

Original Article

Epidemiology and clinicopathological pattern of endometrial carcinoma in Lagos tertiary Hospitals, South-West Nigeria.

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ABSTRACT

Background: Endometrial cancer has become a global health challenge because of its rising morbidity. Understanding the epidemiology and clinicopathological review of this disease may not only aid with treatment but also further the development of prevention strategies. **Objectives:** To review the epidemiology and clinicopathological pattern of endometrial cancer in 2 Lagos Tertiary Hospitals between January 1997 to December 2016. **Methodology:** This is a retrospective study conducted at the oncology clinics of Lagos University Teaching Hospital (LUTH) and Lagos State University Teaching Hospital (LASUTH). Patients' sociodemographic variables, disease characteristics and clinical features were retrieved and analyzed using the statistical package for social sciences (SPSS) version 23.0. **Results:** This 20-year review revealed 162 cases. There was an increasing trend in the incidence with the highest number of cases seen in 2016 (26 patients). The age ranges from 31 to 90 years with a mean of 61.0 ± 10.6 years. The most common histology was endometrioid adenocarcinoma with 98(60.5%). Eighty-four (51.9%) patients presented with stage III disease, 46 (28.4%) with stage IV. All the patients presented with bleeding per vaginum, 73(45%) presented with low backache and vaginal discharge seen in 46(28.4%) patients. **Conclusion:** There was an increasing incidence over the years. More than three quarters presented with stage III or IV diseases. This suggests the need for a high index of suspicion for endometrial cancer especially in women with bleeding per vaginum.

Keywords: *Bleeding per vaginum, Endometrial carcinoma, Epidemiology, Late presentation, Nigeria.*

Introduction

Worldwide, endometrial cancer account for 382,069 cases and 89,929 deaths in 2018 making it the second commonest gynecologic cancer and the six commonest cancer in women.¹ In Nigeria, it is the third most common gynaecological cancer following cervical and ovarian cancers.²⁻⁴ Rising incidence in cases of endometrial cancer has been reported in both developed and developing nations which are attributed to increasing population age and increasing body mass index.⁵⁻⁷ The incidence is however higher in developed countries when compared to less developed ones suggesting the influence of environmental factors.⁸ Cancer predominantly affects a post-menopausal woman.⁶

The actual cause of endometrial cancer is unknown though some risk factors have been identified which is related to high circulating levels of bioavailable estrogens and low levels of progesterone.⁸ Some factors

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like nulliparity, early menarche, or late menopause, diabetes mellitus, and hypertension, which invariably lead to excessive estrogen exposure, has been linked with the disease.⁹ The worldwide increase in obesity and decrease in fertility suggest that the incidence of endometrial cancer will continue to rise.⁵ Other recognized risk factors include older age, white race, family history of endometrial cancer or colon cancer, personal history of breast or ovarian cancer and prior radiation therapy for pelvic cancer among others.^{5,7-8} Hormonal contraceptives for at least 1 year, grand multiparity, breastfeeding, smoking, exercise and coffee intake has been documented to have some protective effect against endometrial cancer.⁹

Endometrial carcinoma developed from the lining of the uterus and it is classified in two different categories based on histology: endometrioid, affecting approximately 80% of patients, and non-endometrioid, affecting approximately 20% of patients.⁵ The endometrioid carcinoma is estrogen-responsive and resembles the proliferative phase of the endometrium.⁸ Its more prevalent among women of premenopausal to early menopausal state and has better prognosis.⁹ Non-endometrioid tumours, however, are hormone-independent with known precursor lesions and it is often seen in older postmenopausal women.⁵ Non-endometrioid histology include serous, squamous, mucinous, clear cell, mesonephric, transitional cell, and undifferentiated among others.⁹

Postmenopausal vaginal bleeding is the commonest presenting complaint in patients with endometrial cancer.⁶⁻⁷ Some patients may present with abnormal vaginal discharge, abnormal Papanicolaou smear while screening for cervical cancer or thickened endometrial on routine transvaginal ultrasound.⁸ This however is not a common presentation in Nigeria where the majority of the patients present with advanced disease.¹⁰ Other patterns of presentation especially in advanced settings include urinary or rectal bleeding, constipation, pain, lower extremity lymphedema, abdominal distension due to ascites, and cough and/or hemoptysis.⁸

