

## Incidence and Management of Ovarian Cancer Cases in a Tertiary Hospital- A 10 Year Review

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**Abstract:** Ovarian cancer was considered to be rare in Nigeria. This study was therefore conducted to look into the current incidence and management of ovarian cancer patients cases seen in the Lagos state University Teaching Hospital, Ikeja, Lagos State. All the case notes of histologically diagnosed cases of Ovarian Cancers seen in LASUTH from 1<sup>st</sup> January 2004-Dec 31<sup>st</sup> 2013 were retrieved from the Medical records department and reviewed. Data was extracted for detailed analysis using a Data Extraction Form. Data extracted was coded and analyzed using Statistical Product and Service Solutions (SPSS) version 20. Ovarian cancer constituted 22.1% of a total of 855 histological diagnosed gynecological malignancies seen over the study period. Mean age of incidence was 40.58 years. Epithelial ovarian cancer was the commonest 67 % ( 140). Serous/Papillary carcinoma accounted for 52.1 % ( 73) of subtypes of epithelial ovarian cancers. 66 % ( 137) of the patients had cytoreductive surgeries due to late presentations. This study showed a decreasing age of incidence in epithelial ovarian cancer cases this is in contrast to previous studies which showed a post-menopausal pattern. Also it was the second most common female genital malignancy and epithelial cancers were the most predominant histopathologic variant.

**Keywords:** Cancer, Incidence, Management, Nigeria, Ovarian.

### I. Introduction

Ovarian cancer is malignant disease arising from the female ovary<sup>1</sup>. These abnormal cells of the ovary divide and grow uncontrollably, forming malignant tumors and invade nearby parts of the body. Ovarian cancer is the eight most common cancer after skin, lymphoma, thyroid, cervix, colorectal, lung and breast. It is the fifth leading cause of death after lung, breast, colorectal and pancreatic cancer.<sup>2</sup> The median age at diagnosis in the U.S was 63 years between 2006-2010, with the highest incidence between 55 and 64. The age adjusted incidence rate was 12.5 per 100,000 women per year. The median age for death of Cancer of the Ovary was 71 years and age adjusted death rates was 8.1 per 100,000 per year.<sup>3</sup> In the UK, incidence rate of ovarian cancer was about 17.1/100,000 for the year 2010. About 8 in 10 cases are diagnosed in women aged 50 years and above. Mortality rate was about 9.1/100,000 in 2010.<sup>4</sup> In Nigeria, studies done by Iyoke.C.A et al in Enugu<sup>5</sup> showed that ovarian cancer constituted 25.0% of all gynecological malignancies seen over a ten-year period giving an incidence rate of 1 per 405 gynecological admissions per year. The mean age of cases at presentation was 45.4 ± 17.1 years. Epithelial ovarian cancer constituted 68.0% of ovarian cancer cases. Approximately 60.0% of women who had epithelial ovarian cancer were aged 50 years or below.<sup>5</sup> Risk factors involved in carcinoma of the ovary include patient related factors and Exposure related factors. Patient related factors include advancing age, low parity, infertility which gives rise to the incessant ovulation hypothesis, also nulliparity, early menarche, first childbirth after age 35, and late menopause that are associated with higher frequency of ovulatory events all may increase the risk of epithelial ovarian cancer and genetic factors. Exposure related factors include metabolic issues, Obesity, diets high in fat, use of fertility drugs and Tamoxifen and so on.<sup>6</sup> The histological classification of ovarian cancers by the World Health Organization (WHO) is based on histogenetic principles, and this classification categorizes ovarian tumors with regard to their derivation from coelomic surface epithelial cells, germ cells, and mesenchyme (the stroma and the sex cord). Epithelial ovarian tumors, which are the majority of malignant ovarian tumors, are further grouped into histological types as follows: serous, mucinous, endometrioid, clear cell, transitional cell tumors (Brenner tumors), carcinosarcoma, mixed epithelial tumor, undifferentiated carcinoma, and others. Clear cell and endometrioid carcinomas are highly associated with endometriosis.<sup>7</sup> Rabiou K.A et al in Lagos<sup>8</sup> showed that 86.5% of patients presented in stage 3 & 4 and associated the delays in presentation to late referrals. There is however a need for more local studies on various histopathology types of ovarian Cancers, The aim of this study is to study the pattern of presentation and management of ovarian cancer cases seen in the Lagos State University Teaching Hospital, Ikeja, and Lagos State.

