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Original article

Incidence, Management and Outcome of Perimenopausal and Postmenopausal Bleeding in Tobruk, Libya

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Abnormal uterine bleeding (AUB) is defined as abnormal volume, duration, or frequency of the menstrual period and is a common symptom in women of all ages (premenopausal, perimenopausal, and postmenopausal). Many new diagnostic modalities are available to clinicians to help the assessment of women presenting with abnormalities in their menstrual pattern. This study aimed to evaluate the incidence, etiology, different diagnostic methods, and treatment of perimenopausal and postmenopausal bleeding in order to ensure the health and comfort of the patient. The study was carried out at the Department of Obstetrics and Gynecology, Tobruk Medical Center, during the period from 1/1/2022 to 1/1/2023. There was a significant difference between perimenopausal and post-menopausal regarding parity, systemic disease, hormonal use, family history of maternal problems, BMI, U/S, histopathological findings, and medical treatment. There is a significant amount of heterogeneity associated with the definition of premenopausal, compared with post menopause.

Introduction

Premenopausal and postmenopausal bleeding causes more concern among patients and physicians because of the higher likelihood of organic causes; however, bleeding from the lower genital tract and of non genital origin should be diagnosed and excluded first. Benign causes like polyps, fibroids, and adenomyosis are more common in the premenopausal group. However, the possibility of genital tract malignancy should be ruled out [1]. In fact, 20-25% of endometrial cancer occurs before menopause (2). Post menopausal bleeding occurs in up to 10% of women over 55 years of age [3]. The main concern is to exclude endometrial carcinoma. It is estimated that the prevalence of endometrial is about 10% in women with post menopausal bleeding and vaginal bleeding is the presenting symptom in 90% of women with endometrial cancer (4) transvaginal ultrasoundis used as an initial diagnostic step which may demonstrate endometrial thickness focal masses the probability of endometrial pathology is strongly reduced when the endometrial thickness is <4mm (5) endometrial thickness of >4mm warrant histological evaluation with either endometrial sampling or hysteroscopy directed biopsy(6). Endometrial sampling with both the papilla device and the vabra device is very sensitive technique for the detection of endometrial carcinoma, but the amount of tissue obtained is sometimes insufficient for accurate histologicaldiagnosis. Also, focal lesions such as polyps or submucous fibroids can be missed (7).
Dilatation and curettage (D&C) was traditionally the method of choice for investigating patients with peri- and postmenopausal bleeding. How it fails to treat cancer. Written consent. Full clinical examination will be conducted, and their height will be measured to calculate body mass index. Also, women then will be subjected to transvaginal ultrasound to asses endometrial thickness and presence of any focal lesion D&D and biopsy will be performed to determine the cause of abnormal uterine bleeding. General anaesthesia will be used throughout the procedure with the patient in the lithotomy position once the bleeding has been evaluated. Treatment options can be determined. Treatment can be medical or surgical. all women will be requested to report their menstrual patterns and the degree of satisfaction with the treatment option. All findings and the results of TVS and D&C, and biopsy will be recorded. Correlation of ultrasonography and histopathological findings of the operative specimens of the curetted tissue will be made. Also, the medical treatmentsuccess of failure will be determined. Women who fail to respond to medical treatment should be reevaluated for the possibility of other pathologies as fibroids or adenomyosis. Another disadvantage of (D&C) is that the procedure is performed under general anesthesia in an impatient setting (8) D&C is now considered to be out patient evaluation using endometrial biopsy

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and outpatient hysteroscopy guided biopsy (9) to improve the diagnostic accuracy of peri and postmenopausal bleeding, hysteroscopy seems to be of value as it allows direct visualization, identification of any focal endometrial lesions as well as directed biopsy of suspicious area. In addition, if a lesion is identified, it can be excised hysteroscopically without the need for hysterectomy (10,11). The study aim was to evaluate the incidence, etiology, different diagnostic methods, and thetreatment of perimenopausal and postmenopausal bleeding in order to ensure the health and comfort of the patient.

