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## **Various endometrial patterns and abnormalities in women with postmenopausal bleeding**

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**Abstract**--Objective: To study the prevalence of various histopathological changes, patterns and lesions of endometrium in women with postmenopausal bleeding. Methodology: All the fixed specimens were processed and embedded in paraffin wax. Multiple serial sections of 4-5 microns thickness were obtained from the paraffin block and then stained with H & E. The observations in our study were analyzed using SPSS software version 11.5. The average values are statistically calculated using Microsoft Excel computer software. Results: This was a prospective, non interventional and observational hospital based cross sectional one year study carried out in histopathology department on endometrial biopsies and hysterectomy specimens. Out of 50 cases, postmenopausal bleeding presented at a mean age of 53.38 years and was most common within 5 years of attaining menopause. Among the endometrial causes of postmenopausal bleeding, 16% were due to benign conditions, 10% were due to malignancy and in 74 % of cases were because of non organic causes comprising of proliferative, secretory and atrophic

endometrium. Atrophic endometrium was most common among non organic causes, endometrial polyp was most common among the benign causes followed by endometrial endometrioid carcinoma was a major finding among the malignant causes. Among the less common entities, 1 case each of carcinosarcoma (MMMT) and endometrial stromal sarcoma low grade was found. Conclusion: Although the incidence of postmenopausal bleeding due to malignancy has fallen, it remains sufficiently high to require immediate and thorough investigation.

**Keywords**--postmenopausal bleeding, endometrial hyperplasia, endometrioid carcinoma, atrophic endometrium.

## Introduction

The definition of menopause given by WHO is permanent cessation of menstruation resulting from loss of ovarian functions. [1] Postmenopausal bleeding is defined as bleeding that occurs from the genital tract after one year of amenorrhoea, in a woman who is not receiving hormone replacement therapy (HRT). [2] It may be heavy bleeding, just spotting or in terms of quantity and duration like normal menstruation. [3] In Asian women the average age of menopause is 46 years. [4] As the life expectancy has increased, the women are spending more part of their life in postmenopausal age. Therefore the evaluation of postmenopausal bleeding is important to see the pattern of endometrial abnormality especially to rule out endometrial carcinoma. Etiology of postmenopausal bleeding include non-gynecological causes like trauma or bleeding disorders, use of hormone replacement therapy, vaginal atrophy, endometrial hyperplasia (simple, complex, and atypical) and endometrial carcinomas etc.. Endometrial carcinoma usually presents as postmenopausal bleeding. Other causes include endometrial polyps or cervical polyps, carcinoma of cervix, uterine sarcoma, ovarian carcinoma (especially estrogen-secreting ovarian tumors) and vaginal carcinoma. Carcinoma of vulva may bleed, but the lesion is obvious. [5-9]

Postmenopausal bleeding represents approximately 5 % of all gynecological visits. [10] Postmenopausal bleeding represents one of the most common reasons for referral to gynecological services; largely due to suspicion of an underlying endometrial malignancy [11] A woman not taking hormone replacement therapy (HRT) who bleeds after the menopause has a 10% risk of having genital cancer and a further 10% risk of significant pathology. [5] Therefore, postmenopausal bleeding should always be investigated no matter how minimal or non-persistent. As indicated by Indian cancer registry, there is an expanding trend for corpus uteri malignancies in the previous 2 decades. [12] Previous studies have demonstrated that 10–20% of endometrial hyperplasia advances to carcinoma when left untreated [13] So early evaluation in the postmenopausal women is essential to find out the precise nature of lesion and to rule out malignancy. The current study was carried out to assess various causes of postmenopausal bleeding in view of histo-pathological findings. This study gave us insight into the presence of various patterns of endometrium including incidence of non-organic,

benign and malignant lesions of endometrium leading to PMB in the rural population of this region (Piparia,Gujarat).

### **Objectives of study**

- To find out relative distribution of various abnormalities of endometrium in this part of country.
- To see the prevalence of endometrial carcinomas.
- To see the distribution of various endometrial patterns occurring in post menopausal bleeding.
- To see the various grades of hyperplasia occurring in patients with post menopausal bleeding.

### **Materials and Method**

#### **Study design**

Hospital based cross sectional study.

#### **Study Group**

The study includes all the cases of postmenopausal bleeding with the established menopause for 1 year and satisfying inclusion criteria.

#### **Sample size of group**

Number of cases - 50 cases with post menopausal bleeding whose uterus had been surgically removed and submitted for histological examination immediately fixed in 10% buffered formalin to Dhiraj hospital during the duration of October 2017 to October 2018.

#### **Study duration**

One year prospective study from October 2017 to October 2018

#### **Source of data**

Study was conducted on the hysterectomy specimens and dilatation and curettage material of the patients admitted and managed in obstetrics and gynecology department of Dhiraj Hospital received in the department of pathology, SBKSMI & RC, Pipariya, Vadodara.

