Original Article

Incidence, Pattern and Management of Ovarian Cancer at a Tertiary Medical Center in Enugu, South East Nigeria

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Abstract

Background: The incidence of ovarian cancer is thought to be increasing in developing countries and little is known about the pattern and incidence of this disease in South-East Nigeria. **Aims:** The objectives of the study were to determine the incidence, describe the pattern and management of ovarian cancer at a tertiary medical center in Enugu South East Nigeria. **Materials and Methods:** This was a retrospective review of cases of histologically diagnosed primary ovarian cancer at the study center over 11 years.Cases of histologically diagnosed primary ovarian cancer were identified through the records of the study center cancer registry and confirmed from the records of the histopathology department. Case notes, admission and theatre records were used to obtain data relating to clinical management, mortality and incidence of primary ovarian cancer. Statistical analysis was dose using SPSS statistical software version 17.0 for windows. Descriptive and inferential statistics were applied to obtain rates, proportions and 95% confidence intervals for these estimates. **Results:** There were 20,227 gynecological admissions during the study period (from January 2000 to December 2010) and 206 gynecological cancers. There were 54 cases of primary ovarian cancer giving an incidence rate of 1/405 gynecological admissions per year or 0.3% (95% confidential interval [CI] 0.23%, 0.38%) or 2.4% (54/206) per gynecological cancer per year. Epithelial ovarian cancer constituted 68% of cases of ovarian cancer (95% CI 54%, 82%): Sex cord and germ cell tumors constituted 16% each (95% CI 6%, 26%). Approximately 60% of women who had epithelial ovarian cancer were aged 50 years or below (95% CI 47%, 74%) and 72% of epithelial ovarian cancer occurred in multiparous women (95% CI 72.1%, 91.9%). Over 84% of ovarian cancer presented in stages 3 and 4 of the disease (95% CI 94%, 72%). The mainstay of management was surgery: Compliance with cis-platinum based adjuvant chemotherapy was poor. Case-specific mortality rate within 1 year of diagnosis was, at least, 70% (95% CI 64%, 84%). **Conclusions:** Primary ovarian cancer was uncommon and consisted mainly of epithelial cancer. Epithelial ovarian cancer occurred more in multiparous women and in women under 50 years in our center contrary to the known pattern of the disease.

Keywords: Management, Ovarian cancer, Pattern, Review

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Introduction

Ovarian cancer is the fourth most common cause of cancer deaths worldwide[1] and also the commonest cause of death among all gynecological cancers.[2-5] The very high case-fatality rate for ovarian cancer is partly because the condition usually presents in advanced stages of the disease.[4] In Enugu, ovarian cancer has been found to be the fourth commonest cause of gynecological mortality.[6] Previous studies done in

Nigeria showed that ovarian cancer constituted 7-22% of all gynecological malignancies.[7-11] Epithelial ovarian cancer is the commonest type of ovarian cancer and is known to be a disease of postmenopausal women.[12]

A global report by the International Federation of Gynecology and Obstetrics (FIGO) has noted that the highest incidence of ovarian cancer was moving towards a younger age group although the majority of patients with epithelial cancer were more than 50 years in age.[13] The reasons for the increased occurrence of epithelial ovarian cancer in younger women are controversial. Risk factors mentioned include an increase in ovulation induction in assisted reproduction techniques, nulliparity and late onset of childbearing due to increasing number of females in the workforce.[14,15]

There is emerging evidence that ovarian cancer may now be commoner in developing than developed countries.[16] A recent estimate indicated that of 240,476 cases of ovarian cancer worldwide in 2009, 155, 835 (64.8%) occurred in developing countries compared to 84,641 in developed countries.[16] There is scanty literature on the current state of ovarian cancer in our center.[17] The aim of this study was therefore, to describe the incidence, pattern and management of ovarian cancer at this major referral medical center in South East Nigeria in the last decade.