Methods

This study was carried out at the Department of Obstetrics and Gynecology, Tobruk Medical Center, during the period from 1/1/2022 to 1/1/2023. Women with abnormal uterine bleeding during perimenopause and with any bleeding after menopause will be recruited in the study from the outpatient clinic. A thorough history was taken from all patients, including age, parity, presence of systemic diseases (e.g. diabetes mellitus, hypertension), and current or past hormonal use. Also, family history of endometrial, ovarian.

Statistical analysis was performed by SPSS version 10.0; percentage, mean, and standard deviation will be used for descriptive statistics; for inferential statistics, chi-square and student T test will be used to detect focal lesions in up to 25% of the cases.

Results

Table 1 shows that more than half (56.3 %) of perimenopausal and postmenopausalbleeding patients were below 52 years. More than half (52.1 %) of patients were below 7 regarding parity. Twenty-five (52.1 %) of patients did not have any systemic disease. Thirty-one cases (64.6 %) of patients did not have any history of hormonal use. Forty cases (83.3 %) of patients did not have any family history of malignancy. Twenty-six cases (54.2 %) of patients were overweight. Half (50%) of patients had endometrial thickness less than 6mm. Regarding histopathological findings by D&C, sixteen cases (33.3 %) of patients had endometrial polyps, and 30 cases (62.5 %) of patients had successful medical treatment.

Table 1. Distribution of Perimenopausal and Postmenopausal Bleeding Patients regarding basic demographic and clinical data.

Characteristics	Frequency (Cases)	Percentage
Age group (median)		
> 52	27	56.3 %
≥ 52	21	43.7 %
Parity		
> 7	25	52.1 %
≥ 7	23	47.9 %
Presence of Systemic Diseases		
Hypertension	5	10.4 %
Diabetes Mellitus	5	10.4 %
Hypertension and Diabetes Mellitus	13	27.1 %
No	25	52.1 %
Past Hormonal Use		
Yes	17	35.4 %
No	31	64.6 %
Family history of endometrial, ovarian or breast cancer		
Endometrial Cancer	3	6.3 %
Breast Cancer	5	10.4 %
No	40	83.3 %
Body Mass Index		
Over-weight	26	54.2 %
Obese	22	45.8 %
Transvaginal ultrasound endometrial thickness (mm)		
> 6	24	50 %
≥ 6	24	50 %
Histopathological findings by D&C		

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Proliferative endometrium	5	10.4 %
Endometrial atrophy	6	12.5 %
Endometrial polyp	16	33.3 %
Cervical polyp	5	10.4 %
Endometrial hyperplasia	8	16.7 %
Endometrial carcinoma	8	16.7 %
Medical treatment		
Success	30	62.5 %
Failure	18	37.5 %
Total	**48**	**100 %**

Table 2 shows that a total of 28(58.3%) of patients had bleeding were perimenopausal, while 20 (41.7%) of patients had bleeding were postmenopausal. The larger proportion (96.3%) of patients who were age >52 years had perimenopausal bleeding as compared with those ≥52 years old (9.5%). A higher proportion (84%) of patients had parity >7 had significantly perimenopausal bleeding. A significantly larger proportion (76%) of patients who didn't have any systemic disease had perimenopausal bleeding than those who had hypertension and diabetes mellitus (39.1%). The majority of women didn't use any hormonal treatment before (74.2%) had highly significant perimenopausal bleeding than those who took hormonal treatment (29.4%). There was a statistically significant difference (P< 0.05).
The majority of patients (65%) who didn't have any family history of endometrial, ovarian, or breast cancer had perimenopausal bleeding compared to those who had a positive family history (25%). Patients who were overweight (76.9 %) had significant perimenopausal bleeding compared to obese patients (36.4%). A higher proportion (75%) of patients who had endometrial thickness >6 mm by transvaginal ultrasound had significantly perimenopausal bleeding than had endometrial thickness ≥6 mm (41.7%). A significantly large proportion (65%) of patients with benign endometrial lesions by histopathological examination after D&C had perimenopausal bleeding compared with patients with malignant endometrial lesions (25%). A significantly higher proportion (73.3%) of patients had success medical treatment with perimenopausal bleeding, while 6 cases (33.3%) had failed medical treatment.