#### **Data collection**

Data of patient's details for age, date, month and year, type of specimen collected from histopathology register and requisition slip for hysterectomy specimens and dilatation and curettage material received in histopathology department from October 2017 to October 2018.

### **Sample selection**

D&C materials, endometrial biopsies and hysterectomy specimen from women with postmenopausal bleeding received for histo-pathological examination in the department of pathology, SBKS medical college were used for the present study. The specimen was received in 10% formaline. The gross examination of the specimen was carried out thoroughly and appropriate sections were taken from various representative sites. Tissue was processed in fully automated tissue processor by passing through various grades of alcohol, xylene and wax. After tissue processing paraffin embedded tissue blocks were prepared. From these blocks 3-5 um thick sections were cut and stained with H&E stain. The sections were studied under light microscope.

### **Inclusion criteria**

All the cases of postmenopausal bleeding with the established menopause for 1 year presenting with spotting per vaginum, scanty flow, moderate to profuse bleeding, brownish discharge will be included in the study irrespective of social background.

### **Exclusion criteria**

- Autolysed specimens.
- Surgical menopause
- Women with cervical pathologies.
- Cases with non endometrial causes of postmenopausal bleeding like fibroid uterus and hormone secreting ovarian tumours etc.

### **Data Analysis**

The observations in our study were analyzed using Statistic Package Programmed for Social Science (SPSS software version 11.5). Distribution & frequency are obtained using statistical Pie Charts and Bar Diagrams. The average values are statistically calculated using Microsoft Excel computer software.

### **Results**

In this study, spanning from November 2017 to October 2018; 50 cases of postmenopausal bleeding were collected consisting of 38 hysterectomy specimens, 10 D & C specimens and 2 specimens of D & C with polypectomy. Of the 50 women recruited with postmenopausal bleeding, 2% of them were between 41-45 years age group 46% between 46-50 years, 30% between 51-55 years, 14% between 56-60 years, and 6% beyond 60 years of age. Postmenopausal bleeding seems to occur most commonly within the next few years of menopause (i.e.) at 46-50 years constituting 46% and the next peak 51-55 years of age at 30%. The mean age of women with postmenopausal bleeding was found to be-53.38 yrs. The following observations were made with regard to endometrial histopathology in relation to Postmenopausal bleeding (Table 1)

Table 1  
Endometrial histopathology in relation to postmenopausal bleeding

Histo-pathological findings	No of patients	Percentage
Proliferative phase	16	32%
Secretory phase	1	2%
Atrophy	20	40%
EHWA	1	2%
EIN	1	2%
Polyp	6	12%
Endometrioid carcinoma	3	6%
Endometrial sarcoma	1	2%
MMMT	1	2%
Total	50	100%

The most common cause of bleeding in the postmenopausal age group was atrophic endometrium, 20 out of 50 (40%) followed by polyps, 06 of 50 (12%). Proliferative endometrium and secretory endometrium were 16 and 1 case respectively out of 50 cases studied. Amongst the proliferative pathologies 1/50 (2%) was of EHWA and 2/50 (4%) were of EIN. Among the malignant causes of postmenopausal bleeding the incidence was 05 of 50 cases (10%). Out of which, 3 of 50 cases were of endometrioid type of endometrial adenocarcinoma; comprising of one case each of papillary variant, villoglandular variant and conventional type each. There was one case each of carcinosarcoma (MMMT) and one case of endometrial stromal sarcoma low grade.

Atrophic endometrium was most commonly noted in the age group of 46-60 years and after duration of menopause of greater than 10 years. Atrophic endometrium showed thinned out endometrium on hysterectomy specimens. Microscopy showed variably sized glands which were cystic and lined by flattened or cuboidal epithelium and diminished amounts of compact stroma. On biopsy/curettage specimens intact glands were uncommon, instead fragmented glands and small clusters of stromal cells were seen. Out of 50 cases; 6 cases (12%) were endometrial polyps. In the present study; endometrial polyps had a higher incidence in the age group of 46-50 years. Majority of the polyps, 3 cases occurred within 5 years of menopause. In all except two, polyps were observed in hysterectomy specimens. The exceptions were case of polypectomy.

On histo-pathological examination 1 was hyperplastic polyps which showed proliferating, irregularly shaped glands resembling non endometrial intraepithelial hyperplasia and stroma was dense which contained thick walled vessels. 3 were functional polyps showing normal proliferative glands with dense stroma and thick walled vessels. 2 were atrophic polyps having cystically dilated glands, reduced glands stroma ratio and thin fibrous stroma. Vessels were thick walled. Most common polyps were functional type comprising of 50% of total polyps found. They were common in the age group of 46-50 yrs followed by 51-55 years age group. Atrophic polyps comprised of 33.33%. Atrophic polyps were common in age group of >65 yrs followed by 46-50 yrs age group. Hyperplastic polyps were found in 16.66% of cases. Glands in hyperplastic polyps showed

complex architecture with focal crowding. Glands were lined by stratified columnar epithelium with presence of mitotic activity and atypical mitotic figures. Endometrium in the background showed the features of EIN.

