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OVARIAN CANCER IN A TERTIARY HOSPITAL IN SOUTH-SOUTH, NIGERIA: A 5-YEAR REVIEW

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ABSTRACT

Background: Ovarian cancer is the second most common gynaecological malignancy in developing countries after cervical and endometrial cancers, with an incidence of 5 per 100,000 and a mortality rate of 3.1 per 100,000. The incidence is higher in whites than others. Blacks and Asians have the lowest incidence. **Objective:** To determine the prevalence and characteristics of patients with ovarian cancer at the Federal Medical Centre (FMC), Yenagoa, Bayelsa State, Nigeria. **Materials and Method:** This was a retrospective study. It involved all the patients with histologically confirmed cervical cancer managed at the gynaecological unit of the FMC, Yenagoa from 1st January, 2016 to 31st December, 2020. Information was extracted from the gynaecological records and entered into a predesigned proforma. Data were analysed using statistical software package and results were then presented in tables and frequencies. **Results:** There were 2,478 gynaecological patients managed, of which 20 had ovarian cancer. The prevalence of ovarian cancer was 0.8%. About 65% of the women were in the seventh and eighth decades of life. Serous cystadenocarcinoma was the most common histological subtype, found in 60% of cases, and 90% of the cases were diagnosed in the advanced stages of the disease. About 45% were managed with surgery and chemotherapy. Six (30%) deaths were recorded in the period under review. **Conclusion:** There is a high number of patients presenting to our hospital with ovarian cancer, especially epithelial ovarian cancer. Contrary to previously held beliefs, more parous women were affected than nulliparous women.

KEYWORDS: Ovarian cancer, Common, Malignancy, Mortality, Whites.

INTRODUCTION

Ovarian cancer is the second most common gynaecological malignancy in developing countries after cervical cancer.[1] It is responsible for 18.8% of all gynaecological cancers in developing countries and 28.7% in developed countries.[1] The incidence is higher in whites than others. Blacks and Asians have the lowest incidence.[1] It is the second most common cause of gynaecological cancer death, with black women who have advanced epithelial ovarian cancer being more likely to die than white women, probably due to less likelihood of receiving guideline-recommended care.[2] The lifetime risk of developing ovarian cancer is 1.4 percent and the average age at diagnosis is 63 years,[3] but in women with a hereditary ovarian cancer (such as BRCA1 and BRCA2 gene mutations and Lynch syndrome), the risk increases with a younger age at diagnosis. Hereditary ovarian cancers generally occur in women about 10 years younger than those with non-hereditary tumours.[4]

Most ovarian cancers are diagnosed at an advanced stage (stage III and IV); 17% of the patients will prevent with spread to regional lymph and 61% with evidence of distant metastasis.[3] The majority of primary ovarian cancers are of epithelial cell origin (about 95%).[5] The others arise from other ovarian cell types – germ cell and sex cord-stroma.[5]

Traditionally, two main hypotheses have been proposed to explain the link between many of the risk factors and development of epithelial ovarian cancers – the incessant ovulation theory and the exposure to gonadotropins hypothesis. The incessant ovulation theory suggests that repeated ovulation results in minor trauma to the ovarian epithelium, which in turn can lead to malignant transformation. Incessant ovulation is thought to play an important role in the underlying mechanism in the development of ovarian cancer and this theory is supported by the observations that multiparity, use of oral contraceptive pills, and a history of breastfeeding are protective.[6] However, it has been observed that even without oral contraceptives, increasing age at first birth reduces the risk of ovarian cancer.[7] Pregnancy is associated with a risk reduction of 13 – 19% per pregnancy.[4] Other factors that have been associated with a reduction in the risk of developing ovarian cancer

are the black race, bilateral tubal ligation and hysterectomy.[4]

The second hypothesis, which suggests that persistent ovarian exposure to gonadotropins and elevated concentrations of oestradiol may be carcinogenic, is supported by the observation that experimentally induced ovarian tumours contain gonadotropin receptors.[3]

Factors that have been associated with an increased risk of ovarian cancer are increasing age, early menarche and late menopause (weak relationship), nulliparity, infertility, endometriosis, polycystic ovarian syndrome, intrauterine device, hormone replacement therapy (non-significant increase in risk), diets high in saturated animal fats, obesity, cigarette smoking, exposure to talc on the external genitalia and genetic factors. Patients with Turner's syndrome are at increased risk of dysgerminoma and gonadoblastoma.[3]

The majority of women have stage 3 disease at diagnosis.[8] Most commonly, women with either early or advanced epithelial ovarian cancer present in a subacute fashion with pelvic or abdominal pain, bloating and gastrointestinal symptoms.[7,9,10] An adnexal mass can also be picked up incidentally following imaging performed for another indication.