Table 10. Association between demographic, clinical, investigations, and treatment characteristics with Perimenopausal and Postmenopausal Bleeding Patients

Characteristics	**Menopausal Bleeding**		**Chi-square test**
	Perimenopausal "28 cases" (58.3 %)	**Postmenopausal "20 cases" (41.7 %)**	
Age group (years)			
> 52 (27 cases)	26 (96.3 %)	1 (3.7 %)	P 0.00001*
≥ 52 (21 cases)	2 (9.5 %)	19 (90.5 %)	
Parity			
> 7 (25 cases)	21 (84 %)	4 (16 %)	P 0.00017*
≥ 7 (23 cases)	7 (30.4 %)	16 (69.6 %)	
Presence of systemic disease			
Yes (23 cases)	9 (39.1 %)	14 (60.9 %)	P 0.00964*
No (25 cases)	19 (76 %)	6 (24 %)	
Past hormonal use			
Yes (17 cases)	5 (29.4 %)	12 (70.6 %)	P 0.00261*
No (31 cases)	23 (74.2 %)	8 (25.8 %)	
Family history of endometrial, ovarian or breast cancer			
Yes (8 cases)	2 (25 %)	6 (75 %)	P 0.03618*
No (40 cases)	26 (65 %)	14 (35 %)	
Body mass index			
Overweight (26 cases)	20 (76.9 %)	6 (23.1 %)	P 0.00451*
Obese (22 cases)	8 (36.4 %)	14 (63.6 %)	
Transvaginal ultrasound endometrial thickness (mm)			
> 6 (24 cases)	18 (75 %)	6 (25 %)	P 0.01917*

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≥ 6 (24 cases)	10 (41.7 %)	14 (58.3 %)	
Histopathological findings by D&C			
Benign lesions (40 cases)	26 (65 %)	14 (35 %)	P 0.03618*
Malignant lesions (8 cases)	2 (25 %)	6 (75 %)	
Medical treatment			
Success (30 cases)	22 (73.3 %)	8 (26.7 %)	P 0.00651*
Failure (18 cases)	6 (33.3 %)	12 (66.7 %)	

Discussion

Abnormal uterine bleeding appears to be one of the most common gynecological problems affecting women's quality of life, especially in thepostmenopausal period. Menopause reduces women's quality of life and affects all aspects of a person's health, including vasomotor, psychosocial, physical, and sexual aspects (12). The main aim of investigating these women was to rule out endometrial cancer and its precursor lesion, and endometrial hyperplasia. The probability of endometrial cancer in women presenting with postmenopausal bleeding is 10%, and approximately 15% for endometrial hyperplasia.

Post menopausal bleeding has been evaluated by clinical examination and pelvic ultrasound in this study. Ultrasound pelvis is an appropriate first-line procedure to identify which woman with post-menopausal bleeding is at higher risk of endometrial cancer. In general, the thicker the endometrium, the higher the probability of important pathology, i.e., endometrial cancer being present. Transvaginal ultrasonography (TVS) is the recommended first-line non-invasive procedure for assessing the endometrium in women with PMB. Measurement of endometrial thickness by TVS, having a cut-off of >4mm, yields 98% sensitivity for the detection of endometrial carcinoma. Hysteroscopy and biopsy (curettage) are the preferred diagnostic techniques to detect benign lesions (13).

For many years, diagnostic curettage has been the method of choice to diagnose endometrial abnormalities. Hysteroscopy combined with histologic examination subsequently became the "gold standard" for such evaluation (11).

Currently, the focus has shifted to TVS as a simple, non-invasive alternative method to hysteroscopy and curettage. The advance of high-resolution transvaginal probes has revolutionized the ability to visualize the endometrium. Transvaginal sonography is an accurate instrument for the evaluation of the endometrium in menstruating as well as postmenopausal women. The use of TVS has reduced risks and burden to patients, as well as costs (14).