## II. Aims And Objectives

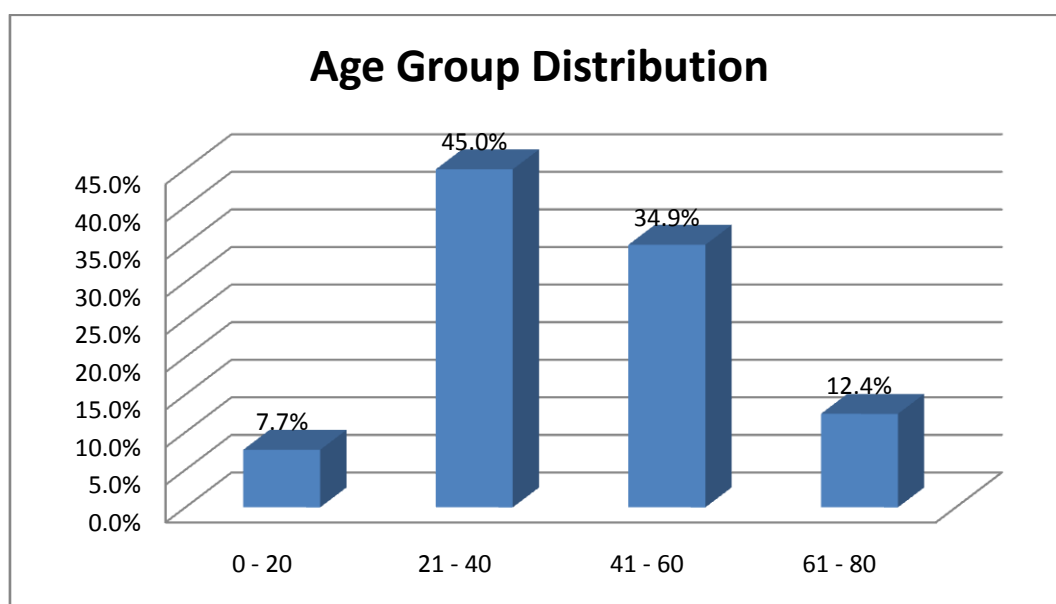
The aim of this study is to study the pattern of presentation and management of ovarian cancer cases seen in the Lagos state University Teaching Hospital, Ikeja, Lagos State.

## III. Materials And Methods

This study was carried out at the outpatient clinic of the Oncology unit and the Gynae-Oncology Unit of the Lagos State University Teaching Hospital Ikeja which is situated within the metropolitan city of Lagos, South Western part of Nigeria. This is a cross sectional retrospective study. Cases of Histological diagnosed ovarian cancer patients were identified from records of the LASUTH Cancer registry and Histopathology department as well as the theatre department of the hospital. Sample size included all the case notes of Histological diagnosed cases of Ovarian Cancers seen in LASUTH from 1<sup>st</sup> January 2004-31<sup>st</sup> December 2013. The case files of such patients with Ovarian Cancer were extracted from the Medical records department and reviewed. The following data was extracted for detailed analysis using a Data Extraction Form containing the following details: Age of patient, Gender of patient, Hospital Number of patient, Address of patient at diagnosis, Presenting complain of the patient, Histological Diagnosis, Clinical stage at presentation, Treatment of patient, Patient's treatment outcome (Partial, Complete or No Response), Side effects of treatment. Inclusion criteria included all cases notes with histology reports of ovarian cases. Data extracted was coded and analyzed using Statistical Product and Service Solutions (SPSS) version 20. Analysis was done using percentages, frequency, chart representation and inferential statistics of chi-square at 5% level of significance. Approval to conduct this study was obtained from the Ethical and research committee of the Lagos State University Teaching Hospital Ikeja.

## IV. Results Presentation And Analysis

The total number of histological diagnosed cases of ovarian malignancy obtained over a ten year period was 290. The records of 209 cases of ovarian cancer were retrieved giving a recovery rate of 75.6%. The cases whose records were available were reviewed and analyzed. Ovarian cancer constituted 22.1% of a total of 855 histological diagnosed gynecological malignancies seen over the study period giving a yearly incidence of 2.21% per gynecological malignancy per year.



**Figure 1: showing age distribution of cases**

The age of patients ranged from 6-78 years (Fig 1). The mean age of all the cases seen was 40.58 (SD = 15.19), while the median age was 39 years and modal age was 30. The mean ages at presentation of the different types of ovarian cancer were as follows: Epithelial tumors  $46.5 \pm 13.7$ , Sex cord stroma tumors  $34.2 \pm 7.8$  and Germ cell tumors  $23.9 \pm 1.3$ .

