

ORIGINAL PAPERS

The Prevalent Cases of Endometrial Carcinoma in Different Life Periods of Women – Clinical and Histopathological Diagnosis

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Abstract

Abnormal uterine bleeding is a term used to describe any irregular bleeding from the uterus that is not part of a woman's normal menstrual cycle and can happen during different life periods. Abnormal uterine bleeding can have structural etiologies (polyp, adenomyosis, leiomyoma, malignancy) or nonstructural etiologies (coagulopathy, ovulatory dysfunction, and not-classified). The post- and pre-menopausal period requires a detailed investigation to establish the etiology of the bleeding because the chances that the woman has a malignancy are plentiful in this period. The treatment plan is determined based on the underlying cause of the bleeding. The main objective of this paper was to determine the prevalence of endometrial carcinoma in different periods, focusing on the postmenopausal period. This research was a cross-sectional study and included 79 cases of abnormal uterine bleeding in different periods of women's lives. Our study found that abnormal uterine bleeding occurs more frequently during the premenopausal period (59%) and that the causes of irregular bleeding during this period were mainly benign. Our study focused on the postmenopausal period, where we found that 32.9% of irregular uterine bleeding occurs during this period, and the leading causes were malignant pathologies (83.3%), mainly endometrial adenocarcinomas. The average age was 66.7 years. During the study, it was observed that 50% of women with abnormal uterine bleeding due to malignancy were classified as overweight, 25% were obese, and 25% had normal weight. It was confirmed that obesity is a co-factor of malignancy in the postmenopausal period, and the pathophysiological mechanism is well understood now. Our study also found a high number of co-morbidities among women with abnormal uterine bleeding due to malignancy. We came to the conclusion that any abnormal uterine bleeding should be initially investigated in a multidisciplinary manner, an accurate diagnosis should be determined, and then a treatment plan should be established. The treatment strategy should be determined depending on the cause of abnormal bleeding.

Keywords: abnormal uterine bleeding; premenopausal period; postmenopausal period; malignancy.

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INTRODUCTION

Abnormal uterine bleeding (AUB) is a term used to describe any irregular bleeding from the uterus that is not part of a woman's normal menstrual cycle. This can include bleeding that is heavier or lighter, and it can happen during different life periods for a woman, including menarche, the reproductive period, perimenopause, and postmenopausal bleeding.

By PALM-COEIN classification, abnormal uterine bleeding can have structural aetiologies (polyp, adenomyosis, leiomyoma, malignancy, and hyperplasia) or nonstructural etiologies (coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, and not-classified)¹.

Diagnosing abnormal uterine bleeding typically involves a combination of medical history, physical examination, and diagnostic tests, including laboratory and imaging tests, as well as an endometrial biopsy^{2,3}.

The specific tests depend on the patient's symptoms and medical history. The post- and pre-menopausal period requires a detailed investigation to establish the aetiology of the bleeding because in this period the chances that the woman has a malignancy are great⁴. Once a diagnosis has been made, the treatment plan is determined based on the underlying cause of the bleeding.

AIM

The main objective of this paper was to determine the prevalent cases of endometrial carcinoma in different periods, focusing on the postmenopausal period.

MATERIAL AND METHOD

This investigation was a cross-sectional study. The study was conducted in patients with abnormal uterine bleeding from the uterus, of different ages, with an interval of 25-85 years, admitted to the Gynecology Department of a public tertiary service institution.

Sample size

The study included 79 cases of abnormal uterine bleeding, in different periods of women's lives.

Materials and path followed

This study was conducted over a period of 10 months, from December 2021 to September 2022, in a public tertiary service institution using the purposive sam-

pling method. After adequate information about the purpose, methodology and benefits of the study, the patient agreed to participate in the study, and informed consent was obtained from them. They were also assured of confidentiality and autonomy.

The socio-demographic data including age, educational level, and economic status are collected. Identifying risk factors for the patient, such as weight, height, BMI, the presence of comorbidities, smoking history, treatment received and period of diagnosis was likewise analyzed.

