

Silent Threats Unveiled: Navigating the Landscape Endometrial Cancer in Women Over 50 - A Comprehensive Analysis of Post-Menopausal Bleeding as a Crucial Diagnostic Indicator

Huma Saleem¹, Rabia Sharif², Saba Iqbal³, Uzma Manzoor⁴, Nosheen Maqsood⁵, Rabia Afzal⁶

¹ Senior Registrar, Department of Gynecology & Obstetrics, Allied Hospital, Faisalabad Pakistan
Manuscript writing and data collection

² Senior Registrar, Department of Gynecology & Obstetrics, Allied Hospital, Faisalabad Pakistan
Discussion writing

³ Senior Registrar, Department of Gynecology & Obstetrics, Allied Hospital, Faisalabad Pakistan
Data collection

⁴ Senior Registrar, Department of Gynecology & Obstetrics, Allied Hospital, Faisalabad Pakistan
Data collection

⁵ Senior Registrar, Department of Gynecology & Obstetrics, Allied Hospital, Faisalabad Pakistan
Data collection

⁶ Senior Registrar, Department of Gynecology & Obstetrics, Allied Hospital, Faisalabad Pakistan
Data collection

CORRESPONDING AUTHOR

Dr. Rabia Sharif

Senior Registrar, Department of Gynecology & Obstetrics, Allied Hospital, Faisalabad Pakistan
Email: rabiasharif104@gmail.com

Submitted for Publication: 23-01-2024

Accepted for Publication 11-03-2024

How to Cite: Saleem H, Sharif R, Iqbal S, Manzoor U, Maqsood N, Afzal R. Silent Threats Unveiled: Navigating the Landscape Endometrial Cancer in Women Over 50 - A Comprehensive Analysis of Post-Menopausal Bleeding as a Crucial Diagnostic Indicator. *APMC* 2024;18(1):31-35. DOI: 10.29054/APMC/2024.1551

ABSTRACT

Background: Endometrial cancer, with a global incidence of 9 per 100,000 women and a 1% lifetime risk, predominantly affects women aged >50 years and commonly manifests as post-menopausal bleeding (PMB). Timely referral for further investigation is imperative in cases of PMB. **Objective:** This study aimed to determine the frequency of endometrial cancer in females with abnormal uterine bleeding (AUB) and compare this frequency between premenopausal and postmenopausal women presenting with AUB. **Study Design:** Descriptive cross-sectional study. **Settings:** Department of Obstetrics & Gynecology, Independent University Hospital, Faisalabad Pakistan. **Duration:** Six months from December 15, 2022 to June 15, 2023. **Methods:** This study aimed to assess endometrial samples from 415 females over. Participants meeting inclusion criteria were enrolled from the Department's outpatient department, providing informed consent and demographic details. Endometrial sampling using Pipelle or D&C under general anesthesia was performed, and subsequent histopathology assessments in the hospital's pathology laboratory categorized findings into premenopausal and postmenopausal groups for comparative analysis. The study, initiated after ERC approval, spanned. **Results:** Out of 415 cases, 61.45% (n=255) were aged 30-50 years, while 38.55% (n=160) were aged 51-70 years, with a mean age of 48.52±7.02 years. The frequency of endometrial cancer in females with AUB was 6.51% (n=27). Comparing premenopausal (4.46%, n=10) to postmenopausal (8.90%, n=17) females with endometrial cancer, the p value was 0.06. **Conclusion:** While the overall frequency of endometrial cancer in females with AUB requires attention, this study emphasizes that the frequency is significantly lower in premenopausal compared to postmenopausal females presenting with AUB.

Keywords: Abnormal uterine bleeding, Endometrial cancer, Pre-menopausal, Post-menopausal.

INTRODUCTION

Abnormal uterine bleeding (AUB) encompasses menstrual bleeding characterized by abnormal quantity, duration, or schedule.^{1,2} It represents a prevalent gynecologic concern and constitutes one-third of the cases seen in outpatient visits to gynecologists.³ AUB can arise from a diverse range of causes, including both local and systemic diseases, as well as medication-related factors.⁴ The term highlights the clinical importance of addressing irregularities in menstrual

bleeding, given its high frequency and association with various underlying health conditions. As a common complaint, understanding and effectively managing AUB are critical for gynecologists in providing comprehensive care to their patients.⁵

