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Prospective study of postmenopausal bleeding and its evaluation in a tertiary care center

Dr Srushti R Kanta[1], Dr Ashwini Mallesara[2], Dr Swathi Bhat[3], Dr Smruthi C Raj[4],Dr Prashanth. S[5],Dr Lepakshi BG[6]

[1,2,3,4]Assistant Professor, Department of OBG, Shimoga Institute of Medical Sciences,Shivamogga, Karnataka, India
[5]AssociateProfessor, Department of OBG, Shimoga Institute of Medical Sciences, Shivamogga, Karnataka, India
[6]HOD, Dept of OBG, Shimoga Institute of Medical Sciences,Shivamogga, Karnataka, India

Corresponding author: Dr Smruthi C Raj

Abstract

Objective: The study aims to identify the clinical correlation between the demographic profile and the risk factors involved in the postmenopausalwomen who later develop endometrial cancer.

Methods: This was a prospective study done in the Obstetrics and Gynaecology department. All patients with the endometrial thickness (ET) equal to or >5 mm were subjected to dilatation and curettage (D&C) andhistopathological studieswere performed. Characteristics of the patient were compared with the use of Univariate and multivariate logistic regression analysis

Results A total of 120 women were enrolled. There were 21 cases and 99 control. The mean age at the time of presentation was 51.9 ± 8.1 years. Out of 21 cases, 9 cases were complex endometrium,5 cases were diagnosed with adenocarcinoma, 7 were atypical endometrium. Using multivariate logistic regression analysis,for ET (AOR = 1.66,CI 0.36–7.55, $P < 0.509$, criteria ET≥11 mm), recurrent episode of bleeding (AOR = 15.86, CI 3.85–65.27.91, p< 0.0001), diabetes (AOR = 3.00, CI 0.89-10.09, p< 0.075) Hypertension (AOR= 1.30 CI 0.39- 4.37, p < 0.664). The Area under Curve (AUC) for Receptor Operating Curve (ROC) for the predictive model was 0.88 to detect adenocarcinoma in postmenopausal bleeding.

Conclusion: High suspicion of endometrial cancer should be considered whenever high-risk factors are present and clinical findings also play an important role in predicting the diagnosis.

Keywords: *Endometrial Cancer, endometrial hyperplasia, postmenopausal bleed, adenocarcinoma, atypical hyperplasia.*

Introduction

World Health Organization (WHO) defines menopause as the cessation of menstruation permanently for more than one year, resulting from a loss of ovarian activity (WHO, 1996). In India,the average age of menopause age is 47.5 years. Projected populationin India by 2026 to be 1.4 billion in that thepeoplemore than 60 yeas to be 173 million andthe total predicted menopausal population to be 103 million(1).

Postmenopausal bleeding refers to any uterine bleeding in a menopausal woman, accounting for nearly 5 % of all outpatient visits to a gynaecologist.(2) Atrophy is the most common cause for Postmenopausal bleeding (PMB). Atrophy accounts as a cause for 60%–80% of all cases of PMB, while endometrial hyperplasia and cancer together account for 20% of cases.(3)Approximately 70% of all gynaecological consultations in perimenopausal and postmenopausal women are for PMB.(4) In about 10% of cases, abnormal postmenopausal or perimenopausal bleeding is associated with endometrial carcinoma and should be considered endometrial neoplasia until proven otherwise.(5)

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As a preliminary investigation,Sonographycan be offered to measure the endometrial thickness inpostmenopausal bleeding. If a thin endometrium is found in Sonography, then chances of cancer and hyperplasia are low.No further evaluation or additional testing is required after routine ultrasonography. Endometrial sampling is also used as a first approach for women with postmenopausal bleeding.(6)In Transvaginal ultrasound images, a thin endometrial echo (< 4 mm) has a greater than 99% negative predictive value for endometrial cancer.(7)

Definitive diagnosis requires a histology report, which can be obtained by dilatation and curettage (D&C). As it's a blind technique and may miss some of the polyps;however, it involves admission and the use of general anaesthesia. In the Grimes et al. study, 10% of the endometrial sample were overlookedwhen (D&C) was used as an only procedure.(8)

There are different types of samplers available, such as the Kevorkian curette, Novak, Vabra aspirator. There is no systematic head to head comparisons. In all sampling methods,chances of missing cancer persist as the sample by these devices is obtained by blind procedure,very little as 4% of the cavity is sampled.

