Original Research Article

Epidemiology of ovarian cancer in Assiut Governorate, Egypt

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ABSTRACT

Background: The aim of this study is to assess ovarian cancer epidemiology and detect its prognostic factors in Assuit, Egypt.

Methods: This retrospective study was performed between January 2010 and December 2015, on all cases attending to Obstetrics and Gynecology Outpatient Clinic in all central hospitals in Assiut. 378 females (≥40 years old) came to Obstetrics and Gynecology Outpatient Clinic from January 2010 to December 2015. Inclusion criteria: All females (≥40 years old), history of current acute or chronic pelvic pain, mass; fixed, hard consistency, history of previous similar condition.

Results: Mean age for whole ovarian cancer cases in this study was 56.44±10.08 (range, 40-85). Nulliparity was found in one case (0.3%), while multiparity was found in 252 cases (66.7%). Grand multiparity was found in 113 cases (29.9%). Twelve cases (3.2%) were virgin. Vaginal ultrasound can find all ovarian cancer cases. Regarding the serum levels of the tumor biomarker, CA-125, the average level of CA-125 is 300-1000 U/ml with 34.9% of cases had readings below to 300-1000 U/ml and 6.1% of cases had readings above to this average level. Regarding treatment, treatment combining surgery with chemotherapy was the main line of management in present study (46.3%). About 33.3% of cases underwent surgery, while only 18.3% took the chance of chemotherapy. Eight cases (2.1%) had no treatment.

Conclusions: Epithelial ovarian cancer is a lethal disease. The age incidence of ovarian cancer in present patients is ten years younger than what is re¬ported in US SEER data and other Western countries. CA-125 level and ultrasonography are increasing the rate of suspicious for diagnosis of malignant tumors.

Keywords: Epidemiology, Ovarian cancer, Ovarian malignancy, Survival

INTRODUCTION

Ovarian cancer (OC) is the most lethal gynecologic malignancy and is the fifth most common cause of cancer-related death among women.[1] In Egypt, Ibrahim et al showed that ovarian cancer represented 2.2 % of all incident cancers and accounted for 4.4% of all newly diagnosed female cancers.[2] Another important regional registry in Egypt is the Aswan regional registry, in which thirty-five cases of ovarian cancer were registered in 2008, representing 5.6% of all female cancers cases.[3]

About 70% of newly diagnosed ovarian cancer patients will have advanced disease and often not totally resectable due to the lack of symptoms in the early stages of ovarian cancer. The prognosis of patients with ovarian cancer is poor, with a 5-year survival of about 35%. Owing to improvements in diagnosis, surgery, and

chemotherapy, during the past 30 years, survival has increased.[4]

The identification of prognostic factors in studies of ovarian cancer may be useful for a variety of reasons. It would increase the understanding of the natural history of the disease, provide clinicians with guidelines for decisions on treatment strategies, and adjust for imbalances in comparing therapeutic regimens.

Numerous studies have attempted to identify the clinical and pathologic correlates of the disease outcomes and the factors that could provide prognostic information for individual patient survival.[5]

Mostafa et al evaluated ovarian cancer cases referred to and presented at the Alexandria Clinical Oncology Department (ACOD).[6] They concluded that the age incidence of ovarian cancer in patients is 10 years younger than that seen in Western countries. OC constitutes the majority among all ovarian cancer cases, followed by border line tumors. Papillary serous cystadenocarcinoma predominates other types of OC. The response rate of OC to first line chemotherapy was high.

Potential screening methods include transvaginal or transabdominal ultrasonography, and measurement of serum cancer antigen 125. Ultrasound scanning detects ovarian enlargement and morphological abnormalities, indicating the presence of a tumour; the transvaginal route is preferred because of the more detailed images obtained.

Recently colour Doppler has been used as an adjunct to grey scale ultrasound, which provides images of ovarian vasculature and estimates of flow velocity, with abnormal blood flow patterns suggestive of malignancy. CA125 is an antigen produced by most primary ovarian malignancies but raised levels may be found in other malignancies and certain benign gynaecological conditions. Measurement of serum level of cancer antigen 125 has been used in screening, in combination with ultasonography.[7]

Hegazi et al described the epidemiological and pathological correlates of ovarian carcinoma cases admitted for surgical treatment at the surgical oncology unit in Mansoura oncology Center, Mansoura, Egypt.[8] They stated that patients present with at a late stage of the disease and age correlates positively with postoperative mortality.

