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Endometrial Cancer: Institutional Experience and Limitations of Management

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ABSTRACT

Endometrial malignancy is the commonest genital tract malignancy encountered in postmenopausal women and the third commonest genital tract malignancy in Nigeria

Methods: This was a retrospective analysis of all cases of endometrial malignancy managed at the University of Port Harcourt Teaching Hospital (UPTH) from 1st January 2011 to 31st December 2016. Relevant information were obtained from the case notes and analyzed using SPSS version 22 software package. The prevalence of endometrial cancer was 1.51% of gynaecological admissions and 8.9% of gynaecological cancers. Postmenopausal women accounted for 82.7% and the most common presenting complaint was post-menopausal bleeding. Obesity was the most identified risk factor in 82.7% of cases. All patients had fractional curettage and none had hysteroscopically directed biopsy as the diagnostic method. Sixty-nine percent of cases had stage 1 disease at surgery. All patients that had surgery had only total abdominal hysterectomy and bilateral salpingoophorectomy. No pelvic or para-aortic lymphadenectomy was performed despite Myometrial involvement in 44.8% of cases. None of the surgeries was performed by a certified oncologist. The case fatality rate was 6.9%. Obesity, a modifiable risk factor was the most important risk factor in this study. There is need to urgently train specialist in the art of lymphadenectomy in order to improve outcome

Keywords: Endometrial cancer, Risk factors, clinical presentation, Treatment outcome

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INTRODUCTION

Endometrial cancer is the most common genital tract malignancy in developed countries but its prevalence in the less developed countries like Nigeria has been overshadowed by the high prevalence of cervical malignancy. Endometrial carcinoma is the commonest gynaecological cancer encountered in postmenopausal women and it is the third commonest cancer of the genital tract in Nigeria.[1] The exact cause of endometrial malignancy is not known but epidemiological studies have linked endometrial malignancy to conditions associated with unopposed estrogen stimulation of the endometrium. Such conditions include use of estrogen replacement therapy, obesity, diabetes mellitus, nulliparity, polycystic ovarian syndrome, early menarche and late menopause.[1,2] A familial tendency has been linked with about 10-15% of cases. Phenotypically, women with endometrial cancer tend to be obese, nulliparous, sub-fertile with late onset menopause. Those with these typical features tend to have well differentiated type 1 tumours with good prognosis whereas women with endometrial malignancy who are thin and of Afro-American descent tend to have poorly differentiated tumours with poor prognosis.[3] According to the SEER study, endometrial malignancy accounts for 1.7% of all cancer deaths.[4] Post-menopausal bleeding is the commonest presenting complaint and it is the main reason for early presentation in women with endometrial cancer.[1] Other complaints are related to superimposed infection or metastasis to other organs as seen in advanced disease.

About 70-80% of endometrial carcinomas are of the adenocarcinoma variety which is usually well differentiated and as such is associated with good prognosis.[1,5] Other histological types such as clear cell and papillary serous adenocarcinoma are deeply invasive and of very poor prognosis.[1,5,6] Transvaginal ultrasound (TVS) is widely recommended as the first line investigative tool in patients with endometrial malignancy essentially to measure the thickness of the endometrium.[7] The major challenge with TVS is reaching a consensus on the cut-off for the various clinical scenario relating to age, ethnicity, use of estrogen replacement therapy and in women with diabetes. Fractional curettage is the traditional method of obtaining endometrial tissue for histological analysis. However, because of the increased anaesthetic risk and complications such as uterine perforation and bleeding, endometrial biopsy which can safely be performed as an outpatient procedure without general anaesthesia is currently gaining popularity.[1] A more reliable procedure which is regarded as the gold standard is hysteroscopically directed endometrial biopsy performed under direct vision.[8] This reduces the chances of missing an occult lesion or other pathologies. Garuti et al reported the sensitivity and specificity of hysteroscopy as 84.6% and 100% respectively.[9] Computerized tomography scan and Magnetic resonance imaging though expensive are very sensitive in detecting myometrial involvement and nodal metastasis and thus useful in pre-operative evaluation of

the patient and in planning the extent of surgery which is the main stay of treatment for endometrial cancer.[10] The extent of surgery is dependent on the stage of the disease. In early stage disease total abdominal hysterectomy (TAH), bilateral salpingo-ophorectomy (BSO), infracolic omentectomy with or without pelvic and paraaortic lymphadenectomy is recommended.[1,10-12] However, with myometrial involvement the need for lymphadenectomy is well established.[1,10-13] In advanced disease, surgical debulking accompanied with TAH, BSO and infracolic omentectomy, removal of clinically palpable lymph nodes followed by radiotherapy or chemoradiation is recommended.[14,15] The aim of surgery is to ensure that the primary tumour is removed as this has been shown to improve outcome. In younger patients with stage 1 disease where fertility preservation is required and in recurrent or advanced cases the use of high dose progestogens is a viable option.[16]

The aim of this study was to review and assess the outcome of the management of endometrial malignancy at the University of Port Harcourt Teaching Hospital (UPTH), to identify gaps and to make recommendations to improve outcome. It also highlights the commoner histologic type in this environment.