With the increasing ageing population and adoption of the western lifestyle by Africans, it is expected that more cases will be diagnosed among Africans in the future. The fact that endometrial cancer has a

poor prognosis in black^{8,11} further justify the need to review the disease. Previous studies in this environment have smaller sample sizes. For example, previous studies done in Ibadan⁷ and Lagos⁶ reviewed 50 and 61 cases respectively. This may not give a true picture of the trends and burden of the disease. Hence the need for this study. This 20-year review addressed the epidemiology and clinicopathological pattern of patients with endometrial cancer referred to the oncology clinics of 2 government-owned tertiary hospitals in Lagos, South West, Nigeria.

Materials and methods

This is a retrospective study of patients with endometrial cancer who presented at the Radiotherapy departments of Lagos University Teaching Hospital and Lagos State University Teaching Hospital between January 1997 and December 2016. Patients who had histologically confirmed endometrial cancer and eventually had treatment were included in the study. Patients whose data could not be retrieved from the medical records were excluded. Out of the 173 documented cases of endometrial cancer seen during this period, 162 met the inclusion criteria. Others have no histology report or the case note could not be retrieved.

The data for this research was obtained from the case notes and treatment cards of the patients retrieved from the Medical Records Department using a data extraction form. The data extraction form consists of two sections; Section A consists of questions on socio-demographic characteristics of the patients while Section B consists of questions on disease characteristics as well as the clinical features.

The data collected was entered into a computer and analyzed using the statistical package for social sciences (SPSS) version 23.0. Analyzed data is presented in the form of frequency tables, charts and cross-tabulations. Approval was obtained from the ethical committee of both LUTH and LASUTH.

Results

The review of endometrial carcinoma during the period of this study revealed 162 cases. The review showed increasing frequency per year with the highest number of cases seen in 2016 (26 patients), none was seen in 1997 and 1998. (figure 1)

The age range was 31 to 90 years with a mean of 61.0 ± 10.6 years. The highest number was seen in the age group 61-70 years which account for seventy-six (46.9%), followed by 51-60 years which account for thirty-two (19.8%) and 41-50 years which account for thirty (18.5%). (figure 2)

Table 1 depicted some socio-demographic variables of these patients. One hundred and six (65.4%) patients were married, fifty (30.9%) were widowed and six (3.7%) were single. Seventy-nine (48.8%) patients were civil servants both active and retired, while sixty-three (38.9%) were traders. The majority of the patients were Christians, 126 (77.8%) while 36(22.2%) were Muslims. Eighty-nine (54.9%) were Igbos by tribe while 69 (42.6%) were Yoruba, and 4 (2.5%) were from minority ethnic groups, none was from the Northern part of Nigeria.

Sixty-nine (42.6%) patients had a tertiary level of education while 56 (34.6%) and 7 (4.3%) had secondary and no formal education respectively. Fifty-six (34.6%) of the patient had documented history of alcohol consumption while only 3(1.9%) had a smoking history. Majority of the patient 105 (64.8%) neither smoke nor consume alcohol. Sixteen (9.9%) patients had a positive family history of cancer. Three (1.9%) patients had a previous history of breast cancer and had taken tamoxifen for

2-5 years. Sixty (37%) patients were hypertensive, 33 (20.4%) were diabetic and 10 (6.2%) were obese ($BM \geq 30\text{kg/m}^2$).

Eighty-four (51.9%) patients presented with stage III disease, 46 (28.4%) with stage IV, 14 (8.6%) stage II, only 4 (2.5%) patients with stage I, while 14 (8.6%) of the patients had no records of their staging at presentation as presented in table 2.

The histological findings are presented in table 2. The most common histological types were endometrioid adenocarcinoma with 98 (60.5%); 22 (13.6%) had papillary serous adenocarcinoma; 12 (7.4%) had a malignant mixed mesodermal tumour; 10 (6.2%) had clear cell carcinoma; 8 (4.9%) had leiomyosarcoma and endometrial stromal sarcoma each, while mucinous adenocarcinoma was 2 (1.2%) and 2 (1.2%) patients had no record of histological type in their case file. (table 2)

The most common presenting complaint was bleeding per vaginum (PV). All the patients 162(100%) had bleeding PV, the low backache was seen in 73(45%) patients, abnormal vaginal discharge was seen in 46(28.4%) patients while pressure symptoms on the bladder/rectum were seen in 23(14.2%) patients.

