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Ovarian Cancers in a Northern Nigerian Hospital: Epidemiology, Clinicopathology and Treatment Options

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Abstract

Background: In Nigeria, Ovarian cancer is the most lethal gynaecologic cancer. The management of disease in developing countries poses a huge challenge due to late presentation and/or diagnosis, poverty, poor health insurance coverage, and the dearth of specialists in the region amongst others. Record keeping is poor. Treatment options are limited with high default rates and mortality. This was a five-year review of clinicopathology and treatment strategies for ovarian cancers in Ahmadu Bello University Teaching Hospital, Zaria.

Methodology: A retrospective study of all primary ovarian cancers diagnosed and or treated in ABUTH Zaria from 1st January 2016 to 31st December 2020 was carried out. A total of 38 cases were retrieved and relevant data was extracted. The data collected were entered into Open Data Kit (ODK) and analysed using descriptive statistics. **Results:** Most patients were aged 35 to 54 years with an overall mean age of 51.2 ± 13.8 years. Only 34% of patients were nulliparous and 63.2% were post-menopausal. The commonest symptoms were abdominal swelling (94.7%), and abdominal pain (68.4%). Epithelial carcinomas (81.8%) were the commonest histotype of which serous adenocarcinoma (85.1%) was the commonest. There was no distinction between high-grade and low-grade serous carcinomas. Rare ovarian tumours (germ cell and sex cord/stromal) accounted for 18.2%. Most patients presented with stage III disease and above (77.7%) with no one presenting at stage I. Thirty-five patients (92.1%) had surgery, twenty-four (63.2%) had chemotherapy and four patients (10.5%) had targeted therapy. No patient had hormonal therapy, genetic testing, Poly-adenosine diphosphate-ribose polymerase inhibitors (PARPi), Hyperthermic intraperitoneal chemotherapy (HIPEC), or palliative radiotherapy. Only 12% had an MDT discussion. One-year post-diagnosis, the majority were lost to follow-up (73.7%) while 21.1% of patients were still on follow-up.

Conclusion: Ovarian cancer patients in ABUTH were relatively younger, unemployed, multiparous, and symptomatic. Some standards of care management practices were omitted. **Keywords:** Ovarian Cancer: Clinicopathology; Treatment; Zaria.

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Introduction

Ovarian cancers are a group of divergent and complex neoplasia of the female gonads. It is the seventh most common female cancer globally and the second most common gynaecologic cancer after cervical among Nigerian women [1]. Globally, ovarian cancer is a highly lethal disease. In Nigeria, it is the most lethal gynaecologic cancer with 72% case fatality in 2020, and remains a public health problem [1,2]. Currently, there are no globally acceptable screening methods for preventing ovarian cancer. Among Nigerians, there is a paucity of data on ovarian cancer epidemiology, clinicopathology, genetics, and survival.

In 2020, ovarian cancer cases accounted for 4.4% of all new cancer cases in Nigeria but 5.1% of deaths from cancer [1]. With the incidence of ovarian cancer projected to surge by 82.9% from 2020 to 2040 in the country, there will be a substantial rise in new cases. The Nigerian National System of Cancer Registries (NSCR) major mandate is gathering, assessing, and preserving data on cancers within the country. There is no national database for ovarian cancers. The National Cancer Control Plans of 2018-2022 [3] and the newly launched 2023-2027 version however had ovarian cancer covered.

A woman's lifetime risk of having the disease is about 1.4% while her risk of dying from the disease is 1% [4]. Globally, the incidence of ovarian cancer has been rising with over 200,000 cases diagnosed annually. The International Agency for Research on Cancer in 2012 estimated that world new cases and deaths from ovarian cancer were 238,700 and 151,900 respectively while in 2020 the incidence and mortality were 313,959 and 207,252 [1,5]. There is a varied trend in the prevalence of ovarian cancer from one geographical region to another. Momenim et al in 2019, showed that the prevalence of ovarian cancer was higher in countries with high human development index (HDI) compared to those with low HDI. Mortality rates however showed an inverse relationship [6]. In the United States, the incidence of the disease has remained static (from 21,290 in 2015 to 21,750 in 2020) while the mortality rate slightly declined (14,180 in 2015 and 13,940 in 2020) [7]. In 2020, there were 3,203 new cases and 2,295 deaths from ovarian cancers in Nigeria [1].

