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ORIGINAL ARTICLE

SIGNIFICANCE OF CLINICAL AND HISTOPATHOLOGICAL EVALUATION IN WOMEN WITH POSTMENOPAUSAL BLEEDING: A HOSPITAL BASED STUDY IN KASHMIR

Rizwana Habib Kant[1], Aasif Iqbal[2], Shaguffta Yasmeen Rather[3], Preeti Sharma[4]

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ABSTRACT: BACKGROUND: Postmenopausal bleeding is a dreaded symptom both for the women and gynaecologist. Though it can be of benign origin, malignancy has to be ruled out and as such needs prompt evaluation. **OBJECTIVE:** (1) To study the etiological factors of postmenopausal bleeding and establish various endometrial causes of postmenopausal bleeding through histopathological evaluation. (2) To investigate the clinical significance of postmenopausal bleeding in terms of risk factors, incidence of malignancy and histopathological evaluation. **METHODOLOGY:** This observational study was conducted at Lalla Ded Hospital Srinagar over a period of 18 months in which 116 cases of postmenopausal bleeding were enrolled in the study. All patients were subjected to detailed history, examination and investigations followed by diagnostic curettage. Endometrial curretings were sent for histopathological examination. **STATISTICAL ANALYSIS:** Statistical Package for Social Sciences (SPSS V.16.0) and Microsoft Excel were used to carry statistical analysis of data. Data was analyzed with the help of descriptive statistics viz. %age, mean S.D. Graphically data was presented by bar and pie diagrams. **RESULTS:** Majority of the patients with postmenopausal bleeding were in the age of 45-55 years (63.8%), majority of cases 64(55.2%) were para 1-3, uterus was of normal size in 53 cases (45.7%). Mean age of onset of menopause was 48.7 years. Obesity was found in 40 cases (34.5%), hypertension in 35 cases (30.2%), and diabetes in 12 cases (10.3%). Out of the 116 cases studied; the most common cause of bleeding in the postmenopausal age group was endometrial hyperplasia in 41 out of 116(35.3%) followed by atrophic endometrium in 39 of 116(33.6%). Endometrial polyps were found in 9 (7.8%) cases, proliferative endometrium was found in 10(8.6%), endometritis was seen in 3(2.6%) cases, secretory endometrium in 1(0.9%) cases and adenofibroma in 1(0.9%) cases. The incidence of endometrial carcinoma in this study was 6% (7 out of 116 cases) mean age being 56.7 years and with duration of menopause more than 3 years. In 5 cases (4.3%) no endometrial tissue was obtained, hence no diagnosis could be made.

KEYWORDS: Postmenopausal Bleeding, Endometrial Curretage, Endometrial Hyperplasia, Endometrial Carcinoma, Atrophic Endometrium.

INTRODUCTION: Postmenopausal bleeding is defined as bleeding that occurs after one year of amenorrhea in a woman who is not receiving hormone replacement therapy. Women on continuous progesterone and estrogen hormone therapy can expect to have irregular vaginal bleeding, especially for the first 6 months. This bleeding should cease after one year. Any unexpected bleeding or significant change in withdrawal bleeding should prompt further investigations.[1] Vaginal bleeding occurs in approximately 4-11% of postmenopausal women.[2,3,4] The incidence of bleeding appears to correlate with time since menopause, with the likelihood of bleeding decreasing over time.

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Postmenopausal bleeding can be due to Vulval causes which include vulvitis, trauma, benign and malignant lesions. The vaginal causes of postmenopausal bleeding include foreign bodies such as ring pessary for prolapse, senile vaginitis, vaginal tumors, vaginal cancer, and post radiation vaginitis. Traumatic bleeding from an atrophic vagina may occur for upto 15% of all causes of postmenopausal bleeding. Cervical causes include benign cervical erosions, polyp, cervicitis, decubitus ulcer in case of prolapse and cervical malignancy. Uterine causes include senile endometritis, tuberculous endometritis, endometrial polyp, endometrial hyperplasia, fibroid uterus and endometrial carcinoma.