Fig.2 illustrates the marital status of patients seen, it shows that 70.8% (148) were married, 13.4% (28) single and others (widowed/separated) 15.8% (33). Furthermore, only 21% were nulliparous (Fig 3) and most cases were in the premenopausal age group (134) 64.1%. Ethnic distribution showed 82.8% Yoruba, 15.2% Igbo, 1% Hausa 1% others.

Table 2 Showing Number Of Children(Parity)

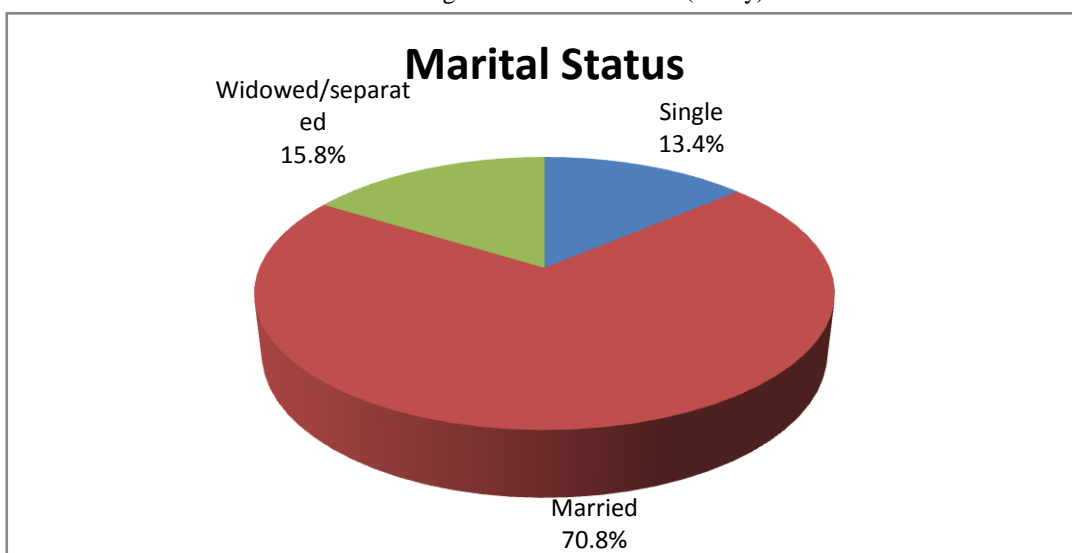


Figure 2 showing marital status

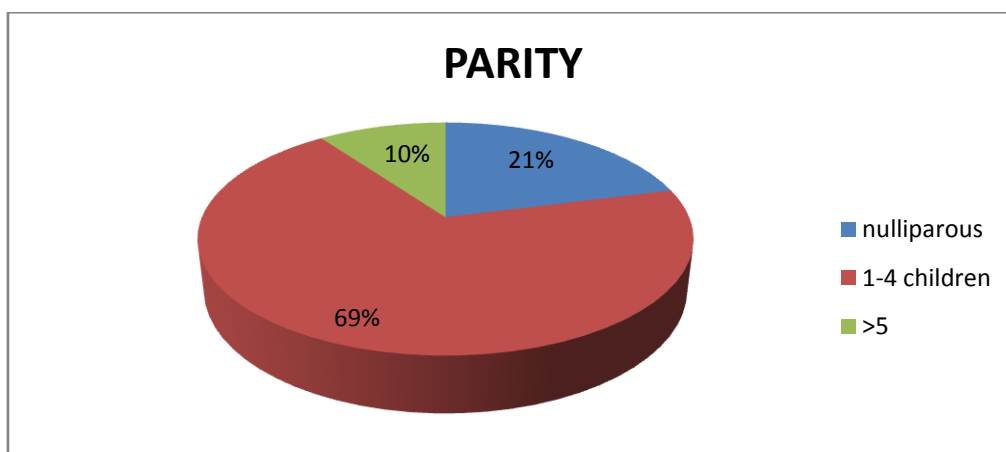


Figure 3 showing parity

Table 1: Showing Histopathologic Variants

HISTOPATHOLOGY	FREQUENCY	PERCENTAGE
EPITHELIAL	140	67
GERM CELL	41	19.6
STROMA	25	12
METASTASIS	3	1.4

The various histopathologic variants of Ovarian cancers are shown in Table 1. Epithelial ovarian cancer constituted 140(67%) of all ovarian cancers seen, followed by Germ cell Tumors with 19.6%.

