



ORIGINAL ARTICLE

# Retrospective analysis evaluating ovarian cancer cases presented at the clinical oncology department, Alexandria University

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## KEYWORDS

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**Abstract** Ovarian cancer is the most common cause of death among women with gynecologic malignancies. The standard management is maximal surgical cytoreduction followed by systemic chemotherapy.

The aim of this retrospective study is to evaluate ovarian cancer cases presented at Alexandria Clinical Oncology Department (ACOD) during the years 2008–2010.

*Methods and materials:* We reviewed the files of all patients presented at or referred to ACOD from January 2008 till December 2010 with the diagnosis of ovarian cancer, ovarian epithelial tumor, ovarian sex cord tumors, border line ovarian tumor and ovarian germ cell tumors.

*Results:* The study included 116 patients, representing 1.4% of all cancer cases; the mean age for all patients was  $47.9 \pm 13.9$  years. Only 13.7% of the patients had positive family history. Stages III and IV were seen in 79.2% of the cases. Epithelial ovarian cancer (EOC) constituted 75% of the cases, border line tumors 12.9%, granulosa cell tumor 6%, and germ cell tumors 4.3%. Among EOC, serous cystadenocarcinoma was seen in 58%. For EOC, surgery was the initial step in 80.4% of the cases. Paclitaxel-carboplatin was the most commonly used regimen as first line chemo-

*Abbreviations:* ACOD, Alexandria clinical oncology department; EOC, epithelial ovarian cancer; PFS, progression free survival; CA125, cancer antigen or carbohydrate antigen 125; TAH & BSO, total abdominal hysterectomy and bilateral salpingo-oophorectomy; MECC, middle east cancer consortium; SEER, surveillance epidemiology and end results; GOG, gynecology oncology group.

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therapy. Response rate to first line chemotherapy reached 87.3% (44.8% complete response). The mean follow up period was 15 months. The progression free survival for EOC after first line chemotherapy was 10.8 months.

*Conclusion:* The age incidence of ovarian cancer in our patients is 10 years younger than that seen in Western countries. EOC constitutes the majority among all ovarian cancer cases, followed by border line tumors. Papillary serous cystadenocarcinoma predominates other types of EOC. The response rate of EOC to first line chemotherapy was high but the progression free survival was lower than that seen in the literature.

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## 1. Introduction

Malignant ovarian tumors include epithelial ovarian cancer, germ cell tumors in addition to other less common tumors of low malignant potential.<sup>1</sup>

Epithelial ovarian cancer EOC is by far the commonest among different malignant ovarian tumors, it is the sixth most frequent cancer in women and the most common cause of death arising from a female pelvic malignancy.<sup>1</sup> More than 50% of epithelial ovarian cancer cases affect patients older than 60 years and 5–10% of the cases are familial.<sup>2</sup> Approximately 75% of women with epithelial ovarian cancer are diagnosed with stage III or stage IV disease. The 5 year survival rates for stage three ranges between 28% and 50%, and for stage four around 13%.<sup>3</sup>

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 I C and up.<sup>4–6</sup> In locally advanced and metastatic EOC either primary surgery or neo-adjuvant chemotherapy followed by surgery is a reasonable modality.<sup>7</sup>

In Egypt, there is no national cancer registry, but one of the important regional registries is Gharbia Population Based Cancer Registry (GPBCR), according to its publications over a three years period (2000–2002), 225 ovarian cancer cases were registered with an average of 75 cases per year. They represented 2.2% of all incident cancers and accounting for 4.4% of all newly diagnosed female cancers.<sup>8</sup>

The other important regional registry in Egypt is Aswan regional registry, in which over the year 2008, thirty-five cases of ovarian cancer were registered, representing 5.6% of all female cancers cases.<sup>9</sup>

In Alexandria Clinical Oncology Department, we have an archive with a filing system for all cancer cases presented at the department together with a manual registry; a new computer based registry is on its way to be established. Studies evaluating the magnitude of the problem of ovarian cancer cases presented at our department are very few and old, so our idea was to conduct such a study aiming at evaluating ovarian cancer cases referred to and presented at the Alexandria Clinical Oncology Department (ACOD) in the last three years.

