ENDOMETRIAL CANCER IN SOKOTO: A 10 - YEAR REVIEW OF EPIDEMIOLOGICAL AND CLINICO-PATHOLOGICAL FEATURES AND OUTCOME

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Abstract

Background: Endometrial cancer is among the most frequently diagnosed malignancy of the female genital tract in the industrialized nation. The disease is 10 times more common in the developed countries than in the developing world, the incidence and the mortality related to the endometrial cancer have increased dramatically in underprivileged regions in the past decades.

Objectives: The objectives were to review the epidemiological and clinico-pathological features and outcome of patients: with endometrial cancer in Sokoto, Nigeria.

Methods: This was a 10- year retrospective study of patients managed for endometrial cancer by the Gynae-Oncology unit of Usmanu Danfodiyo University Teaching Hospital (UDUTH). The case notes of patients were retrieved from the histopathology unit record, Gynae-Oncology ward admissions and discharge books, radio-oncology records and the operating theatre record books. Relevant information were extracted, data were analyzed using Statistical Package for Social Science (SPSS), IBM SPSS statistics Version 21.

Results: A total of 61 patients had a histologically diagnosed cancer of the endometrium, 53 of them had a complete record for analysis. The incidence of endometrial cancer was 9.34%. Most of the patients were Hausa/Fulani with no formal education and from a low socio economic status. The identifiable risk factors in this study were; advanced age 50 years in 94.3%, overweight in 52.8%, low parity in 62.3% and lack of contraception use in 90.6% of the patients. Abnormal vaginal bleeding was the most common presentation and adenocarcinoma the most frequent histological subtype.

Conclusion: Malignant tumours of the endometrium are relatively uncommon in Sokoto afflicting people in the sixth and seventh decades. Late presentation, poverty and aggressive histological type were common risk factors. Education and public enlightenment on the importance of health seeking behaviour and control of the modifiable risk factors will go a long way in reducing the incidence

Key words: Endometrial cancer, Sokoto, advance age, obesity, histological type

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INTRODUCTION

Endometrial cancer occurs globally with wide geographical variation in prevalence and histopathological pattern related to the level of socioeconomic development in the society.¹ In North America, Europe and Australia, it is the most frequently diagnosed malignancy of the female genital tract, representing 6% of all cancer cases and the fourth most common female cancer following breast, lung and colorectal.² Endometrial cancers account for approximately 30 per cent of all gynaecological malignancies, the age-related incidence is 95 per 100 000 women. The life-time risk for developing endometrial cancer is approximately 1 in 90.³ The mean age of diagnosis is 54 years, although cancers can be diagnosed in women throughout their reproductive life. The incidence of endometrial cancer rises sharply in the mid-40s, it should be remembered that 25 per cent of cancers occur before the menopause.³ The incidence of uterine cancer is increasing because of increasing age of the population, use of hormone

replacement therapy (HRT) and obesity.³ However, Asia and Africa have the lowest rates and it is the third most common gynaecologic cancer in most developing countries.^{2,4,5} Endometrial cancer appears most frequently during menopausal period, 75% of cases occur after menopause.⁶

Endometrial cancer is characterized by obvious hyperplasia and anaplasia of the glandular elements, with invasion of underlying stroma, myometrium, and vascular spaces. Although atypical complex hyperplasia is thought to be a precursor lesion, only approximately 25% of patients with endometrial carcinoma have a history of hyperplasia. Type I is almost always preceded by endometrial hyperplasia due to unopposed oestrogen stimulation, while type II is oestrogen independent.⁷ There is a reported rise in incidence of type I cancer, while type II has been relatively stable.⁸ The exact causes of endometrial cancer remain unclear, however there is a clear association with high circulating levels of oestrogen; many of the known risk factors relate to high oestrogen

levels. These include; endometrial hyperplasia, obesity, nulliparity, diabetes mellitus, tamoxifen usage, increasing age, polycystic ovarian syndrome and others.⁷ Approximately 80% of all endometrial cancers are of the endometrioid type (type I) with several variants.⁵ Endometrial adenocarcinomas of the non-endometrioid phenotype (type II) show mucinous, serous, clear cell, squamous, small cell, mixed, or transitional cell differentiation.⁵