METHODS

This retrospective study was performed between January 2010 and December 2015, on all cases attending to Obstetrics and Gynecology Outpatient Clinic in all central hospitals in Assiut.

Technical design

Settings: Obstetrics and Gynecology Outpatient Clinic in all central hospitals in Assiut in the period from January 2010 to December 2015.

Subjects: 378 females (≥40 years old) came to Obstetrics and Gynecology Outpatient Clinic from January 2010 to December 2015.

Inclusion criteria

- All females (≥40 years old) came to Obstetrics and Gynecology Outpatient Clinic from January 2010 to December 2015.
- History of current acute or chronic pelvic pain.
- Mass; fixed, hard consistency.
- History of previous similar condition.

Exclusion criteria

- All females (<40 years old) came to Obstetrics and Gynecology Outpatient Clinic from January 2010 to December 2015.

Study design: Retrospective study. Sample: All females attending outpatient clinics in central hospitals in Assiut from January 2010 to December 2015, including ovarian cancer cases.

Operational design

Process:

All files were reviewed with emphasis on:

Full history

- Personal history: Age, residence, occupation and marital status.
- Menstrual history: Menstrual pattern (premenopausal or postmenopausal), history of irregular uterine bleeding, dysmenorrhea and date of last menstrual period.
- Obstetric history: Gravidity, parity, mode of delivery whether vaginally or abdominally and date of last delivery.
- Present history: Main complaint of female attending the outpatient.
- Presence of infertility: primary or secondary, male or female, duration and any previous therapeutic modality.
- Presence of chronic pelvic pain which is defined as persistent pelvic pain not responding to the usual analgesics, lasting for >6 months after exclusion of non-gynecological causes.
- Contraceptive history: Type of the method, duration of usage and cause of discontinuation (if discontinued).

- Therapeutic history: Use of hormones, ovulation induction agents, drug of certain importance
- Family history and past history.

Clinical examination

- General examination: Vital signs (pulse, blood pressure measurement, temperature and respiratory rate) and breast and lymph node examinations.
- Abdominal examination: Examination of any abdominal or pelvi-abdominal masses.
- Genital examination: Inspection for vaginal discharge or vaginal bleeding.
- Bimanual examination: Size and position of the uterus. Adnexal fullness, tenderness or masses and if a mass was found, its size, consistency and mobility were determined. Douglas pouch was palpated for nodules and fullness.
- Per-rectal examination: Confirming the diagnosis, excluding non-gynecologic causes of adnexal masses.

Investigations

- Routine investigations: Complete blood picture, Random blood sugar, liver, kidney function tests and coagulation profile.
- Radiological investigations: Transvaginal ultrasound was carried out to study the ovarian morphology followed by color Doppler imaging. Abdominal ultrasonography was done to screen for any hepatic focal lesions, ascites, pelvi-abdominal masses, or any other coincidental pathology. Vaginal ultrasonography was done to examine the pelvic organs with special comment on:
- Uterus: Size, position, endometrial thickness and any focal lesion.
- Adnexa looking for any mass(es) with comment on the following points:
- Site: Ovarian or extra-ovarian if possible and whether right, left or bilateral.
- Size: Measured in two perpendicular planes.
- Echogenicity: Whether echo lucent or echogenic.
- Septation: If any was found, its thickness was measured.
- Borders: Whether regular and even or irregular with unclear margins.
- Papillations: Internal or external.
- Wall thickness (in millimeters).

Administrative design

Approval was obtained from Zagazig University Institutional Review Board (IRB).

RESULTS

Table 1 showed demographic data for cases of study regarding age and survival. Mean age for whole ovarian cancer cases in this study was 56.44±10.08 (range, 40-85). Nulliparity was found in one case (0.3%), while multiparity was found in 252 cases (66.7%). Grand multiparity was found in 113 cases (29.9%). Twelve cases (3.2%) were virgin.

Swelling was present in 59 cases (15.6%) and pain was present in 303 cases (80.2%), pain and swelling were present together in 16 cases (4.2%).

Table 1: Demographic data for cases of study regarding age and survival.

	No.	%
Age		
>70 years	52	13.8
50-70 years	221	58.5
<50 years	105	27.8
Range	40 - 85	
Mean±SD	56.44±10.08	
Survival		
Dead	26	6.9
Living	352	93.1

The majority of the patients did not have significant associated conditions with only 28 (7.4%) patients have a diagnosis of diabetes mellitus, 55 (14.6%) patients have a diagnosis of hypertension and 31 (8.2%) patients have a diagnosis of both hypertension and diabetes mellitus. Only, one patient (0.3%) has a diagnosis of both hypertension and stroke.

