10.5005/jp-journals-10032-1151

RESEARCH ARTICLE

Association of Endometrial Thickness with Histopathological Pattern of Endometrium with Postmenopausal Bleeding

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ABSTRACT

Aim: To compare the endometrial thickness with the results of the biopsy and assess the usefulness of endometrial thickness as an indicator of underlying pathology.

Materials and methods: Endometrial thickness measured by ultrasound of 61 patients with postmenopausal bleeding were compared with histopathology of endometrial biopsy. Age of presentation, the duration between menopause and postmenopausal bleeding, parity, associated symptomsand association of risk factors for endometrial hyperplasia and carcinoma were analyzed.

Results: The mean age of patients with menopausal bleeding was 52 years, and that of endometrial cancer was 63.7 years. About one-third of cases with postmenopausal bleeding had hyperplasia and one-tenth was diagnosed as carcinoma. The minimum thickness of endometrium was 6 mm in patients with hyperplasia with a mean of 14.3 ± 5.4 mm, and it was 12 mm in the case of carcinoma with a mean of 20 ± 6.4 mm. Mean thickness of atrophic endometrium was 7.4 ± 3.5 mm.None of the cases with less than 4 mm endometrial thickness had either hyperplasia or cancer.

Conclusion: Ultrasound can be considered as an early diagnostic evaluation tool for patients with postmenopausal bleeding in predicting endometrial hyperplasia and carcinoma which could prevent un-warranted operation in patients with a thin endometrium.

Clinical significance: Thickened endometrium is a predictor of endometrial hyperplasia and cancer.

Keywords: Endometrial pathology, Endometrial thickness, Observational study, Postmenopausal bleeding, Ultrasound.

How to cite this article: Krishnamoorthy P, Balakrishnan N, Prasad G. Association of Endometrial Thickness with Histopathological Pattern of Endometrium with Postmenopausal Bleeding. J South Asian Feder Menopause Soc 2018;6(2):112-116.

Source of support: Nil

Conflict of interest: None

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Date of received: 10 January 2018

Date of acceptance: 27 January 2018

Date of publication: July 2018

INTRODUCTION

Menopause is resulting from the loss of ovarian follicular activity[1] and postmenopausal bleeding (PMB) following established menopause accounts for about 5% of gynecology visits.[2] The most common cause of PMB is endometrial atrophy, contributing to 60–80% of PMB.[3] Though endometrial hyperplasia and endometrial cancer contribute to only 10% of postmenopausal bleeding, it increases the morbidity and mortality of the patients. Endometrial cancer is the most common genital cancer which is the sixth leading cause of death from malignancy among women. Overall, about 2–3% of women develop endometrial cancer during a lifetime.[2] About 90% of women with endometrial cancer have vaginal bleeding, and only less than 5% of endometrial cancer are asymptomatic. 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.[4] Therefore, patients with PMB should always be investigated for early diagnosis of endometrial cancer. Early diagnosis of endometrial cancer could increase the 5-year rate of survival rate up to 95%.

Endometrial hyperplasia and endometrial cancer usually present with thickened endometrium. Dimitraki et al.[5] reviewed the studies on clinical evaluation of women with PMB and stated that there have been many publications indicating that ultrasound may be useful in predicting endometrial pathology. However, they concluded that the accuracy of the above tests in predicting endometrial hyperplasia and endometrial carcinoma is a subject of continuing debate. Transvaginal ultrasound measurement of endometrial thickness has replaced other invasive methods as the first-line investigation of women with PMB, but as yet there is no consensus as to which cut-off value should be adopted to define abnormality.[6] Since advanced endometrial carcinoma has been known to occur in cases without noticeable endometrial thickness on ultrasound, more studies are required to generate

data on this issue. The present study aims at comparing the endometrial thickness with histopathology report of endometrial biopsy of patients with PMB to generate more data on endometrial thickness in the prediction of endometrial hyperplasia and endometrial cancer. Assessment of endometrial thickness is expected to help in decreasing un-warranted operation in patients with a thin endometrium.