### 1.1. Aim of the study

Evaluating ovarian cancer cases presented and referred to the clinical oncology department during the last three years from January 2008 till December 2010, as regards; percentage among different cancer cases, age distribution, clinico-pathological aspect, stage at presentation, grade at presentation,

primary modality of therapy, response to first and second line chemotherapy, and the progression free survival (PFS).

## 2. Methods

We reviewed of the files of all patients who presented at or referred to Alexandria Clinical Oncology Department during the years from January 2008 till December 2010 with the diagnosis of ovarian cancer, ovarian epithelial tumor, ovarian sex cord tumors, border line ovarian tumor and ovarian germ cell tumors. The content of the files were emptied in excel sheets and were referred to the statistician (a member of the team) for statistics.

## 3. Statistical methods

Analysis was done on stats direct statistical package. Descriptive statistics were used to describe the study sample in terms of age, histopathology, stage and grade distribution as well as symptoms and treatment categories. As regards response to treatment, frequency distributions were used to elicit proportion of patients in each response category.

## 4. Results

**Table 1:** Clinico-pathologic criteria in the studied patients.

### 4.1. Age

The mean age for the whole group of patients in this study was  $47.9 \pm 13.9$  (range 25–80 years), and the median age was 46 years, The age distribution showed two age peaks, the first age peak lies between 30 and 50 years of age, half of the patients in the study sample were in this group. The second age peak, which contained approximately one third of the patients, was seen in the age group 60–69 years.

Analysis of EOC patients alone showed a median age of 47 year, mean  $48.5 \pm 12.7$  year and that all age groups were represented within the epithelial tumors category: 1% of epithelial tumors were under 30 years, 48% between 30 and 49 years, 16% were aged 50 and 59 years, 32% between 60 and 69 years and only 3% over 70 years.

### 4.2. Family history

Negative family history for ovarian, breast and colon cancers was present in 100 (86.2%), while 16 (13.7%) patient reported positive family history in first degree relatives for one of the previously mentioned cancers.

**Table 1** Clinico-pathologic criteria in the studied patients.

Age	Number	Percentage
Mean age all patients	47.9 years ± 13.9	–
Mean age EOC	48.5 years ± 12.7	–
Positive Family history	16	13.7
<i>Histopathology</i>		
EOC:	87	75
Border line tumors:	15	12.9
Granulosa cell tumors:	7	6
Germ cell tumors:	5	4.3
Krukenberg tumors	2	1.7
Total number of cases in the study	116	100
<i>Grade of the tumor (all patients)</i>		
GI	11	9.4
GII	37	31.8
GIII	53	45.6
<i>Duration of symptoms</i>		
Maximum:	18 months	–
Minimum:	2 months	–
Mean:	6 ± 2.8 months	–
<i>Common symptoms</i>		
Abdominal discomfort	109	93.9
Abdominal distention	104	89.6
Menstrual irregularities	63	54.3
Pelvic pain	31	26.7
Constipation	11	9.4
Dyspnea	5	4.3
Intermittent intestinal obstruction	3	2.5
Elevated CA 125 level for EOC	87	100

EOC; epithelial ovarian cancer.

#### 4.3. Duration of symptoms

A maximum duration of symptoms prior to presentation of 18 months, and a minimum of 2 months with a mean duration of 6 ± 2.8 months. Duration of symptoms also strongly correlated with stage at presentation by simple linear regression ( $p < 0.001$ ).

#### 4.4. Symptom profile

The most common presenting symptoms were abdominal discomfort (109 patients, 93.9%), abdominal distension (104 patient 89.6%), menstrual irregularities (63 patient 54.3%), pelvic pain (31 patient 26.7%), constipation (11 patient 9.4%), dyspnea (5 patient 4.3%) and intermittent attacks of intestinal obstruction (3 patient 2.5%) .

#### 4.5. Histopathological type

The study included 116 patient with ovarian tumors, EOC constituted 75% (87 cases) of the cases, this was followed by border line tumors accounting for 12.9% (15 cases), then comes granulosa cell tumor 6% (7 cases), and lastly germ cell tumors 4.3% (5 cases). Two cases were found to be krukensberg metastasis from colon cancer.

Among EOC serous cystadenocarcinoma constituted the majority of the cases representing 58% of epithelial ovarian cancers.