Endometrial hyperplasia followed by atrophic endometrium is most common etiology in this group. Fallopian tube malignancy can also present with postmenopausal bleeding, although incidence is rare. Postmenopausal bleeding represents one of the most common reasons for referral to gynaecological services, largely due to suspicion of an underlying endometrial malignancy.[5]

A women not taking hormone replacement therapy who bleeds after the menopause has a 10% risk of having genital cancer and a further 10% risk of significant pathology.[2] The dictum is postmenopausal bleeding indicates malignancy until proved otherwise. Therefore, postmenopausal bleeding should always be investigated no matter how minimal or non-persistent. At least, 25% of postmenopausal women with bleeding are said to have a neoplatic lesion; approximately 15% of which are having endometrial carcinoma.[6]

The recent rise in the incidence of endometrial carcinoma may be related to the decreased incidence of cervical carcinoma, prolonged life expectancy and better diagnostic facilities. The relatively low mortality for this cancer is probably due to the fact that most of these patients turn up for consultation at an early stage with symptoms of postmenopausal bleeding. Clinical evaluation and endometrial curettage is a better option of diagnosis especially in our low resource set up where other diagnostic facilities are not available to all the patients.

OBJECTIVES OF RESEARCH:

1. To study the etiological factors of postmenopausal bleeding and establish various endometrial causes of postmenopausal bleeding through histopathological evaluation.
2. To investigate the clinical significance of postmenopausal bleeding in terms of risk factors, incidence of malignancy and histopathological evaluation.

MATERIAL AND METHODS: Study Design: This observational hospital based study was conducted in Postgraduate Department of Obstetrics and Gynecology LD Hospital, in collaboration with Postgraduate Department of Pathology, Government Medical College, Srinagar for a period of 18 months. The study included 116 women of postmenopausal bleeding with uterine causes. Other causes of postmenopausal bleeding and non-Kashmiri women were excluded from the study.

SELECTION OF CASES: Patients with established postmenopausal bleeding of endometrial origin were included in the study after excluding other causes like vulval, vaginal, cervical, endocrine and systemic causes. Patients on anticoagulants or hormones were also excluded from the study. All patients were subjected to detailed history of symptoms, menstrual history, duration of menopause, interval between menopause and present bleeding, menstrual pattern prior to menopause and thorough general physical, systemic and local examination including perspeculum and bimanual examination.

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Investigations including complete blood picture, blood sugar, trans-abdominal ultrasound and trans-vaginal ultrasound was done. After selection, patients were subjected to diagnostic curettage.

PROCEDURE: Diagnostic curettage was performed under general anaesthesia. Endocervical curettage followed by thorough curettage of entire uterus was done and specimens were collected separately in 10% formaline bottles. The specimens were subjected to adequate fixation and tissue processing followed by formation of blocks. After tissue processing, 5 microns thick sections were cut and stained with hematoxylin and eosin followed by microscopic examination.

RESULTS: This observational hospital based study was conducted in department of obstetrics and gynaecology over a period of 18 months in 116 patients of postmenopausal bleeding. Mean age of onset of postmenopausal bleeding was 54.9 years with majority being in the age range of 45-55 years (63.8%). Mean age of onset of menopause was 48.7 years with majority of women having onset of menopause in the age range of 46-50 years (64.7%). Majority of cases, 64(55.2%) were para 1-3, 50 cases (43.1%) were para 4-6 and only 2 cases were nulli-gravidae.

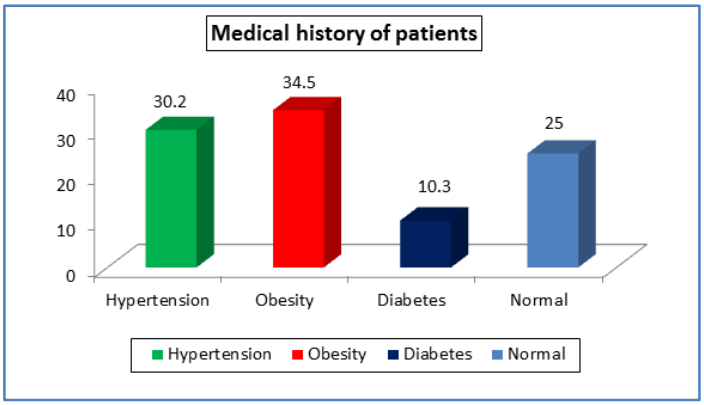

Fig. 1

Obesity was found in 40 case (34.5%), hypertension in 35 cases (30.2%), diabetes in 12 cases (10.3%) as shown in figure 1 above.