MATERIALS AND METHODS

It was a retrospective observational study conducted in the Department of Obstetrics and Gynaecology at Karpaga Vinayaga Institute of Medical Sciences in 2018. The study was conducted after obtaining approval from the institutional ethical committee. All women who were admitted with postmenopausal bleeding in the gynecology ward from December 2016 to November 2017 and who fulfilled the inclusion and exclusion criteria were included in the study. Case sheets of 82 women who were admitted with postmenopausal bleeding during the study were examined and found 61 cases eligible. Patients with premalignant/malignant lesions of vulva/vagina/cervix, bleeding disorders, premature menopause and who were on HRT, tamoxifen, and anticoagulants were excluded.

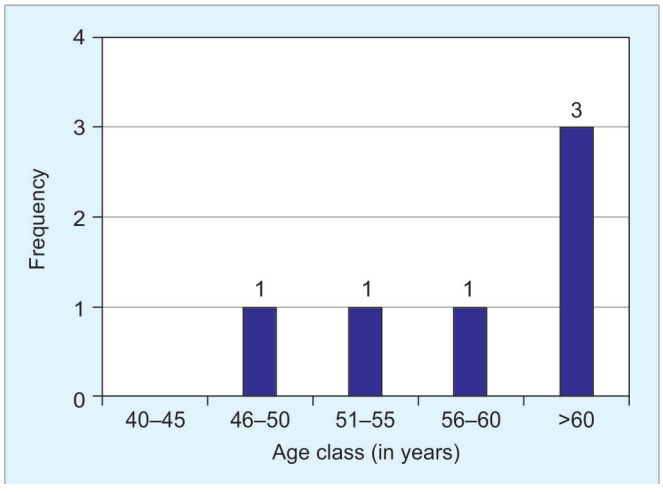
Using a proforma, the relevant history, clinical findings, and investigation details were taken from the case sheets of these patients. The relevant histories included age, parity, the age of menopause, duration since menopause, the age of presentation with postmenopausal bleeding, symptoms of menopause and significant medical and surgical history. Endometrial thickness from the ultrasound findings and histopathological details of endometrial biopsy were collected from the casesheets and were compared using statistical tests such as proportion test and student t-test. None of the patients was contacted, and only case sheets were used with the names of the patient maintained confidential, and hence the study does not have any ethical issue.

RESULTS

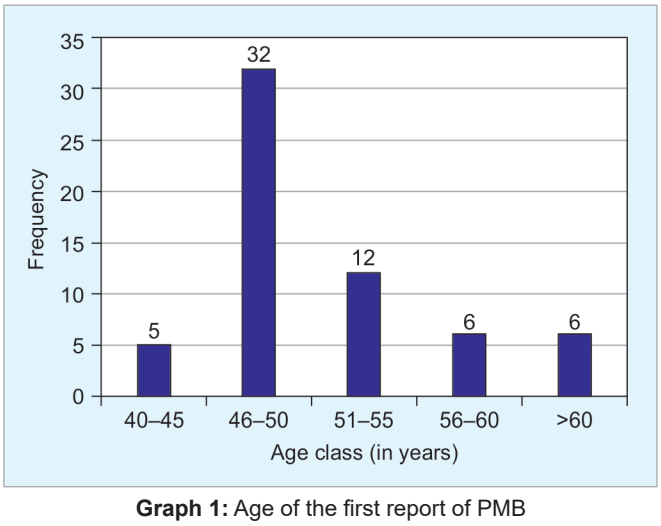
Qualifying reports of 61 patients presented with PMB were analyzed. Patients with age ranging from 43 to 85 years were found to have PMB, with 52.4 % cases reported in the age class of 46 to 50 years (Graph 1). Majority of patients in our study group attained menopause below the age of 50 years through seven (11.4%) cases attained after 50 years and none was above 60 years with the mean age of attaining menopause was 46.8 ± 3.4 years (Graph 1). Age of the first report of PMB.

Age-specific distribution of patients with endometrial cancer (Graph. 2) showed that the presence of cancer was most common in the age class above 60 years. The mean age of patients with endometrial cancer was 63.7 ± 7.4 years, ranging from 49 to 85 years. Hyperplasia was higher in the age class 46 to 50 years (Graph 3).

