



Risk factors associated with postmenopausal bleeding and endometrial carcinoma.

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INTRODUCTION

Endometrial cancer is considered as the most frequent gynecologic cancer in developed countries and accounts for about 5% of total cancer with death rate of approximately 2% in women globally.¹ The prevalence of endometrial cancer is predominantly high in some regions such as North America and areas of Europe, in contrast to other developed countries, which may be recognized

ABSTRACT... Objective: The objectives of the study were to identify the common causes of post menopausal bleeding, benign and malignant causes of post menopausal bleeding and also the identification of risk factors for endometrial carcinoma in women with postmenopausal bleeding. **Study Design:** Cross sectional survey. **Setting:** Fauji Foundation Hospital Rawalpindi. **Period:** August 2018 to January 2019. **Material & Methods:** A total of 224 women with post menopausal bleeding were included in this study. Data was collected through the self structured questionnaire in which we have included patient's demographics, risk factors of Post menopausal bleeding and risk factors of endometrial carcinoma. Histopathological investigations of endometrial sampling were done for identification of benign and malignant causes of post menopausal bleeding. **Results:** Mean age of the women was 59.17 years and mean parity was found to be 2.24. Out of 224 patients 106(47.3%) women had their menopause in duration of 6 to 10 years while 75(33.9%) had menopause in time duration of first 5 years showing high frequency trend of post menopausal bleeding in first ten years duration after menopause. Out of 224 patients 30(13.4) were of normal weight, 94(42.0) were overweight while 100(44.6) were obese according to BMI criteria. Endometrial carcinoma was found in 40 women with post menopausal bleeding. Among them age at menarche was found to be 9 to 13 years in 27(67.5%) patients while more than 13 years in 13(32.5%) women. Age at menopause was found more than 55 years in 20(50%) patients while less than 55 years also in 20(50%) patients. Personal history of breast carcinoma was reported in 6(15%) similarly family history was also found in 6(15%) women. Family history of CA endometrium was observed in 3(7.5%). History of PCOs was also observed in 5(12.5) patients. Menstrual irregularity in perimenopausal period was found in 18(45%) patients with endometrial CA. Nulliparity was reported in 21(52.5%) patients. 12(30%) were on estrogen use while 4(10%) were on Tamoxifen use. **Conclusion:** Diabetes Mellitus and Hypertension were observed as common risk factors for post menopausal bleeding. Endometrial Carcinoma, cervix carcinoma and Hyperplasia with atypia were common malignant causes while endometrial polyp and fibroid uterus were commonly found benign causes of post menopausal bleeding. Early menarche, menopausal duration of more than one year, obesity and diabetes mellitus were common risk factors for endometrial carcinoma.

Key words: Post menopausal Bleeding, Endometrial Carcinoma, Risk Factors, Benign and Malignant Causes.

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for greater pervasiveness of obesity, in addition to other remarkable risk factors for instance early menarche, late menopause, nulliparity, aging, postmenopausal treatment of estrogen therapy.² On the contrary to most cancers, the incidence of endometrial cancer and associated death rates have increased considerably in recent years³⁻⁵ and also anticipated to increase during the period of next 10 years.⁶⁻⁸

Worldwide prevalence of endometrial cancer is 9 for every 100 000 women, with a life span risk of 1%, unopposed estrogen exposure is a worth mentioning risk factor involved, where prolonged exposure cause persistent endometrial proliferation and perhaps, endometrial carcinoma.⁹ Various other risks factor influence estrogen exposure involved obesity, polycystic ovarian syndrome, anovulation, nulliparity and diabetes mellitus type II.¹⁰ and these are also familiar to augment the risk of endometrial carcinoma. In some conditions, an irregular excessive proliferation of endometrial glands, endometrial hyperplasia, may be consider a reason for developing endometrial carcinoma. 'Atypical' hyperplasia pose the highest risk and, as with endometrial cancer, is treated by hysterectomy.¹¹

Endometrial carcinoma clinically manifested with postmenopausal bleeding (PMB).¹⁰ therefore it is recommended that women presenting with PMB are referred for further evaluation.^{12,13}

To rule out the endometrial carcinoma, the possible indicators for biopsy is controversial¹⁴ and current guidance vary. Current guidelines suggest an age cutoff, above which patients are referred; in some it is consider as 40 years.¹⁵