The significance of Abnormal Uterine Bleeding (AUB) lies in its profound impact on women's quality of life, productivity, and healthcare utilization.^{6,7} Histopathological examination of endometrial samples is pivotal for AUB diagnosis.^{8,9} Among females aged 18-70

years, normal cyclical endometrium was observed in 40.94% of cases, disordered proliferative endometrium in 13.40%, hyperplasia in 10.92%, and malignancy (carcinoma) in 2.48%.¹⁰ Abnormal perimenopausal or post-menopausal bleeding is linked to endometrial cancer in about 10% of cases, with a notable increase to 23.8% in women over 80 years.^{11,12} Although 20 to 25% of cases will be diagnosed pre-menopausally.¹³ Contrasting findings exist in the literature, with some studies indicating predominantly postmenopausal occurrences of endometrial carcinoma, while others suggest substantial premenopausal cases, ranging from 5% to 30% in women aged 18-40 years.^{14,15,16} The complexity of age-related variations underscores the need for a comprehensive understanding of AUB's age-specific implications, contributing to enhanced clinical management and tailored preventive strategies.

The underlying rationale for this investigation is to methodically examine and compare the incidence of endometrial cancer in premenopausal and postmenopausal females presenting with Abnormal Uterine Bleeding (AUB). Despite the widely held belief that endometrial carcinoma is more prevalent among postmenopausal women,¹⁷ existing literature yields conflicting results.^{10,13,15,16} Notably, there is a notable absence of local evidence regarding the prevalence of this disease within the regional female population, and specific information pertaining to high-risk age groups is lacking. This study seeks to address these gaps by supplying substantiated evidence on the prevalence of endometrial carcinoma in females experiencing AUB, with a specific focus on identifying age groups at elevated risk. The outcomes of this research endeavor are anticipated to enhance our understanding, contributing to the refinement of existing knowledge and aiding in the development of effective surveillance and early screening strategies for the timely detection and intervention in the local female population.

The objective was to determine the frequency of endometrial cancer in females with abnormal uterine bleeding and compare the frequency of endometrial cancer in premenopausal versus postmenopausal females presenting with abnormal uterine bleeding.

METHODS

This descriptive cross-sectional study was carried out at Department of Obstetrics & Gynecology, Independent University Hospital, Faisalabad and Allied Hospital, Faisalabad. The duration of the study was six months from December 15, 2022 to June 15, 2023.

After approval of Ethical Review Committee (ERC No. Eth/248/IUH), a sample size of 415 cases was calculated with 95% confidence level, 1.5% margin of error and

taking expected percentage of endometrial carcinoma i.e. 2.48%¹⁰ in females presenting with AUB.

Non-Probability Purposive Sampling Technique was used.

Abnormal Uterine Bleeding is defined as all or any of the followings menstrual cycle length <21 days or >35 days, duration of bleeding more than 7 days, amount of bleeding >80ml/7days¹⁸ measured by soaked pads on weighing machine, where 1gm=1ml for >6 months.

Endometrial Carcinoma was labeled if abnormal cell shape and size, numerous, small, crowded glands with varying degrees of nuclear atypia, mitotic activity, and stratification on histopathology.¹⁹

Patients of age 30-70 years, presenting with AUB (as per operational definition) both premenopausal and postmenopausal females were included.

Pregnancy (through USG and medial record), females with palpable pelvic masses (on clinical examination), patients with coagulation and medical disorders like liver disease (AST>40IU, ALT>40IU), renal disease (creatinine >1.2mg/dl) and females taking Hormonal replacement therapy (on medical record) were excluded.

A total of 415 females fulfilling the inclusion criteria were enrolled in the study from the OPD of Department of Obstetrics & Gynecology, Independent University Hospital, Faisalabad and Allied Hospital, Faisalabad. Informed consent and demographic profile (name, age, duration of AUB, parity and contact) was obtained. Endometrial sampling was done either in outdoor with Pipelle endometrial sampler or indoor department by D&C under general anesthesia. Samples were sent to the pathology laboratory of the hospital for histopathology. Reports were assessed and findings were noted. Then groups were formed i.e. premenopausal and postmenopausal and frequency of endometrial cancer was compared. All the data was documented using a proforma

Data was entered and analyzed by SPSS version 20. Mean and standard deviation was calculated for the quantitative variables like age and duration of AUB. Frequency and percentage were calculated for all qualitative variables like parity, menstrual groups (premenopausal and post-menopausal) and endometrial carcinoma. Chi square test was used to compare the endometrial carcinoma in both groups. P-value ≤ 0.05 was considered as significant. Effect modifiers like age, duration was controlled by stratification. Post-stratification chi-square test was applied. P-value ≤ 0.05 was significant.