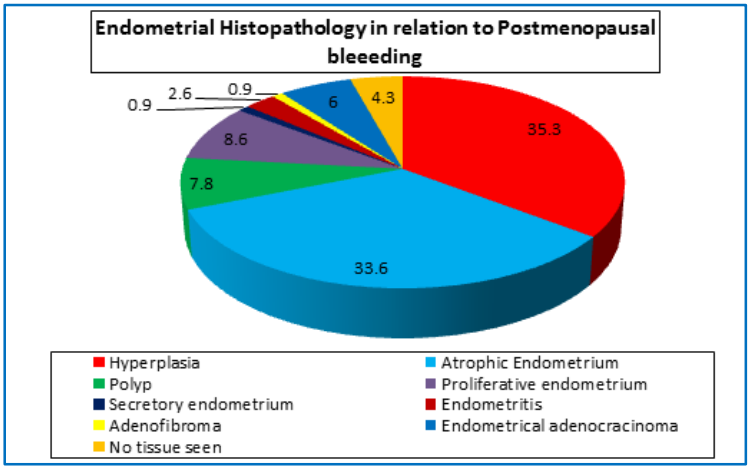

Fig. 2

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Out of the 116 cases studied; the most common cause of bleeding in the postmenopausal age group was endometrial hyperplasia 41 out of 116(35.3%) followed by atrophic endometrium 39 of 116(33.6%) cases. Endometrial polyps were found in 9(7.8%) cases, proliferative endometrium was found in 10(8.6%) endometritis was seen in 3(2.6%) cases, secretory endometrium in (0.9%) case and adenofibroma in 1(0.9%) case. In 5 cases (4.3%) no endometrial tissue was obtained, hence no diagnosis could be made. The cause of postmenopausal bleeding in 89.7% cases was found to be benign lesion whereas 6% had malignant lesion. In 5 cases (4.3%) no endometrial tissue was obtained hence no diagnosis could be made as shown in figure 2.

Endometrial Histopathology	Age (45-55)	Age (56-65)	Age (66-75)
Hyperplasia (simple & complex)	28	12	1
Atrophic Endometrium	12	22	5
Polyp	8	1	0
Proliferative endometrium	8	1	1
Secretory endometrium	0	1	0
Endometritis	0	3	0
Adenofibroma	1	0	0
Endometrial adenocarcinoma	3	4	0
No tissue seen	5	0	0
Total	**65**	**44**	**7**

Table 1: Relation of age with different Endometrial Lesions

Age of patients ranged from 45 years to 75 years. In the age group of 45 to 55 years, the commonest endometrial lesion was found to be endometrial hyperplasia in 28 cases (37.8%) followed by endometrial atrophy 12 cases (18.4%), polyps 8 cases (10.8%) and proliferative endometrium was observed in 8 cases (10.8%). There were 3 cases (4%) having endometrial adenocarcinoma. There was a single case of adenofibroma in this age group, whereas in 5 cases (6.7%) no endometrial tissue was obtained. In the age group of 56-65 years, the highest incidence was of endometrial atrophy 22(50%) cases followed by endometrial hyperplasia 12 cases (27.27%). There were 4 cases (9%) of endometrial adenocarcinoma and 3 cases (6.8%) having endometritis. In the age group of 66-75 years, there were total 7 cases only out of which 5 cases (71.4%) showed atrophic endometrium, 1 case (14.2%) of a 75 years old patient showed proliferative endometrium which was an unusual finding as described in Table 1.

In the study the duration of menopause ranged from 1 year to >10 years. In the span of 1-2 years there were 14 cases (40%) which were diagnosed as endometrial hyperplasia, 7 cases (20%) were having atrophic endometrium and 3 cases (8.57%) were found to have polyps. There was no case of malignancy. In 3-5 years span, there were maximum number of cases (37 cases). Out of these 14 cases (37.83%) were found to have endometrial hyperplasia, 11 cases (29.7%) were of endometrial atrophy and 4 cases (10.8%) of endometrial polyps. There were 4 cases (10.8%) of endometrial adenocarcinoma in this age group. The single case of adenocarcinoma was seen after a gap of 3 years of menopause. In the span of 6-10 years, there were 25 cases of which 10(40%) showed endometrial hyperplasia, 9(36%) has endometrial atrophy; 1 case (4%) had endometrial adenocarcinoma, 2 cases (8%) were of polyp and endometritis each. After 10 years, duration of

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menopause there were 19 cases in this study out which majority 12(63.15%) showed endometrial atrophy followed by 3 cases (15.78%) of endometrial hyperplasia and 2 cases (10.5%) of malignancy. Majority of cases, 64(55.17%) were seen in the para 1-3. Out of these 22(34.4%) cases had endometrial hyperplasia (simple and complex) , 20(31.25%) cases had atrophy, 6 (9.3%) cases had proliferative endometrium, 5(7.8%) cases had malignancy, 5(7.8%) cases had polyps and 1(1.5%) each had adenofibroma and endometritis.