**Table 2** Stage information in the studied patients.

Stage	EOC (%)	Border lie tumors (%)	Granulosa cell tumors (%)	Germ cell tumors (%)
I	6.8	86.6	28.5	40
II	8.2	–	–	–
III	50.6	13.3	28.5	–
IV	34.4	–	42.8	60

#### 4.6. Stage

**Table 2:** Stage information in the studied patients.

For all patients in the study, typical presentation was late; stage III was the initial presentation in 48 patients (41.3%) and stage IV in 44 patients (37.9%). Simple linear regression showed that stage at presentation was strongly correlated to age at presentation ( $p < 0.001$ ) which shows that younger patients are more likely to present early.

For border line tumors; the majority of the cases were presented in an early stage (86.6% of the cases were stage I and II); 5 patients (33.3%) had stage I, 8 patients (53.3%) had stage II, while only 2 patients (13.3%) had stage III c.

Three out of the 5 patients (60%) with germ cell tumor had stage IV at presentation while the other two patients (40%) had stage I.

As regards granulosa cell tumor; three out of the seven patients had stage IV (42.8%), two out of the seven patients had stage III (28.5%), while only two patients had stage I (28.5%).

The stage distribution for malignant epithelial tumors was as follows:

Stage I in 6.8% (50% of them having stage I c), stage II in 8.2% (42% having stage II c), stage III in 50.6% (86% having stage III c presentation) and stage IV in 34.4% of the cases.

All patients who were clinically staged had stage IV disease and were referred to us from Elshatby university hospital after biopsy to receive neoadjuvant chemotherapy, as they were considered inoperable.

#### 4.7. Grade

For the whole group of patients, grade III dominates in 53 patients (45.6%), grade II in 37 patients (31.8%) and grade I in 11 patients (9.4%), while 15 patient (12.9%) were having border line tumor.

For epithelial tumors; grade I accounted for 9/87(10.3%) of the patients, grade II 32/87 (36.7%) of the patients and grade III 46/87 (52.8%) of the patients.

#### 4.8. CA-125

CA-125 was elevated in all patients with epithelial tumor in this study, normal in sex cord and germ cell tumors. Elevated inhibin was recorded in two patients with granulosa cell tumors.

#### 4.9. Treatment

##### 4.9.1. Surgery

**Table 3:** Summary of surgery in the studied patients.

4.9.1.1. For epithelial tumors. Surgery was performed initially in 70/87 cases (80.4%), of which 59 (84.2%) had total abdominal

**Table 3** Summary of surgery in the studied patients.

Surgery as a treatment modality for the whole studied patients:	Number of patients	Percentage
Patients started initial surgery	94*	81
Patients underwent surgery after neo-adjuvant chemotherapy	8	6.8
Total patients received surgery during treatment.	102/116	87.9
<i>Type of surgery</i>		
EOC	70/87	80.4
TAH & BSO	59/70	84.2
Debulking	9/70	12.8
Unilateral oophorectomy	2/70	2.8
No residual or residual < 2 cm	24/70	34.2
Residual > 2 cm	46/70	65.8
<i>Border line tumors</i>		
Unilateral oophorectomy	13/15	86.6
TAH & BSO	1/15	6.6
Debulking	2/15	13
<i>Sex cord tumors</i>		
TAH & BSO	3/7	42.8
Unilateral oophorectomy	2/7	28.5
<i>Germ cell tumor</i>		
Unilateral oophorectomy	2/5	40

\* the number includes the two patients with krukemberg metastasis.

hysterectomy with bilateral salpingio-oophorectomy (TAH BSO), 9 (12.8%) patients had debulking and 2 (2.8%) underwent unilateral oophorectomy.

Of those who underwent surgery 24 patients had no residual or residual less than 2 cm (34.2% of those who did surgery) while the majority of those who underwent surgery had a residual tumor more than 2 cm (65.8%).

**4.9.1.2. For border line tumors.** 13 out of 15 patients had unilateral oophorectomy, one patient underwent TAH and BSO and one patient had debulking and the pathology of the last 2 cases revealed in addition to the border line pathology positivity of the cytology for malignant cell.

**4.9.1.3. For germ cell tumors.** 3/5 Patients were treated with primary chemotherapy and 2/5 had unilateral oophorectomy.