Material and methods

Our study was a prospective study done in the Obstetrics and Gynaecology department of tertiary care hospital and medical college, Shivamogga,to evaluate the postmenstrual beading patient.Inthis study, we have included patients all the new referrals patients who came with PMB symptoms. We have excluded all the symptomatic postmenopausal women with vaginal bleedingfrom cervical or vulvar disease.Previously diagnosed cervical cancer, women with bleeding disorders, patients on anticoagulants therapy were also excluded.

Patients with the above satisfying criteria were enrolled in this study; A detaileddemographic profile was collected with the help of performed proforma, history regarding the age, time and duration of presentationsince menopause. Any use of MHT, unscheduled vaginal bleeding with MHT, single/recurrent episodes of vaginal bleeding. Presence of hypertension and diabetes.We have defined recurrent episodes of vaginal bleeding as any bleeding episode lasting≥ 7 days,or there was two or more separate bleeding episode within the past 12 months. All patients were subjected to routine gynaecological check-up where both the pelvic and abdomenexaminations were performed, followed by TVS for uterine volume, ovarian volume, and endometrial thickness.All patients with ET equal to or >5 mm were subjected to dilatation and curettage (D&C) under anaesthesia. Pathologists performed all histopathological studies.

The study was done after the approval of the Institutional Ethics Board and after taking informed consent from women.

Statistical analysis

All the data were summarised using standard descriptive methods.For the frequency and percentage categorical variables and mean, SD or median and range for continuous variables.Chi-square was used to compare between categorical variables. We have used the Student t-test to compare normally distributed continuous variables and categorical variables. In contrast, the nonparametric Mann–Whitney and Kruskal–Wallis tests were used for continuous asymmetric variables. A separate logistic regression model was used to compare case and control for some of the high-risk factors. AOR was calculated with the help of multivariate analysis, the corresponding 95% CI was calculated.A predictive model was done withArea under Curve (AUC) for Receptor Operating Curve (ROC).

Results

A total of 120 women were enrolled who came with a history of Postmenstrual bleed and endometrial thickness measurement more than 5 mm. All the patientswere subjected to D and C. The average age at the time of presentation was 51.9 ± 8.1 years. The mean menopausal age was 46.7 ± 3.25 years and the duration of menopause was 5.25 ± 6.98 years. Allwere multiparous. About22.5% (27/120) of the study participants had diabetes, 33.3% (40/120) were hypertensive, 30%(37/120) has recurrent episodes of vaginal bleeding. In this study, the mean thickness of the endometrial was 12±5.3 6 mm.

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All the samples were subjected to a histological examination. There were 57/120 (47.5%) women with endometrial atrophy,21(17.5%) with proliferative endometrium, 5(4.1%) with EC, 26(21.6%) with endometrial hyperplasia, of which 10(8.3%) cases of simple endometrial hyperplasia, 9 (7.5%) cases of complex hyperplasia with atypia, 7/120(5.8%) cases of atypical hyperplasia.21/120(17.5%) with disordered proliferative endometrium, and 5/120(4.1%) cases of endometrial polyps [Table 2].

There are 21 casesand 99 control. Out of 21 cases, 9 cases are complex endometrium.Five cases are diagnosed with adenocarcinoma, 7 are atypical endometrium.In the control group, out of 99 cases, 21 cases are proliferative endometrium.One case is fibroid with heterogeneous myometrium, 10 cases are of simple hyperplasia, 57 cases are of atrophic endometrium, 10 cases are polyp, 5 cases are of cervical cancer.