Investigations in ovarian cancer will include abdominopelvic ultrasound scan which will characterise the tumour and indicate likelihood or otherwise of malignancy which may be bilateral, have solid components, multiple septations >2 – 3 mm in size and presence of ascites.[10] Others include computerised axial tomographic scan (CT scan) which will help to determine the extent of the spread to the liver, spleen and other intra-abdominal structures and lymph nodes. Tumour markers like CA–125, alpha-fetoprotein, carcinoembryonic antigen, β-HCG; may give further insight into the originating cell type and aid in patient's monitoring.[11] Baseline investigations like full blood count, blood grouping, electrolytes, urea, and creatinine and urinalysis are also helpful.

Risk of malignancy index (RMI) is a reliable, cheap, readily available and cost-effective method of pre-operatively distinguishing benign from malignant ovarian masses and aids in triaging patients into different treatment groups. Risk of malignancy index is calculated by finding the product of menopausal status, ultrasound scan features (multilocular septations, solid components, bilaterality, metastasis, and ascites) and the absolute value of CA–125. A score of 1 and 3 are given for premenopausal status and postmenopausal status respectively. A score of 1 and 3 are given for one and more than one ultrasound scan features respectively. If the score is less than 25, there is a 3% chance that the tumour is malignant, and the patient should be managed by a general Gynaecologist. If the score is between 25 and 250, there is a 20% chance that the tumour is malignant, and the patient should be managed in a gynaecological oncology unit. If the score is greater than 250, there is a 75% chance that the tumour is malignant, and the patient should be managed in an oncology Centre.

The diagnosis is surgico-pathological. Surgical staging and cytoreduction followed by adjuvant chemotherapy is the management approach used for most women with epithelial ovarian cancer.[3] Optimal debulking (maximum diameter of tumour left behind less than 1 cm) is aimed at. The extent of success at cytoreductive surgery is the most important determinant of survival and outcome in ovarian cancer.[12]

Post-operative adjuvant chemotherapy should generally be considered for patients with advanced disease and currently the most effective regimen uses a combination of paclitaxel and carboplatin administered systemic for 6 cycles at 3- to 4-week intervals.[4] This platinum-taxane doublet is the gold standard chemotherapy for epithelial cell ovarian malignancy in many countries.[13]

In the past, a second surgery was done after about 12 months of treatment, to assess the response and to plan for further management. Presently, with effective radiological investigations such as ultrasound scan, CT scan and MRI, second look surgery is now obsolete, except for research purposes.

Other modalities of adjuvant therapy in the treatment of ovarian cancer include radiotherapy and immunotherapy.[13] Gene therapy and viral therapy are novel modalities of cancer therapy.

Enormous efforts in search of a comprehensive screening test, for ovarian cancer has been froth with varying challenges. There is no proof that routine screening with serum makers, sonography, or pelvic examination decreases mortality rate.[14] Compared to cervical cancer and other gynaecological cancers, ovarian cancer does not have an ideal and reliable screening method.[14] However, CA–125, a glycoprotein produced both in benign and malignant ovarian epithelia tumours, is usually raised in serous cystadenocarcinoma and can be used to monitor the progress of the disease and evaluate response to treatment.[14]

Following all first-line treatment for epithelial ovarian cancer, monitoring should include the routine history, physical examination, assessment of CA–125 (or other tumour markers if they were elevated on initial presentation) and other testing if clinically indicated. The objective of this study was to determine the prevalence of ovarian cancer and characteristics of patients with ovarian cancer at the Federal Medical Centre, Yenagoa.

MATERIALS AND METHOD

This study was carried out at the Department of Obstetrics and Gynaecology, Federal Medical Centre,

Yenagoa. It was a retrospective study which involved all the patients with histologically confirmed ovarian cancer managed at the gynecological unit of the Centre from 1st January, 2016 to 31st December, 2020. Information was extracted from the gynaecological clinic, gynaecological emergency and gynaecological ward registers, and patients' medical records and entered into a pre-designed proforma. Data were analysed using statistical software (SPSS for windows® version 23, SPSS Inc.; Chicago, USA). Result was presented in tables, frequencies and percentages.

RESULTS

There were 2,478 gynaecological cases managed in the Federal Medical Centre, Yenagoa in the period under review, of which 20 cases were ovarian cancers. The prevalence of ovarian cancer was 0.8% of all the gynaecological cases in the period under review.

Sociodemographic characteristics and anthropometric measures of patients

Of the 20 women with ovarian cancer, 65% were in the seventh and eighth decades of life with a mean age of 63.3 years and standard deviation of 9.0 years. Slightly above half are widows (55.0%) and the same proportion were without formal education (Table 1).

Table 1: Sociodemographic characteristics and anthropometric measures of patients with ovarian cancer.