3 patients out of 50 with postmenopausal bleeding had endometrial hyperplasia as the endometrial pathology. Out of 3 cases; 1 (33.33%) has endometrial hyperplasia without atypia (EHWA) and 2 case (66.67 %) were having endometrial intraepithelial neoplasia (EIN). Majority of patients with EHWA were in age group of 46-50 years and patients of EIN were in 51-55 years of age group. On microscopy; EHWA showed an increased glands/stroma ratio and the glands varied in size and shape. There were cystically dilated glands with occasional outpouching surrounded by an abundant cellular stroma in most cases; at other times the glands were minimally dilated but focally crowded. The lining epithelium was columnar and pseudostratified with amphophilic cytoplasm. Mitotic activity was variable. Nuclei were typically oval, basally oriented, and bland with smooth uniform contours.

EIN had increasing architectural abnormality with irregular outline and papillary infoldings; compressed intervening stroma resulting in back-to-back glandular crowding. Epithelial stratification and mitotic activity were present. They had atypical cytology of the glandular lining which showed loss of polarity of the nuclei; irregularity of nuclear membranes and cleared chromatin. Out of total 50 patients presenting with PMB 5 patients were of malignant tumors accounting for the total 10 % of study group population. Among the malignant endometrial category 60% of cases were due to endometrioid carcinoma and ESS LG and MMMT accounting for 20% each respectively. The incidence of endometrioid carcinoma in this study was 6% (3 out of 50 cases). It was higher in the age range of 51-55 years accounting for 40% of cases followed by 20% cases in 55-60 years of age group, mean age of 56.66. The incidence was higher when the duration of menopause was greater than 10 years; mean duration of menopause was 10 years.

There were different histologic subtypes of endometrial carcinoma found in this study. Out of 3 patients, 1 (33%) had endometrioid carcinoma conventional type; 1 (33%) had endometrioid carcinoma villoglandular type and 1 (33%) had papillary variant of endometrioid carcinoma. Carcinosarcoma (MMMT) was Found in 1 out of 50 cases comprised 2% of endometrial tumors and was found in the age group of 46-50 yrs: occurring in early post menopausal age. Grossly, after bisecting uterus, one polypoidal mass present in endometrial cavity. Carcinomatous components are of glandular type and mesenchymal component consist of few spindle cell and cartilaginous - biphasic appearance. Immunological tests were performed and whorled basaloid areas were positive for cytokeratin. The stromal component of the tumor was highlighted on vimentin. Her 2 neu was positive.

Endometrial stromal sarcoma was found in 1 out of 50 cases comprised 20% of endometrial tumors and was found in the age group of 46-50 yrs: occurring in early post menopausal age. Stromal sarcoma was of low grade variety. No cellular pleomorphism and necrosis was noted. Tumor was limited to uterus involving half of myometrium. Mitotic count was less than 4/10 hpf was noted. Tumor expressed

CD 10 and Vimentin IHC markers strongly. Tumor was immunonegative for SMA and Desmin .ER and PR markers were also not expressed by tumor cells.

## Discussion

The term “postmenopausal bleeding” generally implies bleeding from the uterus, and that is essentially the only bleeding of importance at the postmenopausal age. Few analyses of the causes of uterine bleeding in postmenopausal women are based on representative populations. This study includes women presenting with an endometrial cause of uterine bleeding after menopause is a defined health care region during a period of 24 months. Microscopic study of the endometrial specimen is imperative for proper diagnosis and therapy of benign as well as malignant lesions.<sup>65</sup>

In the present study and the study by Dr. Pragati (2014)<sup>66</sup>, majority of patients presenting with PMB were in the age group of 46-50 years, that is 46% and 31.6% respectively. Lowest numbers of patients were in the age group of 61-65 years age group (2%) and in the study group of Dr. Pragati was lowest in 66-70 yrs age group comprising of 3.2 %.

