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HISTOPATHOLOGICAL FINDINGS IN POSTMENOPAUSAL BLEEDING

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ABSTRACT

Introduction: *Postmenopausal bleeding is commonly considered a significant and alarming indicator of genital diseases. The term "postmenopausal bleeding" typically refers to uterine bleeding. Since it is a sign of many different etiologies and has a strong correlation with malignancy and conditions with substantial morbidity and mortality, prompt identification and treatment are desired for postmenopausal bleeding.*

Methods: *It is a retrospective cross-sectional observational study carried out in the pathology division of KIST Medical College and Hospital, Lalitpur, Nepal. From July 2017 to July 2022, 270 endometrial and endocervical biopsy samples with a history of postmenopausal bleeding were included. Following microscopic analysis, frequencies of histological findings in various age groups were generated. To determine whether the difference was significant, chi-square and proportions were used; the cutoff value was set at p 0.05.*

Results: *On average, the patients were 51.9 years old, plus or minus 6.6 years. Of the 270 samples included, 222 (82.2%) were endometrial biopsies, and the remaining samples were cervical biopsies. Endometrial hyperplasia was the most common histological finding overall, occurring in 67 (24.8%) of the patients. With a mean age of 65.33 years, endometrial and cervical cancer patients were between the ages of 51 and 79. Endometrial and cervical carcinomas were together present in 31 (11.48%) of the patients. Leiomyoma was one discovery; others included endometritis, adenomyosis, endometrial polyps, hormonal deviations, and disordered proliferative endometrium. Endometrial hyperplasia was discovered in 20 patients over the age of 50 and 47 patients under the age of 50; this finding is statistically significant at a p-value of 0.05.*

Conclusions: *In postmenopausal bleeding, benign diseases predominated, but the proportion of endometrial and cervical cancers and pre-malignant disorders was rather high. Our study demonstrates the significance of the endometrial sample, particularly in peri/postmenopausal women who have atypical uterine bleeding.*

Keywords: *Cervical Carcinoma, Endometrial Carcinoma, Endometrial Hyperplasia,Endometrial Sampling, Postmenopausal Bleeding*

INTRODUCTION

Greek words "meno" (month), "pause," and "halt" make up the phrase "menopause." Approximately 50 years old is when women begin the physiological process of menopause. Asian women reach menopause on average at the age of 46. It signals the end of the reproductive years, is connected to signs of an estrogen shortage, and has a big impact on women's health and quality of life[1,2]. Postmenopausal bleeding is referred to as "bleeding via the female vaginal canal, 12 months after the cessation of menstrual cycles (menopause)" (PMB)[3].

Postmenopausal bleeding is typically seen as a serious and concerning indicator of genital disorders. It can just be your typical menstrual cycle, spotting, or excessive bleeding. Postmenopausal bleeding accounts for 5% of all gynecological appointments[4]. Postmenopausal bleeding can occur at any age and be brought on by a variety of illnesses that affect any of the female genital tract organs, but most frequently the uterus and cervix. Infections, benign lesions like polyps, hyperplastic (pre-malignant) diseases, aggressive malignant disorders, and normal physiologic atrophic alterations can all cause PMB. This symptom is also linked to a number of systemic diseases, particularly blood dyscrasias[3]. The dictum is postmenopausal bleeding indicates malignancy. Hence, any postmenopausal bleeding, no matter how slight or intermittent, needs to be investigated. At least 25% of postmenopausal bleeding is thought to be caused by neoplastic lesions, with endometrial cancer accounting for about 15% of this cases[5]. In order to reduce morbidity and mortality related to neoplastic and non-neoplastic disorders associated with postmenopausal bleeding, timely intervention is needed. Any disease that affects any of the female genital tract organs, but most frequently the uterus and cervix, can cause

postmenopausal bleeding at any age. PMB can be brought on by infections, benign lesions such as polyps, hyperplastic (pre-malignant) diseases, aggressive malignant disorders, and common physiological atrophic changes. Additionally, this symptom has been connected to certain systemic illnesses, including blood dyscrasias[3]. Postmenopausal bleeding is thought to be a sign of cancer. Therefore, it is important to look into any postmenopausal bleeding, no matter how minimal or irregular. Neoplastic lesions are considered to constitute the root of at least 25% of postmenopausal bleeding, with endometrial cancer representing roughly 15% of these cases[5]. Early management is required to lower the morbidity and mortality linked to neoplastic and non-neoplastic illnesses associated with postmenopausal hemorrhage.