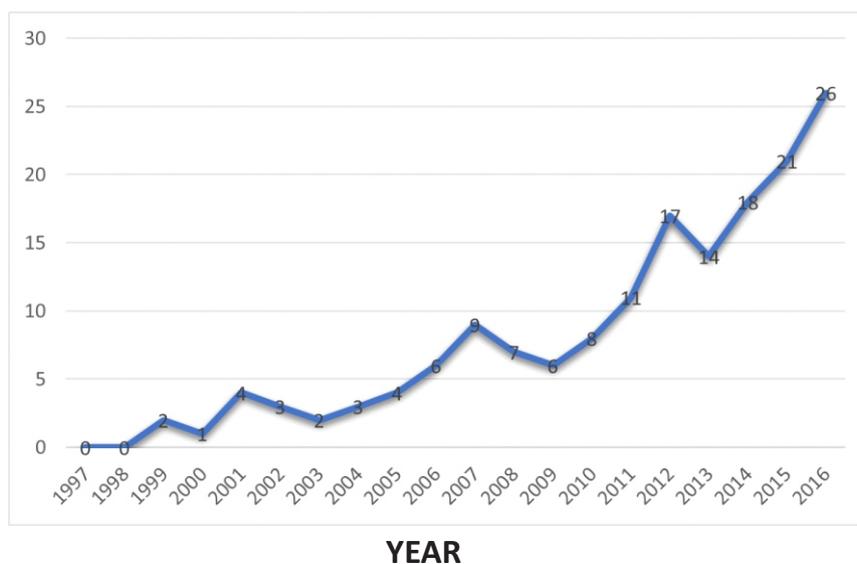


Figure 1. drt66

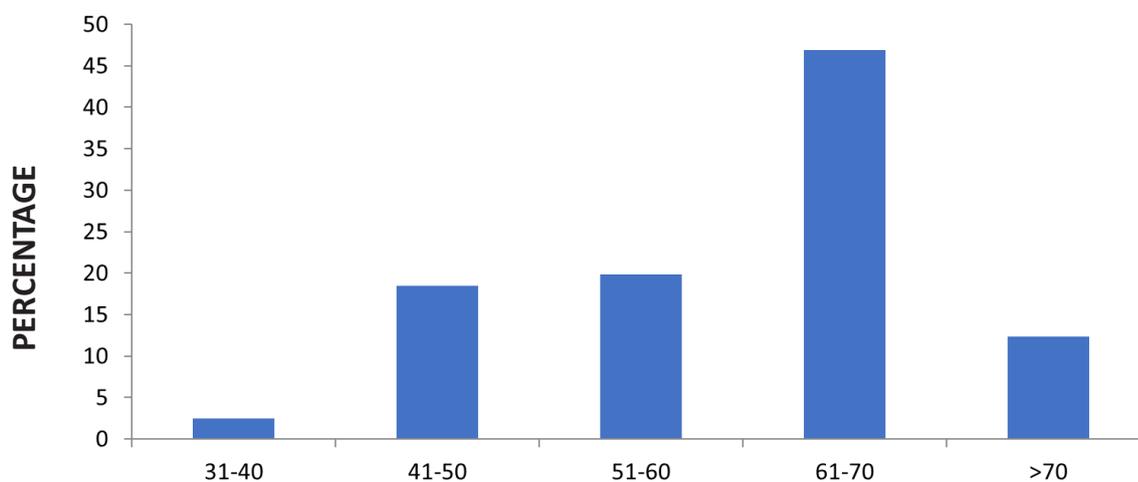


Figure 2: Age group distribution of the 162 cases of endometrial cancer seen in Lagos, SW Nigeria.