**4.9.1.4. For sex cord tumors.** 3/7 Patients were treated with TAH BSO, 2/7 with unilateral oophorectomy and 2/7 with primary chemotherapy.

So, for the whole study group 94 patients had initial surgery (TAH BSO, unilateral oophorectomy, debulking) including the two patients diagnosed as having krukemberg tumor. For those who started chemotherapy, further 8 patients had surgery after primary chemotherapy. So that in total 102/116 (87.9%) patients had some sort of surgery during their treatment.

#### 4.9.2. Chemotherapy

**Table 4:** Types of chemotherapy regimens used in different lines in EOC.

**Table 4** Type of chemotherapy regimens used in different lines of treatment for EOC.

Chemotherapy used for EOC*	Number of patients	Percentage
<i>First line</i>		
Did not receive adjuvant chemotherapy	3	3.4
Carboplatin–adriamycin–cyclophosphamide (CAP)	6	6.8
Carboplatin	21	24.1
Carboplatin–cyclophosphamide	1	1.1
Paclitaxel–carboplatin	56	64.3
<i>Second line</i>		
Gemcitabine- carboplatin	17	47.2
Paclitaxel- carboplatin	15	41.6
Gemcitabine	2	5.5
Oral etoposide	2	5.5
<i>Third line</i>		
Paclitaxel- carboplatin	2	14.2
Liposomal doxorubicin	3	21.4
Gemcitabine	1	7.1
Tamoxifen	7	50
Etoposide	1	7.1

\* Epithelial ovarian carcinoma.

**Table 5:** The response rate after different chemotherapy lines in EOC.

**4.9.2.1. Non-epithelial ovarian cancer.** Twelve non-epithelial ovarian tumors were included in our study (in addition to border line tumors), two did not receive chemotherapy, while the other ten patients had received chemotherapy; complete response was achieved in 50% of the cases, 20% had partial response and 30% had stable disease. The median progression free survival was 15 months.

While germ cell tumors were consistently treated with BEP (bleomycin–etoposide–cisplatin), sex cord tumors were either treated with BEP (3/7), carboplatin–paclitaxel (2/7) or no chemotherapy (2/7).

For border line ovarian tumors 2/15 patients (13.3%) received chemotherapy because of the presence of malignant cells in the pathology specimen, which was in the form of 6 cycles (paclitaxel, carboplatin).

**4.9.2.2. Epithelial ovarian cancer.** Seventeen patients (19.5%) with epithelial ovarian cancer received primary chemotherapy.

For epithelial ovarian cancer and as a first line chemotherapy;

- Three patients did not receive any adjuvant chemotherapy after surgery; all of them were having stage IA, GII epithelial ovarian cancer (3.4%).
- CAP (Cisplatin, Adriamycin, and Cyclophosphamide) was the initial regimen in 6 patients (6.8%).
- Carboplatin alone was the starting regimen for 21 patients (24.1%).
- Carboplatin, cyclophosphamide were the starting regimen for one patient (1.1%).
- Paclitaxel, carboplatin were the initial regimen in 56 patients (64.3%).

**Table 5** The response rate after different chemotherapy lines in epithelial ovarian cancer.

	CR (%)	PR (%)	SD (%)	PD (%)
Response rate to first line chemotherapy	44.8	42.5	6.8	5.7
Response rate to second line chemotherapy	27.7	41.6	22.2	8.3
Response rate to third line chemotherapy	–	–	50	50

Response rate after three cycles first line chemotherapy in EOC (Table 5);

- 39 Patients 44.8% achieved complete response, and retained their response after 6 cycles.
- 37 Patients 42.5% achieved partial response, of them 7 patients converted to complete response after three more cycles.
- 6 Patients 6.8% had stable disease, both after three and six cycles.
- 5 Patients 5.7% had progressed after receiving three cycles.

For epithelial ovarian cancer, 36 patients (41.3%) received second line chemotherapy, as follows;

- Gemcitabine, carboplatin in 17 patients (47.2%).
- Paclitaxel, carboplatin in 15 patients (41.6%).
- Gemcitabine in 2 patients (5.5%).
- Oral Etoposide tablets in 2 patients (5.5%).

Response rate for patients after second line chemotherapy (Table 5);

- 10 Patients had complete response (27.7%).
- 15 Patients had partial response (41.6%).
- 8 Patients stable disease (22.2%).
- 3 Patients had progressive disease (8.3%).