Table 2  
Comparison of histopathology of endometrium in postmenopausal bleeding

Endometrial Pathologies	Pacheco	Kinitis	Lidor	Gredmark	Escoffery	Naik	Pragati	Present study
histopathology	(1968) <sup>65</sup>	(1982) <sup>72</sup>	(1986) <sup>73</sup>	(1995) <sup>74</sup>	(2002) <sup>7</sup>	(2005) <sup>75</sup>	(2013) <sup>47</sup>	2018
	n = 288	n = 87	n=226	n=442		n=53	n=140	n=50
Prolif. Endo	10%	1.10%	14%	4.30%	4%	17%	13%	32%
SecretoryEndo		1.10%		1.40%			3.70%	2%
Atrophic Endo	27.70%	33.30%	46%	51.50%	26.7%	32%	41%	40%
Hyperplasia		18.30%	15%	10.10%	28%	26.40%	12.97%	6%
Polyp	32.30%	10.30%	8%	9.50%		5.70%	4.63%	12%
Endometrioid ca	21.80%	16%	7%	8.40%	12%	19%	13%	6%
Sarcoma	0.34%	-	-	-	4.40%	-		2%
Carcinosarcoma	0.34%	-	-	-	-	-		2%

The above table 2 represents the summary of the different endometrial patterns reported by various authors. All the aforementioned studies have dealt with all causes of postmenopausal bleeding and have shown their own respective incidences of non endometrial causes also which has been excluded from this discussion since this particular study deals exclusively with endometrial causes of postmenopausal bleeding. Proliferative endometrium was found in 32% of cases in this study which was highest amongst all the studies correlated with the observation of Pacheco,10%. Naik found 17% of cases to have proliferative endometrium in postmenopausal women but Kinits had only 1.1% of cases. None of the studies found disordered proliferative endometrium in any of their cases as in our study. The incidence might be higher because of exclusion of patients with hormonal therapy.

Secretory endometrium was found in 1 case in this study accounting for 2% of all the cases. Gredmark had 1.4% of cases of secretory endometrium and Kinitis had 1.1%. This discrepancy must be because of the lower sample size in our study. Atrophic endometrium as the cause of postmenopausal bleeding in the present study was 40 %. This was comparable with Lidor (1986) (46%) and Arati Mallick (41%) .Gredmark 51.55% (1995) had a higher percentage in their series with an incidence of 51.5%. It is not known why some patients tend to bleed from an atrophic endometrium. Anatomical vascular variations or local abnormal hemostatic mechanisms in the uterus have been proposed.<sup>74</sup> The lowest incidence of endometrial hyperplasia in the present study dealing with postmenopausal bleeding, (6%) was not observed in any of the previous studies. The studies by Escoffery (2002),28% and Naik(2005),26.4% had a slightly higher incidence of hyperplasia than the present study. In the present study, none of the patients had received exogenous oestrogens. That was our exclusion criteria. So that must be the reason for lower incidence of hyperplasia in our study

The incidence of endometrial polyps in this study was 12% which was comparable to studies by Kinnitis1982 having 10.3%. Lidor and Gredmark studies had relatively lesser incidence having 8% and 9.5% respectively. In this study; endometrioid carcinoma accounted for 6% of cases; this was in agreement with Lidor (1986) (7%) and was comparable with Gredmark (1995),8.4%. Pacheco and Naik had higher incidence of endometrial carcinoma, 21.8% and 19% respectively. Among the less common malignant neoplasms causing postmenopausal bleeding; this study detected 1 case of carcinosarcoma and 1 case of endometrial stromal sarcoma of the uterus. Pacheco (1968) presented in his study also 1 case of carcinosarcoma (0.34%) and 1 case of sarcoma (0.34%).

### **Endometrial atrophy**

Various studies have quoted endometrial atrophy as one common finding in postmenopausal women. Out of 50 cases in this study 22 cases (44%) of postmenopausal women with bleeding had atrophic endometrium on histopathology. In women with PMB; the present study observed an incidence of 40% of atrophic endometrium as the cause. It was in comparison to the study done by Arati Mallick. Gredmark noted the highest incidence of 51.5%. The studies by Escoffery and Pacheco were comparable to the present study in this regard with an incidence of 26.7% and 27.7% respectively.

(Figure 1.)



Figure 1. Endometrial atrophy Atrophic HSP, with thinned out endometrium

### **Endometrial polyps**

The prevalence of endometrial polyps in the general female population has been quoted to be as high as 25%; and it has been noted that polyps are most common at 50 years of age.<sup>13,50</sup> In the present study comprising of 50 cases of PMB, 6 (12 %) cases were due to endometrial polyps. Various studies have quoted varying incidence of endometrial polyps in women with PMB. Pacheco et al had observed the highest incidence, 32.3%. Incidence in our study is comparable with studies of Kinnitis (10.3%). Polyps were commonly observed in the 46-50 age group with a mean age of 55.33 years in the present study and 55.5 years in the study by Savelli. Histopathologic types of polyps prevalent in postmenopausal women with bleeding varied. The present study had 1 of 6 (16.67%) of hyperplastic polyps and 3 (50%) functional polyps. And 2 of 6 (33.33%) had atrophic polyps. (Figure 2). The histologic types of polyps in PMB in the present study indicated a high incidence of benign polyps 83.33% approximately same as Savelli and Robboy found a higher incidence of benign polyps in postmenopausal women.<sup>14</sup>