Table 1

Variable		Frequency	Percentage (%)
Marital status	Married	106	65.4
	Widow	50	30.9
	Single	6	3.7
Occupation	Civil servant	79	48.8
	Traders	63	38.9
	Others	20	12.3
Education	None	7	4.3
	Secondary	56	34.6
	Tertiary	69	42.6
	Others	30	18.5
Ethnicity	Yoruba	69	42.6
	Igbo	89	54.9
	Other	4	2.5
Religion	Christianity	126	77.8
	Islam	36	22.2
Social habits	None	105	64.8
	Smoking	3	1.9
	Alcohol intake	56	34.6
	Alcohol + smoking	3	1.9
Co-morbidity	Hypertension	60	37.0
	Diabetes	33	20.4
	Obesity (BMI ≥ 30 kg/m ²)	10	6.2
	None	59	36.4

Table 2: Stage of the disease, histology type and presenting complains of patients with endometrial cancer

Variable		Frequency	Percentage
Stage	I	4	2.5
	II	14	8.6
	III	84	51.9
	IV	46	28.4
Histology	Endometrioid adenocarcinoma	98	60.5
	Papillary serous adenocarcinoma	12	7.4
	Malignant mixed mesodermal	12	7.4
	Clear cell carcinoma	10	6.2
	Leiomyosarcoma	8	4.9
	Endometrial stromal sarcoma	8	4.9
	Mucinous adenocarcinoma	2	1.2
	Presenting Complaints	Vaginal bleeding	162
Lower back pain	73	45.1	
Vaginal discharge	46	28.4	
Pressure symptoms on the bladder/rectum	23	14.2	

Discussion

The study showed a rising incidence of endometrial cancer. This may suggest that the incidence of endometrial cancer is increasing over the studied period. This increase can partly be due to increasing population age and increasing body mass index.^{9,12-13}

Apart from this, the low number (and non-cases) reports in some years during the study period may be due to lack of radiotherapy machine, machine breakdown or facility shut down during industrial action of health workers.¹⁴ These factors reduced the number of patients referred from other centres. Patients who do not require radiotherapy would rather receive their treatment (surgery or chemotherapy) at their primary centres since facilities for these treatments are available in most tertiary institutions as opposed to radiotherapy which is available in a few centres.¹⁴

The distribution of patients according to the geographical region indicated that the highest number of patients were from the southern part of the country, with the northern region accounting for none. This may not be a true representation as the patients may have been referred to other radiotherapy centres closer to them. Previous studies done in the northern part of the country showed a similar result.^{2,10}

The majority of patients reviewed were civil servants (both serving and retired) by occupation. This may not be due to occupational hazards they are exposed to at work but may be attributed to their literacy level which has influenced their level of awareness and thus their decision to present for treatment.

The mean age of the patient in this study was 61.0 ± 10.6 years. This is in keeping with the finding of a similar study in northern Nigeria. Endometrial cancer is most commonly diagnosed after menopause, with the peak incidence occurring between the ages of 60 and 70 years.¹³

Ten patients were documented to be obese. Obesity is a strong risk factor for endometrial cancer. Women with a normal body-mass index ($BMI < 30 \text{ kg/m}^2$) have a 3% lifetime risk of endometrial cancer, but for every 5-unit increase in the BMI, the risk of cancer increases by more than 50%.¹² In obesity, androstenedione produced in the ovary and adrenal gland gets converted into estrone, and the testosterone produced by the ovaries gets converted into estradiol in adipose tissues leading to hyperestrogenic state which lead to increased risk of endometrial hyperplasia and cancer.⁹ There is also a

positive correlation between obesity and mortality with endometrial carcinoma.¹⁵

Thirty-three of the patients were diabetic while 60 were hypertensive. Non-insulin-dependent diabetes mellitus and hypertension also increase the risk of endometrial cancer.⁸ Given the strong association between obesity and type 2 diabetes and that many patients with endometrial cancer are obese, the relationship between diabetes and endometrial cancer was often attributed to confounding.¹⁶ However, data are showing that these risk factors could be independent of obesity.¹⁷

In this study, 16 patients had a positive family history of cancer. Endometrial cancer has some genetic predisposition. Inherited genetic predisposition, especially in the setting of hereditary nonpolyposis colorectal cancer (HNPCC), probably accounts for <5% of all endometrial cancer cases.⁸ Cowden syndrome (CS) and Peutz-Jeghers syndrome (PJS) are other genetic diseases that are related to endometrial cancer. Whether the endometrial cancer of these 16 patients with a positive family history of cancer is from genetics, shared lifestyle or coincidence could not be ascertained from this study.