Table 2: Showing the Subtypes of Various Histologic Variants

HISTOLOGIC SUBTYPES	FREQUENCY	PERCENTAGE
<b>EPITHELIAL</b>	140	100
Serous/Papillary Carcinoma	73	52.1%
MucinousCytadenocarcinoma	47	33.6%
Squamous cell Carcinoma	9	6.4%
Clear Cell Carcinoma	5	3.6%
Endometriod Carcinoma	6	4.3%
<b>SEX CORD STROMA TUMOR</b>	25	100
Granulosa Cell Tumour	23	92
Fibroma	1	4
Thecoma	1	4
<b>GERM CELL TUMOR</b>	41	100
Dysgerminomas	21	51.2%
Teratoma	10	24.4%

Immature Teratoma	9	22%
Endodermal sinus	1	2.4%
<b>METASTASIS FROM COLON</b>	<b>3</b>	

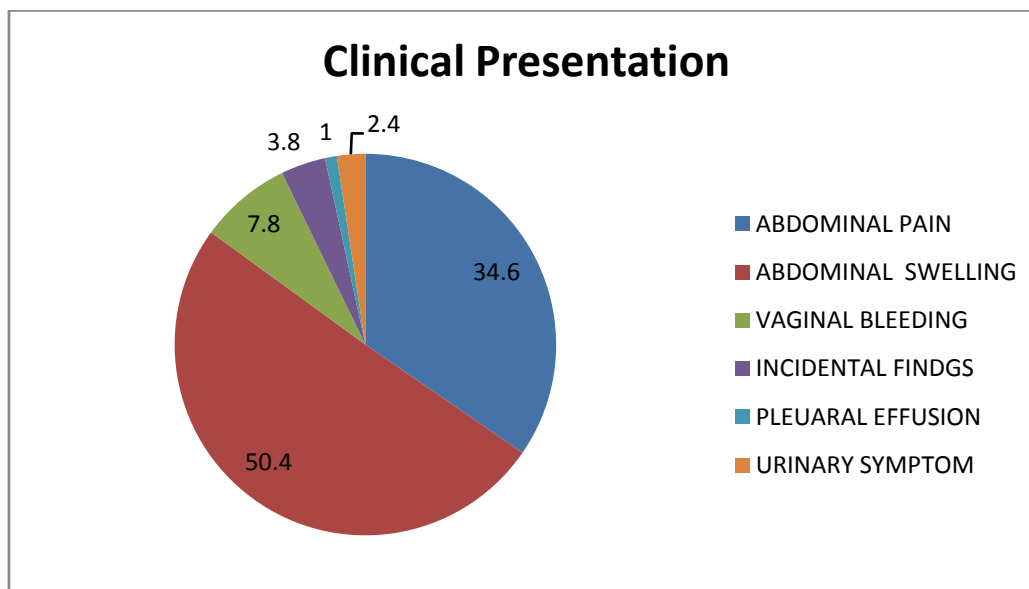
The different subtypes of histopathologic variants are shown in Table 2. Serous /Papillary Carcinoma was the most common subtype among the Epithelial cancers being 52.1 % ( 73). It was followed by mucinous cystadenocarcinoma which accounted for 33.6 % ( 47). Granulosa Cell Tumor and Dysgerminomas were the commonest subtypes in the Sex Cord/Stroma and Germ cell Tumor groups respectively.

Table 3 shows the relationship between parity and the different histological variants. Ovarian cancer occurred mostly in multiparous (1->5 children) women accounting for 67% of cases. It also demonstrates that most of the multiparous cases were of the epithelial ovarian cancer histological variant.

**Table 3: Showing relationships between parity and histologic variants**

PARITY				
HISTOLOGIC VARIANT	NULLIPARITY	MULTIPARITY (1->5 Children)	TOTAL	PERCENTAGE
Epithelial	2	138	140	67
Germ Cell Tumor	23	18	41	19.6
Sex Cord/Stroma	19	6	25	12
Metastasis	-	3	3	1.4
TOTAL	44	167	209	100

Fig .4 shows the clinical presentation of cases. Patients presented with a range of symptoms but the most common was abdominal swelling/mass which constituted 50.4%, others included abdominal pain 34.6%, vaginal bleeding 7.8%, 2(1%) cases of pleural effusion, 2.4% had urinary symptoms and while the remaining 4 cases were incidental findings during surgery (3.8%) About 50% of these cases had overlapping symptoms.