We found no significant difference for the age of late menopause, endometrial thickness <25 mm and recurrent menstrual bleeding from the univariant analysis to develop endometrial carcinoma.But there was asignificant difference noticed in hypertension, endometrial thickness >25mm, age of presentation, duration of menopause and mean endometrial thickness.

Table 1 Basic character of women with postmenopausal bleeding

	Median (IQR) or n(%) or mean SD 95% CI with range (whichever applicable for data)
Age at presentation	51.9±8.1
Duration of menopause	5.25±6.9
Age of menopause	46.7±3.25
Diabetes	27(22.5)
Hypertension	40(33.3)
Recurrent episode of bleeding use of HRT	33(27.5)
Endometrial thickness in PMW	12.8±5.3
Use of HRT	0

Data are presented as mean±SD or *n* (%). The mean age of presentation was 51.9±8.1years. The mean menopausal age was 46.7±3.25years and the duration of menopause (YSM) was 5.25±6.9years. All are multiparous with risk factors of diabetes, hypertension, obesity, recurrent episodes of vaginal bleeding with HRT. Mean thickness of endometrial was 12.8±5.3mm, SD: Standard deviation, PMW: Postmenopausal women, HRT: Hormone replacement therapy, IQR: Interquartile range, CI: Confidence interval, YSM: Year Since menopause

Table 2 Histopathology of the endometrium

Histopathology of endometrium	**Case(19)**	**Control (101)**	**Total**
Proliferative endometrium	0(0)	21(20.7)	21
Cervical cancer	0(0)	5(4.9)	5
Complex hyperplasia	9(47.3)	0(0)	9
Fibroid with heterogeneous myometrium	0(0)	1(0.9)	1
Simple hyperplasia	0(0)	10(9.9)	10
Adenocarcinoma	5(26.3)	0(0)	5
Atypical hyperplasia	7(36.8)	0(0)	7
Atrophic endometrium	0(0)	57(56.4)	57
Polyp	0(0)	10(9.9)	10

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Histological examination revealed the most common cause of bleeding in postmenopausal women in this study is endometrial atrophy, followed by other reasons in descending sequence of proliferative endometrium, endometrial cancer, endometrial hyperplasia, disordered proliferative endometrium, endometrial polyps

Table 3Demographic profile of the population

	Case(21)	Control(99)	p
Age in years	60.3(9.3)	50.3(6.8)	0.0001
Age at menopause	48(3.6)	46.4(3.1)	0.03
Duration of menopause	11.7(9.4)	3.8(5.5)	0.0001
Associated with diabetes	12	32	0.032
Associated with hypertension	12	18	0.0002
Late menopause	2	3	0.179
Pt on HRT	0	0	-
Endometrial thickness (mm) <10 10-25 >25	 2 14 5	 31 67 0	 0.04 0.92 0.0001
Frequency of bleeding • Recurrent • single	 4 17	 19 80	 0.995 0.991
Mean endometrial thickness	17.6(7.4)	11.8(4.1)	0.0001

*Univariate comparison. **Strongly Significant,*Moderately significant. Patient characteristics showed significant differences in diabetes, recurrent vaginal bleeding episodes, presence of hypertension, presence of obesity/ overweight, and endometrial thickness. PMC: Past menstrual cycle, HRT: Hormone replacement therapy*

In the multivariate analysis, recurrent bleeding per vagina, the endometrial thickness of more than 10mm, presence of Diabetes Mellitus and Hypertension were included. Recurrent vaginal bleeding in the postmenopausal period was the only factor found to be significant on multivariate analysis. (Table 4)

Table 4:Risk factors associated with adenocarcinoma.

