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Endometrial histopathological pattern in post-menopausal women with bleeding in Kano, northwest Nigeria

Enemona Sunday Achanya,[1] Abdullahi Abba Habib,[2] Olayinka Taiwo Hassan,[1] Agbogo Onyilo Emmanuel,[1] Ifesinachi Omeje,[3] Usman Aliyu Umar,[3] Muhammed Ibrahim Imam,[3] Ibrahim Adamu Yakasai[3]

[1]Department of Obstetrics and Gynaecology, Federal University of Health Sciences/Federal University of Health Sciences Teaching Hospital, Azare; [2]Department of Obstetrics and Gynaecology, Federal University Dutse/Rasheed Shekoni Federal University Teaching Hospital, Dutse; [3]Department of Obstetrics and Gynaecology, Bayero University/ Aminu Kano Teaching Hospital, Kano, Nigeria

Abstract

Post-Menopausal Bleeding (PMB), as one of the common presentations of endometrial pathology, requires prompt and efficient evaluation to exclude or diagnose malignancy. Endometrial sampling is one of the initial screening tests for evaluating endometrial pathology in these women in order to determine those that will require further evaluation, hence early diagnosis and treatment.
The aim of this study was to determine the histopathological pattern of endometrial sample among women presenting with post-menopausal bleeding in Kano. It was a multicenter cross-sectional study of women with PMB who presented at the gynaecological emergency and clinics of Aminu Kano Teaching Hospital (AKTH), Muhammadu Abdullahi Wase Specialist Hospital (MAWSH) and Murtala Muhammad Specialist Hospital (MMSH) from January, 2018, to June, 2019. The patients were selected using convenient sampling technique after obtaining ethical clearance. Clinical histories were obtained, clinical examination carried out. Endometrial sample was obtained by suction curettage and subjected to histopathologic diagnosis. Forty-five women with PMB were evaluated in our study. The mean age of the patients was 58.2±6.0 years and mean parity was 4.4±1.9. The mean age at menopause was 51.3±1.4 years while the mean duration from menopause to symptom of bleeding per vaginam was 6.9±4.9 years. In 19 (42.2%) of patients, endometrial hyperplasia was found out of which 10 (52.6%) were simple hyperplasia and 9 (47.4%) atypical hyperplasia. Endometrial cancer was found in 12 (26.7%) while 14 (31.1%) had normal histology. Endometrial hyperplasia was the most common pathology among women with PMB in Kano.

Key words: transvaginal ultrasound, endometrial thickness, biopsy, post-menopausal bleeding.

Correspondence: Achanya Enemona Sunday, Department of Obstetrics and Gynaecology, Federal University of Health Sciences, Azare, Nigeria.
E-mail: sunday.achanya@fuhsa.edu.ng

Introduction

Abnormal uterine bleeding occurring at any age in a woman's life is distressing and worrisome, but post-menopausal bleeding is of special concern because it is a common clinical indication of the presence of endometrial carcinoma.[1] Post-menopausal Bleeding (PMB) can be defined as abnormal uterine bleeding occurring at least one year after menopause other than the expected bleeding in women taking sequential hormone replacement therapy, and its incidence can be as high as 10% in (Netherland) Europe.[2] Post-menopausal bleeding significantly impacts quality of life, results in loss of time for work, increases risk of surgical intervention including hysterectomy and ultimately impacts negatively on the health care system. It is a common problem representing 5-10% of all gynaecology outpatient attendance[3] and 25% of indications for gynecological surgeries in Jos, Nigeria.[3]

The differential diagnosis of post-menopausal bleeding includes endometrial polyp, endometrial hyperplasia, endometrial carcinoma, cervical cancer and uterine leiomyosarcoma.[3] It is estimated that 10-15% of patients who present with post-menopausal bleeding end up having endometrial cancer.[3]

Endometrial cancers most commonly occur in the sixth and seventh decades of life with less than 5% of cases are diagnosed in women less than 40 years of age. Furthermore, it has been estimated that the risk of a woman developing endometrial cancer is 1.1% and the life-time risk of dying from it is 0.4%.[4] Therefore, early clinical evaluation of post-menopausal bleeding and prompt diagnosis of endometrial cancer will permit timely treatment and good prognosis. Our study aimed to determine common endometrial histopathological pattern in women with PMB in Kano.