MATERIALS AND METHOD

This was a retrospective study of all cases of endometrial cancer that were confirmed histologically at the University of Port-Harcourt Teaching Hospital between 1st of January 2009 and 31st of December 2016.

Permission was obtained from the Heads of the department of Gynaecology, Anatomical pathology and medical records for the use of patient records for the conduct of this study. The folder numbers of patients who had endometrial cancer were obtained from the gynaecological ward and theatre records. The folder numbers were then used to trace the case files of the patient from the medical records department and relevant data were extracted from the case files. The data extracted include age, occupation, educational level, marital status, parity, menopausal state, known risk factors, clinical presentation, duration of symptoms, diagnostic method, treatment modality, findings at surgery, stage of the disease, histological type and grade as well as management outcomes. Also histologic slides of participants were collected and reviewed. Also obesity was objectively assed with measuring the Body mass index (BMI).The data was entered and analyzed using the SPSS 21.0 (IBM, Armonk, NY USA). The results obtained were represented in percentages, means and frequency tables.

RESULTS AND DISCUSSION

There were 1,924 gynaecological admissions within the study period and 326 of these admissions were for gynaecological malignancies. Twenty-nine patients had histologically

confirmed endometrial cancer giving a prevalence of 15.1 per 1000 gynaecological admissions and 8.9% of gynaecological malignancies. Ten patients that had fractional curettage were negative for malignancy.

The mean age of patients was 59.32 (±8.26) years with a range of 44 – 78 years. The peak age of the disease was between 50 and 59 years (53.0%). Post-menopausal patients accounted for 82.7%. Most (38.0%) of the patients had secondary level of education. The parity of the study population ranged from 0-3 and nulliparity accounted for 24.1%. Table 1 shows the sociodemographic characteristics of the patients.

Twenty-four (82.7%) patients were obese. Sixteen patients (55.1%) had early menarche while 12 (41.4%) patients had late menopause as shown in table 2. None of the patients was on estrogen replacement therapy and none was on tamoxifen. History of use of combined oral contraceptive pills was noted in 2 (6.9%) patients.

Most frequent presenting symptoms were post-menopausal bleeding (82.7%) and offensive vaginal discharge (55.2%). Only 2 (6.9%) patients reported history of weight loss. Table 3 shows the clinical presentation of the patients with endometrial cancer. The mean duration of symptoms was 9 months ± 4.2 and ranged from 5-24 months. Seventeen (58.6%) patients presented within a year of developing symptoms.

All patients had fractional curettage to obtain tissue for histological diagnosis. None had endometrial biopsy as an office procedure and none had hysteroscopically directed biopsy. Histologically, 24 (82.7%) reports were adenocarcinoma while 3 cases were papillary serous and 2 cases were clear cell tumours. All cases of adenocarcinoma were well differentiated while the clear cell and papillary tumours were poorly differentiated.

Twenty-six (89.7%) patients had surgery while 3 patients with advanced disease were treated with high dose progestogen using Depo-Provera. Surgery performed consisted of total abdominal hysterectomy and bilateral salpingo-ophorectomy. Thirteen (44.8%) of the 29 patients that had surgery had myometrial involvement but no lymphadenectomy was performed. Table 4 shows the stages of endometrial cancer among the study population. Most patients (82.7%) had early stage disease (stage 1 and 2) while (17.3%) had advanced disease (stages 3 and 4). None of the surgeries was performed by certified gynaecological oncologist. Three patients with advanced disease were on high dose progestogens. Most (93.1%) patients were lost to follow up within 6 months of treatment. There were two cases of mortality recorded within the study period giving a case fatality rate of 6.9%. The patients had advanced stage disease and they died within 4 months of diagnosis.

Tables 1: Sociodemographic factors

Indices	Frequency (29)	Percentage (%)
AGE		
40-49	3	10.3
50-59	16	55.2
60-69	8	27.6
70 and above	2	6.9
PARITY		
0	7	24.1
1	12	41.4
2	7	24.1
3	3	10.3
Educational level		
None	1	3.4
Primary	7	24.1
Secondary	11	38.0
Tertiary	10	34.5

Table 2: Risk Factors

Factor	Frequency	Percentage
Obesity	24	82.7
Early menarche	16	55.1
Late menopause	12	41.4
Diabetes mellitus	10	34.5
Nulliparity	**7**	24.1
Diabetes mellitus	**7**	24.1
Previous PCOS	2	6.9

Table 3: Clinical presentation

Presentation	Frequency	Percentage (%)
Postmenopausal bleeding	24	82.8
Offensive vaginal discharge	16	55.2
Abdominal distension	8	27.6
Pre/peri-menopausal bleeding	5	17.2
Weight loss	2	6.9

Table 4: Duration of symptom and stage of disease

Duration (years)	Frequency	Percentage
<_1	17	58.6
1 – 2	7	24.1
>2	5	17.2
Stage		
1	20	69.0
2	4	13.7
3	2	7.0
4	3	10.3