MATERIALS AND METHODS

At the pathology department of Kist Medical College and Hospital in Lalitpur, Nepal, a retrospective cross-sectional descriptive study was undertakenafter Institute Ethical Committee clearance. A large number of gynecological cases are seen daily at KISTMCTH, a tertiary medical facility. Postmenopausal bleeding cases were identified for whom endometrial samples were obtained for histological analysis between the years of 2017 and 2022 in July.The gross examination was carried out in accordance with the recommendations from the third and fourth editions of Susan Lester's Manual of Surgical Pathology, which are editions [6,7]. Hematoxylin& Eosin was used to stain formalin-fixed, paraffin-embedded tissue sections (H&E). It took two pathologists to conduct the microscopic inspection. A pre-made proforma was used to collect data on variables like age and histopathology findings.

Data was analyzed by using SPSS Version 29. Chi-square test was applied to see the distribution with 95% confidence interval and 5% level of significance, p-value of < 0.05 was considered significant.

Inclusion criteria were postmenopausal women with vaginal bleeding manifested as spotting per vagina, brownish discharge, scanty flow and moderate to profuse bleeding. Exclusion criteria were Premature menopause whether surgical or natural, age less than 40 years and patients on hormone replacement therapy.

RESULTS

The average age of the patients was 51.9±6.6 years, with a range of 41 to 73 years. Nearly half (44%) of the patients were in their fifth decade. Distribution of study subjects according to the age group is shown in table 1 and figure 1. Out of 270 samples, 48 (17.8%) of them were cervical biopsies and 222 (82.2%) were endometrial biopsies. The most frequent histological result overall, observed in 67 (24.8%) patients, was endometrial hyperplasia. In no case was there evidence of atypical endometrial hyperplasia. Cervical carcinoma was the most prevalent condition in the group of cervical biopsies, accounting for 24 (8.9%) cases. In 31 (11.48%) patients, both cervical and endometrial carcinoma were present. All cases of endometrial cancer were endometrioid carcinomas. The age group for endometrial and cervical carcinoma ranged from 51-79 years with mean at 65.33 years. Leiomyoma was discovered in 17 (6.3%), Endometritis in 32 (11.85%), and Adenomyosis in 15 cases, Endometrial polyps and hormonal alterations were each found in 12 (4.44%) instances, and disordered proliferative endometrium was seen in 18 (6.7%) cases. Figure 2 shows causes of postmenopausal bleeding.

Twenty individuals over the age of 50 and 47 patients under the age of 50 were both found to have endometrial hyperplasia, which is statistically significant at a p-value of <0.05 (Table 2).

Table 1: Distribution of study subjects according to age group (n=270)

Age (years)	No. of study subjects	Percentage (%)
41-45	30	11.1
46-50	126	46.7
51-55	57	21.1
56-60	33	12.2
61-65	12	4.4
66-70	3	1.1
>70	9	3.3
Total	270	100%