Materials and Methods

It was a prospective study of consenting women with post-menopausal bleeding who met the inclusion criteria at the gynaecological emergency and clinic of three tertiary hospitals in Kano Northwest, Nigeria from January, 2018, to June, 2019. Convenient sampling technique was used to select these women with post-menopausal bleeding who met the inclusion and exclusion criteria. For the purpose of the study, post-menopausal bleeding was any vaginal bleeding in a post-menopausal woman whose last menstru-

al period is at least one year (12 months) to time of the study. Cervical lesion was ruled out by pelvic examination and bleeding disorder by clinical history, simply doing bedside clotting time and those found to have deranged results were excluded from the study, asked to do clotting profile and linked with their managing consultants. The total sample size was 45.

Structured questionnaires were administered to these women. The questionnaire contained sociodemographic and clinical information. The information obtained consisted of age, parity, marital, educational status, socioeconomic status, religion, number of months between menopause and time of recruitment, number of weeks of post-menopausal bleeding and the time of recruitment, and phone number, Other information included history of hypertension, diabetes mellitus, use of Hormone Replacement Therapy (HRT) or Anti-Retroviral Therapy (ART), tamoxifen, personal and family history of breast or other pelvic cancers, patient height, weight and Body Mass Index (BMI).

The Karman's syringe was assembled and charged. The patient was asked to empty her urinary bladder and then placed in lithotomy position cleaned and draped under a good light source. Bimanual examination was performed to determine the uterine size and position. Sterile disposable Cuscos speculum was inserted and the cervix displayed. The cervix was then cleaned with providone iodine. The anterior cervical lip was held with vulsellum forceps and traction. Size 4 Karman's cannula was inserted through the *os* into the uterine cavity using a non-touch technique, and slowly advanced until the fundus was felt. It was then withdrawn backward 1 cm and the charged Karman's syringe was then attached to the cannula. The valve on the syringe was released, to transfer the vacuum through the cannula into the uterine cavity. A 180° twisting motion was used as the cannula was moved between the uterine fundus and the internal *os* while making sure that at least 4 up and down excursions were made to allow adequate tissue to be taken by the cannula. The valve was then locked and the syringe disconnected from the cannula, followed by removal of the cannula. The content of the cannula was poured on sterile gauze to soak away the blood, after which blood clots were removed and the tissue sample was then placed in a labeled bottle containing 10% formalin. The vulsellum was then removed and the cervix examined for bleeding. The speculum was then removed and the patient cleaned. The patient was then briefed on the findings and given a two-weeks appointment to the gynaecology clinic. The sample was then taken to the histopathology laboratory for slide preparation and analysis by the pathologist. The sample was allowed to stand for minimum of 6-12 hours to allow for sufficient tissue fixation.

The formalin-containing tissue was then transferred into a centrifuging test-tube containing density reagent (BD diagnostic) to remove blood clots and mucus after a two-stage centrifugation at 1000 rpm for 2 minutes 15 seconds and then 2000 rpm for 10 minutes 15 seconds (Rotina 465; Hettich Corporation, Westphalia, Germany). The tissue was then placed in a cassette, loaded into a tissue processor for waxing and passed through a series of a dehydrating and a cleaning solvent, ethanol and xylen respectively for about 5-10 minutes each and rinsed with water resulting in a formalin-fixed paraffin-embedded tissue block.

Tissue from the block was then sectioned thinly to 0.4-0.5 um size using a microtome, placed a glass slide, then stained with hematoxylin and eosin (H & E) and covered with a cover slip for examination under the microscope by the consultant pathologist. The slides were examined with both low (x10) and high (x40, x60) power magnifications and the diagnosis recorded.

Data were analyzed using the Statistical Package for Social Sciences, (SPSS) version 20.0 (IBM Corp., Armonk, USA). Measured variables were expressed in descriptive statistics; numeric variables were summarized using range, mean and standard deviation while categorical variables were presented in percentages. Categorical variables were compared, and tests of significance done with Chi-square. A p-value less than 0.05 was considered statistically significant.

Ethical considerations

Approval for the study was given by Kano State Ministry of Health (MOH/Off/797/T.I/686). The provision of the Helsinki Declaration for an investigation on humans was considered.

Results

Eighty-four patients with post-menopausal bleeding were seen during the course of the study. Thirty-nine of these patients were excluded: 11 did not consent to participate in the study, 27 had cervical lesions (23 had cervical cancer while 4 had cervical polyp), and one patient who had ahistory of bleeding disorder and prolonged bedside clotting time (even though endometrial pathology could not be excluded, but may also be the reason for the bleeding). A total of 45 patients who met the inclusion criteria were recruited for this study. They all had endometrial biopsy using manual vacuum aspiration system.