**Figure 4: showing clinical presentation**

Stages of disease at time of presentation are shown in Fig5. Majority of patients presented with stage 3 constituting 48.3 % ( 101) cases.

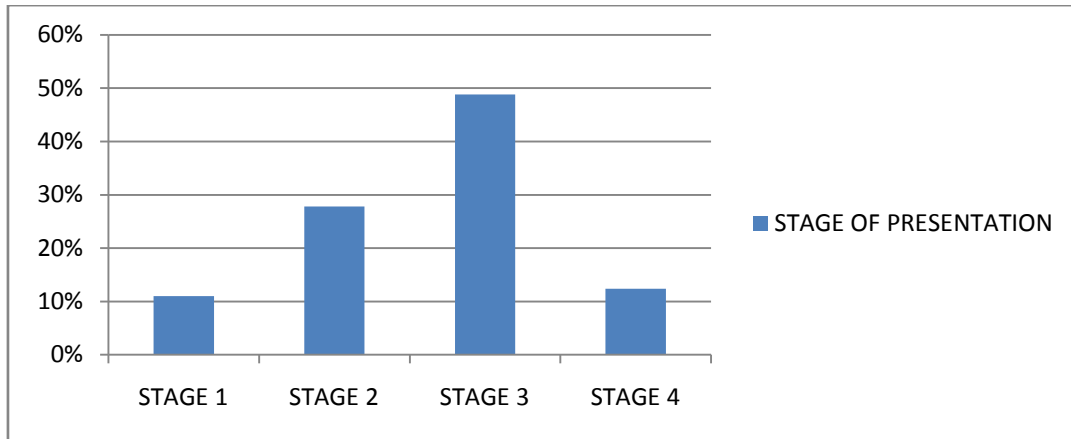


Figure 5: showing stages of disease at time of presentation

Table 4 shows a Cross tabulation of the histological variants and stages of presentation. Most of the advanced cases were epithelial ovarian cancer cases, while the Germ cell and Sex Cord /Stromal tumors constituted most of the early cases (stages 1&2).

Table 4: Showing stages of presentation and histologic variant

HISTO VARIANT	STAGE				TOTAL
	1	2	3	4	
Epithelial	4	19	94	23	140
Germ Cell Tumor	14	22	4	1	41
Sex Cord/Stroma	5	15	4	1	25
Metastasis	-	-	-	3	3
TOTAL	23	57	101	28	209
PERCENTAGE	11%	27%	48%	14%	100%

Fig 6 illustrates the different surgical procedures done. About 66 % ( 137) of the patients had cytoreductive surgeries which included surgical staging, maximal debulking, total abdominal hysterectomy, bilateral salpingo-oophorectomy, different degrees of omentectomies and appendectomy. Some had fertility preserving surgeries involving unilateral oophorectomy (14%) and bilateral oophorectomy (17%). the remaining 7 cases had inoperable tumors at surgery and only had tumor biopsy.