RESULTS

A total of 415 cases fulfilling the inclusion/exclusion criteria were enrolled to determine the frequency of endometrial cancer in females with abnormal uterine bleeding and to compare the frequency of endometrial cancer in premenopausal versus postmenopausal females presenting with abnormal uterine bleeding.

Age distribution of the patients was done, it shows that 61.45%(n=255) were between 30-50 years of age while 38.55%(n=160) were between 51-70 years of age, mean ± sd was calculated as 48.52±7.02 years. (Table No. 1)

Table 1: Age Distribution (n=415)

Age (in years)	No. of patients	%
30-50	255	61.45
51-70	160	38.55
Total	415	100
Mean ± SD	48.52 ± 7.02	

Mean duration of abnormal uterine bleeding was recorded as 7.05 ± 2.09 months. Parity distribution of the patients was done, it shows that 78.07%(n=324) were between 1-3 paras while 21.93%(n=91) had >3 paras, mean ± sd was calculated as 2.55 ± 1.12 paras.

Frequency of endometrial cancer in females with abnormal uterine bleeding was recorded in 6.51%(n=27) while 93.49%(n=388) had no endometrial cancer. (Table No. 2)

Table 2: Frequency of endometrial cancer in females with abnormal uterine bleeding (n=415)

Endometrial cancer	No. of patients	%
Yes	27	6.51
No	388	93.49
Total	415	100

Comparison of frequency of endometrial cancer in premenopausal versus postmenopausal females presenting with abnormal uterine bleeding shows that out of 224 cases 4.46%(n=10) in pre-menopausal women while 8.90%(n=17) out of 191 cases had endometrial cancer, p value was 0.06. (Table No. 3)

Table 3: Comparison of frequency of endometrial cancer in premenopausal vs postmenopausal females presenting with abnormal uterine bleeding (n=415)

Endometrial cancer	Pre-menopausal women (n=224)		Post-menopausal women (n=191)	
	No. of patients	%	No. of patients	%
Yes	10	4.46	17	8.90
No	214	95.54	174	91.10
Total	224	100	191	100

P value= 0.06

Figure 1: Comparison of frequency of endometrial cancer in premenopausal vs postmenopausal females presenting with abnormal uterine bleeding (n=415)

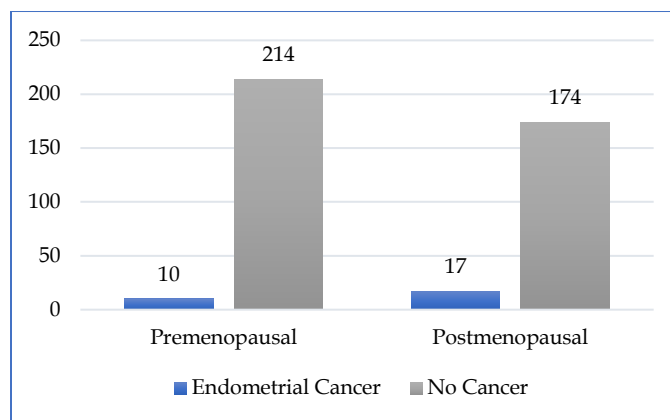


Table 4: Stratification for frequency of endometrial cancer in premenopausal vs postmenopausal females presenting with abnormal uterine bleeding with regards to age

Age (Years)	Group	Endometrial Cancer		P-value
		Yes	No	
30-50 Years	Premenopausal	10	192	0.46
	Postmenopausal	4	49	
51-70 Years	Premenopausal	0	22	0.13
	Postmenopausal	12	125	

Table 5: Stratification for frequency of endometrial cancer in premenopausal vs postmenopausal females presenting with abnormal uterine bleeding with regards to duration of disease

Duration	Group	Endometrial Cancer		P-value
		Yes	No	
1-6 months	Premenopausal	3	93	0.12
	Postmenopausal	8	90	
>6 months	Premenopausal	7	121	0.23
	Postmenopausal	9	84	

DISCUSSION

Endometrial cancer has a worldwide incidence of 9 per 100,000 women, with a 1% lifetime risk. Most cases are in women aged >50 years. Unopposed oestrogen exposure is a significant risk factor, where prolonged exposure causes continual endometrial proliferation and, potentially, endometrial carcinoma. Other factors influencing oestrogen exposure include obesity, polycystic ovarian syndrome (PCOS), anovulation, nulliparity, and type 2 diabetes mellitus and these are also thought to increase the risk of endometrial cancer.²⁰ Postmenopausal bleeding (PMB) is the predominant manifestation of endometrial cancer. Consequently, it is advised to refer women who exhibit PMB for additional investigations. Premenopausal abnormal uterine bleeding is common and estimated to interfere with daily life in more than one-fifth of women. Nevertheless, the existing body of evidence regarding abnormal uterine bleeding in premenopausal women and its association with the risk of endometrial cancer remains inconclusive.