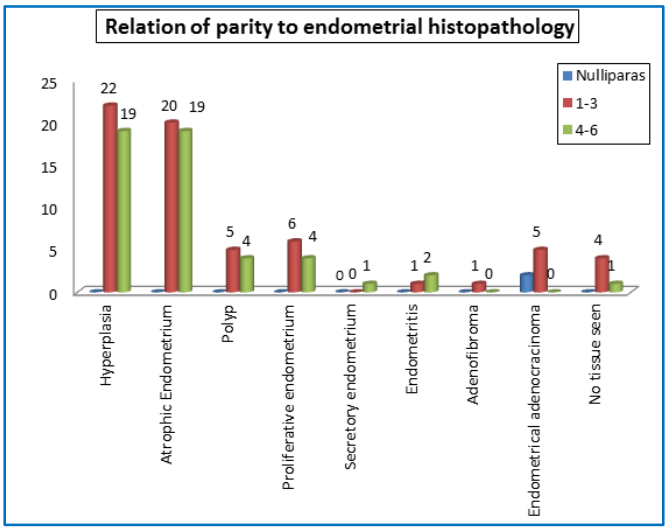

Fig. 3

As shown above, majority of cases 64(55.17%) were seen in the para 1-3. Out of these 22(34.4%) cases had endometrial hyperplasia (Simple and Complex), 20 (31.25%) cases had atrophy, 6(9.3%) cases had proliferative endometrium, 5(7.8%) cases had malignancy, 5(7.8%) had polyps and 1(1.5%) each had adenofibroma and endometritis. In the para 4-6, there were 50 cases, (43.10%). 19 cases (38%) had endometrial hyperplasia, 19 cases (38%) had endometrial atrophy, 4 cases (8%) had polyp and proliferative endometrium. 2 cases (4%) had endometritis and 1(2%) had secretory endometrium. There were 2 nulligravida women (1.7%) and both had endometrial adenocarcinoma.

Bulky uterus was found in 40 cases (34.4%) where the predominant pathology was endometrial hyperplasia in 23 cases (57.5%), 5 cases (12.5%) had malignancy, 6 cases (15%) had polyp, 3 cases (7.5%) had proliferative endometrium, and 2 cases (5%) had atrophic endometrium and 1 case (2.5%) had endometritis.

Type of hyperplasia	No. of Cases	Percentage
Simple hyperplasia	38	92.68
Complex hyperplasia	1	2.4
Complex hyperplasia with atypia	2	4.8
Total	**41**	**100**

Table 2: Types of Hyperplasia (Simple and Complex)

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There were 38 cases (92.68%) of simple hyperplasia, 1 case (2.4%) of complex hyperplasia and 2 cases (4.8%) of complex hyperplasia with atypia as shown in table3. Majority of the patients with endometrial hyperplasia (Simple and Complex) were in the age group of 45-55 years (68.3%). In the age group of 56-65 years there were 12 cases (29.3%). In the age group of 66-75 years, 1 patient had endometrial hyperplasia.

Out of 116 cases of postmenopausal bleeding, 39 cases (33.6%) showed atrophic endometrium. It was most commonly noted in the age group of 56-65 years and after a duration of menopause of 8.6 years. Mean parity in patients with atrophic endometrium was 3.7. Out of 116 cases; 10(8.6%) showed proliferative endometrium in the age group of 45-55 years and within a duration of menopause of 2 years and with mean parity of 3.4. Only 1 case showed proliferative endometrium after a gap of 10 years of menopause which was an unusual finding. Out of 116 cases, 9 cases (7.7%) were having endometrial polyps. In the present study, endometrial polyps had a higher incidence in the age group of 45-55 years. Majority of cases i.e., 7 occurred within 5 years of menopause. Mean parity in patients with polyps was 3.22.There were no polyps with atypia or cancerous polyps. All the hyperplastic polyps showed simple hyperplasia of surrounding endometrium.