Figure 2. Endometrial polyp in atrophic uterus

### Endometrial carcinoma

The incidence of endometrial carcinoma varied between 3.7 and 17.9% in various studies on endometrial patterns in PMB published since 1930.<sup>74</sup> The present study reported an incidence of 6% (3 of 50). The mean age of patients with endometrial carcinoma was 53.4 years. The mean duration of menopause was 10 years after which the cases were diagnosed. The age specific incidence of endometrial carcinoma was compared in various studies. (Figure 3). In the present study majority of cases (66%) occurred in the age range of 45-55 years and only 1 case occurred at 60 years of age. Gredmark had the maximum no. of cases of endometrial carcinoma in the age group of 66-75 years (40.5%), whereas Naik reported 56-65 years of age group. In the age group of 56-65 years the incidence was in comparison to Gredmark studies. There was a definite risk for endometrial carcinoma in postmenopausal patients with advancing age. Gredmark observed that the incidence of bleeding decreased with increasing age, while the probability of endometrial cancer as the underlying cause increased.<sup>40</sup>



Figure 3. Endometrial carcinoma showing irregular growth filling endometrial cavity

### Endometrial stromal sarcoma

ESS was found in 1 patient with PMB (2%). It has been reported in PMB series study by Pacheco et al (1968) with the incidence of 0.34 % and 4.4 % in Escoffery (2002). In the study done by Nathaniel L Jones<sup>78</sup> out of 3133 uterine cancers submitted for a molecular profiling test from March 2011 to July 2014, 143 ESSs were identified based on reported pathology accounting for 4.56 % of cases. Of 143 ESSs, 52 (36%) were ESS-HG, 44 (31%) ESS-LG, and 47 (33%) unspecified. Compared with ESS-HG patients with ESS-LG were on average 2 years younger (54.7 vs 56.9). In our study series it was a case of ESS-LG presented at the age of 49 yrs. Hormone receptor expression was significantly greater in ESS-LG than ESS-HG: ER $\alpha$  (90% vs 21%), PR (86% vs 21%) and AR (60% vs 17%), respectively. 69% of ESS-HG were ER and PR negative while only 7% of ESS-LG were ER and PR negative<sup>78</sup> Our case was immune non reactive for ER and PR receptors.



Figure 4. Endometrial stromal sarcoma: Irregular nodular yellowish growth with few cystic areas

### **Uterine carcinosarcoma**

Hart (1995) studied 29 cases of carcinosarcoma where the mean age of patients was 68 years and 58% of cases had endometrioid type of carcinomatous component; 71% of cases had heterologous sarcomatous component of which the most common was rhabdomyosarcoma. The current study includes a single case of carcinosarcoma in a patient aged 50 years with PMB. This case also showed endometrioid type of carcinomatous component and heterologous sarcomatous component which had cartilage and osteoid elements.

### **Conclusion**

Bleeding from the genital tract occurring after menopause is much more sinister than premenopausal bleeding. The incidence of a malignant cause increases as the time lapse between menopause and onset of bleeding increases. Although the incidence of postmenopausal bleeding due to malignancy has fallen, it remains sufficiently high to require immediate and thorough investigation.

### **References**

1. ACOG – Endometrial hyperplasia 147 May 2011.
2. Alakananda, Das N, Das BP. Age of Menopause and Menopausal Symptoms among women attending Gauhati Medical College and Hospital, Guwahati, Assam: A cross-sectional study. *Scholars Journal of Applied Medical Sciences (SJAMS)*. 2015;3(7C):2621-9.
3. American Cancer Society Cancer Facts and Figures 2015
4. Archer DF, McIntyre-Seltman K, Wilborn WW Jr et al, Endometrial morphology in asymptomatic postmenopausal women. *Am J Obstet Gynecol* 1991;165:317-20.
5. Astrup K, Olivarius Nde F. Frequency of spontaneously occurring postmenopausal bleeding in the general population. *Acta Obstetrica et Gynecologica Scandinavica* 2004; 83(2):203-7.
6. BalaSubramaniam, Sushama, Rasika Hospital based study of endometrial cancer survival in India *Asian Pacific Journal Cancer Preview* 2013;14 ;(2):977-980.