The management of ovarian cancer in low- and middle-income countries including Nigeria is plagued with enormous challenges [1,8]. The early stage of the disease is usually characterized by vague symptoms and is often missed; thus, many patients present with advanced disease. In addition, the cost of chemotherapy is high, especially without health insurance coverage. In Nigeria, most patients pay out of pocket and are unable to complete the course of chemotherapy. Compounding this problem is the growing incidence of fake and adulterated chemotherapeutic agents in the region which are usually cheaper but not efficacious. Consequently, some patients who receive chemotherapy show little or no improvement [9]. Additionally, there are few gynaecological oncologists practicing in the region [9]. There has not been a single clinical trial in our centre on ovarian cancers. Targeted therapy use is low, as PARPi is not available in the country. The interplay of all these factors accounts for the late diagnosis, high default rate, and poor prognosis of ovarian cancer reported in the region.

The standard of care for diagnosis and treatment has clearly been documented. We therefore conducted a five-year review of ovarian cancer in our institution to determine the sociodemographic characteristics, clinical presentation, diagnosis, histological types, and treatment strategies, while comparing this with standard of care.

Methodology

The study was carried out at Ahmadu Bello University Teaching Hospital (ABUTH). The hospital is a cancer referral centre from other parts of Nigeria. Ethical approval was obtained from the Health Research Ethics Committee (NHREC/10/12/2015). The study was retrospective in which all cases of primary ovarian cancer that were histologically diagnosed and/or treated at our institution from 1st

January 2016 to 31st December 2020. Only records of patients with a histologic diagnosis of ovarian cancer at ABUTH and patients treated for ovarian cancer in ABUTH irrespective of where they were diagnosed were included.

The variables were extracted from eligible case notes of patients with ovarian tumours. The number of gynaecological malignancies managed during the period and the total number of gynaecological admissions were obtained from the gynecological ward register. The patients with histologically confirmed ovarian cancer were obtained from the Department of Pathology and Morbid Anatomy. Case notes of patients with histological diagnoses of ovarian cancer were obtained from the Department of Health Information Management. Relevant data such as age, tribe, religion, occupation, marital status, parity, clinical presentation, stage at presentation, histological types, treatment options, and outcomes were extracted from case notes using a structured form. The data collected were de-identified and stored in a passworded computer accessible only to the researcher.

Data was extracted and entered in the Open Data Kit (ODK) software version 1.16.1 using Android handheld smart devices, which was scripted to prevent or minimize data entry errors, ease timely data collection, ensure completeness of the information and subsequent processing and analysis, and results were presented using frequency tables, pie, and bar charts.

Results

During the 5-year period, there were 3,010 gynecological admissions. The total number of histologically diagnosed cases of primary ovarian malignancy obtained was 42, therefore ovarian cancers accounted for about 1.4% of all gynaecological admissions within the period of this study. Complete records were available for 38 cases retrieved, giving a recovery rate of 90.4%. Thus, only cases with complete records were analyzed. Figure 1 shows the annual numbers of ovarian cancers over a five-year period.



Figure 1: Cases by Year of Ovarian Cancer seen in Ahmadu Bello University Teaching Hospital Shika-Zaria from 2016-2020.

The sociodemographic characteristics of patients with ovarian cancer is shown in Table 1. Thirty four percent (34%) of patients were nulliparous and 63.2% were post-menopausal, with majority of patients in the 35 - 54-year age group.