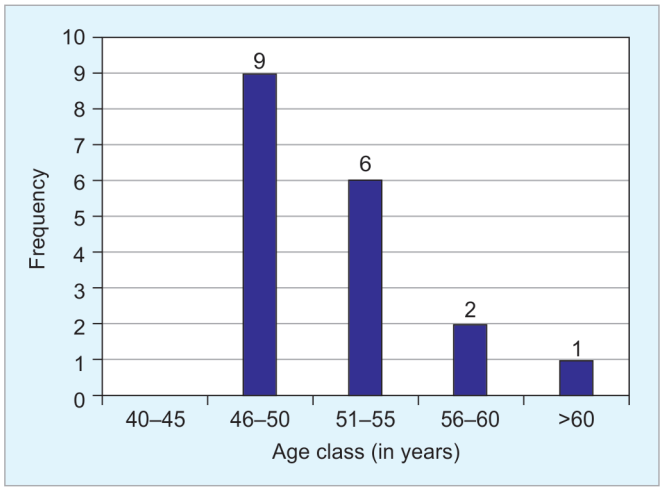
The interval between menopause and first presentation of PMB was found to range between one and 40 years with a mean of 5.8 ± 6.6 years. The mean interval in relation to the major pathological findings is shown in Table 1. The mean gap was minimum in atrophic endometrium (5.2 ± 4.2 years) and hyperplasia (5.4 ± 5.2 years) cases



Graph 2: Age distribution of patients with adenocarcinoma



Graph 1: Age of the first report of PMB



Graph 3: Age distribution of patients with hyperplasia

Table 1: Mean interval (in years) of menopause and PMB in relation to major pathology

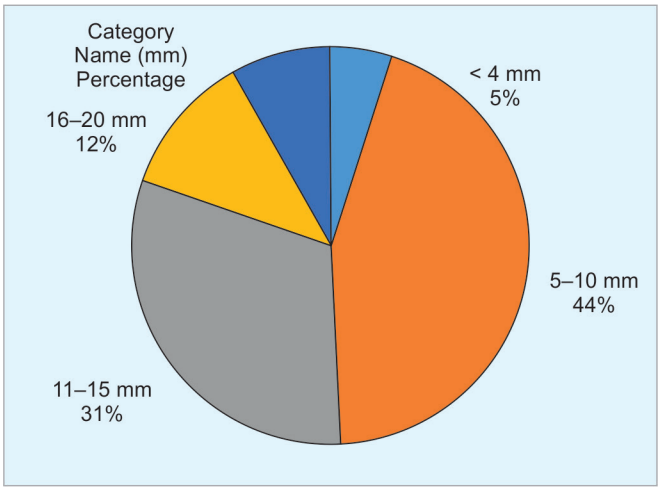
Interval (in years)	*No. of cases*	*Atrophic endometrium*	*Adenocarcinoma*	*Hyperplasia*
1–5	41	12	1	14
6–10	11	3	2	2
11–15	5	2	0	1
16–20	3	0	2	2
>20	1	0	1	0

while it was as wide as 16.2 ± 13.7 years among carcinoma cases. This shows that endometrial cancer presentation was delayed.

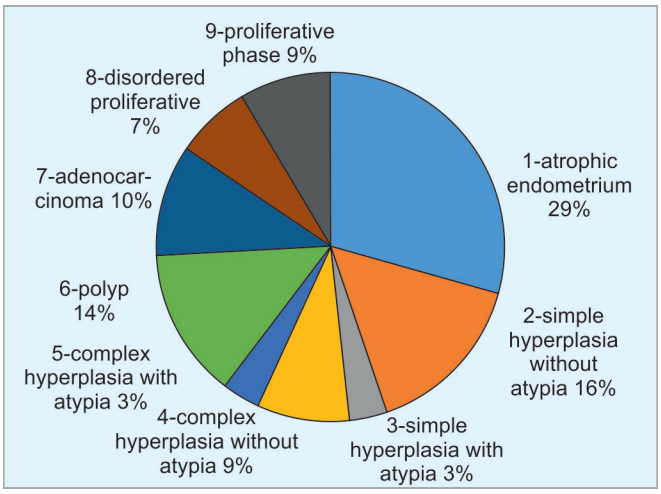
The scan findings of the patients based on endometrial thickness are shown in Graph 4. Endometrial thickness ranged from 3.3–30 mm and the mean was 11.2 ± 5.4 mm. It was less than 4 mm only in 3 (5%) of the cases. Majority of the cases were in the range of 5 to 10 mm thickness followed by 11–15 mm thickness. Distribution of cases in relation to histopathological report is given in Graph 5. The most common histopathological findings were hyperplasia and atrophic endometrium, constituting about 29.5 and 29% of the cases, respectively.