S. No	Risk factor	Adjusted Odds Ratio (95% CI)	p-value
1.	Endometrial thickness > 10mm	1.66 (0.36 to 7.55)	0.509
2.	Recurrent per vaginal bleeding	15.86 (3.85 to 65.27)	0.000
3.	Diabetes Mellitus	3.00 (0.89 to 10.09)	0.075
4.	Hypertension	1.30 (0.39 to 4.37)	0.664

When multivariant logistic regression analysis was used, there was a positive association with Diabetes, recurrent episodes of bleeding, endometrial thickness,hypertension which was significant. The analysisalso showed the significant predictive variables associated with endometrial cancer. AOR: Adjusted odds ratio, CI: Confidence interval

Further, it was noted that the Area under Curve (AUC) for Receptor Operating Curve (ROC) for the predictive model was 0.88 for the detection of adenocarcinoma in postmenopausal bleeding. (0.5*Endometrial thickening of more than 10 mm+2.7*Recurrent vaginal bleeding +1.10*Diabetes Mellitus+0.26*Hypertension). (Figure 1)

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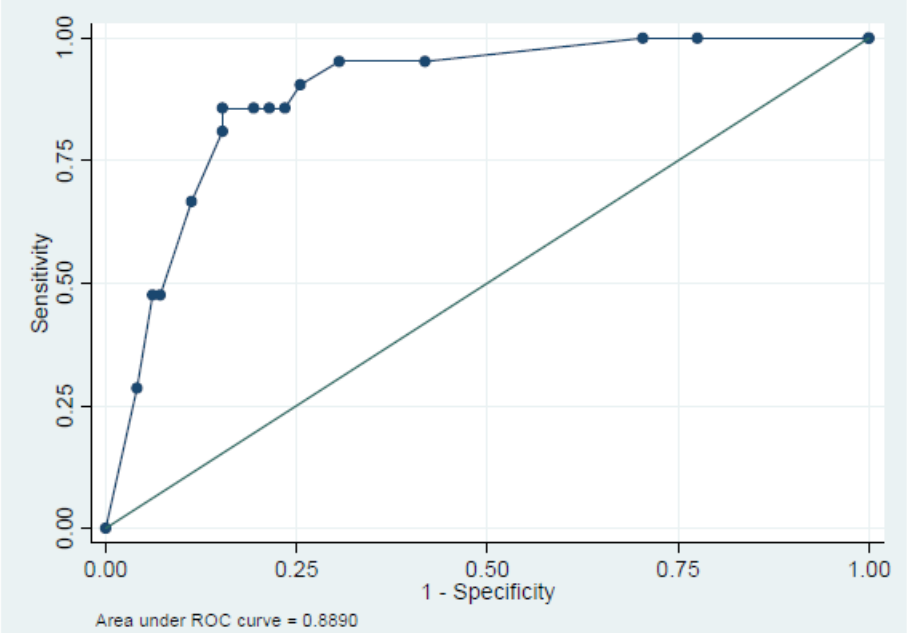

Figure 1: ROC for 0.5*Endometrial thickening of more than 10 mm+2.7*Recurrent vaginal bleeding +1.10*Diabetes Mellitus+0.26*Hypertension)

Discussion

Patients with a history of postmenopausal bleed were initially assed with either endometrial biopsy or transvaginal ultrasonography. No further evaluation was done for the women with ET<5 mm Women with endometrial thickness <5 mm were not evaluated for further management(9)(10).This study investigated the correlation between hypertension, diabetes, endometrial thickness, and a recurrent bleeding episode with endometrial carcinoma. An individualised adjusted odd ratio can be calculated and help the clinician decrease false-negative results and unnecessary patient exposure for further unnecessary investigation.