Variable		Frequency	Percent
Age in years	< 15	1	2.6
	15 - 34	2	5.3
	35 - 54	20	52.6
	≥55	15	39.5
Tribe	Fulani	2	5.3
	Hausa	20	52.6
	Idoma	3	7.9
	Igbo	3	7.9
	Other	8	21.1
	Yoruba	2	5.3
Religion	Christianity	11	28.9
	Islam	27	71.1
Occupation	Artisan	2	5.2
L.	Civil servant	1	2.6
	Retired	1	2.6
	Student	1	2.6
	Teaching	5	13.2
	Trading	5	13.2
	Unemployed	22	57.9
	Unskilled employed	1	2.6
Marital status	Never married	1	2.6
	Married	30	78.9
	Widowed	7	18.4
Highest Educational Qualification	Not indicated	27	71.1
Ingliest Educational Qualification	Our'anic Only	27	79
	Primary Education	1	26
	Graduate	7	18.4
Menopausal Status	Pre-menopausal	14	36.8
*	Post-menopausal	24	63.2

 Table 1: Sociodemographic Characteristics of Patients with Ovarian Cancer in Ahmadu Bello University

 Teaching Hospital Shika-Zaria 2016-2020.

The clinical presentation of the patients with ovarian cancer is presented in Table 2. The commonest clinical presentation was abdominal swelling (94.7%), others were abdominal pain (68.4%), easy satiety (57.9%), and weight loss (47.4%). Vaginal bleeding was seen in 26.7% of patients. While the common clinical signs were abdominal distention (60.5%), ascites (63.2%), abdominal mass (44.7%), and cachexia (34.2%). Other symptoms/signs are shown in Table 2.

Symptom	%	Sign	%
Abdominal swelling	94.7	Pallor	30.8
Abdominal pain	68.4	Jaundice	0.3
Easy satiety	57.9	Pedal oedema	6.9
Nausea	2.3	Cachexia	34.2
Anorexia	7.8	Abdominal distention	60.5
Weight loss	47.4	Abdominal mass	44.7
Constipation	5.2	Ascites	63.2
Vaginal bleeding	26.7	Lymphadenopathy	5.2
Cough	5.1	Hepatomegaly	4.8
Chest pain	0.2		
Shortness of breath	2.0		

Table 2. Symptoms and Signs of Ovarian Cancer in Ahmadu Bello University Teaching Hospital Shika-Zaria 2016-2020.

The histological pattern of ovarian cancer is presented in Table 3. Most patients with sex-cord tumour (80%) presented with vaginal bleeding while epithelial cell tumour (81.8%) was the commonest histotype. Five patients (15.2%) had Sex cord tumours while one patient (3%) had Germ cell tumour. The commonest epithelial tumour was serous (85.1%) followed by endometroid cancers (11.1%). Dysgerminoma and immature teratoma were the germ cell cancers seen. Granulosa cell tumour was the only type of Sex cord cancer seen.

Table 3: Histological Types of Ovarian Cancer in Ahmadu Bello University	Teaching Hospital Shika-Zaria
2016-2020.	

Histological type	Histological Subtype	Frequency	Percent
Epithelial	Endometroid	3	7.9
	Mixed	1	2.6
	Serous	23	60.5
Germ cell	Dysgerminoma	1	2.6
	Immature teratoma	1	2.6
Sex cord	Granulosa cell	5	13.2
Missing		4	10.5

The distribution of the stage of ovarian cancer at presentation in the patients is presented in Table 4. Most patients (73.7%) presented with advanced disease above stage III. The patients with stage II disease had Granulosa cell tumours (50%) and Serous carcinoma (50%). The disease stage at presentation was not indicated for five patients (13.9%). No patient had genetic testing during their management.

Surgical Stage	Frequency	Percent (%)
1	-	-
П	3	7.9
Ш	16	42.1
IV	12	31.6
Not Indicated	7	18.4

 Table 4: Stage at Presentation of Ovarian Cancer in Ahmadu Bello University Teaching Hospital Shika-Zaria 2016-2020.

The treatment modalities for the patients is displayed in Table 5. Thirty-five patients (92.1%) had surgery, twenty-four (63.2%) had chemotherapy and 4 patients (10.5%) had Bevacizumab targeted therapy. No patient had HIPEC, hormonal therapy, PARPi, or palliative radiotherapy.

Table 5: Treatment Modalities for Ovarian Cancers in Ahmadu Bello University Teaching Hospital Shika-Zaria 2016-2020.