In the peri-menopausal period the patient may experience bleeding with an acyclical pattern and in the post-menopausal woman bleeding is often the first sign of an endometrial carcinoma.⁴ Investigation of this abnormal bleeding usually consists of a cytological smear of the cervix to exclude cervical pathology followed by imaging of the endometrial cavity for endometrial thickness and endometrial sampling. In advanced cancer, patients may present with evidence of fistula, bony metastases, altered liver function or respiratory symptoms.³

The mainstay of treatment is surgery, including a total hysterectomy with bilateral salpingo-oophorectomy and staging with pelvic and periaortic lymphadenectomy.¹⁻⁴ Further postoperative therapy depends on the particular histologic characteristics and the extent of the tumor. Primary radiation therapy is used only in patients with medical contraindications for surgery or advanced pelvic disease. Primary chemotherapy is used infrequently and mostly in patients with metastatic disease.⁴ High-dose progesterone therapy, commonly with medroxyprogesterone acetate or megestrol acetate, may be used for patients who are inoperable or in younger patients who elect for fertility preservation.⁴ Adjuvant treatment is dependent on the results of surgical staging and histology. The overall prognosis is considerably better than for the other major gynecologic cancers with 5-year survival rates of 96%, 67%, and 17% for local, regional, and distant disease at diagnosis, respectively.¹¹ The most important prognostic factors for endometrial cancer are stage, histologic type, grade, myometrial invasion, and the presence of lymphovascular

space invasion.¹¹

There is a paucity of information on endometrial cancers in our facility despite the gradually increasing incidence in Nigeria.⁹ The objectives of this study were to review the epidemiological, clinico-pathological features and outcome of patients with endometrial cancer in Sokoto, Nigeria.

MATERIALS AND METHODS

This was a 10- year retrospective study of patients that were managed for endometrial cancer by the Gynae-Oncology unit of Usmanu Danfodiyo University Teaching hospital (UDUTH) from 1st January 2007 to 31st December 2016. The case notes of patients were retrieved from the histopathology unit record, gynae-oncology ward admissions and discharge books, radio-oncology records and the operating theatre record books. Relevant information was extracted from these case notes using a proforma. The information retrieved included, the socio-demographic characteristics including menopausal status, contraceptives use and duration, presence of Diabetes Mellitus and or Hypertension and family history of cancer. Others include the histological type and grade, stage at presentation, method and outcome of treatment. The height and weight were those recorded at presentation. These were used to calculate each patient's BMI and were categorized according to WHO scoring system.

The data was analyzed using Statistical Package for Social Science (SPSS), IBM SPSS statistics Version 21. The results obtained were expressed in descriptive statistics. Simple percentages were used to describe categorical variables. Similarly, quantitative variables were described using measures of central tendency (mean, median) and measures of dispersion (range, standard deviation) as appropriate. Tables and figures were also used to summarize variables.

RESULTS

During the study period (2007-2016), a total of 3933 cancer patients were registered at the

histopathology department of Usmanu Danfodiyo University Teaching Hospital (UDUTH), 2260 (57.5%) were females. About 653(28.9%) of the cases were female genital tract malignancies. Endometrial cancer accounted for 9.34% (61/653 patients).

Fifty eight case notes were retrieved; giving a retrieval rate of 95.1%, and 53 of these case notes had a complete record for analysis. Hence 91.4% (53/58) of the total case notes were analysed.

Table 1 summarises the socio-demography of the patients.

The mean age of women presenting with endometrial cancer in this study was 65.5 ± 1.68 . The youngest at presentation was 45 years and the oldest was 91 years. The mean age at menopause was 52.83 years. Most of the patients were in the 6th and 7th decade of life 20 (37.7%). Fifty patients (94%) were post-menopausal. Those with low parity (Para 0 - 3) accounted for 33 (62.3 %). The majority of the patients were Hausa/Fulani 40(75.5%), Muslims 42(79.2%), and House wives 50 (94.3%) and had no formal education 40 (75.5%).