The age of the patients ranged between 53-69 years with a mean age of 58.2±6.0 years. Twenty-seven (60%) were aged 50-54 years, 3 (6.7%) were 55-59 years and 15 (33.3%) were aged 60 years and above (Table 1, Figure 1).

The parity of these patients ranged from 1-7 with a mean of 4.4±1.9. Low parity (0-4) constituted 44.4% of the study population and high parity (5-7) constituted 55.6% (Figure 2).

Table 1. Socio-demographic and menstrual characteristics of the patients.

Variable	Frequency	Percentage
Age		
50-54	27	60
55-59	3	6.7
≥60	15	33.3
Parity		
0	8	17.7
1-4	12	26.7
≥5	25	55.6
Age at menarche		
12-13	31	68.9
14-15	14	31.1
Age at menopause		
<50	2	4.4
≥50	43	95.6
Level of education		
Quranic	32	71.1
Primary	8	17.8
Secondary	3	6.7
Tertiary	2	4.4
Socioeconomic status		
Low	36	80
Middle	6	13.3
High	3	6.7

The age at menarche ranged between 12-14 years, with the mean age at menarche being 13.2±0.6 years. Five (11.1%) patients attained menarche at age 12, 26 (57.8%) at age 13, while 14 (31.1%) had it at age 14 (Figure 3).

The age at menopause of these patients ranged between 49-54 years with a mean of 51.3±1.4 years. The menstrual span of the study population ranged between 36-42 years with a mean of 38±1.6 years while the years since menopause (time from menopause to presentation) ranged between 3-16 years with a mean of 6.9±4.9 years.

The majority of the patients (71.1%) had Quranic (informal) education, 17.8% primary education, 6.7% secondary education and 4.4% tertiary education (Figure 4).

Most of the patients were of low socioeconomic class (80%), 13.3% were middle socioeconomic class, while 6.7% were of high socioeconomic class (using the protocol of social classification by Olusanya O, Okpere EE and Ezimokhai M.)[5] (Figure 5).

Table 2 shows the histological spectrum of endometrial pathology of the patients. Twelve patients (26.7%) had endometrial cancer, 19 (42.2%) endometrial hyperplasia while 14 (31.1%) patients had normal histology (proliferative and secretory endometrium). The incidence of endometrial cancer was 26.7% while that of endometrial hyperplasia was 42.2%.

The bivariate analysis of these patients by their risk factors as shown in Table 3 revealed that Body Mass Index (BMI) and diabetes mellitus are risk factors for endometrial pathology (endometrial hyperplasia/cancer).

The logistic regression analysis showed that the significant predictive variable for endometrial pathology was BMI (Table 4).

Discussion

The incidence of endometrial cancer of 26.7% in this study is similar to the findings in studies conducted by Sharma J. *et al*. and Van Doorn *et al*. of 21% and 23.8%, respectively.[7,8] However, it is higher than the 11.5% and 19.5% reported by Ferrazzi *et al.* and Jacobs *et al*., respectively.[6,9] The large sample size coupled with the fact that these studies were carried out in developed countries where there are programs and interventions in post-menopausal women to mitigate the major risk factors for endometrial cancer could have accounted for the low incidence. Also, the different population studied could have been responsible for the difference in the incidences. Considering the high incidence of endometrial

Table 2. Endometrial histopathological pattern of patients with post-menopausal bleeding.

Endometrial pattern	Frequency	Percentage
Normal	14	31.11
Secretory endometrium	9	20
Proliferative endometrium	5	11.11
Hyperplasia without atypia	18	40
Hyperplasia with atypia	1	2.22
Cancer	12	26.67
Endometroid	7	15.56
Papillary serous	3	6.67
Clear cell	2	4.44
Total	45	100

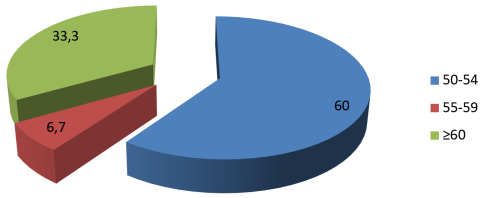

Figure 1. Age group of respondents.