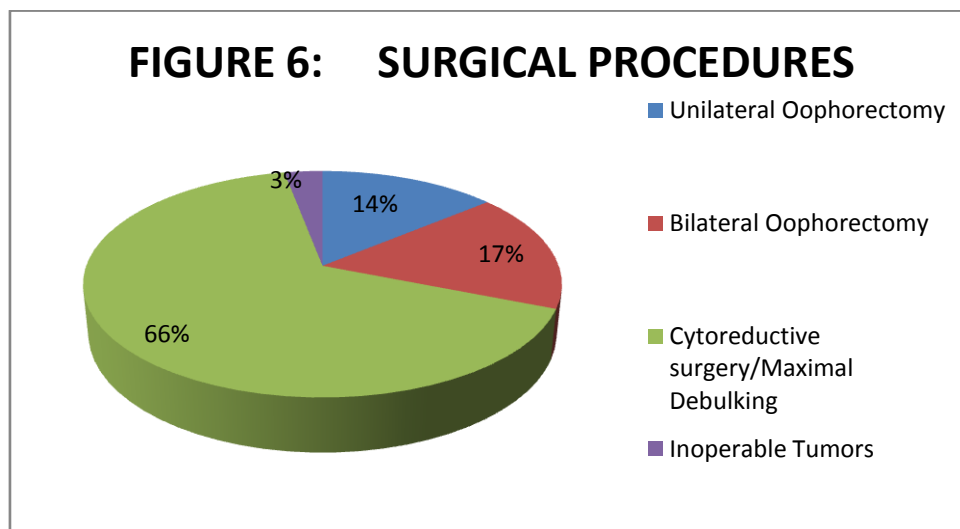
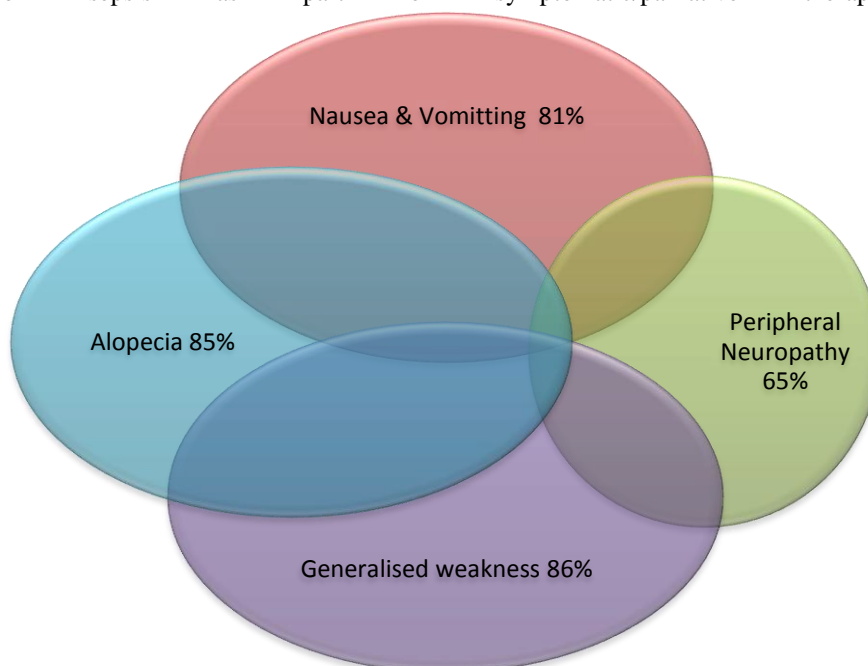


Figure 6 showing surgical procedures done

Eighty-five percent of the patients had chemotherapy involving platinum based combination chemotherapy. The combinations included a platinum agent i.e. Cisplatin (100mg/m<sup>2</sup>) or Carboplatin(6AUC) and paclitaxel (175mg/m<sup>2</sup>) or cyclophosphamide(600mg/m<sup>2</sup>) for epithelial/ stroma tumors and a combination of Bleomycin/Etoposide/Cisplatin for Germ cell tumors.

However, approximately 81% of patients completed prescribed courses of chemotherapy while 3% patients died before commencement of chemotherapy due to advanced nature of disease and there were 4(2%) cases of recurrence about 1year after. the remaining 29(14%) did not receive chemotherapy. Noneof the cases in this study received Radiotherapy

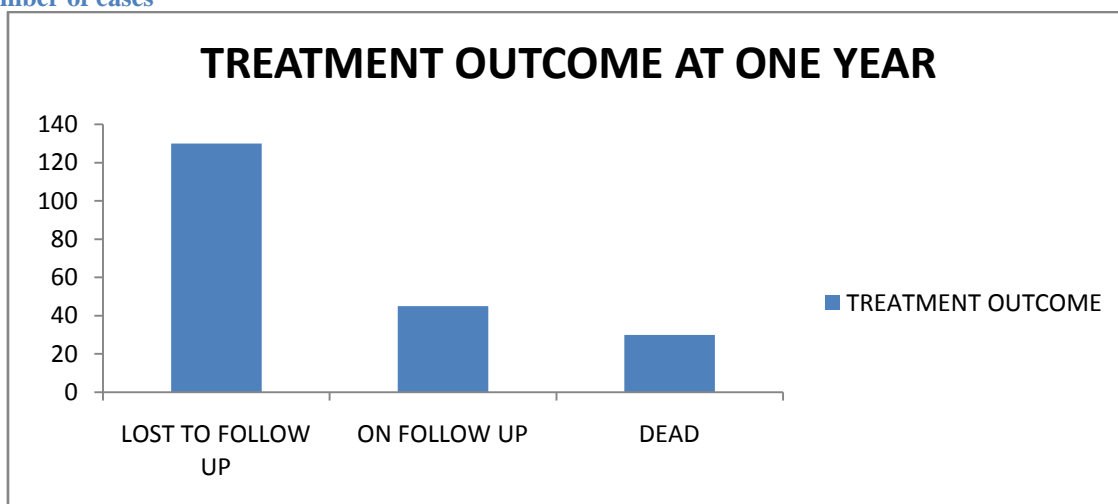
Most cases had overlapping side effects which included nausea & vomiting 81%, alopecia 85%, weakness 86% and peripheral neuropathy 65%. All patients had injectable and/or oral analgesics, and antiemetic for relief and antibiotics for sepsis as part of symptomatic/palliative therapy(Fig 7).