Table 1: Socio-Demographic Characteristics of Patients with Endometrial Cancer in Sokoto

Characteristics	Frequency (n)	Percentage (%)
Age		
40 – 49	3	5.7
50 – 59	17	32.1
60 – 69	20	37.7
70 and above	13	24.5
Total	53	100
Parity		
0 – 3	33	62.3
4 and above	20	37.7
Total	53	100
Tribe		
Hausa	40	75.5
Yoruba	6	11.3
Igbo	6	11.3
Others	1	1.9
Total	53	100

Religion

Islam	42	79.2
Christianity	10	18.9
Others	1	1.9
Total	53	100

Educational status

None	40	75.5
Primary	3	5.7
Secondary	9	17
Tertiary	1	1.9
Total	53	100

Table II: Risk Factors / Presentation of Patients with Endometrial Cancer in Sokoto

Characteristics	Frequency (n)	Percentage (%)
Family history of cancer		
Yes	4	7.5
None	49	92.5
Total	53	100
History of Hypertension		
Yes	16	30.2
No	37	69.8
Total	53	100
History of Diabetes Mellitus		
Yes	4	7.5
No	49	92.5
Total	53	100
Body Mass Index (BMI)		
Underweight	1	1.9
Normal weight	22	41.5
Over weight	28	52.8
Obese	2	3.8
Total	53	100
Vaginal Bleeding		
Yes	53	100
No	0	0
Total	53	100
Abdominal Swelling		
Yes	12	22.6
No	41	77.4
Total	53	100

Diabetes mellitus and Hypertension occurred in 4(7.5%) and 16(30.2%) respectively. Family history of cancer was found in 4(7.5%). Obesity was observed in 2(3.8%). Twenty eight were

(52.8%) were overweight and 22 (41.5%) women had normal weight. All the patients had history of abnormal vaginal bleeding, however only 12 (22.6%) had an abdominal swelling. About 48 (90.6%) of them had never used any form of contraception.

Table III: Histological Types and Grades Endometrial Cancer in Sokoto

Characteristics	Frequency (n)	Percentage (%)
Histological Type		
Adenomatous	32	60.4
Squamous	7	13.2
Adenosquamous	5	9.4
Mucinous	4	7.5
Others	4	7.5
Total	53	100
Grade		
Well Differentiated	9	17.0
Moderately Differentiated	10	18.9
Poorly Differentiated	23	43.4
Others	7	73.2
Total	53	100

Adenocarcinoma was the commonest histological type 32(60.4%), others were Squamous type 7(13.2%), Adenosquamous 5 (9.4%) and other histological subtypes accounted for 4 (7.5%). The majority of these were poorly differentiated in 23(43.4%), while 10(18.9%) were moderately differentiated and only 9(17%) were well differentiated. The stage at presentation was mostly late stage in 36 (67.6%), only 17 (32.4%) presented early.

Surgery was offered for 18 (34%) of the patients, 6 (11.3%) received chemotherapy, while the rest had combined therapy (either of surgery or chemotherapy with radiation) 54.7%.

FIGURE 2: Outcome of Patients Endometrial Cancer in Sokoto

As at the time of this research, 26 (49.1%) were still on follow up, 10 (18.9%) were lost to follow up, 8(15.1%) had died and 9(17%) signed against medical advice.

DISCUSSION

Female malignancies accounted for 57.5% of all malignancies diagnosed in the histopathology department of UDUTH, 28.9% affected the female genital tract, and 9.34% were primarily from the endometrium. This implies that the incidence of endometrial cancer in our centre was 9.43 %. This value is higher to that found in Ibadan 3.1%¹⁵ and 4.8% in Enugu¹², it is however closer to that found in Kano¹³ 10.6% and Abakaliki 10.1%.¹⁴