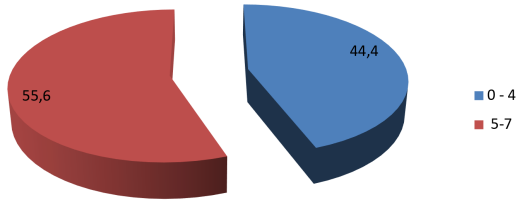

Figure 2. Parity of respondents.

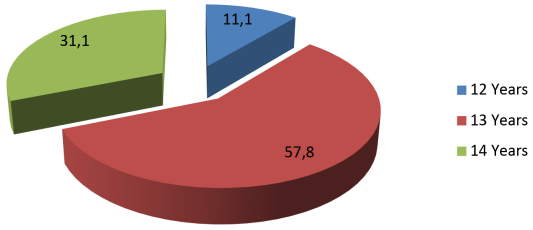

Figure 3. Age at menarche of respondents.

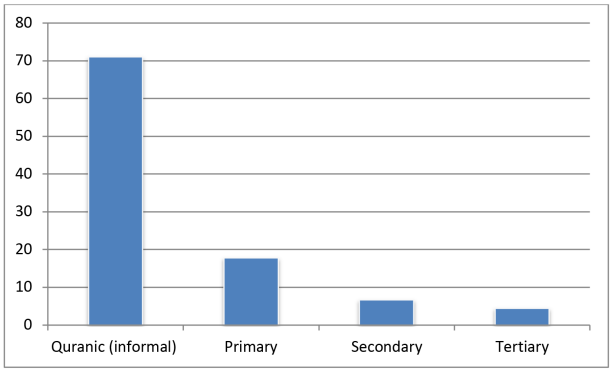

Figure 4. Educational status of respondents.

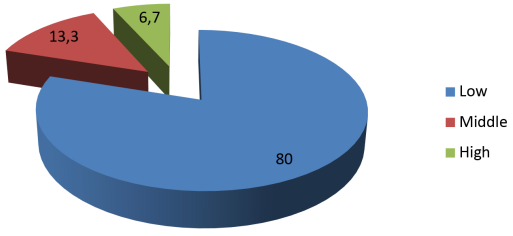

Figure 5. Socioeconomic status of respondents.

cancer in this study, patients with PMB should be promptly referred for transvaginal ultrasound endometrial thickness assessment and those with abnormal results should have endometrial biopsy. This has also been supported by recommendation from international bodies as it has been found to guarantee early diagnosis and treatment.[10,11]

In this study, the socio-demographic characteristics showed that the mean age of post-menopausal women who presented with PMB was 58.2±6.0 years with the range of 53-69 years. This was similar to the studies conducted by Russel *et al*. and Von Doorn *et al*., both of which reported a mean age of 62 years, but lower than the 64 years reported by Van Den Bosch *et al*. and Yakasai *et al.*[12-15] The difference could be due to the variation in average life expectancy and improved healthcare in those countries compared to our study population. The study showed that 44.4% of the patients were of low parity (0-4). This is similar to the finding in the study conducted by Singh *et al.* in which patients with low parity accounted for 40%, but much lower than that reported by Viswanathan and colleagues who found out that 76.7% of their patients were between para 2-3.[16,17] However, low parity being a risk factor for endometrial cancer was not found to be significantly associated in this study.

It was also shown in this study that most of the women belong to the low socio-economic class (80%) as per Odusanya, Okpere and Ezimokhai's social scale.[5] Similar results were also found in study conducted by Sharma *et al*. and Viswanathan *et al*.[7,17] This finding could have been due to the fact that the study was conducted among the populace where culturally the women are full-time

Table 3. Distribution of patients with post-menopausal bleeding with endometrial biopsy by their risk factors.