**Figure 7: showing overlapping side effects**

Follow up of patients was by clinical examination and trans-abdominal/Vaginalultrasonography and Computerized tomography scans. CA125 assays were not routinely done until 2010 for lack of facilities within the hospital. The outcome of patients following treatment varied, 57.9 %( 121) were lost to follow up or defaulted treatment (Fig 8).About 45 cases (21.5%) were seen in follow up clinic within a year after treatment.About 43 cases of ovarian cancers died (20.6%) within a year after treatment.

**Number of cases**



**Figure 8: showing treatment outcome**

The survival period within a year following treatment in this study is as follows (Table 5), 69% survived within 0-6months after treatment, 20% survived for 7-12months and 54% survived beyond a year after treatment.

**Table 5: Showing Survival Periods For Ovarian Cancer Patients**

Time Interval	Frequency of Cases	Percentage
0-6 months	145	69%
7-12 months	15	7%
>12 months	49	23%
Total	209	100%

## V. Discussion

Ovarian cancer accounted for almost a quarter of all gynecological malignancies in this study and was also the second most common malignancy among cases reviewed. This finding was in agreement with several studies done across Nigeria.<sup>5, 10, 11, 22</sup> Several studies across Nigeria showed that an average of 43-62 cases of ovarian cancer would be seen over a 10-year period, this tends to support the rarity of this cancer in this country.<sup>10, 12, 13</sup> However, the incidence of ovarian cancer in this study showed an increased occurrence of patients, this is similar to the findings by Iyokeet al<sup>5</sup> where the incidence of ovarian cancer suggested an 85% increase in relation to other gynecological malignancies at the center, however, the incidence of ovarian cancer in this study suggested an astronomical increase when compared with previous studies, several factors may be attributed to this increase these include, the fact that Lagos is the most populous city in Nigeria, the second fastest-growing city in Africa and the seventh in the world, and its nature being a cosmopolitan city with a population of 21 million<sup>32</sup>, and highly enlightened citizenry. This is likely to increase the tendency of seeking orthodox care.

The findings of this study showed that majority of cases reviewed presented below the age of 50 years, the mean age was 40.58 (SD±15.19) with a median age of 39 years. This is closely related to the findings of previous studies done in Enugu<sup>5</sup> where it was noted that majority of the cases presented below 50 years with a mean age of 45.4 while the median age was 48. This result is also consistent with a related study done in Ibadan<sup>15</sup> However, this observation differed from an earlier study done in Lagos by Ketiku et al<sup>16</sup> which found a mean age of 58 years (Postmenopausal) among ovarian cancer. The high incidence within the premenopausal age bracket may suggest a shift to an earlier age of occurrence in the population which is a worrisome development. The ovarian cancer patients in this environment are premenopausal<sup>15</sup> it is however in contrast with international studies done in the United States, United Kingdom and Australia which showed higher incidence in the postmenopausal age bracket.<sup>3, 4, 17</sup> Previous literature postulated nulliparity as a risk factor for ovarian cancer due to repeated cycles of ovulation, resulting in increased trauma and scar tissue formation on the surface epithelium of the ovary thereby increasing risk of malignant transformation.<sup>18, 19</sup> The findings of this study reveal that majority of cases in the parous group and are consistent with a similar work done in the southern part of Nigeria.<sup>15</sup> The most common histological variant was Epithelial ovarian cancer which accounted for 67% of cases and this is in agreement with previous literature.<sup>20, 21</sup> Epithelial ovarian cancer has been known to be a disease of the 6<sup>th</sup> and 7<sup>th</sup> decade of life. Serous Epithelial carcinoma was the most predominant subtype of Epithelial ovarian cancer. This finding is in agreement with a previous ten-year study on Ovarian cancer in Sokoto, North western part of Nigeria<sup>9, 20</sup> and an earlier study done in Lagos by Ketiku et al.<sup>16</sup> However, a previous study from Kano had identified mucinous subtype as being more prevalent.<sup>10</sup> Dysgerminomas were the most common Germ cell tumors, similar findings were noted from previous studies<sup>10, 20</sup> Granulosa cell tumor was the commonest of Sex cord stroma tumor this is in agreement with a related work in Benin City.<sup>23</sup> The findings from this study showed that majority of patients 60.2% presented in late stages of the disease. This is attributable to the fact that women often have vague symptoms of abdominal bloating/distention and are often treated for gastrointestinal problems. Unfortunately, given the vague nature of the symptoms, nearly 80% of these have advanced-stage (metastatic) disease.<sup>24</sup> This finding is in agreement with previous studies in Nigeria.<sup>11, 15, 21, 24</sup> This suggests that clinicians must have a high index of suspicion when patients present with vague symptoms and signs of ovarian cancer. It is important for women and medical practitioners to know the symptoms of ovarian cancer so that early diagnosis can be made, bearing in mind that 80-90% of women who develop ovarian cancer will not have a family history and screening in general population is not yet effective.<sup>25</sup>