About 9.8% of the PMB patients were diagnosed as carcinoma. Endometrial pathologies and their corresponding endometrial thickness are given in Table 2. None of the patients with adenocarcinoma and hyperplasia had endometrial thickness <4 mm. The three cases with an endometrial thickness of less than 4 mm had only atrophic endometrium. The mean endometrial thickness for adenocarcinoma was as high as 20 ± 6.4 mm and is significantly (t = 2.9; p <0.05) higher than the mean of 14.3 ± 5.4 mm in hyperplasia cases.The mean endometrial thickness in atrophic endometrium was least (7.4 ± 3.5 mm) is significantly (p < 0.05) different when compared to both carcinoma and hyperplasia.

The association of PMB with other symptoms is shown in Graph 6. Abdominal pain is the most common symptom followed by white discharge. Back pain is a least reported symptom of PMB. Analysis of cases in relation to parity shows that 22 (36.1%) of the cases had parity of <2 and remaining were above two parities. Out of 61 patients, 27 patients (44%) had associated risk factors such as diabetes and or hypertension (Table 3). In the case of endometrial cancer, 4 out of 6 patients had risk factors (66.7%), followed by hyperplasia (55.6%). However, the proportion



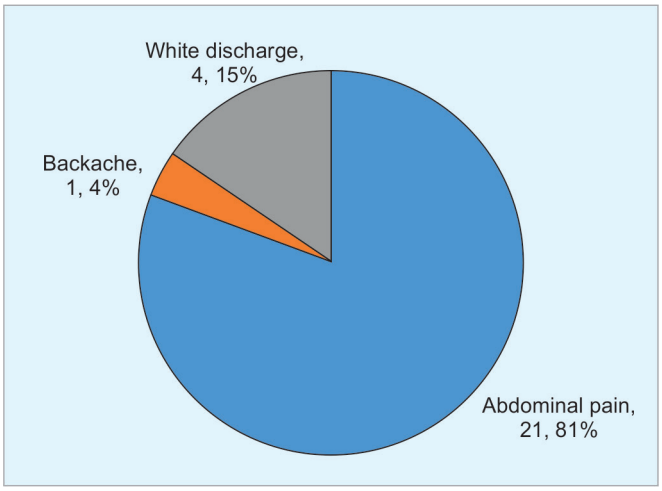
Graph 4: Distribution of cases in relation to ET thickness (n = 61)



Graph 5: HPE profile (n = 61)

Table 2. Endometrial thickness (in mm) in relation to histopathology

HPE	*No. of cases*	*mean*	*Min*	*Max*	*Standard deviation*
Atrophic endometrium	17	7.4	3.5	16.3	3.45
Simple hyperplasia without atypia	9	11.5	6.0	16.5	5.03
Simple hyperplasia with atypia	2	13.0	12.5	13.5	0.71
Complex hyperplasia without atypia	5	15.2	13.0	18.0	2.16
Complex hyperplasia with atypia	2	17.5	16.0	19.0	2.12
Polyp	8	11.0	8.0	12.0	2.72
Adenocarcinoma	6	20.0	12.0	30.0	6.42
Disordered proliferative	4	7.1	6.0	9.5	1.65
Proliferative phase	5	9.3	4.4	15.0	3.82
Secretory phase	3	10.8	8.5	15.0	3.64



Graph 6: Associated symptoms of postmenopausal bleeding (n = 27)

Table 3: Distribution of cases in relation to risk factors

HPE	*Total cases*	*No. patients with risk factors*	*%*
Atrophic endometrium	17	7	41.18
Simple hyperplasia without atypia	9	3	33.33
Simple hyperplasia with atypia	2	1	50.00
Complex hyperplasia without atypia	5	4	80.00
Complex hyperplasia with atypia	2	2	100.00
Polyp	8	1	12.50
Adenocarcinoma	6	4	66.67
Disordered proliferative	4	2	50.00
Proliferative phase	5	2	40.00
Secretory phase	3	1	33.33

of cases with risk factors in these two conditions (58.4 %) is significantly higher × (Chi-square) = 1.14; $p = 0.28$) when compared to atrophic endometrium (41.2%).