Ethical issues

The patient's right to informed consent and voluntary participation was taken into consideration. Anonymity and confidentiality of women's data are ensured. There is no conflict of interest.

RESULTS

Out of a total of 79 cases with irregular uterine bleeding; 56.9% (45 cases) of the women were in the perimenopausal period, 32.9% were in the postmenopausal period, while 10.2% were in the reproductive period (**Figure 1**).

Abnormal uterine bleeding, percentages

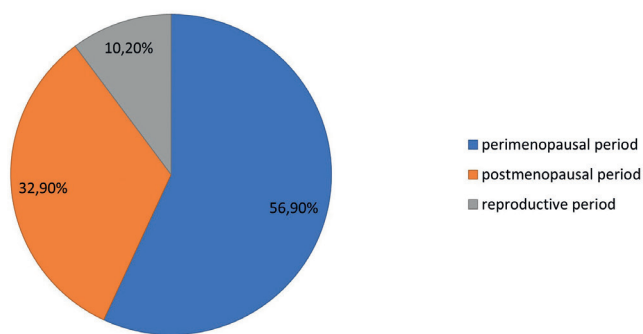


Figure 1. The percentage of abnormal uterine bleeding, according to the periods.

The average age of women with irregular uterine bleeding in the postmenopausal period was 62.03 years, in the perimenopausal period 47.5 years, and in the reproductive period it was 33.3 years. 46.8% of women with irregular uterine bleeding were smokers, while 53.2% were non-smokers (**Table 1**).

Table 1 Socio-demographic data

Socio-demographic data	Postmenopausal bleeding	Perimenopausal bleeding	Reproductive ages uterine bleeding	Total
The average ages of women	62.03 years	47.5 years	33.3 years	
Smoking YES NO	5 cases 21 cases	25 cases 20 cases	7 cases 1 cases	37 cases or 46.8% 42 cases or 53.2% Total 79 cases 100%
Educational level High Secondary Lower	6 cases 15 cases 5 cases	18 cases 20 cases 7 cases	3 cases 4 cases 1 cases	27 cases 34.2% 39 cases 49.4% 13 cases 16.4% Total 79 cases 100%
Economic status High Middle Low	2 cases 13 cases 11 cases	5 cases 19 cases 21 cases	2 cases 3 cases 3 cases	9 cases 11.4% 35 cases 44.3% 35 cases 44.3% Total 79 cases 100%

In 79 cases with irregular uterine bleeding in different lifestyles, exploratory curettage and histopathological analysis were performed, resulting in 67 cases (84.8%) of abnormal uterine bleeding due to benign causes such as endometrial hyperplasia simplex, endometrial polyp, endometrial atrophy, submucous fibroids, etc. Meanwhile, 12 cases (15.2%) of abnormal uterine bleeding were due to malignant causes such as endometrial adenocarcinoma (Figure 2).

Aetiology of bleeding/percentage

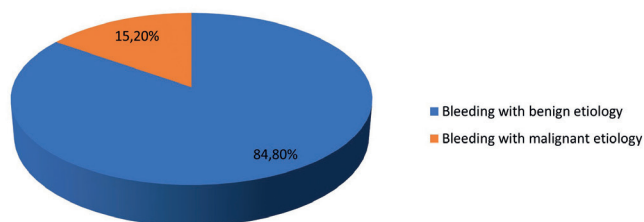


Figure 2. The percentage of abnormal uterine bleeding, according to the etiology.

Out of a total of 12 cases with malignant pathology, 10 cases (83.3%) were women with abnormal uterine bleeding in the postmenopausal period, while 2 cases (16.7%) were women with irregular bleeding in the perimenopausal period. All women with abnormal uterine bleeding in the reproductive period had benign

causes such as endometrial polyp, ovulatory dysfunction, etc. (Figure 3).