	Normal n (%)	Hyperplasia/cancer n (%)	Test χ^2	p
Age				
<55	8 (57.1)	19 (61.3)	0.417	0.519
≥55	6 (42.9)	12 (38.7)		
Total	14 (100)	31 (100)		
Parity				
Low (0-4)	4 (28.6)	16 (51.6)	2.704	0.202
High (>4)	10 (71.4)	15 (48.4)		
Total	14 (100)	31 (100)		
Menstrual span				
<40	12 (85.7)	24 (77.4)	0.415	0.520
≥40	2 (14.3)	7 (22.6)		
Total	14 (100)	31 (100)		
Years since menopause				
<8	9 (64.3)	20 (54.5) 0	0.986	
≥8	5 (35.7)	11 (35.5)		
Total	14 (100)	31 (100)		
BMI				
<25	6 (42.9)	1 (3.2)	11.532	0.001
≥25	8 (57.1)	30 (96.8)		
Total	14 (100)	31 (100)		
Hypertension				
Present	8 (57.1)	19 (61.3)	0.069	0.793
Absent	6 (42.9)	12 (38.7)		
Total	14 (100)	31 (100)		
Diabetes mellitus				
Present	1 (7.1)	11 (35.5)	3.961	0.047
Absent	13 (92.9)	20 (54.5)		
Total	14 (100)	31 (100)		
Family history first degree relation				
Present	1 (7.1)	3 (9.7)	0.137	0.711
Absent	13 (92.9)	28 (90.3)		
Total	14 (100)	31 (100)		

BMI, Body Mass Index

Table 4. Determination of predictive variable for endometrial pathology.

Variable	Odd ratio	95% confidence interval Lower level	Upper level	p
BMI	4.035	-3,66	-0.045	0.045
Diabetes	2.121	-0.569	3.857	0.145

BMI, Body Mass Index.

housewives with low levels of education which is a key factor in social stratification in terms of employment and income generation.

In this study, 20% of the patients had menstrual span ≥40 years. This is similar to the finding in the study conducted by Pattersson *et al*.[18] Menstrual span has been identified as one of the risk factors for endometrial cancer. However, it has not been found to be significantly associated in this study.

The mean number of years since menopause (duration of menopause) in this study was 6.93±4.9 which differs from the study by Van Den Bosch et al that reported 13.39±8.0.[14] The difference could have been due to reduced life expectancy in this part of the world. Another reason could be due to the fact that most of the present study population are illiterate and may have recall bias about their date of birth, menarche and age at menopause.

The study revealed that 84.4% of these women had BMI ≥25 kg/m^2 which agreed with the study conducted by Rusell M. *et al*. where 96.7% had BMI ≥25 kg/m^2.[19] However, this was higher than 29% obtained in the study by Sharma *et al*.[7] The difference could be due to variation in nutrition and environment factors as Sharma's study population were mountain dwellers who also engaged in strenuous physical work unlike the population in this study who were mostly housewives. Also BMI ≥25Kg/m^2 was found to be the most significant predictor of endometrial pathology in the study subjects. Therefore, special consideration should be given to overweight/obese patients presenting with PMB (ensuring they have both transvaginal ultrasound scan of ET and endometrial biopsy at a single clinic visit/one stop clinic); also programs and interventions that will help to reduce incidence of obesity in peri and post-menopausal women will invariably reduce incidence of endometrial cancer.

This study also showed that majority of these women who presented with PMB had hypertension (60%) which agreed with the finding by Sharma J. *et al*.[7] It is not surprising as hypertension is a disease of advancing age. However, it was not significant. Furthermore, 26.7% of the study subjects had diabetes which was in agreement with study by Singh *et al*. but low compared to 48% that was found in the study by Wiswanathan M *et al*.[16,21] The difference could have been due to higher prevalence of type 2 diabetes mellitus among Asian population. Despite this difference, there was association between diabetes and histopathology of endometrial biopsy among this study population with PMB with p-value=0.001. However, from the logistic regression analysis this association was not significant (p-value=0.045).

Endometrial hyperplasia accounting for 42.2% was the most common pathology found in these women. This was higher than 12.0% in the study by Saha J. *et al*., Kumari *et al*. but quite lower compared to 59% found in the study by Forae and Aligbe.[22,23] This was followed by secretory and proliferative endometrium 31.1% in this study but lower than 48.6% by Kumari *et al.* Endometrial cancer in this study was 26.67% of which 15.56% were endometroid carcinoma, 6.67% were papillary serous type while 4.44% were of clear cell carcinoma.

Conclusions

Endometrial hyperplasia was the most common pathology and BMI was a significant predictor of endometrial pathology in women with PMB in Kano.

Recommendations

Special consideration should be given to overweight/obese patients presenting with PMB (ensuring they have both transvaginal ultrasound scan of ET and endometrial biopsy at a single clinic visit/one stop clinic); also programs and interventions that will help to reduce incidence of obesity in peri and post-menopausal women will invariably reduce incidence of endometrial cancer.

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Patient's consent for publication: the patients gave their written consent to use their personal data for the publication of this paper and any accompanying images.

Availability of data and materials: all data generated or analyzed during this study are included in this published article.