This study showed that the most predominant clinical symptoms in majority of cases reviewed were abdominal swelling/mass with or without abdominal pain 85%, findings are consistent with previous studies<sup>15, 21, 26</sup> other documented symptoms include bloating, urinary tract symptoms, pelvic discomfort and bowel irregularities.<sup>26</sup> Treatment modalities of ovarian cancer almost always involve a combination of surgery followed by platinum-based chemotherapy.<sup>27</sup> The recommended surgical procedure is total hysterectomy, bilateral salpingo-oophorectomy and omentectomy aimed at radical cytoreductive treatment. Majority of the patients in this study had surgical staging and maximal debulking surgeries. Others had fertility preserving surgeries involving unilateral and bilateral oophorectomies. This mode of management was consistent with previous study done which showed that only a limited number of patients will benefit from cytoreductive surgery as a result of late presentation. Majority (85%) of cases received platinum-based combination chemotherapy. The combinations were of a platinum agent (Cisplatin or carboplatin) and paclitaxel, cyclophosphamide for

Epithelial/ Stroma Tumors and a combination of bleomycin, etoposide cisplatin for Germ cell Tumors. These combinations were in agreement with standard recommended chemotherapy regimens in the management of ovarian cancers.<sup>28, 29, 30</sup> however the FDA recently approved the use of Bevacizumab, which is a monoclonal antibody, in the management of platinum resistant ovarian cancer.

Most cases had overlapping side effects which included nausea & vomiting, alopecia, weakness and peripheral neuropathy. All patients had injectable and/or oral analgesics, and antiemetic for relief and antibiotics for sepsis as part of symptomatic/palliative therapy.

CA 125 is recommended for clinical use in the diagnosis and treatment of ovarian cancer. However, in this study, CA125 assays were not routinely done until 2010 for lack of facilities within the hospital. None of the cases in this study had Radiotherapy primarily due to lack of Radiotherapy facilities in at the center and also logistics of referring cases to other center was not feasible since most cases present in late stages and had financial constraints. Long term survival in ovarian cancer is known to be poor because majority of cases present in late stages.<sup>24, 31</sup> A large number of patients default after treatment making it difficult to determine the actual rate of survival.

## VI. Conclusion

Cancer of the ovary is the second most common female genital malignancy in Lagos with declining age of incidence. Options now exist for prevention, detection, treatment and palliative care for ovarian cancer. However, in our low resource setting women cannot avail these options. In view of this, it is important to increase awareness, public enlightenment and routine screening and treatment of ovarian cancer. It is important for women and clinicians to know the symptoms of ovarian cancer so that early diagnosis can be made and appropriate treatment to be given on time. This will help to improve results and survival rate. The limitations of this study were lack of follow up and poor documentation of vital information, and poor record keeping. Data were scanty on management outcome and records of deaths from this gynecological malignancy. Based on the findings of this study, there is need for increased awareness, public enlightenment programs and screening on ovarian cancer. Clinicians should have a high clinical index of suspicion when female patients present with vague abdominal symptoms. More research work on ovarian cancer in order to determine the risk factors in women of African descent, also reasons for increased incidence in premenopausal age group.

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