Distribution of cases with malignant pathology according to periods

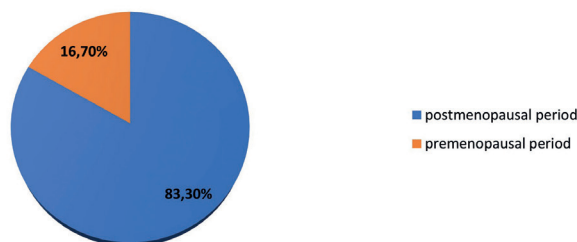


Figure 3. Distribution of cases with malignant pathology according to periods.

The average age of women with malignant pathology was 66.7 years, while the average postmenopausal period was 17.3 years. The average age of menopause onset was 49.4 years. Out of 12 cases with malignant pathology, 6 cases (50%) had Class I obesity with an average BMI of 31.63 kg/m², 3 cases (25%) were overweight with an average BMI of 28.0 kg/m², and 3 cases had normal weight with an average BMI of 23.3 kg/m². All women with abnormal uterine bleeding due to malignant causes had co-morbidities and used daily medication therapy, with the most common co-morbidities being: arterial hypertension, Class I obesity, type II diabetes mellitus, chronic anemia, etc. (Table 2).

Table 2 Distribution in percentages of co-morbidities

Co-morbidities	Cases (percentage)
Arterial Hypertension	12/12 (100%)
Class 1 Obesity	6/12 (50%)
Type 2 diabetes mellitus	5/12 (41.6%)
Anemia chronic disease	4/12 (33.3%)
Overweight	3/12 (25%)

DISCUSSION

Abnormal uterine bleeding can occur at any stage of a woman's life, and depending on when it happens; it can have different causes and treatments. Our study found that abnormal uterine bleeding occurs more frequently during the premenopausal period (56.9%), and the causes of irregular bleeding during this period are mainly benign, similar to the results of a study by Berndt-Johan Procopè⁵. Although less frequent, the most common cause of abnormal bleeding during the postmenopausal period is malignancy. Due to the malignancy-related causes of irregular uterine bleeding that occur in the postmenopausal period of a woman, our study focused on this period, where we found that 32.9% of irregular uterine bleeding occurs during this period, and the main causes were malignant pathologies (83.3%), mainly endometrial adenocarcinoma. With an average age of 66.7 years, the same results were found in a large number of studies on the malignant causes of abnormal uterine bleeding in the postmenopausal period^{6,7,8,9}. The diagnosis of the cause of abnormal uterine bleeding was made in our study using exploratory curettage and histopathological analysis for the postmenopausal, perimenopausal, and reproductive periods, while the adolescence period was excluded from this diagnostic plan, respecting the age-specific characteristics, as was done in many other studies^{10,11,12,13}. In our study, the average age of women entering menopause was 49.4 years, which was found to be similar to the average age of menopause in the world, which is between 47.5 and 51.4 years¹⁴. During the study, it was observed that 50% of women with abnormal uterine bleeding due to malignancy were classified as overweight, 25% were obese, and 25% had normal weight. It was confirmed that obesity is a co-factor of malignancy in the postmenopausal period, and the pathophysiological mechanism is well understood now these findings are also described in many

other studies^{15,16,17}. Additionally, our study also found a high number of co-morbidities among women with abnormal uterine bleeding due to malignancy, such as hypertension, class I hypertension, class I obesity, type II diabetes mellitus, chronic anemia, and overweight, which is also confirmed by Yang X et al. study¹⁸.

CONCLUSION

We came to the conclusion that any abnormal uterine bleeding should be initially investigated in a multidisciplinary manner, the accurate diagnosis should be determined, and then a treatment plan should be established. The treatment strategy should be determined depending on the cause of abnormal bleeding. In any abnormal uterine bleeding in the premenopausal period, especially in the postmenopausal period, it is cost-effective to perform an exploratory curettage and confirm the histopathological diagnosis first, and then determine the treatment strategy. Since the role of metabolic syndrome in endometrial cancer is well known, all women in the pre and postmenopausal periods are recommended to have regular physical activity, reduce stress, maintain a normal weight, and properly manage hypertension, diabetes mellitus, anemia, and hyperlipidemia.