In the current cross-sectional study, patients with postmenopausal bleeding were assigned to TVS measurement of endometrial thickness, endometrial sampling, and histopathological examination. In the present study, the age at presentation was >52 years, with a mean age was 56.3%, and the age at menopause was ≥52 years, with a mean age was 43.7% years. El-Mowafi et al. have observed a higher mean age in Egyptian women having postmenopausal bleeding, which was 52.6+2.8 years, range 48-58 years (15). The results are different from the study done by Lidor et al. in 226 PMB cases and revealed that the ages of patients ranged from 40 to 81 years, with a mean of 56 years. In another study, the mean age was reported to be 49.6 years, which differs from this study (16). Whereas a similar study done by Ubeja and Singh in 100 PMB cases, it was observed that the age of presentation was 41–70 years with a mean age of 54.51 years (17) was similar to our study. Comorbidities observed in these women are hypertension and diabetes mellitus, which are similar to a study.

It was found that the mean BMI was 25.55±2.7, ranging from 19 to 33. However, half of the women were overweight. An increase in BMI is usually caused by an increase in body fat. Obesity plays an important role during menopause. The higher the body fat, the more reproductive hormones thus disrupting the physiology of menopause. In this study, a statistically significant positive correlation was found between endometrial thickness at menopause and BMI (r=0.282, P=0.001). Women of all parity represented in the study, which is similar to (33), and the duration of postmenopausal bleeding it ranged from 1 to 10 months, with a mean of 4.08 months.

Endometrial thickness was assessed using transvaginal sonography, with a mean of 10.71 ± 5.374 mm, ranged from 3–25mm. In this study majority of the patients, 37.1% had endometrial thickness in the range of 5 -10mm followed by 11-15mm in 21 %. Studies by Shrestha et al and Sur D & Chakravorty R had majority of patients in the endometrial thickness range of 11-15mm (48.57% and 42.07%) followed by 5-10mm (35.24% and 32.32%). The extreme ranges of thicknesses, ie <5mm and > 20mm, were seen in 17.4% and 4.2% of cases, which was different from to study by Shrestha et al (1.90% and 2.86%).

This study showed that since this particular study deals exclusively with endometrial causes of postmenopausal bleeding. The highest incidence of cystic hyperplasia in 55.7% in the present study

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dealing with postmenopausal bleeding. The studies by Krishnani (2022), had a slightly lower incidence of hyperplasia 28% and 26.4% respectively, than the present study (18). In Egypt study, the ET was measured by TVS in all cases, and an endometrial pathology was found, endometrial hyperplasia (42%) [6]. The higher incidence of endometrial hyperplasia shows that the postmenopausal endometrium in cases of bleeding exhibits an estrogenic effect of varying degree. According to Kinitis (1982), the postmenopausal estrogen presumably originates from androstenedione of ovarian and adrenal origin. Thus, the postmenopausal ovary is seemingly capable of some 'steroidogenesis' (19).

A trophic endometrium was the cause of postmenopausal bleeding in the present study was 18.6%. This was comparable to Aravazhi (2022), Escoffery (2002), 26.7%. Lidor (1986), Kant (2015), and Rotenberg et al. (2022) had a higher percentage in their series with an incidence of 46%,51.5% and 51.66%, respectively. It is not known why some patients tend to bleed from an atrophic endometrium. Anatomical vascular variations or local abnormal haemostatic mechanisms in the uterus have been proposed (20-23). Among the included postmenopausal women, complex hyperplasia in 8.4% and endometrial polyps in 3.6 %. In contrast with the results of other studies, 12.5% of patients had complex hyperplasia, 9% endometrial polypand the frequency of endometrial polyps was found to be 9.2%.(24) In Egypt study the a polyp was found in (32%)

However, endometrial malignancy was high in the postmenopausal women (13.8%). Similar findings were also noted by Shrestha et al, where 12.5% of patients had endometrial malignancy (25), and a higher incidence of malignancy was seen in a postmenopausal group in the study done by Dangal G (24.3%).(26) In Egypt study, endometrial carcinoma was the histopathological report of 8%.