7. Baloglu H, Cannizzaro LA, Jones J, Koss LG. Atypical endometrial hyperplasia shares genomic abnormalities with endometrioid carcinoma by comparative genomic hybridisation. *Hum Pathol*. 2001;32:615-622
8. Bani-Irshaid and A. Al-Sumadi Histological findings in women with postmenopausal bleeding: Jordanian figures I. *Eastern Mediterranean Health Journal* vol 7 2011.
9. Bartosch C, Manuel Lopes J, Oliva E. Endometrial carcinomas: a review emphasizing overlapping and distinctive morphological and immunohistochemical features. *Adv Anat Pathol*. 2011;18(6):415-437.
10. Bentley RC, Mutter GL, Robboy SJ. The normal endometrium. In: Robboy SJ, Mutter GL, Part J, Bentley RC, editors. *Robboy's Pathology of the Female Reproductive Tract*. 2<sup>nd</sup> ed. Churchill Livingstone Elsevier; 2009 .p.314.
11. Blake Gills . *Uterus corpus ,Rosai and Ackerman's surgical pathology*; : 11th edition , Elsevier publication 2018 ; 1334
12. Blake Gills. *Uterus corpus ,Rosai and Ackerman's surgical pathology*; : 11th edition, Elsevier publication 2018 ; 1320-22
13. Board of IMS on October 11, 1999, in Yokohama, Japan.
14. Bokhman JV. Two pathogenetic types of endometrial carcinoma. *GynecolOncol*. 1983;15(1):10-17.
15. Borker SA, Venugopalan PP, Bhat SN. Study of menopausal symptoms, and perceptions about menopause among women at a rural community in Kerala. *J Midlife Health*. 2013;4(3):182-7.
16. Brand AH. The woman with postmenopausal bleeding. *Australian Family Physician* 2007; 30:97-192.
17. Brinton LA, Felix AS, McMeekin DS, et al. Etiologic heterogeneity in endometrial cancer: evidence from a Gynecologic Oncology Group trial. *Gynecol Oncol*. 2013;129(2):277-284.
18. Burbos N, Musonda P, Giarenis I, Shiner AM, Giamougiannis P, Morris EP, et al. Predicting the risk of endometrial cancer in postmenopausal women presenting with vaginal bleeding: the Norwich DEFAB risk assessment tool. *Br J Cancer* 2010;102(8):1201-6.
19. Carlos RC, Bree RL, Abrahamse PH, Fendrick AM. Cost effectiveness of saline assisted hysterosonography and office hysteroscopy in the evaluation of postmenopausal bleeding. *Acad Radiol* 2001; 8: 835-44.
20. Chamlian LD, Taylor HB. Endometrial hyperplasia in young women. *Obstet Gynecol*. 1970;36:659-666.
21. Cooke ID. Endocrine changes associated with menopause and postmenopausal years. In : Campbell S. editor. *Management of Menopause and Postmenopausal years*. New York : MTP; 1976 .p.49-55.
22. Cote ML, Ruterbusch JJ, Ahmed Q, et al. Endometrial cancer in morbidly obese women: doracial disparities affect surgical or survival outcomes? *Gynecol Oncology* 2014; 133:38.
23. Dal Cin P. Cytogenetics of mesenchymal tumors of the female genital tract. *Surg Pathol Clin*. 2009; 2:813-821.
24. Dietel M. The histological diagnosis of endometrial hyperplasia: is there a need to simplify? *Virchows Arch*. 2001;439:604-608.
25. Escoffery CT, Blake GO, Sargeant LA. Histopathological findings in women with postmenopausal bleeding in Jamaica. *West Indian Medical Journal* 2002;51(4):232-5.