For early detection of endometrial carcinoma could focus on females at high risks of developing endometrial cancer, while excluding most women at lower risks. Most common symptom of endometrial cancer is postmenopausal bleeding (PMB) and accounts for about two-thirds of all gynecologic visits amongst perimenopausal and postmenopausal women.^{16,17} Even though, PMB is commonly associated with endometrial polyps or/and might result from spontaneous bleeding in women treating with hormone therapy.¹⁸ In some studies, the risks of developing endometrial cancer in females with post menopausal bleeding vary widely from 3% to 25%.^{19,20} Most endometrial cancer is diagnosed at a localized stage and is usually treatable with surgery, with a -year survival rate of about 95%. In comparison, 5-year survival rate for stage IV (late stage) endometrial cancer range from 16% to 45%.^{21,22}

The objective of this study was to determine the risk factors associated with endometrial carcinoma in women with postmenopausal bleeding and to identify the benign and malignant causes of post menopausal bleeding.

MATERIAL & METHODS

This cross sectional survey was carried out from August 2018 to January 2019 at Fauji Foundation Hospital, Rawalpindi. In this study a total of 224 women with post menopausal bleeding were included. Sample size was calculated by using Raosoft software keeping in view 5% margin of error, 95% of confidence interval, 20000 population size with 50% response distribution. Written informed consent was taken from the patients. Ethical consent was taken from Ethical review committee.

Data was collected through the self designed structured questionnaire in which we have included patient's demographics, risk factors of Post menopausal bleeding and risk factors of endometrial carcinoma. Histopathological investigations of endometrial sampling were done for identification of benign and malignant causes of post menopausal bleeding.

RESULT

Mean age of the women was 59.17 years and mean parity was found to be 2.24. Out of 224 patients 106(47.3%) women had their menopause in duration of 6 to 10 years while 75(33.9%) had menopause in time duration of first 5 years showing high frequency trend of post menopausal bleeding in first ten years duration after menopause. Out of 224 patients 30(13.4) were of normal weight, 94(42.0) were overweight while 100(44.6) were obese according to BMI criteria. When asked about hormonal treatment 67(29.9%) were on contraceptive use, 24(10.7%) were on HRT, 67(29.9%) were taking drugs for menstrual regularity while 20(8.9%) were on ovulation induction. Regarding the duration of post menopausal bleeding, 144(64.3%) had it for less than 1 year while 79(35.3%) had it for more than 1 year. According to the management, TAH+BSO done in 113(50.4) patients while 27(12.1) received oncology treatment, in 6(2.7) marina insertion

done, 28(12.5) received oral hormonal treatment and 48(21.4) were on conservative management.

Endometrial carcinoma was found in 40 women with post menopausal bleeding. Among them age at menarche was found to be 9 to 13 years in 27(67.5%) patients while more than 13 years in 13(32.5%) women. Age at menopause was found more than 55 years in 20(50%) patients while less than 55 years also in 20(50%) patients. Personal history of breast carcinoma was reported in 6(15%) similarly family history was also found in 6(15%) women. Family history of endometrium carcinoma was observed in 3(7.5%). History of PCOs was also observed in 5(12.5) patients.

Menstrual irregularity in perimenopausal period was found in 18(45%) patients with endometrial carcinoma. Nulliparity was reported in 21(52.5%) patients. 12(30%) were on estrogen use while 4(10%) were on Tamoxifen use.

Conditions	Frequency	Percentage (%)
Diabetes mellitus	63	28.1
Hypertension	70	31.3
Smoking	27	12.1
History of tumor	19	8.5
HCV positive	25	11.2
Thyroid disease	14	6.3
No co morbidity	4	1.7
Total	224	100

Table-I. Risk factors for post menopausal bleeding

Malignant Causes			Benign Causes		
Frequency		%	Frequency		%
Carcinoma cervix	20	8.9	Endometrial polyp	27	12
Carcinoma endometrial	40	17.8	Cervical polyp	09	4
High grade intraepithelial cervical lesion (CIN)	4	1.7	Pyometra	06	2.6
Uterine sarcoma	2	0.89	Hyperplasia without atypia	11	4.9
Hyperplasia with atypia	20	8.9	Fibroid uterus	12	5.3
Cyst adenocarcinoma	2	0.89	Secretory endometrium	02	0.89
			Senile atrophy of endometrium	08	3.5
			Chronic cervicitis	02	0.89
			Atrophic vaginitis	10	4.46
			Scanty biopsy	10	4.46
			Disordered proliferative endometrium	05	2.23
			Inactive endometrium	05	2.23