The incidence of endometrial carcinoma in the present study (13.8%), which is less than that noted in other studies by Liu et al, may be because of the difference in the size of the sample and demographic variations of the population studied. However, in this study, only eight of patients had a family history of endometrial cancer (27).

Thus, all patients with PMB need preliminary evaluation by TVS for ET and endometrial sampling to rule out premalignant and malignant pathology as early as possible. Conduction of hysteroscopy to the diagnostic armamentarium of gynecologists has been beneficial in early diagnosis and treatment in women with PMB. Hysteroscopic guide biopsy can help further evaluation and to guide the choice of treatment in women with PMB.

In postmenopausal women the normal length of uterus is usually between 4- 6cm in this study, regard to size of uterus, 30.5% of patients were 6cm, 16.2% patients were 7cm and 47.9% patients were 8cm; while 5.4% patient were 9cm with majority of women were the position of their uterus was retroverted uterus (RVF). In another study mean ET in atrophic endometrium was (4.69±2.19 mm) and malignancy (14.39±4.83 mm), which is similar to the findings of the fifteen cases with ET <5 mm were atrophic endometrium on histopathology (28). In our study for the ET of <5mm, we had 15% cases of Atrophic endometrium, which is higher than the findings observed by Bishnu Prasad Das. With the thickness range of 11-15mm, we observed hyperplasia of 15% and carcinoma of 4.2%. Hyperplasia was reported by Pillai SS (3.4%) and Sur D & Chakravorthy R (4.26%), which is in lower than this study. Carcinoma was seen in 0.95 of % cases of the study done by Shrestha et al, which is again lower than this study (29,30). With the increase in the endometrial thickness from < 5mm to >20 mm, we observed that there is an increase in the cases of hyperplasia and endometrial carcinoma. These findings were similar to other studies. The study by Sattanakho et al concluded that endometrial thickness of 8 mm or less is less likely to be associated with malignant pathology (31).

The current study showed there was a highly statistically significant difference between histopathological patterns according to endometrial thickness —mm‖ with p-value (<0.001). The highest value was found in complex hyperplasia of uterus (15.43±4.01) followed by malignancy (14.39±4.83), as for the endometrial polyp, it was (10.33±1.36), while the lowest value was found in atrophic endometritis (4.69±2.19). It is similar to a study done by Abdel-Rahman. et al., (2021), which found there was a highly statistically significant difference between histopathological pattern and ET —mm‖ with (p<0.001). In their study reported the highest value was found in AC of the uterus (15.67±3.71), followed by endometrial hyperplasia (8.57±2.60), endometrial polyp (7.33±1.03) and the lowest value was found in Atrophic endometritis (2.96±0.85) (6).

The highest mean age was found in cystic hyperplasia (65.09±7.81), and the endometrial carcinoma was found in women their mean 59.83±4.93 between 55 and 76 years of age. In the study by Helena C. Van Doorn et al. (32) in women under 55 years, the probability of having malignancy was 3% vs 18.9% in women over 70 years. In the present study women under 55 years are <1% vs 20% in women>55 years. The difference in the mean ages of similar probability could be because of the difference in sample size and the demographics of patients attending this institute. In the current study, there was a highly

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statistically significant correlation between histopathological pattern according to ET—mmǁ with r=0.449 and p-value (<0.001). This is in concordance with several studies (6).

Conclusion

Lifestyle modification and awareness programs will be beneficial among women in menopausal transition, to reduce the morbidity later in the post-menopausal stage. There is a significant amount of heterogeneity associated with the definition of premenopause, compared with post menopause. We propose three key suggestions/recommendations, which can be distilled from these findings. Firstly, premenopause, which is not currently explicitly stated in STRAW or STRAW + 10, should be transparently operationalized and reported. Secondly, as a minimum requirement, regular menstruation should be defined as the number of menstrual cycles in a period of at least 3 months. Finally, the utility of introducing normative age ranges as a supplementary criterion for defining stages of reproductive ageing should be considered.

Conflict of interest. **Nil**

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