This study was planned to evaluate and compare the frequency of endometrial cancer in premenopausal versus postmenopausal females presenting with AUB.

In this study, out of 415 cases, 61.45% (n=255) were between 30-50 years of age while 38.55% (n=160) were between 51-70 years of age, mean±sd was calculated as 48.52±7.02 years, frequency of endometrial cancer in females with abnormal uterine bleeding was recorded in 6.51% (n=27), comparison of frequency of endometrial cancer in premenopausal versus postmenopausal females presenting with abnormal uterine bleeding shows that out of 224 cases 4.46% (n=10) in pre-menopausal women while 8.90% (n=17) out of 191 cases had endometrial cancer, p value was 0.06.

Previous studies reveal that abnormal perimenopausal or post-menopausal bleeding is associated with endometrial cancer in approximately 10% of cases.^{4,5} While another study reported the probability of endometrial carcinoma in postmenopausal women rises from 1% in women <50 years to 23.8% in women >80 years.⁶ Although 20 to 25% of cases will be diagnosed premenopausally.⁷ While another study reported 5% to 30% of cases occur in premenopausal women (18-40 years).^{8,9}

Contrary to the above, another study showed that endometrial carcinoma was present in 0.65% cases of age 18-40 years, 1.61% in cases of age 41-50 years and 9.4% in cases of age >50 years.³ The findings of our study are in agreement with this study.

A postmenopausal woman may experience a harmless episode of uterine bleeding from a single "rogue ovulation" after more than a year without periods.²¹ Also, it's normal for women who take hormone therapy in

continuous combined doses of estrogen and a progestogen to experience bleeding or spotting during the first several months – and for women on cyclic hormone regimens to sometimes have light monthly bleeding. But apart from that, bleeding in a postmenopausal woman is abnormal and should be investigated right away. About 10% of postmenopausal women who experience bleeding have endometrial cancer – cancer that arises in the uterine lining, or endometrium. In almost all cases, bleeding is the first sign. If it's discovered and treated early, it's highly curable. Fortunately, the most common causes of postmenopausal bleeding are far less serious. Typically, the issue stems from age-related thinning (atrophy) of endometrial or vaginal tissues, a benign condition attributed to decreasing estrogen levels. It requires little or no treatment, although vaginal estrogen can help if, for example, the atrophy causes vaginal bleeding after intercourse. Uterine polyps (noncancerous growths in the endometrial lining) are another possible source of bleeding; it may or may not be necessary to remove them. Bleeding may also signal a condition called endometrial hyperplasia – the overgrowth of cells lining the uterus. It's not cancer but in some cases results in the growth of cells that could turn into cancer (atypical hyperplasia). Endometrial hyperplasia is typically treated with medications.

This study was planned to get the evidence that how much endometrial carcinoma is common in females having problem of AUB and at what ages, it is more common. This is helpful to improve our knowledge and can also help us to plan better surveillance and early screening tools for early detection and deterioration at early stages.

CONCLUSION

We concluded that the frequency of endometrial cancer in females with abnormal uterine bleeding is not very higher but needs attention, however, the frequency of endometrial cancer in premenopausal is significantly lower than postmenopausal females presenting with abnormal uterine bleeding

LIMITATIONS

Size of the sample is small and population covered a single city.

SUGGESTIONS / RECOMMENDATIONS

This study should be considered as pilot study, needs more research by involving different cities.

CONFLICT OF INTEREST / DISCLOSURE

None.

ACKNOWLEDGEMENTS

We acknowledged all patients who contributed in this study and Prof. Dr. Tasnim Tahira for her guidance.