References

1. Munro MG, Critchley HO, Broder MS, Fraser IS, FIGO Working Group on Menstrual Disorders. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in non-gravid women of reproductive age. *International Journal of Gynecology & Obstetrics*. 2011 Apr 1;113(1):3-13.
2. Albers J, Hull SK, Wesley RM. Abnormal uterine bleeding. *American family physician*. 2004 Apr 15;69(8):1915-26.
3. Van Dongen H, De Kroon CD, Jacobi CE, Trimbos JB, Jansen FW. Diagnostic hysteroscopy in abnormal uterine bleeding: a systematic review and meta analysis. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2007 Jun;114(6):664-75.
4. Cooper NA, Barton PM, Breijer M, Caffrey O, Opmeer BC, Timmermans A, Mol BW, Khan KS, Clark TJ. Cost-effectiveness of diagnostic strategies for the management of abnormal uterine bleeding (heavy menstrual bleeding and post-menopausal bleeding): a decision analysis. *Health technology assessment (Winchester, England)*. 2014 Apr 1;18(24):1-201.
5. Procopè BJ. Aetiology of postmenopausal bleeding. *Acta Obstetrica et Gynecologica Scandinavica*. 1971 Jan 1;50(4):311-3.
6. Gredmark T, Kvint S, Havel G, Mattsson LÅ. Histopathological findings in women with postmenopausal bleeding. *BJOG: An International Journal of Obstetrics & Gynaecology*. 1995 Feb;102(2):133-6.

7. Astrup K, Olivarius ND. Frequency of spontaneously occurring postmenopausal bleeding in the general population. *Actaobstetriciaetgynecologica Scandinavica*. 2004 Jan 1;83(2):203-7.
8. Opmeer BC, Van Doorn HC, Heintz AP, Burger CW, Bossuyt PM, Mol BW. Improving the existing diagnostic strategy by accounting for characteristics of the women in the diagnostic work up for postmenopausal bleeding. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2007 Jan;114(1):51-8.
9. Keirse MJ. Aetiology of postmenopausal bleeding. *Postgraduate medical journal*. 1973 May 1;49(571):344-8.
10. Sung S, Abramovitz A. Postmenopausal bleeding. In *StatPearls [Internet]*. 2022 May 1. StatPearls Publishing.
11. Wouk N, Helton M. Abnormal uterine bleeding in premenopausal women. *American family physician*. 2019 Apr 1;99(7):435-43.
12. Kaunitz AM. Abnormal uterine bleeding in reproductive-age women. *Jama*. 2019 Jun 4;321(21):2126-7.
13. Hernandez A, Dietrich JE. Abnormal uterine bleeding in the adolescent. *Obstetrics & Gynecology*. 2020 Mar 1;135(3):615-21.
14. Sharman Moser S, Chodick G, Bar-On S, Shalev V. Healthcare utilization and prevalence of symptoms in women with menopause: a real-world analysis. *International Journal of Women's Health*. 2020 Jun 3:445-54.
15. MacKintosh ML, Derbyshire AE, McVey RJ, Bolton J, Nickkho Amiry M, Higgins CL, Kamieniorz M, Pemberton PW, Kirmani BH, Ahmed B, Syed AA. The impact of obesity and bariatric surgery on circulating and tissue biomarkers of endometrial cancer risk. *International journal of cancer*. 2019 Feb 1;144(3):641-50.
16. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. *Obesity Reviews*. 2021 Dec;22(12):e13337.
17. Smrz SA, Calo C, Fisher JL, Salani R. An ecological evaluation of the increasing incidence of endometrial cancer and the obesity epidemic. *American Journal of Obstetrics and Gynecology*. 2021 May 1;224(5):506-e1.
18. Yang X, Wang J. The role of metabolic syndrome in endometrial cancer: a review. *Frontiers in oncology*. 2019 Aug 8;9:744.