followed by adenocarcinoma. The propor-

tion of mucinous carcinomas among Egyptians in this study was 16.1% and among Jordanians it was 11.7%, whereas in Israeli and Cypriot registries, the percentage was low, ranging from 6% to 8.7% [13].

In our study, sex cord tumor accounted for 3.8% of the cases. This was close to the results of the MECS where the percentage of sex cord stromal tumors was very low, especially in Jews and Israeli Arabs [13].

In our study, the percentage of germ cell tumors was 13.6% of all ovarian cancer cases presented to our department. Our results mimic those of US SEER but it is slightly higher than other Arabian countries where the incidence of germ cell tumors is higher (7.2-12.1%) [13].

For all patients in this study, stages III and IV were seen in 58.1% of the cases, including epithelial and non-epithelial ovarian cancer (56.2% vs 78%). But when we calculated only epithelial ovarian cancer, stage III and IV were 70%, which is more similar to many international results. As reported by Beth., *et al,* approximately 70% of patients with EOC present with stage III or IV disease.

In our study, CA-125 was elevated in more than 90% of all epithelial tumors, which is similar to the report by [9] where it was elevated in about 80% of cases, especially late stage.

About 44.5% of all ovarian tumors in this study were having bilateral disease, a result which is much more than the 17.2% incidence that was seen in an Asian study evaluating ovarian cancer at a cancer hospital in a developing country [18].

More than 90% of our patients were treated initially with surgery. In a review of 372 consecutive patients with advanced ovarian cancer in a university hospital in Berlin, it was found that 89% of the cases underwent surgery [19].

In our study, only 14 patients having epithelial ovarian carcinomas did not receive any adjuvant or neoadjuvant chemotherapy, all of them were having stage IA and GI (5.3%), while 4.9% of the cases in our study started neo-adjuvant chemotherapy.

Based on international guidelines, Paclitaxel-carboplatin was the standard first line in cases of EOC (83.2%).

BEP (Bleomycin, Etopside and Platinol) was the standard treatment in cases of NEOC (13.9%). The response rate to first line chemotherapy after chemotherapy cycles was seen in about 55.4% of the cases, 44.6% of the cases progressed after first line chemotherapy.

The response rate to paclitaxel followed by either cisplatin or carboplatin in the study done by Neijt., *et al,* ranged between 64-74% [20]. The response rate in our study is similar to those of the international studies**.**

There were 112 patients (44.6%) diagnosed as having ovarian cancer and received second-line chemotherapy. Platinum based was the most frequently used regimen of second line chemotherapy in 88.4% and non-platinum based was used in 11.6% of the cases. What was very evident in our study was the response rate to second-line chemotherapy which reached 58%. In the western studies, the response rate for platinum sensitive patients ranged roughly from 30% to 60%. The response rate in platinum resistant patients is much less [21].

Nearly 25 patients (9.4%) received third-line chemotherapy. Platinum based was the most frequently used as third-line chemotherapy (68%) while non platinum was used by 32%.

Forty-four patients received third line chemotherapy with a response rate of 41% in a retrospective study evaluating 172 patients with ovarian epithelial cancer treated at the National Cancer Institute in Japan from the year 1999-2005, this was reported in a study [22].

Five years overall survival in our study was 85%, which is much higher than other western countries where 5 years OS is 44.2% as reported by SEER US. As per the American Cancer Society, 5 year OS in stage I, II, III and IV were 89%, 66%, 34% and 18% respectively [11].

The most reliable long-term survival data on accurately staged early-stage ovarian cancer is derived from studies of the GOG. In these studies, patients with stage I disease with well or moderately well differentiated tumors have a greater than 90% five year survival rate. Patients with unfavorable prognosis early stage ovarian cancer have a 5 year survival rate of approximately 80%. Patients with stage III

disease have a 5 year survival rate of approximately 35%, which is dependent in large part on the volume of disease present in the upper abdomen. Patients with stage IV disease have less than a 10% five year survival rate [23].

This difference between our study and international literature can be explained by two reasons: First, we studied all types of ovarian cancer including epithelial ovarian cancer, germ cell tumor and sex cord tumor. Second, the median of OS of all patients wasn't reached because 20% only of the whole group were dead and the rest of the group are either free or lost to follow-up with no available communication to know if they are either still alive or if they have died.

Epithelial ovarian cancer is a lethal disease. The age incidence of ovarian cancer in our patients is ten years younger than what is reported in US SEER data and other Western countries. EOC constitutes the majority among all ovarian cancer cases, followed by germ cell tumors. Papillary serous cyst adenocarcinoma predominate other types of EOC.

Presentation of patients in this study was late and stages III and IV were predominant. The response rate of EOC to first line chemotherapy was high but the progression free survival was lower than what is reported in the western literature. Despite a high response rate to first-line chemotherapy, prognosis remains poor due to recurrence and development of resistance to chemotherapy. FIGO staging, histopathological grade and type of surgery have a clear impact on overall survival.

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