Vaginal ultrasound can find all ovarian cancer cases. Regarding the serum levels of the tumor biomarker, CA-125, the average level of CA-125 is 300-1000 U/ml with 34.9% of cases had readings below to 300-1000 U/ml and 6.1% of cases had readings above to this average level.

Regarding treatment, treatment combining surgery with chemotherapy was the main line of management in present study (46.3%). About 33.3% of cases underwent surgery, while only 18.3% took the chance of chemotherapy. Eight cases (2.1%) had no treatment.

Table 2: Histological types of the ovarian tumors.

Histology	No.	%
Epithelial tumors	205	54.2
Germ cell tumors	2	0.5
Metastatic tumors	86	22.8
Non-neoplastic ovarian	18	4.8
Sex cord tumors	42	11.1
Soft tissue tumors nonspecific to ovary	15	4.0
Unclassified tumors	10	2.6

Epithelial tumors constituted 54.2% of the cases, this was followed by metastatic tumours accounting for 22.8%, then came sex-cord tumors (11.1%), and lasting germ cell tumours (0.5%) (Table 2).

DISCUSSION

Ovarian cancer is second most common cancer of the female reproductive system and the leading cause of the death from gynecologic malignancies. 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.[9]

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.[10]

The American Cancer Society estimated 21,880 new cases of ovarian cancer in 2010 and 1,385 deaths from disease in 2010. Ovarian cancer is more common among White American women than it in the Black American women. Epithelial ovarian cancer can occur in girls 15 years, but mean age is 56 years. In United States, it is approximately 15 cases per 100,000 women per year aged 50-54 years rising to 35 cases per 100,000 women aged 70-74 years.[9]

Studies in Egypt, Dey et al and Italy, Minelli et al have found ovarian cancer rates to be higher in urban compared to rural areas.[11,12]

A regional registry, the Gharbia Population Based Cancer Registry (GPBCR), showed data of 225 ovarian cancer cases during a three years period (2000-2002). Ovarian cancer represented 2.2 % of all incident cancers and accounted for 4.4% of all newly diagnosed female cancers (Ibrahim et al).[2] Another important regional registry in Egypt is the Aswan regional registry, in which thirty-five cases of ovarian cancer were registered in 2008, representing 5.6% of all female cancer cases (Egypt National Cancer Registry, Aswan Profile, 2008).[3]

Factors associated with an increased risk for invasive epithelial ovarian cancer include: age, race, nulliparity, family history of ovarian cancer and history of endometrial or breast cancer.[13]

Factors associated with a reduced risk are history of one or more full-term pregnancies, use of oral contraceptives, history of breast feeding, tubal ligation and hysterectomy. Other factors such as infertility drugs, hormone replacement therapy, age at menarche, age at menopause, dietary factors, lactose intolerance, talc use, and alcohol consumption have been suggested, but their role is still inconclusive.[14]

Advances in molecular genetics have found mutations in the $BRCA_1$ and $BRCA_2$ tumours suppressor genes responsible for the majority of hereditary ovarian cancer. Additional risk factors include nulliparity and refractory infertility. Protective factors include multiparity oral contraceptives and tubal ligation or hysterectomy. With 5 years of oral contraceptive use, women can cut their risk of ovarian cancer, approximately in half. This also holds true for individuals with a family history.[15]

Stage of diagnosis, maximum residual disease following cytoreductive surgery and performance status are the three major prognostic factors. Using a multimodality approach to treatment, including aggressive cytoreductive surgery and combination. Chemotherapy five-year survival rates are as follow: stage I 93%, stage II (70%), stage III (37%) and stage IV (25%). The highest ovarian cancer rate is reported from industrial countries with exception of Japan. United States and Denmark respectively have a higher incidence of ovarian cancer. A few aspects of ovarian cancer epidemiology are well documented such as an inverse association with parity and oral contraceptive pills. A role for other menstrual, reproductive and hormonal therapy and diet has been suggested, but remains to be confirmed.[16]

There was a weak association with duration of longest pregnancy attempt, total duration of unprotected intercourse and history of clinically diagnosed infertility.[1] The aim of this retrospective study is to assess ovarian cancer epidemiology and detect its prognostic factors on 378 cases enrolled to Obstetrics and Gynecology Outpatient Clinic in all central hospitals in Assiut (from January 2010 to December 2015). All patients were subjected to thorough clinical evaluation and transabdominal and transvaginal ultrasound. Complete blood picture and random blood sugar. If cases were operated surgically, liver and kidney function tests and coagulation profile were done.