Materials and Methods

This was a retrospective review of all cases of histologically diagnosed ovarian cancer treated at the study center. The study population included all women admitted and treated in the gynecology department of the hospital during the study period. The study covered the period from January 1st 2000 to December 31st 2010. A purposive sample of all cases of primary ovarian cancer seen during the period was done because of the rarity of the disease in previous studies. A written application for data was made to the cancer registry of the study center following which all cases of gynecological cancer seen during the study period and their biographic, clinical and mortality data were compiled by the cancer registry. From this list, all cases of ovarian cancer were compiled separately. Using this list as a template, the histological diagnoses of these cases were retrieved from the Histopathology Department of the hospital and cases of primary ovarian cancer were selected. The case notes of these selected cases were retrieved from the Records Department and data relating to age, parity, clinical presentation and treatment were abstracted and coded into SPSS Statistical Software Version 15.0 (Chicago Illinois, USA) for Windows for analysis. Where case notes were not available or had missing data, efforts were made to obtain patient data from ward admission records and operating theatre records. Mortality data were compiled from the cancer registry records, case notes and Mortuary records. Data analysis was by descriptive and inferential statistics at 95% level of confidence. Rates and proportions were determined and their 95% confidence intervals calculated as estimates of their values in the population.

The main outcome measures were the incidence rate of ovarian cancer overall and incidence rates based on socio-demographic and disease characteristics, the proportions of cases that received surgery and chemotherapy, as well as the estimated case-fatality rate for ovarian cancer. Ethical clearance for the study was duly obtained from the Research Ethics Committee of the hospital.

Results

There were 20,227 gynecological admissions and 206 gynecological cancers seen during the period. The total number of histologically diagnosed cases of primary ovarian malignancy obtained over an 11-year period was 54. The socio-demographic and treatment records of 50 cases were retrieved giving a recovery rate of 92.6% (50/54). The cases whose records were available were used for analysis. The incidence rate of ovarian cancer was 1/404 gynecological admissions per year or 0.3% (54/20227) 95% confidence interval (CI) 0.23%, 0.38%. The incidence rate of ovarian cancer per gynecological cancer per year was 2.4% (54/206).

Table 1 shows the incidence of ovarian cancer based on the characteristics of the patients. The overall mean age (SD) of the cases was 45.4 (17.1) (95% CI 40.7, 50.1) while the median

Table 1: Showing the distribution of cases of ovarian cancer according to socio-demographic characteristics as seen at the University of Nigeria teaching hospital Enugu from 2000 to 2010

Characteristic	Ovarian cancer *n*=50	Percentage
Age (years)		
10-20	5	10
21-30	9	18
31-40	6	12
41-50	10	20
51-60	8	16
61-70	9	18
71-80	3	6
Parity		
0	17	34
1-4	15	30
≥5	18	36
Ethnic group		
Igbo	49	98
Non-Igbo	1	2
Occupation		
Unemployed	8	16
Farmer	14	28
Civil servant	3	6
Trader	9	18
Teacher	4	8
Nurse	2	4
Student	10	20
Menstrual group		
Pre-menopausal	24	48
Post-menopausal	26	52

age was 48 years. The mean ages (SD) at presentation of the different types of ovarian cancer were epithelial 50.3 (13.2) years (95% CI 46.6, 54.0), sex cord 53.1 (13.3) years (95% CI 49.4, 56.8), and germ cell tumors 18.5 (8.3) years (95% CI 16.2, 20.8).

Epithelial ovarian cancer constituted 68% (34/50) of ovarian cancers (95% CI 54%, 82%). Approximately 55% (30/50) of epithelial ovarian cancer occurred at 50 years or below (95% CI 47%, 74%). Parous women constituted 72.40% (36/50) of epithelial ovarian cancer (95% CI 71.9%, 72.1%). Approximately 38% (19/50) of parous women with ovarian cancer were grand multiparous. Premenopausal women constituted about 36% (17/50) cases of epithelial ovarian cancer (95% CI 23%, 48%).

Table 2 shows clinico-pathologic features of ovarian cancer seen during the study period. Most patients presented in the stages 3 and 4 of the disease. All cancers in premenarcheal girls were germ cell tumors.