26. Fenoglio CM, Crum CP, Ferenczy A. Endometrial hyperplasia and carcinoma. Are ultrastructural, biochemical and immunocytochemical studies useful in distinguishing between them? *Pathol Res Pract.* 1982;174:257-284
27. Ferenczy A. Pathophysiology of endometrial bleeding. *Maturitas* 2003; 45:1.
28. Global epidemiology of cancer Randall E Harris
29. Gordon MD, Ireland K. Pathology of hyperplasia and carcinoma of the endometrium. *Semin Oncol.* 1994;21:64-70
30. Gredmark T, Kvint S, Havel G, Mattsson LA. Histopathological findings in women with postmenopausal bleeding. *British Journal of Obstetrics and Gynaecology* 1995;102(2):133-6.
31. Gusberg SB, Kaplan AL. Precursors of corpus cancer. IV. Adenomatous hyperplasia as stage 0 carcinoma of the endometrium. *Am J Obstet Gynecol.* 1963;87:662-667.
32. *Gynecol Oncology* 2004; 94:256.
33. Hawwa ZM, Nahhas WA, Copenhaver EH. Postmenopausal bleeding. *Lahey Clinic Foundation Bulletin* 1970; 19:61-70.
34. Hayes MP, Wang H, Espinal-Witter R, et al. PIK3CA and PTEN mutations in uterine endometrioid carcinoma and complex atypical hyperplasia. *Clin CancerRes.* 2006;12(20, pt 1):5932-5935
35. Hendrickson MR, Longacre TA, Kempson RL. The Uterine Corpus. In : Mills SE, Carter D, Greenon JK, Oberman HA, Reuter VE, Stoler MH, editors. *Sternberg's Diagnostic Surgical Pathology.* 4<sup>th</sup> ed. Vol.3, Philadelphia: Lippincott Williams; 2004 .p.2453.
36. Indian Menopause Society Consensus Guideline No.4 2010.
37. Jose C. Pacheco and Roger D. Kempers. Etiology of postmenopausal bleeding. *Obstet & Gynecol* 1968 July; 32(1):40-46.
38. Joseph J. Sreenan, and William R. Hart. Carcinosarcoma of the female genital tract – A pathologic study of 29 metastatic tumors: Further evidence for the dominant role of the epithelial component and the conversion theory of histogenesis. *Am J Surg Pathol* 1995; 19 (6):666-674.
39. Khan RL. Postmenopausal bleeding. In text book of Gynaecology, 3rd edition. Medical Publications, Lahore 2000; 260-262.
40. Kintis GA and Calvert W. Postmenopausal bleeding – one hospital – one year. *J Obstet & Gynecol India* 1982;676-683.
41. Korhonen MO, Symons JP, Hyde BM, Rowan JP, Wilborn WH, Histologic classification and pathologic findings for endometrial biopsy specimens obtained from 2964 perimenopausal and postmenopausal women undergoing screening for continuous hormones as replacement therapy (CHART 2 Study). *Am J Obstet Gynecol* 1997;176:377-80.
42. Kurman RJ, Kaminski PF, Norris HJ. The behavior of endometrial hyperplasia. A long-term study of 'untreated' hyperplasia in 170 patients. *Cancer.* 1985;56:403-412
43. Lax SF, Kurman RJ. A dualistic model for endometrial carcinogenesis based on immunohistochemical and molecular genetic analyses. *Verh Dtsch GesPathol.* 1997;81:228-232.
44. Lax SF, Xavier G, et al. Endometrial adenocarcinoma (Ch.16) In: Robboys SJ, Mutter GL, et al, editors. *Robboy's pathology of female reproductive tract.* 2<sup>nd</sup> ed. Churchill Livingstone Elsevier; 2009 .p.396-415.
45. Lax SF. Molecular genetic changes in epithelial, stromal and mixed neoplasms of the endometrium. *Pathology.* 2007;39(1):46-54.

46. Lee CH, Hoang LN, Yip S, et al. Frequent expression of KIT in endometrial stromal sarcoma with YWHAE genetic rearrangement. *Mod Pathol*. 2014;27(5): 751–757
47. Lee WH, Tan KH, Lee YW. The aetiology of postmenopausal bleeding—a study of 163 consecutive cases in Singapore. *Singapore Medical Journal*. 1995;36(2):164-8.
48. Lidor A, Ismajovich B, Confino E, David MP. Histopathological findings in 226 women with postmenopausal uterine bleeding. *Acta Obstet Gynecol Scand* 1986;65:41
49. Lidor A, Ismajovich B, Confino E, David MP. Histopathological findings in 226 women with post-menopausal uterine bleeding. *Acta Obstet Gynecol Scand* 1986 (65):1:41-43.
50. Mahajan N, Aggarwal M, Bagga A. Health issues of menopausal women in North India. *Journal of Midlife Health*. 2012;3(2):84-7.
51. McCluggage WC. Mesenchymal uterine tumours other than pure smooth muscle neoplasm and adenomyosis. In : Robboy SJ, Mutter GL, et al, editors. *Robboy's pathology of female reproductive tract*. 2<sup>nd</sup> ed. Churchill Livingstone Elsevier; 2009.p.443-447.
52. Murali R, Soslow RA, Weigelt B. Classification of endometrial carcinoma: more than two types. *Lancet Oncol*. 2014;15(7):e268–e278.
53. Mutter GL, Nucci, MR, and Robboy SJ. Endometritis, metaplasia, polyps, and miscellaneous changes. In: *Robboy's Pathology of the Female Reproductive Tract*, 2nd ed., Robboy SJ, Mutter GL, Pract J, et al. (Eds), Churchill Livingstone Elsevier, Oxford 2009. p.343.
54. Mutter GL, Zaino RJ, Bentley RC. Benign endometrial hyperplasia and EIN. In : Robboy SJ, Mutter GL, Prat J, Bentley RC, editors. *Robboy's Pathology of the Female Reproductive tract*. 2<sup>nd</sup> ed. Churchill Livingstone Elsevier; 2009 .p.367-388
55. National Institute of Cancer Prevention and research – Globocan 2012 data.
56. New Insights into Pathology of endometrial carcinoma. *Current Topics in Menopause*
57. Padubidri VG, Paftary SN. Menopause, premature menopausal and postmenopausal bleeding. In : Howkins and Bourne Shaw's text book of Gynecology. 13<sup>th</sup> ed. Elsevier; 2004 .p.66.
58. Pragati J karmakar, Anne Wilkinson, Mayuri Rathode. Histopathological evaluation of postmenopausal bleeding e-ISSN: 2279-0853, p-ISSN: 2279-0861. Volume 13, Issue 10 Ver. III (Oct. 2014), PP 53-57
59. Ronghe R, Gaudoin M. Women with recurrent postmenopausal bleeding should be re-investigated but are not more likely to have endometrial cancer. *Menopause International* 2010;16(1):9-11.
60. Ronnet BM, Zaino RJ, Kurman RJ. Endometrial carcinoma. In : Kurman RJ, editor. *Blauster's pathology of female genital tract*. 5<sup>th</sup> ed. New York: Springer Verlag; 2002 .p.501-535.
61. Ronnett BM, Kurman RJ. Precursor lesions of endometrial carcinoma. In: Kurman RJ, editors. *Blaustein's Pathology of Female Genital tract*. 5<sup>th</sup> ed. New York : Springer – Verlag; 2002 .p.468-477.
62. Sabini G, Chumas JC, Mann WJ. Steroid hormone receptors in endometrial stromal sarcomas. A biochemical and immunohistochemical study. *Am J Clin Pathol*. 1992; 97:381-386.