Characteristics	Frequency (N = 20)	Percent (%)
Age group		
<50 years	3	15.0
50 - 59 years	4	20.0
60 - 69 years	9	45.0
≥ 70 years	4	20.0
Mean Age ± SD in years	63.3 ± 9.0	
Marital status		
Married	7	35.0
Separated/Divorced	2	10.0
Widowed	11	55.0
Highest level of education		
None	11	55.0
Primary	3	15.0
Secondary	4	20.0
Tertiary	2	10.0
Occupation		
Unemployed	6	30.0
Civil Servant	4	20.0
Trader	4	20.0
Farmer	6	30.0
Mean weight ± SD in Kg	64.8 ± 7.9	
Mean height ± SD in m^2	1.58 ± 0.03	
Mean BMI ± SD in kg/m^2	25.7 ± 2.7	
Body mass index categories		
Normal	10	50.0
Overweight	9	45.0
Obese	1	5.0

Gynaecological cancers in the Federal Medical Centre, Yenagoa.

Table 2 revealed the incidence of the major gynaecological cancers seen in the period under review in our Centre. Ovarian cancer was second after cervical cancer. Endometrial cancer was third (Table 2).

Table 2: Gynaecological cancers in the Federal Medical Centre, Yenagoa.

	Cervical cancer	Ovarian cancer	Endometrial cancer	Total
Number of cases	31	20	17	68
Percentage (%)	45.6	29.4	25	100

Gynaecological features of patients with ovarian cancer

Table 3 revealed that 80% of the women were multiparous and grand multiparous. About 75% had normal menopause, while 10% had late menopause (Table 3).

Table 3: Gynaecological features of patients with ovarian cancer.

Characteristics	Frequency N = 20	Percent (%)
Menarche		
Early menarche	4	20.0
Normal menarche	16	80.0
Mean age of menarche ± SD in years	12.6 ± 1.2	
Parity		
Nulliparous	3	15.0
Primiparous	1	5.0
Multiparous	8	40.0
Grand multiparous	8	40.0
Median Parity (Range)	4 (0 – 10)	
Menopause		
Early	2	10.0
Normal	15	75.0
Late	2	10.0
Pre-menopause	1	5.0
Mean age of menopause ± SD in years	51.4 ± 5.1	

Presenting complaints, clinical features, and risk factors among women with Ovarian cancer

All patients with ovarian cancer presented with abdominal swelling (Table 4). Other presenting complaints were abdominal pain (85%), weight loss (70%) and early satiety (55%). Ascites was observed in 75% of cases (Table 4). There was hypertension, diabetes, and family history of gynaecological cancers in 55%, 25% and 20% of these patients, respectively (Table 4).

Table 4: Presenting complaints, clinical features, and risk factors among women with ovarian cancer.

Characteristics	Frequency (N = 20)	Percent (%)
Presenting Complaints*		
Abdominal swelling	20	100.0
Abdominal pain	17	85.0
Weight loss	14	70.0
Early satiety	11	55.0
Post-menopausal bleed	3	15.0
Anorexia	3	15.0
Leg swelling	3	15.0
Constipation	2	10.0
Urinary frequency	2	10.0
Vaginal protrusion	1	5.0
Clinical features*		
Abdominal Distention	20	100.0
Abdominal Mass	20	100.0
Ascites	15	75.0
Cachexia	10	50.0
Abdominal tenderness	10	50.0

Pallor	5	25.0
Hepatomegaly	4	20.0
Pleural effusion	5	5.0
Pedal edema	1	5.0
Risk factors		
Positive family history of Gynaecological Cancer	4	20.0
History of Hypertension	11	55.0
History of Diabetes mellitus	5	25.0

*More than one of the variables apply in a patient.

Staging and Histological types of Ovarian cancer

Table 5 revealed that Serous cystadenocarcinoma was the most common histological subtype, found in 60% of cases, and 90% of the cases were diagnosed in the advanced stages of the disease (Stage III and Stage IV).

Table 5: Staging and Histological types of ovarian cancer.

Characteristics	Frequency N = 20	Percent (%)
FIGO Tumour staging		
Stage 1	0	0.0
Stage II	2	10.0
Stage III	9	45.0
Stage IV	9	45.0
Histological Subtype		
Serous Cystadenocarcinoma	12	60.0
Endometroid Cystadenocarcinoma	1	5.0
Mucinous cystadenocarcinoma	3	15.0
Clear cell Cystadenocarcinoma	1	5.0
Granulosa cell tumour	3	15.0

Treatment modality and outcome

As presented in Table 5, 45% were managed with surgery and chemotherapy, while half of the patients (50%) were managed with chemotherapy alone. Six (30%) deaths were recorded in the period under review (Table 6). A little above half of the patients defaulted in their treatment (55.0%), while 15% had a recurrence after initial resolution of the cancer.

Table 6: Treatment modality and outcome of Management.