Three patients in this study had a previous personal history of breast cancer. The three patients had a history of use of Tamoxifen for breast cancer. Tamoxifen increases the risk of endometrial cancer in breast cancer survivors.⁸ There has been documented an association between tamoxifen use and endometrial cancer.¹⁸ The mechanism of action of tamoxifen is in competition with that of endogenous estrogen for estrogen receptors because tamoxifen has some weak estrogenic effects especially in postmenopausal women.⁸ Gynecological assessment and symptoms monitoring for endometrial cancer is recommended for breast cancer survivors taking tamoxifen.¹⁹

As regards histology, endometrioid adenocarcinoma was the commonest type found in this study which is in keeping with previous studies which have shown that it is the commonest histology seen in endometrial cancer.⁶ The frequency seen in this study (60.5%) was however lower than the documented frequency in the literature where endometrioid constitute 75-80% of endometrioid

cancer.^{8,12} This did not come as a surprise since this study is among the black population and blacks are more likely than whites to present with non-endometrioid tumours.¹¹ Non-endometrioid carcinoma is known to have a poorer prognosis.⁸ This may suggest the possibility of poorer survival in these patients. A survival study would be needed to establish this.

More than three-quarters of the patients presented with stage 3 or 4 diseases. This is similar to the pattern of presentation of most cancer in this part of the world.²⁰ Late presentation connotes poor prognosis. Some studies have attributed the delay in presentation in this environment to poverty and ignorance on the part of the patients.²¹⁻²² It is however surprising that although a large number of patients reviewed in this study were civil servants, most of them presented late. This may be due to the aggressive nature of the disease in blacks,^{8,11} compounded by the incompetence of some primary physicians in suspecting the disease and effecting early referral and lack of adequate treatment facilities.²¹⁻²² This suggests that more needs to be done by all and sundry to ensure cancer patients present early and receive treatment promptly.

All of the patients present with one or more symptoms at presentation. Patients with early-stage endometrial cancer may present with abnormal Papanicolaou smear or thickened endometrium on routine transvaginal ultrasound scan without any clinical symptoms.⁸ Though routine screening is not recommended for endometrial cancer,²³ screening for cervical cancer can aid early detection of endometrial cancer.²⁴ Having no asymptomatic patients in this study further expose our poor screening culture. It could also be explained by the fact that black patients often present with more aggressive disease.⁶ All the patients in this study had vaginal bleeding as their presenting complaint. This is in keeping with the findings of a similar study in the northern part of the country.¹⁰ Some other studies however reported vaginal bleeding in 75-90% of patients with endometrial cancer.^{6,8}

Other complaints that patients present with include low backache seen in 73(45%) patients, abnormal vaginal discharge in 46 (28.4%) of the cases and pressure symptoms on the bladder/rectum occurred in 23 (14.2%) patients. These symptoms are often seen in advanced diseases.⁸

Conclusion

The study showed an increased incidence of endometrial cancer and abnormal vaginal bleeding is the commonest symptom. Though endometrioid adenocarcinoma was the commonest histology seen in this study, the frequency of non-endometrioid carcinoma is higher than previously reported. Late presentation is the norm as seen in more than three-quarters of the cases presenting in stage 3 or 4 diseases. More needs to be done by all and sundry to create awareness on abnormal uterine bleeding as a possible early warning sign of endometrial cancer.

Limitation

Being a retrospective study, there were missing data that limit the full analysis of some parameters. It studied patients with endometrial cancer referred to the oncology clinics of 2 tertiary hospitals in Lagos. Patients who had surgery but not referred for adjuvant treatment were not captured in the study. This will not give the true picture of the burden of endometrial cancer. Despite these limitations, the study gave a good picture of the disease condition in this environment which can be useful as baseline data for a future prospective study.

Recommendation

More needs to be done by all and sundry to create awareness on abnormal uterine bleeding as a possible early warning sign of endometrial cancer. Women, especially postmenopausal women should be aware of the risks and symptoms of endometrial cancer and report any abnormal uterine bleeding. Government and non-governmental organizations should make cancer treatment available, easily accessible and affordable. There is a need for unified standardized cancer registries in the country to provide reliable data on cancer. This will assist policymakers in developing interventions that can mitigate against the rising trend of the disease.

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