Our study mean age of presentation of endometrial carcinoma and menopause was 60.3±9.3 and 48±3.6, the duration of menopause was 11.7±9.4. All the results are similar to 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(11). Asimilar finding was observedin Ubeja and Singh study et al. study. It was observed that the age of presentation was 41–70 years with a mean age of 54.51 years, the mean year since menopause was 7.20 years which was similar to our study.(12)

In our study, the mean and SD of ET was 11.8(4.1) in the control group and 17.6(7.4) in the case. Kadakola *et al*. reported that the mean±SD of PMB women has of 8.84 ± 8.04.(12). The PMB wasmost commonly found in multiparous women associated with risk factors like diabetes (22.5%) and hypertension (33.3%); these results were similar to studies done by Nirupama *et al.* (13),

The most important finding of our study is that, when we applied multivariate logistic regression analysis for ET, diabetic and recurrent episode of bleeding and hypertension which showed significant predictive variables associated with endometrial neoplasia

We have performed a histological examination on only those with endometrial thickness of more than 5 mm thickness. We have collected all cases prospectively. All patients who are with ET more than 5 mm were subjected to histopathological examination.

High suspicion of endometrial cancer should be kept whenever high-risk factors are present and clinical findings also play a significant role in predicting the diagnosis. Any patient with a history of postmenopausal women with a new or recurrent episode of bleeding symptoms should be advised for further evaluation.

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In the prediction model, we have seen that incorporating clinical information aided with initial investigations like TVS allows us to guide the subsequent investigations and treatment strategies. The beneficial effects are evident for disease detection and improved patient care.

Conclusion

Detail clinical information along with initial investigationssuch as TVS and minimal procedures like endometrial biopsy will guide for the subsequent appropriate management.

Reference

1. Unni J. Third consensus meeting of Indian Menopause Society (2008): A summary. J Midlife Health. 2010;1(1):43.
2. Chopra K. Clinical perspective to postmenopausal bleeding and its diagnostic evaluation: a mini review. Women's Heal. 2019;8(1):63–4.
3. Brand AH. The woman with postmenopausal bleeding. Aust Fam Physician. 2007;36(3):116–20.
4. Moodley M, Roberts C. Clinical pathway for the evaluation of postmenopausal bleeding with an emphasis on endometrial cancer detection. Journal of Obstetrics and Gynaecology. 2004.
5. Sousa R, Silvestre M, Almeida E Sousa L, Falcão F, Dias I, Silva T, et al. Transvaginal ultrasonography and hysteroscopy in postmenopausal bleeding: A prospective study. Acta Obstet Gynecol Scand. 2001;80(9):856–62.
6. Cancer E. Endometrial Cancer. Practice Bulletin No. 149. American College of Obstetricians and Gynecologists. Obstet Gynecol. 2015;125(4):1006–26.
7. Briley M, Lindsell DRM. The role of transvaginal ultrasound in the investigation of women with postmenopausal bleeding. Clin Radiol. 1998;53(7):502–5.
8. Grimes DA. Diagnostic dilation and curettage: A reappraisal. Am J Obstet Gynecol [Internet]. 1982;142(1):1–6. Available from: http://dx.doi.org/10.1016/S0002-9378(16)32276-1
9. P DM, P DE, M DPV. Role of transvaginal Sonography in the evaluation of postmenopausal bleeding. Int J Clin Obstet Gynaecol. 2019;3(1):212–5.
10. Smith-Bindman R, Kerlikowske K, Feldstein VA, Subak L, Scheidler J, Segal M, et al. Endovaginal ultrasound to exclude endometrial cancer and other endometrial abnormalities. J Am Med Assoc. 1998;280(17):1510–7.
11. Lidor BA, Ismajovich B, Confino E, David MP. Histopathological findings in 226 women with postmenopausal uterine bleeding. Obstet Gynecol Surv. 1988;43(1):67–8.
12. Begum J, Samal R. A clinicopathological evaluation of postmenopausal bleeding and its correlation with risk factors for developing endometrial hyperplasia and cancer: A hospital-based prospective study. J Midlife Health. 2019;10(4):179–83.
13. Nirupama V, Suneetha Y, K PD. Post Menopausal Bleeding : An Analytic Study of 100 Cases. 2015;4(6):2588–90.