Characteristics	Frequency N = 20	Percent (%)
Treatment Modality		
Surgery	1	5.0
Chemotherapy	10	50.0
Surgery and Chemotherapy	9	45.0
Outcome		
Recurrence	3	15.0
Defaulted	11	55.0
Death	6	30.0

DISCUSSION

In this study, 20 patients were managed for ovarian cancer within the study period of five years which is lower than findings from a tertiary hospital in Lagos (50 cases in 5 years),[15] University of Benin teaching hospital (49 cases in 10 years),[16] a tertiary hospital in Enugu (50 cases in 10 years),[9] and much lower than what was observed in Aminu Kano Teaching Hospital by Yakasai et al (76 cases in 3 years).[17] It is however, comparable to a study done by Odukogbe et al in Ibadan, where 21 cases of ovarian cancer were managed within a five-year period.[18]

Ovarian malignancy consisted of 29.4% of all gynaecological cancers in this study, second to cervical cancer (45.6%) and followed by endometrial cancer (25%). This pattern is common in studies done across the country,[19,20,21,22] but differs from the pattern seen in developed countries where most often ovarian cancer is second to endometrial cancer which is the most common cancer.[23,24]

In this study 29.4% of gynaecological malignancies were ovarian, which is comparable to the study by Yakasai et al (30.5%).[17] It is however, higher than many other studies done across the country (8.2% in Lagos,[15] 9.8% in Ibadan,[18] 22.1% in Abuja,[21] 21.2% in Ilorin,[19] 25% in Enugu[9]). We also noted that ovarian cancer accounted for 0.8% of all gynaecological admissions, which compares with findings from Jos and Abuja (0.7% respectively).[20,21] In a study carried out by Iyoke et al in Enugu, ovarian cancer constituted 0.3% of all gynaecological admissions which was much lower than what we got in our study.[9] Our rates were however, lower than those in Lagos, Ibadan and Abakaliki (1.5%, 1.7%, 1.6% respectively).[15,18,22]

It is known that ovarian cancer (epithelial) is a disease of the sixth and seventh decades of life, and so not surprising that most of our cases were menopausal and above the age of 60 years. This is similar to the study by Agboeze et al with a peak age of occurrence of 60-69 years.[22] However, studies done by Sharafadeen et al and Odukogbe et al were at variance with ours with most of their patients being <50-year-old and premenopausal.[15,18] It may be possible that there may be a high rate of non-epithelial ovarian cancers or hereditary cancers (which are more likely to occur in younger people) in these studies. Many other studies also show a shift in the age of occurrence to an earlier age (the fifth decade).[9,19,25]

Most of the women (80%) in this study were either multiparous or grand multiparous. This is not consistent with the incessant ovulation theory where nulliparous women are more at risk of the disease. In this study, only one out of twenty patients with ovarian cancer were nulliparous. This might suggest that nulliparity may not be a strong risk factor in the development of ovarian cancer in this environment. Similar to our study was that of Iyoke et al in South East, Nigeria with up to 72.4% of their ovarian cancer patients being parous.[9]

All patients in this study presented with abdominal swelling. Other common symptoms were abdominal pain (85%), weight loss (70%) and early satiety (55%). These features suggest advanced disease and such presentations were seen in various other studies in Nigeria.[16,18,19] At presentation, 90% of the patients had advanced disease (stage 3 and 4), with 60% being epithelial in origin. Many other studies have a similar pattern.[16,17,18,19]

Combination treatment with surgery and chemotherapy is the standard management of ovarian cancer. Almost half of the patients in this study (45%) had this modality of treatment, with 50% of patients having chemotherapy alone. Many of these patients presented very late and were not fit for surgery or had inoperable tumours at presentation. There was a high rate of defaulters (probably due to financial constraint), and thus never had cytoreductive surgery. Only one patient had surgery without adjuvant chemotherapy and this was due to financial constraint. Six (30%) patients died of ovarian cancer in the study period. This goes to show that ovarian cancer is highly lethal, especially when the patients present late for treatment in the advanced stages of the disease.

CONCLUSION

There is a high number of patients presenting to our hospital with ovarian cancer, especially epithelial ovarian cancer. Contrary to previously held beliefs, more parous women were affected than nulliparous women and this would require more research to elucidate the possible reasons for this observation.

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Conflict of Interest
The authors declare that there are no conflicts of interest.

Authors' Contributions
EST participated in literature searches and wrote the discussion. PCO conceptualised and designed the study, managed literature searches, supervised data collection/collation and wrote the first draft of the manuscript. DOA wrote the protocol of the study and supervised the entire research. LO participated in literature searches and wrote the results. NCN and GA collected and collated data. All authors read and approved the final manuscript.

Ethical Approval
The research work was examined and approved by the hospital research and ethics committee.

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