Management of Ovarian cancer in the center is a multidisciplinary approach involving gynecological oncologists, general gynecologists and general nurses. General surgeons participated in most surgeries involving bowel resection.

Table 2: Clinico-pathologic features of ovarian cancer seen at the UNTH, Enugu from 2000 to 2011

Clinical/pathological feature	Number of cases	Percentage
Major presenting symptoms		
Abdominal swelling	32	64
Abdominal pains and discomfort	50	100
Weight loss	25	50
Stage of disease at presentation		
1	0	0
2	4	8
3	32	64
4	14	28
Histological type		
Epithelial tumours		
Serous cystadenocarcinoma	18	36
Mucinous cystadenocarcinoma	12	24
Poorly differentiated adenocarcinoma	4	8
Sex cord tumor		
Granulosa cell tumor	4	8
Poorly differentiated Sertoli-leydig cell tumor	2	4
Invasive alveolar rhabdomyosarcoma	2	4
Germcell tumor		
Malignant teratoma	4	8
Dysgerminoma	2	4
Endodermal sinus tumor	2	4

UNTH: University of Nigeria teaching hospital

Approximately 76% (38/50) of the patients (95% CI 64%, 84%) had surgical staging, and maximal debulking surgery involving total abdominal hysterectomy, bilateral salpingo-oophorectomy and different degrees of omentectomy, appendectomy, bowel resection and adhesiolysis. The remaining 24% (12/50) were treated as follows: One patient, a 9-year-old girl had excision of tubo-ovarian mass; four of the patients were referred to the study center for histological diagnosis and chemotherapy after surgery had been done in private clinics; seven patients or 14% (7/50) (95% CI 4.2%, 23.8%) had inoperable tumors at surgery and all had staging and biopsy.

Eighty-four percent (42/50) (95% CI 72%, 94%) of the patients had chemotherapy involving cis-platinum based combination chemotherapy. The combinations were of a platinum agent (Cisplatin or carboplatin) and paclitaxel, cyclophosphamide or doxorubicin. However, approximately 81% (34/42) of these had one or two courses of chemotherapy only and abandoned further chemotherapy. Approximately 28.6% (6/42) had 6 courses while 4.8% (2/42) had four courses. All patients had injectable and/or oral analgesics for pain relief and antibiotics for sepsis as part of symptomatic/palliative therapy. The use of patent-controlled analgesia was not found in the records.

Follow up of patients was by clinical examination and trans-abdominal/transvaginal ultrasonography. CA125 assays were not routinely done for lack of facilities within the hospital. Only 2 patients who had stage 2 disease had records of CA125 assays done outside the study center. The values were 108.3 u/ml and 84.7 u/ml. Both were serous cystadenocarcinoma.

Approximately seventy percent (38/54) (95% CI 64%, 88%) of cases died of the disease within 1 year of initial presentation. All the deaths occurred within 1 year of initial presentation. The mortality or survival data of the remaining 29.6% (16/54) were not available.

Discussion

This study showed that ovarian cancer is uncommon in the study center. This is consistent with a previous audit of gynecological cancers in this center three decades ago and as well as the findings of a more recent report.[6,17] Similarly, studies across Nigeria showed that 43-62 cases of ovarian cancer would be expected to be seen in about 10 years.[7-11] These underlie the rarity of ovarian cancer in Nigeria. Compared to an audit of gynecological cancers in this center three decades ago in which the incidence of ovarian cancer was 1.3% per gynecological cancer per year, the incidence of ovarian cancer in this study suggests about 84% increase in the incidence of ovarian cancer in relation to other gynecological cancers in this center. Considering that most cases of cancer would end up in the teaching hospital because of lack of expertise and facilities for its treatment elsewhere in the state, this may represent an

actual increase in the incidence of ovarian cancer in the area or a mere increase in reportage of the disease perhaps due to an increased tendency to seek orthodox care for the disease.