Advanced age is an associated risk factor for developing endometrial cancer with a peak incidence among women in their 70s.¹¹ Overall, approximately 80% of diagnosis occurred in post-menopausal women older than 55 years.¹¹ As this is a disease of the elderly, average age at diagnosis is the 60s.¹¹ In this study, the mean age at presentation was 65 years, with a peak at the 6th and 7th decade. The same finding was seen in Ibadan 55-64 years,¹⁵ 54-74 years in Kano¹³, 61-70 in Enugu and 60-69 years in Abakaliki¹⁴. It was however much less in Maiduguri.¹⁸ Over ninety two percent of the patients had no family history of cancer, similar finding was found in Ibadan 92%. Majority of the patients were overweight 52.8% and only 3.8% were obese, 41.5% were of normal weight. Ibadan recorded similar findings with 40% overweight, however more patient in that study were obese 32% and only 24% had a normal weight.¹⁵ Contraception use was not popular among the patient in this study, as 90.6% of them had never used any form of contraception. Though a different study also showed less usage of contraception among its patient 72%,¹⁵ The use of combine oral contraception for at least 1 year confers as much as 30-50% reduced risk of endometrial cancer, and the risk reduction extends to 10-20 years.¹¹

Diabetes Mellitus and Hypertension were seen in 7.5% and 30.2% respectively, but lower values were reported in Ibadan 2.0% and 26%

respectively.¹⁵ As these medical conditions were often found co-existing with endometrial cancer. They were often sequelae of obesity and an environment of chronic excess estrogen.¹¹ The low association of these disease conditions with patients in this study may be as a result of lower frequency of obesity seen.

The most common presentation of endometrial cancer is an abnormal vaginal bleeding.¹¹ Two third of patient will present with post-menopausal bleeding.¹¹ All our patient had history of abnormal vaginal bleeding and 22.6% had abdominal swelling. This is also seen in 96% of patient in Ibadan with vaginal bleeding and 4% with abdominal swelling.¹⁵

The most common histological type of endometrial cancer is endometrioid adenocarcinoma, accounting for 75% of all cases.¹¹ This is also in keeping with this study where 60.4% are of the adenocarcinoma type, similar to 67.4% seen in Maiduguri.¹⁸ Though of lower percentages in others studies, it is however the most frequent histological type in Kano 46%¹³ and 36% in Ibadan¹⁵. Majority of these patients presented with poorly differentiated histological pattern 43.4%, similar to those found in Ibadan 56%.¹⁵

Patients with endometrial cancer should undergo total hysterectomy, bilateral salpingectomy and surgical staging using the revised FIGO system.¹¹ This is often the case in advanced countries where three quarter of patients with endometrial cancer present in an early stage of the disease.¹¹ This is not the case in developing countries like ours, as only 32.1% of the patients in this study presented early and had this form of surgery. Majority, 60.4% presented late, with an already advanced disease hence had combination therapy. These combination therapies include surgery and chemotherapy or chemo-radiation. These are mostly as adjunct or palliative.

The outcome of all the patients that were analysed in this study was not favourable. As only 49.1% were still on follow up at the time of the study, 15.1% died during evaluation or treatment, 18.9%

were lost to follow up, while 17% signed against medical advice. The poor outcome may be due to late presentation, lack of access to health care, low socio-economic status, cultural barriers and tumour biological behaviour among other factors.

CONCLUSIONS

In conclusion, endometrial cancers are relatively common in developing countries as demonstrated in this study. Lack of awareness, poor socio-economic status, cultural and religious barrier has made presentation for care to be delayed. This is further complicated by the poor differentiated histological subtypes and unavailability of diagnostic and therapeutic machines. These and many other compounding factors have made the morbidity and mortality high.

RECOMMENDATIONS

It is recommended here that creation of more expanded, concise and easily comprehensible awareness campaign on endometrial cancer should be embarked upon. This can be achieved through the media, organized medical outreaches and very importantly utilizing the powers of religious clerics and community leaders. Women identified as high risk should be screened periodically (annually NICE guide line).¹¹ Communities, NGO, Philanthropist and Government should improve access to health, provide health insurance and provide diagnostic and therapeutic gadgets like magnetic resonance, computer tomographic scan and radiotherapy machines in all tertiary health centres.

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