Treatment	(%)
Surgery	35(92.1)
Chemotherapy	24(63.2)
Hormonal therapy	0(0.0)
Targeted therapy (use of Bevacizumab)	4(10.5)
Palliative use of radiotherapy	0(0)

Among patients that had surgical treatment, 26 (74.28%) had staging laparotomy/primary debulking surgery while 7 patients (20%) had delayed debulking surgery. Sixty-three percent of patients had chemotherapy while 10% had both chemotherapy and targeted therapy. The common agents used in the treatment of ovarian cancer were Platinum-based agents (Cisplatin/ Carboplatin) and Taxanes (Paclitaxel/Docetaxel). Others were Bleomycin, Etoposide, and Gemcitabine. Bevacizumab was the only form of targeted agent used. Seven patients (33.3%) had neoadjuvant chemotherapy while 20 patients (83.3%) had adjuvant chemotherapy. Four patients (16.7%) had second-line chemotherapy while one patient (4.8%) had third- and fourth-line chemotherapy. Other forms of treatment received were blood transfusion (52.6%), Analgesics (44.7%), Haematinics (21.1%), Antibiotics (15.8%), Deep Venous Thrombosis (DVT) prophylaxis and nutritional rehabilitation (10.5%) respectively while 2.6% had DVT treatment. As of the time of this study in 2022, 21.1% of patients were still on follow-up, 5.3% had died and 73.7% were lost to follow-up. Those who defaulted did so in an average of 4 months from the commencement of the first form of treatment. All deaths occurred after 1 year of the commencement of the first form of treatment.

Discussion

This study investigated the clinicopathology and treatment strategies of ovarian cancer at Ahmadu Bello University Teaching Hospital Zaria. The study showed that ovarian cancer accounted for 1.33% of all gynaecological admissions and 20.39% of gynaecological cancers. It was consistent with a previous study of ovarian cancer in this center about a decade ago [14]. The prevalence of ovarian cancer from this study was lower than the 2.4% reported by Iyoke et al in Enugu and 11.5% by Umar et al in Kano [15,16].

Ovarian cancer has been described as the disease of the elderly, typically developing after menopause with more than 50% of cases occurring after the sixth decade of life [17]. On the contrary, this study showed that most of the ovarian cancer (52.6%) occurred between 35 years and 54 years of age with a mean age of 51.2 ± 33.8 years, indicating a difference in age-related incidence of ovarian cancer among populations. A similar pattern of the age distribution of ovarian cancer was described in a previous study in this center by Zayyan et al as well as Iyoke et al. in Enugu [14,15]. According to FIGO 2021 report, the largest number of patients with epithelial ovarian cancer is found in the 60–64 years age group. The median age is about a decade earlier in low-income countries [18].

Nulliparity is a strong risk factor for ovarian cancer. This study however revealed a high incidence of the disease among grand multiparous women (36.8%) with an overall mean parity of 4.3 ± 2.3 , putting to question the seemingly protective effect of parity on ovarian cancer in our women. A previous study in this centre reported that 83% of the patients were parous with a mean parity of 4.5 [14]. The overall mean parity in this study was higher than the mean parity of 3.4 ± 1.7 by Ayogu et al in Abuja [2]. There must be a strong driver of malignant transformation in our women that even grand multiparity and significant ovulation interruptions aren't enough to meaningfully impact risk. Further research is needed to investigate this. A study by McGuire et al showed clear patterns of decreasing risk of ovarian cancer with increasing parity [19].

Post-menopausal women accounted for 63.2% of cases of ovarian cancer, showing a deviation from a previous study done in this centre in which young premenopausal women accounted for 79.5% of cases of ovarian cancer. The finding is however consistent with findings from other parts of the world where the majority of women with ovarian cancer are post-menopausal [17].

The most common clinical presentations were abdominal swelling (94.7%) and abdominal pains (68.7%). Majority of patients with sex-cord tumour (80%) presented with vaginal bleeding. These findings were consistent with those documented in other studies [15].

Globally, it has been shown that about 75% of patients with ovarian cancer present with advanced disease.² This was consistent with the findings in this study. The majority of the patients (77.7%) presented with advanced disease with stage III and IV constituting 44.4% and 33.3% respectively. This was slightly higher than the universal value but lower than the value (80%) reported in a previous study in this centre [14]. Late presentation of patients with ovarian cancer could be due to misdiagnosis because of non-specific gastrointestinal symptoms, initial use of non-orthodox therapies, high level of illiteracy, and low socio-economic status as evidenced by low wealth quintiles of women in northern Nigeria. Less than 10% of patients have some form of health insurance. Late presentation poses a huge challenge in the management of the disease and is associated with poor treatment outcomes [2,6].