As a third line, 14 patients (14.7%) received third line systemic therapy, as follows;

- Paclitaxel, carboplatin in 2 patients (14.2%).
- Liposomal doxorubicin, in 3 patients (21.4%).
- Gemcitabine single agent in one patient (7.1%).
- Tamoxifen in 7 patients (50%).
- Etoposide tablets in one patient (7.1%).

Response rate for third line (Table 5);

- 7 Stable disease (50%).
- 7 Progressive diseases (50%).

#### 4.10. Duration of response

The mean follow up period was 15 months (minimum 3 and maximum 24 months); the progression free survival (PFS) after first line chemotherapy for epithelial ovarian cancer was 10.8 months.

## 5. Discussion

### 5.1. Age

The study included 116 patients diagnosed as having ovarian tumors, representing 1.4% of all cancer cases presented at

Alexandria Clinical Oncology Department ACOD during the period from January 2008 till December 2010.

For EOC the median age was 47 year and the mean age was  $48.5 \pm 12.7$  years, an age incidence peak which is about one and a half decade lower than what is seen in Western populations.<sup>10</sup>

In the Gharbia population based cancer registry, ovarian cancer represented 2.2% of all incident cancers and 4.4% of all newly diagnosed female cancers. The mean age at diagnosis was 47.2 years and the median age was 49 years.<sup>8</sup>

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 and compared it to the US SEER data base, and noticed that, while in Cypriots, Israeli, and US SEER data, 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.<sup>10</sup>

Paes et al., in a retrospective study evaluating clinic-pathologic characteristics of ovarian tumors in the state of Espirito Santo in Brazil found that the mean age of diagnosis of ovarian cancer was 54.6 years.<sup>11</sup>

Malik, in their study evaluating 286 patients with ovarian epithelial cancer presented at the national cancer institute in Pakistan during the period from 1993 to 1998, found that the mean age of presentation was  $49.5 \pm 13$  years.<sup>12</sup>

So, the age incidence of our patients is similar to that of other parts of Egypt (Gharbia), Jordan, Israeli Arab and Pakistan, while it is nearly 10 years younger than US seer data, Israeli, Cypriots, a notification that needs to be studied more deeply.

### 5.2. Family history

In our study positive family history for ovarian, breast and colon cancers was present in 13.7% of the patients. In a recent study evaluating epithelial ovarian cancer among Pakistani women, the number of patients with positive family history for cancer was 18.7%.<sup>15</sup> In another older study from Pakistan,<sup>12</sup> 20% of the cases had positive family history of cancer. The results of our study stand midway between the consistent higher percentages of positive family history in Pakistani studies and the lower percentage in western data in which only 5–10% of epithelial ovarian cancer cases have strong family histories,<sup>16</sup> further epidemiologic studies are needed to explain these results.

### 5.3. Pathology

In our study, EOC predominates constituting 75% of all ovarian cancer cases. Sarwar et al.,<sup>13</sup> in a study evaluating epithelial ovarian cancer at a cancer hospital in Pakistan, mentioned that epithelial tumors constituted 83.3% of all ovarian cancer cases in this hospital. These incidences were close to the (66–70%)

range seen in Indian hospitals, and a little bit less than what was written in western literature (90%).<sup>13,14</sup> In the Middle East consortium study<sup>10</sup>, epithelial ovarian tumors ranged between 77.8% and 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%).

Among our patients with EOC, 58% were serous carcinomas, and 17.2% were mucinous carcinomas. In the Middle East consortium study,<sup>10</sup> serous carcinomas predominate with percentage ranging between 27.2% and 49.9%, followed by adenocarcinomas, the proportion of mucinous carcinomas among Egyptians in this study was 16.1% and among Jordanians was 11.7% whereas in Israeli and Cypriot registries the percentage was low ranging from 6% to 8.7%.

Paes et al., in their study found that 30% of the epithelial tumors were serous while 13.7% were mucinous.<sup>11</sup>

In our study, granulosa cell tumor accounted for 6% of the cases; this was close to the results of the Middle East consortium study where the percentage of the sex cord–stromal tumors was very low especially in Jews and Israeli Arabs.<sup>10</sup>

In our study, the percentage of germ cell tumors was 4.3% of all ovarian cancer cases presented to our department. According to the Middle East consortium study,<sup>10</sup> our results mimic those of US SEER, Cypriot, and Israeli Jewish but less than other Arabian countries where the incidence of germ cell tumors is higher (7.2–12.1%).