Endometrial malignancy is still an important gynaecological cancer in developing countries but results from the management of this condition is at variance from what is obtainable in developed countries. The prevalence of 15.1 per 1000 gynaecological admissions and 8.9% of gynaecological malignancies is higher than the 25.1 per 100,000 reported among white

American from the SEER study and also higher than the 4.9% reported by Ogunbiyi et al amongst Nigerian women.[4,17] The varying incidence of the various risk factors as well as environmental factors may account for the wide disparity in incidence of endometrial cancer between geographical locations. The mean age in this study was 59.32 years which is slightly lower than the 61 years reported by Howlander et al.[18] Similarly. as noted by Brinton et al endometrial cancer is rare in women of reproductive age with only 10.3% reported in this study in women less than 50 years (Brinton).[19]

Obesity is the single and most important risk factor for endometrial cancer identified in this study accounting for 82.7% of cases. Brinton reported a relative risk of obesity of 2-5 and the role of obesity as an independent risk factor for endometrial cancer is well established.[20] The importance of obesity as a significant risk factor in this study lies in the fact that it is a modifiable risk factor unlike early menarche and late menopause, thus encouraging weight reduction amongst the study population may reduce the prevalence of endometrial cancer as also postulated by Zhang X et al. [21]

In consonance with other studies postmenopausal bleeding was the commonest clinical presentation as observed in 82.8% and it is the most importance reason for early presentation as observed in this study where 58.6% reported within one year of symptoms.[1] Unlike, premalignant conditions of the cervix which are asymptomatic, complex and atypical endometrial hyperplasia which are generally regarded as premalignant conditions of endometrial malignancy usually present with abnormal vaginal bleeding therefore, encouraging early and prompt evaluation of all cases of peri/postmenopausal bleeding may lead to early detection of premalignant conditions and thus reduce the incidence of endometrial cancer.[1,22]

It is worrisome that none of the patients had hysteroscopicallly directed biopsy which is the preferred method of obtaining tissue for histological confirmation with better sensitivity and specificity as reported by Garuti et al and Tinelli et al.[9,23] Ten of the patients that had fractional curettage with negative results may have had an occult lesion missed because fractional curettage as a blind procedure is less reliable than hysteroscopy performed under direct vision. A tertiary hospital that serves as a major referral centre in the South-south geopolitical zone should have a functional hysteroscope in order to offer optimum services, not just for the purpose of evaluating patients with endometrial cancer but also for other gynaecological procedures. There is also need to ensure training of consultants in the use of the hysteroscope which is regarded as the stethoscope of the gynaecologist depicting its availability and importance.

As observed in other reports endometroid adenocarcinoma was the commonest histological type with only few cases of clear cell and serous histological types.[5] It is noteworthy that despite the fact that most of the cases were well differentiated tumours a significant number (44.8%) had evidence of myometrial involvement at the time of surgery. As stated earlier, patients with myometrial involvement and apparently early stage disease require pelvic and paraaortic lymphadenectomy to exclude lymph node metastasis which depicts stage 111C disease. Muallem et al stated patients with deep myometrial infiltration carries a 5-time risk of involvement of pelvic lymph nodes, a 14-time risk of paraaortic lymph node involvement and in patients with poorly differentiated tumours the risk of lymph node involvement was over 50%.[11] Similarly, Fotopoulou also advocated that when pelvic and paraaortic lymphadenectomy is required for high risk patients with early and advanced disease lymphadenectomy should be performed up to the level of the renal vessels to ensure accuracy in the evaluation of all potentially positive nodes.[13] However, none of the patients within the study period had lymphadenectomy. TAH and BSO which was performed for the patients with myometrial involvement in this study without lymphadenectomy was insufficient as patients with lymph node metastasis and high risk cases require additional therapy with chemotherapy[24] or chemoradiation/radiotherapy as suggested from findings of the various Post-Operative Radiation Therapy in Endometrial Carcinoma (PORTEC) study.[14,25] The main reason for this under-treatment of patients with endometrial cancer at the study centre is not due to lack of knowledge but lack of expertise considering the fact that lymphadenectomy is a delicate procedure due to the close relationship between lymph nodes and the major blood vessels of the pelvis and aorta. Therefore, provision of radiotherapy services, specialist training in the art of lymphadenectomy and gynaecological oncology practice in general will improve patient care. The case fatality rate reported in this study of 6.9% may not be a true reflection of mortality from endometrial cancer as most of the patients were lost to follow up within few months of treatment. There is need for care givers to improve on patient's counselling and to emphasis that these patients should be followed up for life.

CONCLUSION

Obesity as a modifiable risk factor is the most important risk factor identified in this study. Though most patients presented in early stage disease a significant proportion had myometrial involvement necessitating lymphadenectomy which were not performed due to lack of expertise. There is need to train specialist in the art of lymphadenectomy, general oncology practice and provision of hysteroscopy and radiotherapy services in order to improve patient care and outcome.

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