Epithelial ovarian cancer was the commonest histological type of ovarian cancer accounting for 81.8% of cases, followed by sex cord tumour (15.2%). Serous adenocarcinoma was the most common histological type, constituting approximately 70% of total ovarian cancer cases managed in our facility. This is higher than the 55.9% variant reported in Kano as the most common histological subtype [16]. Dysgerminoma and immature teratoma were the only germ cell cancers seen and granulosa cell tumour was the only sex cord tumours during the study period. A recent large multicenter study has revealed an increase in the

diagnosis of non-serious histology from Nigeria [20]. Whether this is because non-serous tumours have a better prognosis and are operated more.

Thirty-five patients (92.1%) had surgery. Twenty-six patients (74.28.1%) had primary debulking surgery while 7 patients (20%) had delayed debulking surgery and 2 patients (5.72%) had inoperable tumours respectively. Those with inoperable an tumour had a biopsy taken for histology. This was not consistent with findings in Abuja where the majority (32) 55.2% of the patients had cytoreductive surgery for ovarian cancers [15].

Sixty-three percent (63%) of patients had chemotherapy. Seven patients (33.3%) had neoadjuvant chemotherapy while 20 patients (83.3%) had adjuvant chemotherapy. Those who didn't have chemotherapy are mainly due to financial toxicity or poor performance status. This was higher than reports in Kano where only 48.3% of patients had chemotherapy treatment following cytoreductive surgery but lower than a study in Enugu where 84% of patients with ovarian cancer received chemotherapy [16]. The main factors why patients don't get chemotherapy are their low-performance status (ECOG) and the inability to pay for it. Clinical oncologists give chemotherapy and as a rule, patients with ECOG 3 and below do not get chemotherapy. The most common agents used in the treatment of ovarian cancer were Platinum-based agents (Cisplatin/ Carboplatin) and Taxanes (Paclitaxel /Docetaxel). This was consistent with reports from other studies [2,16,21]. Bevacizumab was the only form of targeted agent used. Only 10% had both chemotherapy and targeted therapy. This could be due to the high cost of targeted therapy.

This study revealed that majority of patients 28/33 (73.7%) were lost to follow up and 2 patients (5.3%) died more than a year after the first form of treatment. A high rate of default among patients undergoing treatment for ovarian cancer has been reported in sub-Saharan Africa and other developing nations. The default rate in this study was higher than those in Sudan (40%) and Abuja (55.2%) but was lower than the default rate of 81% in Enugu [2,15,21]. The high default rate may be due to the poor socioeconomic status of the patients as most patients were unemployed or low-income earners and could hardly afford the cost of investigation, surgical, chemotherapeutic treatment, and targeted therapy. Chemotherapeutic agents were not covered by the National Health Insurance Authority during most of the period under review. The scheme was extended to cover chemotherapy drugs in late 2019. Hence, up to this time, patients paid for every care they received. Better health insurance coverage, less out-of-pocket payment, patient education, availability, accessibility, and affordability of care can reduce loss to follow-up. The confirmed mortality rate from ovarian cancer from this study was lower than 16% reported in Abuja and 70% in Enugu [2,15] even though some of the loss to follow-up could be due to mortality. The documented challenges to ovarian cancer management from our centre [8] are equally reflected in the findings from this study such as poor record keeping, low uptake of immunohistochemistry, lack of genetic testing, et cetera.

Strengths and Limitations of the study: The small sample size of the study, selection, information bias, confounding variables, lack of generalizability of the study, and limited statistical power are limitations identified. The strengths include the provision of insights into the current management of ovarian cancer patients and the need for more research.

Conclusion

The management of ovarian cancer in our environment remains challenging. Ovarian cancer patients in ABUTH were relatively younger, unemployed, multiparous, symptomatic, and presented very late. Some standard-of-care practices like genetic testing were omitted in their management. Quite worrisome is a loss to follow up in over two-thirds of patients

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