Variable	Mean	SD	Range
Age	56.7	6.601	48-65
Duration of menopause	7.9	6.719	3-20
Parity	1.3	1.113	0-3

Table 3: Clinical parameters in relation with endometrial carcinoma

The incidence of endometrial carcinoma in this study was 6% (7 out of 116) cases. It was higher in the age range of 56-65 years, mean age being 56.7 years. The incidence was higher when the duration of menopause was greater than 3 years; mean duration of menopause being 79.9 years. Mean parity of patients with endometrial carcinoma was1.3 as shown above.

DISCUSSION: There have been many studies on postmenopausal bleeding from India and outside. In this study, we have tried to determine various causes of postmenopausal bleeding in patients referred to our hospital. In our study and study by Das et al,[7] majority of women presenting with postmenopausal bleeding are in the age group of 45-55years that is 63.8% and 85% respectively. Both the studies show that incidence of postmenopausal bleeding decreases with increase in age. The present study and the studies conducted by Saxena et al[8] and Das et al[7] found that postmenopausal bleeding was more common within 1-5 years of duration of menopause.

There was found to be decline in incidence of postmenopausal bleeding with increase in duration of menopause. The present study showed that 64.7% of women attained their menopause between 46-50 years with mean age of onset being 48.7 years. Study conducted by Kavitha et al[9] found 43.3% of women have attained menopause between 46-50 years of age. In our study, there was history of hypertension in 30.2% of women, diabetes mellitus in 10.3% of women and 34.5% of women were obese. Our observation was comparable to a study conducted by Kavitha et al[9] in which hypertension was found in 36.6% of women, diabetes in 13.3% of women and 43.3% of women were obese. The studies by Escoffery et al[10] and Naik et al[11] had 28% and 26.4% incidence

respectively, slightly lower incidence of hyperplasia than the present study in which incidence was 35.3%. The higher incidence of endometrial hyperplasia shows that postmenopausal endometrium in cases of bleeding exhibits an oestrogenic effect of varying degree. Incidence of atrophic endometrium as a cause of postmenopausal bleeding was 33.6% (39/116) in present study. This was comparable with study conducted by Pacheco et al (27.7%)[12] and Escoffery et al (26.7%).[10]

The study conducted by Lidor et al[13] and Gredmark et al[14] had a higher percentage in their studies with an incidence of 46% and 51.5% respectively. It is not known why some patients with atrophic endometrium tend to bleed. Anatomical vascular variations or local abnormal hemostatic mechanisms in the uterus have been proposed as the cause of bleeding. In this study, adenocarcinoma accounted for 6% (7/116) and was in agreement with studies conducted by Lidor et al (7%)[13] and Gredmark et al (8.4%).[14] While as studies conducted by Pacheco et al[12] and Naik et al[11] had higher incidence of endometrial carcinoma, 21.8% and 19% respectively. The incidence of endometrial polyps in this study was 7.8% (9/116) which was comparable to studies by Lidor et al[13] and Gredmark et al[14] who reported 8% and 9.5% respectively. Proliferative endometrium was found in 8.6% (10/116) of cases in this study which correlated with the observation of study by Pacheco et al (10%).[12] Naik et al[11] found that 17% of cases have proliferative endometrium in postmenopausal women but study by Kinitis et al[15] had only 1.1% of cases. Secretory endometrium was found in 1 case in the present study accounting for 0.9% of all the cases. Gredmark et al[14] found secretory endometrium in 1.4% cases and Kinitis et al[15] in 1.1% cases in their respective studies. Endometritis was found in the present study with an incidence of 2.6% (3 cases). Samal et al[16] found an incidence of 3.57% of cases in his study of postmenopausal women with dysfunctional uterine bleeding. Among the benign causes of bleeding in postmenopausal women, the present study showed an incidence of 89.7% which was comparable with studies done by Lidor et al [13]and Gredmark et al[14]. Choo et al[17] has divided the various endometrial lesions causing postmenopausal bleeding into organic and non-organic causes. Non organic causes basically consisted of atrophic endometrium, proliferative endometrium and secretory endometrium in his study which accounted for 90% of causes of bleeding. Incidence of endometrial hyperplasia and proliferative endometrium were more common in the age group of 45-55 years in the present study which was comparative to the study conducted by Naik et al.[11] Endometrial malignancy was more frequent in the age group of 56-65 years in the present study and also in the study of Naik et al.[11] There were 9 cases (7.8%) of endometrial polyps in this study and was comparable with the study conducted by Naik et al.[11]