DISCUSSION

It is known that post-menopausal bleeding contributes to about 5% of all gynecological outpatient department visits.[2] The present study showed that the probability of endometrial cancer was about 10% and endometrial hyperplasia wasabout 29%. Our study corroborates with a similar observation on the mean age of post-menopausal bleeding, and the interval between menopause and menopausal bleeding reported elsewhere.[7-10] Mean age of attainment of menopause was 46.8 years which is comparable to that of 48.4 years reported by Kumari and Hafsa.[8] The mean age of presentation of post-menopausal bleeding in the present study was 52.7 years which is closer to the mean age of 55.5 and 55.9 years reported by Manjusha et al.[7] and Kumari and Hafsa[8] respectively. According to a study conducted by Gredmark et al.,[11] the incidence of post-menopausal bleeding decreases with age which corroborates with a present study where about 90% of cases with post-menopausal bleeding are under the age of 60 years. Endometrial cancer was observed in the older age class with 50% of the cases presenting above 60 years of age, showing an increase in incidence with age as has been reported earlier.[12] The mean interval between the age of menopause and menopausal bleeding was 16.2 years for the cases with adenocarcinoma, indicating an increased risk with the interval. In the case of other pathological conditions, it was around 5–6 years.

Out of six cases of adenocarcinoma, four cases had either diabetes, hypertension or both, indicating the likelihood of adenocarcinoma with these factors. Association of endometrial cancer with obesity, diabetes, and hypertension has already been reported.[8] Meta-analysis of epidemiological studies related to endometrial cancer reported parity may be associated with a decreased risk of cancer. However, the present study showed that the mean parity among cancer patients was 3.6 against the overall parity of 3. A relatively smaller number of endometrial cancer cases could have limited the inference on its association with parity.

Certain studies emphasis on evaluating the intracavitary uterine lesions only if endometrial thickness is more than 4 mm in PMB[13-15] whereas some authors recommend for endometrial biopsy for all patients presenting PMB,[16,17] irrespective of endometrial thickness as there are reports of prevalence of endometrial cancer with less than 4 mm thickness.[18] Dimitraki et al.[5] while reviewing the studies on PMB concluded that since advanced endometrial carcinoma has been known to occur in cases without noticeable endometrial thickness on ultrasound, the clinician should beware of the diagnostic evaluation of postmenopausal women with vaginal bleeding.

A meta-analysis[19] showed that several studies suggest that an endometrial thickness of >15 mm is highly suggestive of endometrial carcinoma. In our study, the mean endometrial thickness for adenocarcinoma was 20 mm which is close to 21 mm reported by Karlson et al.[20] It was 14.3 mm among cases of hyperplasia and 7.4 for atrophic endometrium. None of the cases of hyperplasia and adenocarcinoma had less than 4 mm which is in agreement with the study of Karlsson et al.[20] who reported that the risk of finding pathologic endometrium at curettage when the endometrium is <4 mm, is only 5.5%. Similarly, using the same cutoff of 4 mm, the sensitivity of detecting cancer was reported to be over 90%.[13,16,17]

There are different ways of evaluating the postmenopausal bleeding which includes transvaginal sonography (TVS), hysteroscopic evaluation and endometrial biopsy. Of these hysteroscopies and endometrial biopsy are inva-

sive as well as expensive[21] procedures whereas TVS is noninvasive, easy and inexpensive procedure and does not require anesthesia. Hence TVS can be used as the first mode of evaluation of patients with PMB and based on endometrial thickness further tests can be undertaken. Our study results corroborate with the study from over 4000 patients spread over 10 years[6] which concluded that transvaginal ultrasound using a 3 mm cutoff can identify women with PMB who are highly unlikely to have endometrial cancer, thereby avoiding more invasive endometrial biopsy.

Though data from 61 cases provided valid information, data from more cases could have provided stronger evidence on the inferences and this can be considered as a limitation of the study.

CONCLUSION

It can be concluded that TVS can be used as the first mode of investigation for PMB cases. Endometrial biopsy can be recommended only when the thickness is >4 mm as it has 100% sensitivity for both hyperplasia and adenocarcinoma.

CLINICAL SIGNIFICANCE

Thickened endometrium is a predictor of endometrial hyperplasia and carcinoma.

ACKNOWLEDGMENTS

Authors wish to acknowledge the support provided by the Department of Obstetrics and Gynaecology, Karpaga Vinayakar Institute of Medical Sciences. Thanks are also due to the participants of the study for their cooperation.

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