63. Samal S, et al. Clinicopathological study of dysfunctional uterine bleeding in postmenopausal women. *J Obstet Gynecol India* 1996; 40:286.
64. Sarah E. Ferguson, Carmen Tornos, Amanda Hummer, Richard R. Barakat and Robert A. Soslow. Prognostic features of surgical stage I uterine carcinosarcoma. *Am J Surg Pathol* 2007 Nov; 31(11):1653-1661.
65. Saseendran Pallikadavath, Reuben Ogollah, Abhishek Singh, Tara Dean, Ann Dewey, William Stones. Natural menopause among women below 50 years in India: A population based study *Indian J Med Res.* 2016 Sep; 144(3): 366–377.
66. Sherman BM. Endocrinologic and menstrual alterations. In : Mishell DR, editors. *Menopause – Physiology and Pharmacology*. Chicago : Year Book Medical Publishers; 1987 .p.41-52
67. Sherman ME, Mazur MT, Kurman RJ. Benign diseases of the endometrium. In : Kurman RJ, editors. *Blaustein's Pathology of Female Genital Tract*. 5<sup>th</sup> ed. New York : Springer Verlag; 2002 .p.437-453.
68. Silverberg SG, Mutter GL, Kurman RJ, Tavassoli FA. Tumors of the uterine corpus. In : Tavassoli FA, Devilee P, editors. *World Health Organization classification of tumours. Pathology and genetics of tumors of the breast and female genital organs*. IARC Press : Lyon 2003 .p.229
69. Singh A, Pradhan SK. Menopausal symptoms of postmenopausal women in a rural community of Delhi, India: A cross-sectional study. *J Midlife Health.* 2014;5(2);62-7.
70. Soslow RA, Bissonnette JP, Wilton A, et al. Clinicopathologic analysis of 187 high-grade endometrial carcinomas of different histologic subtypes: similar outcomes belie distinctive biologic differences. *Am J Surg Pathol.* 2007;31(7): 979–987.
71. Speroff L, Glass R, Kase N. *Clinical gynaecological endocrinology and infertility*. Baltimore: Williams and Wilkins 1994.
72. Takkar N, Goel P, Dua D, Mohan H, Huria A, Sehgal A. Spectrum of gynaecological disorders in older Indian women: a hospitalbased study. *Asian J Gerontol Geriatr* 2010; 5: 69–73.
73. Tandulwadkar S, Deshmukh P, Lodha P, Agarwal B. Hysteroscopy in postmenopausal bleeding. *J Gynec Endosc Surg* 2009;1: 8993.
74. Thomas Gredmark, Sonja Kvint, Guillaume Havel, Lars Ake Mattsson. Histopathological findings in women with postmenopausal bleeding. *Br J Obstet & Gynecol* 1995 Feb; 102:133-136.
75. Veena S. Naik, Jyoti D. Rege, Kusum D. Jashnani. Pathology of genital tract in postmenopausal bleeding. *Bombay Hospital J.*
76. W.H.O. Research on the menopause in the 1990s. Report of a WHO Scientific Group. World Health Organization technical report series 1996;866:1-107.
77. YC, Mak KC, Hsu C, Wong TS, Ma HK. Postmenopausal uterine bleeding of nonorganic cause. *Obstet Gynecol* 1985; 66:225-228.
78. Zaino R, Carinelli SG, Ellenson LH et al. Tumours of the uterine Corpus: epithelial Tumours and Precursors. In: Kurman RJ, Carcanglu ML, Herrington CS, Young RH, eds. *WHO Classification of Tumours of female reproductive Organs*. 4th ed. Lyon: WHO Press; 2014: 125–126