In the duration of menopause of 1-5 years, the present study had the highest incidence of endometrial hyperplasia whereas the study done by Saxena et al[8] had atrophic endometrium as the commonest endometrial pattern. In the duration of menopause of 6-10 years, the present study as well as study conducted by Saxena et al[8] had the highest incidence of endometrial hyperplasia followed by atrophic endometrium and malignancy. Saxena et al[8] in his study observed a higher incidence of endometrial hyperplasia even after 10 years of menopause whereas the present study had a higher incidence of atrophic endometrium in that period. In the present study endometrial hyperplasia was the predominant finding in women with postmenopausal bleeding, being 41 out of 116 cases (35.34%). It included 38 cases (92.68%) of simple hyperplasia, 1 case of complex hyperplasia (2.4%) and 2 cases of complex hyperplasia with atypia (4.5%).

The incidence of endometrial hyperplasia was highest in the present study. Escoffery et al (28%)[10] and Naik et al (14%)[11] had slightly lower incidence comparatively.

Simple hyperplasia was the commonest finding among the types of hyperplasias in postmenopausal bleeding in the present study and study by Allison et al whereas Gredmark et al[14] and Reed et al[18] have noted complex hyperplasia as more common entity in postmenopausal age.

The incidence of atypical hyperplasia in our study was 4.5%. Other authors have reported slightly higher incidence. The incidence of endometrial hyperplasia in present study and studies by Allison et al and Reed et al[18] was highest among women aged 45-55 years. The comparative studies show that there was decrease in the incidence of endometrial hyperplasia with advancing age. Regarding the type of hyperplasia prevalent in different age groups, the present study showed 28 out of 41(68.3%) , simple hyperplasia in the age group of 45-55 years, 12 out of 41(29.3%) cases were in the age group of 56-65 years and 1 out of 41 was found in the age group of 66-75 years. A single case of complex hyperplasia in this study was found at 60 years of age.2 cases of atypical hyperplasia were found at 48 and 55 years of age respectively.

Out of 116 cases in this study 39 cases (33.6%) of postmenopausal women with bleeding had atrophic endometrium on histopathopogy. Study conducted by Gredmark et al[14] noted the highest incidence of 51.5%. The mean age of patients (60.4%) with atrophic endometrium was lowest in the present study whereas in the studies by Choo et al[17] and Sivridis et al[19] the mean age was 68 and 66.08 years respectively. The incidence of endometrial carcinoma in present study was 6% (7 of 116) with mean age of 56.7 years and mean duration of menopause of 7.9 years. Majority occurred in age group of 56-65 years which was comparable with the study conducted by Naik et al.[11] There were 3 cases of endometrial carcinoma with a systematic illness of diabetes mellitus. One women had obesity and hypertension while as three women had obesity with diabetes but the sample size is too small to make a significant conclusion regarding the association with endometrial carcinoma.

CONCLUSION: From our study it was observed that the most common cause of postmenopausal bleeding was endometrial hyperplasia (35.3%), followed by atrophic endometrium (33.6%), endometrial polyp (7.8%), proliferative endometrium (8.6%) and 6% cases had endometrial adenocarcinoma. Incidence of endometrial carcinoma though low but cannot be ruled out until proved otherwise by histopathological examination. Obesity, Diabetes and Hypertension were not found to be significant risk factors in our study, the cause of which may be small sample size. More studies need to be done to establish the association between risk factors and endometrial carcinoma. Prompt clinical evaluation followed by histopathological examination is important for diagnosing cause of postmenopausal bleeding and formulating an appropriate therapeutic strategy.

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AUTHORS:

1. Rizwana Habib Kant
2. Aasif Iqbal
3. Shaguffta Yasmeen Rather
4. Preeti Sharma

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Obstetrics & Gynaecology, GMC Srinagar.
2. Senior Resident, Department of Obstetrics & Gynaecology, GMC Srinagar.
3. Consultant, Department of Obstetrics & Gynaecology, GMC Srinagar.
4. Junior Resident, Department of Obstetrics & Gynaecology, GMC Srinagar.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Rizwana Habib,
Associate Professor,
Department of Obstetrics & Gynaecology,
Lalla Ded Hospital,
Govt. Medical College,
Srinagar-190006.
E-mail: habibrizwana@gmail.com

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