So, the incidence of EOC among all ovarian cancer cases in our study is similar to the incidence in Pakistani and Indian hospitals, and some Middle East countries, but differs from US SEER, Israeli data.

#### 5.4. Stage

For all patients in this study, typical presentation was late; stages III and IV were seen in 79.2% of the cases. Our results were similar to results presented by Malik,<sup>12</sup> where 78% of the cases were having stages III and IV at presentation. Another Asian study showed higher stage at presentation in Pakistan and south Asian countries compared to the Western population (stages III & IV 67% in this study).<sup>13</sup> Paes et al.,<sup>11</sup> found that stages III and IV accounted for only 56.2% of his cases.

#### 5.5. Tumor markers

In our study CA-125 was elevated in all epithelial tumors, while in the study done by Sarwar et al.,<sup>13</sup> CA-125 was elevated in only 70% of the cases of epithelial ovarian cancer.

#### 5.6. Bi-laterality

Only 13% of all ovarian tumors in this study were having bilateral disease, a result which is close to the 17.2% incidence that was seen in an Asian study evaluating ovarian cancer at a cancer hospital in a developing country,<sup>13</sup> and is much less than 35% in Gharbia population bases cancer registry.<sup>8</sup>

#### 5.7. Treatment

##### 5.7.1. Surgery

5.7.1.1. *For epithelial tumors.* 80.4% of our patients were treated initially with surgery. Singh et al.,<sup>14</sup> in the study evaluating

ovarian cancer in oriental women from Singapore found that surgery was the primary treatment modality in 97% of the cases, while Sehouli et al.,<sup>17</sup> in their review to 372 consecutive patients with advanced ovarian cancer in a university hospital in Berlin found that 89% of the cases underwent surgery. Thrall et al.,<sup>18</sup> in their report evaluating patients with advanced ovarian epithelial carcinoma in the Medicare population found that surgery was performed initially in 58.8% of the women.

The slightly lower incidence of our patients' starting surgery in comparison to the German and the Singapore trials could be explained by the fact that there is no established multidisciplinary team between our department and the gynecology department evaluating every case and putting plans for further management.

Of those who underwent surgery 34.2% of our cases had optimum cytoreduction surgery (no residual or residual less than 2 cm). Gerestein et al.,<sup>19</sup> in the study evaluating surgery in 115 patients with stages III and IV ovarian cancer in the south west of the Netherlands found that optimal surgery was done in only 45% of the cases. Brand et al.,<sup>20</sup> in the survey study among gynecologist performing surgery for ovarian carcinoma in Australia and New Zealand found that about 65% of the surgeons perform optimal cytoreductive surgery.

It is obvious from the comparison that in our series, optimal cytoreductive surgery is performed in a much less frequency than done in Western countries, and this can be explained by; the very late presentation in most of our cases, and absence of multidisciplinary team evaluating all the cases before surgery.

5.7.1.2. *For border line tumors.* All our patients with border line tumors underwent surgery, 86.6% of the patients had unilateral oophorectomy (all stage I and II tumors had conservative surgery), 6.6% underwent TAH and BSO and 6.6% had debulking surgery. In contrast to our series, only 35% of the cases in an Italian study done by Lervollno et al.<sup>21</sup>, (evaluating 20 patients with border line ovarian tumors) had conservative surgery, while 63% of the cases had TAH & BSO. Darai et al.<sup>22</sup> in the study evaluating 43 cases of ovarian border line tumors found that conservative surgery was done in 51.1%.

The small number of the cases with sex cord and germ cell tumor in this study will prevent further discussion of the different surgical approaches.

##### 5.7.2. Chemotherapy

In our study, only three patients having epithelial ovarian carcinoma did not receive any adjuvant or neo-adjuvant chemotherapy, all of them were having stage IA and GII (3.4%), while 19.5% of the cases in our study started neo-adjuvant chemotherapy.