In terms of the pattern of occurrence, the finding in this study that most cases of epithelial ovarian cancer occurred at 50 years or below is different from what is known about epithelial ovarian cancer. Epithelial Ovarian cancer has been known as a disease of the sixth and seventh decades of life.[12] In a recent report by FIGO, most cases of ovarian cancer were above 50 years.[13] In the previous study at this center three decades ago, the peak age of incidence was in the sixth decade of life. The findings in this study may therefore, indicate a shift to an earlier occurrence in this population. This is similar to results of a study done in Ghana where the fifth decade of life was the peak period of presentation of epithelial ovarian cancer.[18]

The apparent trend of increased occurrence of epithelial ovarian cancer in younger women in the population is worrisome. In a society where birth records are poorly kept or do not exist, the possibility of inaccurate age declarations by patients must be borne in mind while evaluating this finding. Besides, given that the average life expectancy at birth for Nigeria is about 53 years,[19] the influence of the shorter lifespan women in the study area in comparison to Western populations must also be considered. Despite these considerations, this study suggests that epithelial ovarian cancer may be occurring in relatively younger women in Nigeria. Further studies, using a design that will permit collection of more reliable and comprehensive data, are required to clarify if there is an actual reduction in the age of occurrence of this disease. The possible influences of genetic factors and lifestyle in the etiology of ovarian cancer in this environment will also need to be explored. Acquisition of technical and human capacity for genetic studies and antigen assays is desirable in order to fully define the pattern of this disease in this area. Besides, the development of institutional protocols for data collection and management will facilitate the building up of a database for the disease.

Nulliparity has been known to be a strong risk factor for epithelial ovarian cancer;[14,15] however, this study shows a high incidence of ovarian cancer among parous women with a substantial contribution from grand multiparous women. Less than a third of cases of epithelial ovarian cancer occurred in the nullipara. In a previous study from this center, all cases of ovarian cancer occurred in parous women with grand multipara constituting 50%.[11] This suggests that in this environment, nulliparity may not be a strong factor in the etiology of epithelial ovarian cancer.

With respect to management of cases, this study suggests that most patients presented in stages 3 and 4 of the disease and that most cases abandoned their chemotherapy mid-way. The pattern of late presentation of cases in advanced stages of the disease was also noted by a previous study from this center[11] and appears to be a worldwide phenomenon.[13] Late presentation poses a surgical challenge and results in poor treatment outcome.[13] In fact, 14% of cases in this study were inoperable as at presentation. Peculiar factors associated with this pattern of presentation in our environment include ignorance and illiteracy which perpetuate poor health seeking behavior and a first recourse to alternative health practitioners and prayer houses before orthodox medical care.[7,9,10]

The trend of abandonment of chemotherapy may be due to financial incapacitation arising from expensive cost of care or due to frustration arising from lack of apparent clinical progress following suboptimal debulking surgery for advanced disease. The drugs used for chemotherapy could be expensive. Increased cost of care can also arise from longer hospital stays needed for advanced disease. Absence of any form of health insurance during the period of the study meant that patients paid at points of service. Unfortunately, most packages available in the recently introduced Nigeria National Health Insurance scheme do not cover cancer care.

The main strength of this study is that it gives the most comprehensive picture of the current state of ovarian cancer incidence, pattern and management in this center and it could be a good basis for further studies on this disease in the South East zone of Nigeria. The major limitations of this study, however, include the small sample size and the non-comparative retrospective design both of which limit the external validity of the findings. Given the rarity of ovarian cancer, a prospective design would have taken too long a time to accumulate this number of cases. Despite these limitations, we conclude that the study shows a low incidence of ovarian cancer and in comparison with previous reviews, it suggests an emerging pattern of increasing incidence and younger age of onset of epithelial ovarian cancer in this center. There is also a substantial involvement of parous woman in epithelial ovarian cancer among patients treated at this center. All these are contrary to established facts from previous studies.[4,12,15] Population-based studies are required to determine the possible explanation for these observed trends in this environment. We recommend funding of cancer care by government to reduce cost and improve compliance with treatment as well as public health education to encourage early presentation for treatment.

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