REFERENCES

- Marnach ML, Laughlin-Tommaso SK. Evaluation and Management of Abnormal Uterine Bleeding. *Mayo Clin Proc.* 2019 Feb;94(2):326-335.
- Elmaogullari S, Aycan Z. Abnormal Uterine Bleeding in Adolescents. *J Clin Res Pediatr Endocrinol.* 2018 Jul 31;10(3):191-197.
- Mutakha GS, Mwaliko E, Kirwa P. Clinical bleeding patterns and management techniques of abnormal uterine bleeding at a teaching and referral hospital in Western Kenya. *PLoS One.* 2020 Dec 2;15(12):e0243166.
- MacGregor B, Munro MG, Lumsden MA. Therapeutic options for the management of abnormal uterine bleeding. *Int J Gynaecol Obstet.* 2023 Aug;162 Suppl 2:43-57.
- Davis E, Sparzak PB. Abnormal Uterine Bleeding. 2023 Sep 4. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-.
- Takashima Y, Bruno-Gaston J, Israel J. Management of Abnormal Uterine Bleeding: Later Reproductive Years. In: *Handbook of Gynecology* 2023 Dec 2 (pp. 513-525). Cham: Springer International Publishing.
- Chodankar R, Harpur A, Mahmood T. Heavy menstrual bleeding. *Obstetrics, Gynaecology & Reproductive Medicine.* 2018 Jul 1;28(7):196-202.
- Mehta S, Gupta B. Recent Advances in Endometrial Cancer [Internet]. Springer Nature Singapore; 2020. Available from: <https://books.google.com.pk/books?id=-HyDwAAQBAJ>
- Vijayaraghavan A Sr, Jadhav C, Pradeep B, Bindu H, Kumaran S. A Histopathological Study of Endometrial Biopsy Samples in Abnormal Uterine Bleeding. *Cureus.* 2022 Nov 8;14(11):e31264.
- Asuzu IM, Olaofe OO. Histological Pattern of Endometrial Biopsies in Women with Abnormal Uterine Bleeding in a Hospital in North Central Nigeria. *Int J Reprod Med.* 2018 Nov 1;2018:2765927.
- Ellenson LH, Ronnett BM, Soslow RA, Zaino RJ, Kurman RJ. Endometrial Carcinoma. In: Kurman RJ, Ellenson LH, Ronnett BM, editors. *Blaustein's Pathology of the Female Genital Tract* [Internet]. Boston, MA: Springer US; 2011. p. 394-452. Available from: <https://www.infona.pl/resource/bwmeta1.element.springer-a5e19c76-43e1-348b-ba25-b8d0e106f8c5>
- Clarke MA, Long BJ, Del Mar Morillo A, Arbyn M, Bakkum-Gamez JN, Wentzensen N. Association of Endometrial Cancer Risk With Postmenopausal Bleeding in Women: A Systematic Review and Meta-analysis. *JAMA Intern Med.* 2018 Sep 1;178(9):1210-1222.
- Renaud MC, Le T. No. 291-Epidemiology and Investigations for Suspected Endometrial Cancer. *J Obstet Gynaecol Can.* 2018 Sep;40(9):e703-e711.
- Sreedhar VV, Jyothi C, Rao MN, Sailaja V, Paul MC, Lakshmi GV. Study of Histopathological Pattern of Endometrium in Abnormal Uterine Bleeding—A Study of 150 Cases. *Saudi Journal of Pathology and Microbiology.* 2017 Apr.
- Singh S, Best C, Dunn S, Leyland N, Wolfman WL, Wolfman W, Allaire C, Awadalla A, Heywood M, Lemyre M, Marcoux V. Abnormal uterine bleeding in pre-menopausal women. *Journal of obstetrics and gynaecology Canada.* 2013 May 1;35(5):473-5.
- Son J, Carr C, Yao M, Radeva M, Priyadarshini A, Marquard J, Michener CM, AlHilli M. Endometrial cancer in young women: prognostic factors and treatment outcomes in women aged ≤ 40 years. *International Journal of Gynecologic Cancer.* 2020 May 1;30(5).
- Wu Y, Sun W, Liu H, Zhang D. Age at Menopause and Risk of Developing Endometrial Cancer: A Meta-Analysis. *Biomed Res Int.* 2019 May 29;2019:8584130.
- O'Brien SH. Evaluation and management of heavy menstrual bleeding in adolescents: the role of the hematologist. *Hematology Am Soc Hematol Educ Program.* 2018 Nov 30;2018(1):390-398.
- Mills AM. Endometrial carcinoma. *Gynecologic and Obstetric Pathology, Volume 1.* 2019:455-513.
- Ignatov A, Ortmann O. Endocrine Risk Factors of Endometrial Cancer: Polycystic Ovary Syndrome, Oral Contraceptives, Infertility, Tamoxifen. *Cancers (Basel).* 2020 Jul 2;12(7):1766.
- Kadhim IM. Diagnostic approach to Perimenopausal bleeding by Pipelle or Dilatation and Curettage. *Research Journal of Pharmacy and Technology.* 2021;14(11):5764-8.