As regards the type of chemotherapy regimen used, Paclitaxel-carboplatin was the most frequently used regimen as first line in 64.3% of the cases, followed by carboplatin single agent in 24.1% of the cases (carboplatin was used alone for fragile patients with moderate performance status or when there is shortage in paclitaxel because of the limited resources).

The response rate to the first line chemotherapy (including both neo-adjuvant and following surgery) after three chemotherapy cycles was seen in 87.3% of the cases (CR 44.8%), if we added cases with stable disease after three cycles chemotherapy, the overall response will increase to 94.1%, only

5.7% of the case progressed after three cycles of first line chemotherapy.

Different response rates were seen in the literature, with different percentages of complete responses;

Thigpen et al.,<sup>23</sup> in the GOG study protocol 47, found that the complete response rate for the cisplatin containing arm reached 51%. The response rate to paclitaxel followed by either cisplatin or carboplatin in the study done by Neijt, et al.,<sup>24</sup> ranged between (64–74%), while the pathological complete response in the study done by Ozols et al.,<sup>25</sup> comparing paclitaxel plus cisplatin versus paclitaxel plus carboplatin, was nearly similar among both groups (46 vs. 53%).

McGuire et al.,<sup>26</sup> compared cisplatin–paclitaxel vs. cisplatin–cyclophosphamide in patients with stage IV or suboptimally debulked stage III EOC, found that the overall response was (73% vs. 60%), and the clinical CR (51% vs. 31%).

It is obvious after comparing our results to those of the large international studies that the response rate including clinical complete response in our patients is closely similar to those of the international studies.

In our study, for epithelial ovarian cancer, the mean follow up period was 15 months (a minimum period of 3 months and a maximum of 24 months) and the progression free survival (PFS) after first line chemotherapy was 10.8 months.

After reviewing the PFS in different international studies, it ranged between 11 and 21 months which is much higher than that was seen in our study.<sup>23–27</sup>

The possible explanation of that difference in progression free survival between our study and the different international studies could be explained by; first; the number of the patients in our study was small in comparison to those studies, second; no standard chemotherapy protocol was given among all patients in our study, and third; the high frequency of chemotherapy under-dosage and frequent interruption of the treatment were due to limited resources and unavailability of the drugs specially paclitaxel.

Thirty-six patients (41.3%) diagnosed as having epithelial ovarian cancer received second line chemotherapy.

Gemcitabine-carboplatin was the most frequently used regimen as second line chemotherapy in 47.2% followed by paclitaxel-carboplatin in 41.6% of the cases, and then comes gemcitabine and Etoposide as single agents 5.5% each.

What was very evident in our study was the response rate to second line chemotherapy which reached nearly 69.3% of them 27.7% achieved second complete responses (the response was assessed radiologically and by tumor markers).

In the western studies the response rate for platinum sensitive patients ranged roughly from 30% to 60% with a complete response ranging between 10% and 30%. The response rate in platinum resistant patients is much less.<sup>28</sup>

The high response rate to platinum containing second line chemotherapy in our study could be explained by the high incidence of platinum sensitive patients in our study, but also the small number of the patients in the study may contribute to these results.

Nearly fourteen percent (14.7%) of the patients diagnosed as having epithelial ovarian cancer received third line chemotherapy, tamoxifen, liposomal doxorubicin, gemcitabine, paclitaxel and etoposide were the most frequently used agents in the third line.

On the contrary to the high response rate in the first and second line chemotherapy, none of our patients had complete

or partial response to any of the previously mentioned agents, only stable disease in 50% of the cases and progressive disease in the other 50% of the cases.

Tangjitgamol et al.,<sup>29</sup> reported the response rate in 51 patients receiving third line chemotherapy for epithelial ovarian carcinoma at MD Anderson Cancer Center, and found the response rate was modest; the overall response rate was 16% (eight cases), with 2% complete response (one case) and 14% partial response (seven cases). Stable disease was achieved in 31% (16 cases).

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 by Nishio et al.<sup>30</sup>

For sex cord tumors and germ cell tumors, the number of the cases was too small for comparison or any statistical conclusions.

## 6. Conclusions

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 our ovarian cancer cases, followed by border line tumors. Papillary serous cystadenocarcinoma predominates other types of EOC. For all patients in this study, typical presentation was late; stages III and IV predominate. 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.

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