Early age of menarche before age 12 or late age of menopause after 50 years are associated with increased risk of ovarian cancer. The recent reduction associated with a month of pregnancy was greater for younger women than for old women.[17]

DiSilvestro et al observed that the mean age in the study that included one hundred and thirty seven cases was 58 years old, while Mostafa et al evaluated Egyptian ovarian cancer cases, the median age was 47 year and the mean age was 48.5±12.7 years, an age incidence peak which is about one and a half decade lower than what is seen in Western populations.[18,19] In 2008, 35 cases of ovarian cancer were registered in Aswan represent (5.62%) of all female cancers cases. The mean age of these cases was 51.1 years with a median age of 52.5.

Hegazi et al investigated the epidemiological and pathological correlates of postoperative mortality of ovarian cancer at a tertiary care center in Mansoura, Egypt.[8] They identified 95 patients with primary ovarian cancer undergoing different types of surgeries. The mean

age of patients in this study was 52.18 ranging from 14 to 98 years, and the median age was 53 years. The age distribution showed an age peak that lied between 45 and 62 years of age. Seven cases (7%) were at the age of 30 years or less.

Hegazi et al found that the majority of the patients did not have significant comorbidity with only 10 (10%) patients have a diagnosis of hypertension and 3 (3%) have a diagnosis of type 2 DM.[8]

U/S can sometimes but not always tell the difference between ovarian cancer and other more common conditions (ovarian cyst and endometriosis). As a result, pelvic U/S is not recommended as standard alone screening test of ovarian cancer.

Sassone et al have looked at using CA-125 and pelvic U/S together to detect ovarian cancer.[13] Many women had unnecessary surgery because of false positive test result. The CA-125 or pelvic U/S was abnormal, but no cancer was found. CA-125 and pelvic U/S have found more cancers at an early, more treatable stage. Sensitivity of CT and U/S about 100% helps to diagnose ovarian cancer of all cases with combination of CA-125.

Hegazi et al studied the serum levels of the CA-125 biomarker in association with the pathological type of the tumor.[8] The average level is 325.38 U/ml with 50 % of cases had readings below or equal to 233.15 U/ml. Patients with serous tumors had statistically significantly greater values of CA-125 than patients with mucinous tumors. Moreover, the granulosa cell tumors were associated with the least serum levels of CA-125 and generally occurred in younger patients (average age 42 years).

Singh et al, in the study evaluating ovarian cancer in oriental women from Singapore found that surgery was the primary treatment modality in 97% of the cases.[20] Eisenkop et al have achieved better results using more extended surgery.[21] However, Bristow et al reported in a meta-analysis that two-thirds of patients are not candidates for optimal primary cytoreduction.[22] Whether suboptimal cytoreduction is the consequence of a more aggressive tumor or a less aggressive surgical approach is still controversial. This significant subset of patients undergoing suboptimal debulking will not derive any benefit from this procedure but will suffer the morbidity of such an intervention. The alternative to primary surgery in patients with an unresectable tumor or poor performance status is neoadjuvant chemotherapy.

In the cohort done by Hegazi et al, the majority of cases received neo adjuvant chemotherapy.[8] This may be attributed to the large proportion of cases first diagnosed at later stages of the disease.

It is obvious from the comparison that in present 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 present cases, and absence of multidisciplinary team evaluating all the cases before surgery.

Sarwar et al, 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.[23] 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%).

The current study has some methodological limitations notably the rather small sample size and the incomplete accrual of some variables.

CONCLUSION

Epithelial ovarian cancer is a lethal disease. The age incidence of ovarian cancer in present patients is ten years younger than what is reported in US SEER data and other Western countries. CA-125 level and ultrasonography are increasing the rate of suspicious for diagnosis of malignant tumours. In addition, MRI examination and histological examination result in small improvement in positive value. Presentation of patients in this study was late. The response rate of EOC to first line chemotherapy was high. Prognosis remains poor due to recurrence, development of resistance to chemotherapy and late stage of presentation. FIGO staging, histopathological grade and type of surgery have a clear impact on overall survival. Patients present with at a late stage of the disease and age correlates with postoperative mortality.

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