Table-II. Histopathology of endometrial sampling n = 224

BMI	Frequency	Percentage (%)
>25	7	17.5
25-35	13	32.5
<35	20	50.0
Total	40	100

Table-III. BMI levels in patients with endometrial carcinoma

Risk Factors	Frequency	Percentage
Obesity	20	50
Diabetes Mellitus	23	57.5
Early menarche (9-13 years)	27	67.5
Late menopause (>55 years)	20	50
Menstrual irregularity in perimenopausal period	18	45
Menopausal duration(> 1 year)	27	67.5
Nulliparity	21	52.5
Estrogen use	12	30
Tamoxifen use	4	10
Personal history of CA breast	6	15
Family history of CA breast	6	15
Family history of CA endometrium	3	7.5
History of Polycystic ovarian syndrome	5	12.5

Table-IV. Risk factors of endometrial carcinoma

DISCUSSION

American Cancer Society documented in 2001 that there were an inadequate details to suggest screening for endometrial cancer in females at average or increased risks due to history of diabetes, hypertension, infertility, obesity, late menopause, nulliparity, tamoxifen or unopposed estrogen therapy.²³ At the stage of menopause every woman should be informed about the risk factors and symptoms of endometrial cancer and highly appreciated to document any unexpected bleeding to their clinicians.²⁴

KJ Jung et al. have documented that, in western world early menarche, late menopause and long period between menarche and menopause were significantly associated with a high risk of developing breast cancer. For endometrial carcinoma, there was a statistically significant trend with the duration between menarche and menopause.²⁵

Menarche is an event referring the commencement of female reproductive cycle. Increasing evidence suggested the importance of menarche as both a footprint for chronic disease risks and a compass for developmental trajectory and overall health status. Unfavorable effect due to earlier age at menarche embrace risks for developing breast^{26,27} and endometrial cancer²⁸ In our study early menarche was found in 67.5% women. Our study confirm the findings of previous studies demonstrating that an earlier age at menarche was associated with increased risk of developing endometrial cancer (Table-II).

Menopause is considered as the permanent cessation of ovulation and menstruation, the final menstrual period definite by the subsequent 12 successive months in an absence of menses. It depicts the loss of reproductive capability, and the menopausal age is an indicator for overall health and aging.^{29,30} Undesirable effects from a late menopausal age comprise risks for developing endometrial and breast cancer.^{31,32} A European prospective investigation demonstrated a strong protective association with the use of oral contraceptives, parity and ovarian cancer risk, a high risk of advance age at menopause,

and no association with other reproductive factors. Our study is in keeping with reports from previous studies in finding that an advance age at menopause was associated with an increased risk of developing endometrial cancer. Our study confirms the findings of previous studies demonstrating that advance age at menopause was associated with high risk of endometrial carcinoma, as our study documented 50% women with late menopause (Table-II).

Several other studies have demonstrated the role of reproductive factors – such as age at menarche, parity, lactation and menopause, – on the risk for the development of hormone-related cancers, including breast cancer and ovarian cancer.³³ Our study is consistent with this hypothesis, demonstrating that about a 10-year increase in the duration of menopause was associated with around a two-fold increase in the risk of endometrial carcinoma.

CONCLUSION

Diabetes Mellitus and Hypertension were observed as common risk factors for post menopausal bleeding. Endometrial Carcinoma, cervix carcinoma and Hyperplasia were common malignant causes while endometrial polyp and fibroid uterus were commonly found benign causes of post menopausal bleeding. Early menarche, menopausal duration of more than one year, obesity and diabetes mellitus were common risk factors for endometrial carcinoma.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Nadia Ahmed Bukhari	Conceived the study and designed the model.	
2	Wardah Ajaz Qazi	Carried out the survey, manuscript search.	
3	Saira Jahan	Did the literature search, analyzed the data.	
4	Sadia Asmat	Did the literature search, analyzed the data.	
5	Nosheen Akhter	Analyzed the data, performed the calculations.	
6	Robina Jabeen	Performed the calculations, Manuscript writing.	