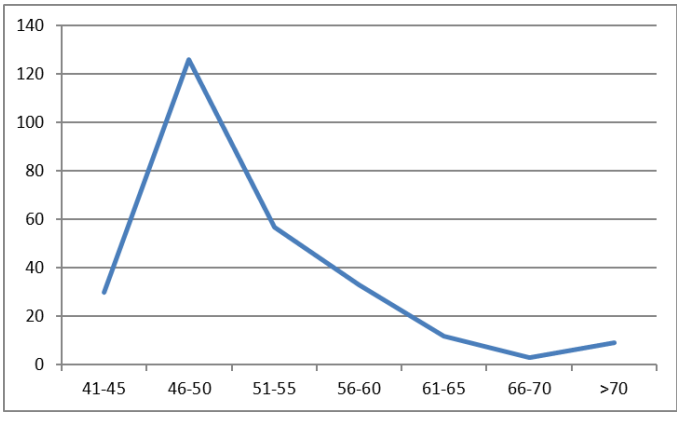

Figure 1: Age distribution graph

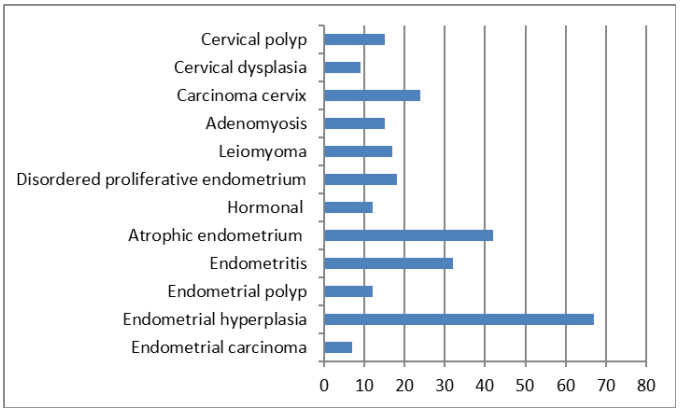

Figure 2: Endometrial and cervical causes of post-menopausal bleeding

Table 2: Statistical significance between age and endometrial hyperplasia

Age	PMB with EH	PMB without EH	Marginal row totals
< 50 years	47(31%)	103(69%)	150
> 50 years	20 (17%)	100(83%)	120
Margin column totals	67	203	270 (Grand total)

The chi-square statistic is 7.6865. The p-value is .005564. Significant at p < .05.

PMB: Postmenopausal bleeding

EH: Endometrial hyperplasia

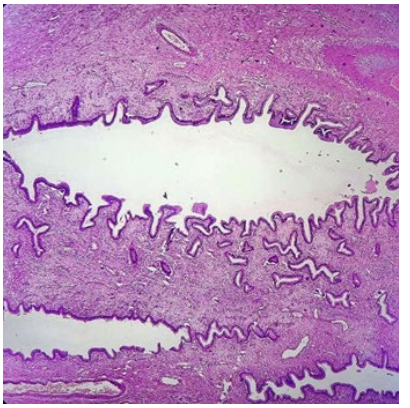

Figure 3 showing endocervical polyp

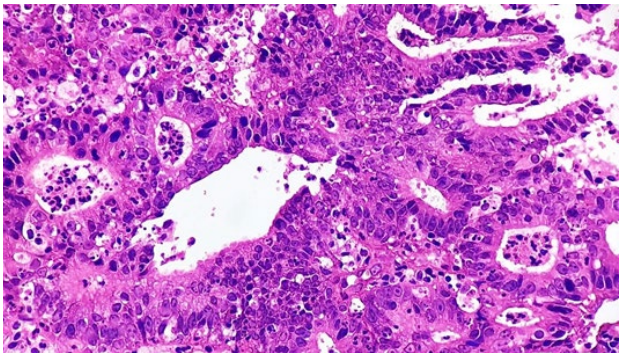

Figure 4 showing endometrioid carcinoma

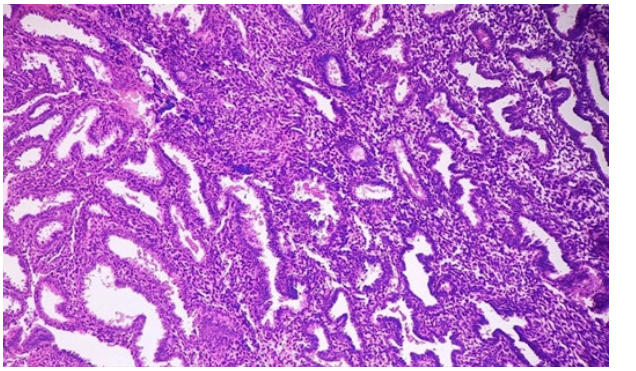

Figure 5 showing endometrial polyp

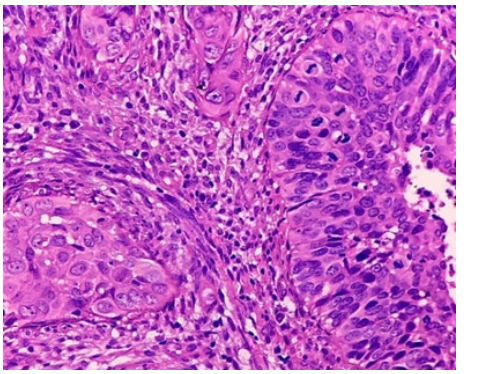

Fig. 6 showing SCC of cervix

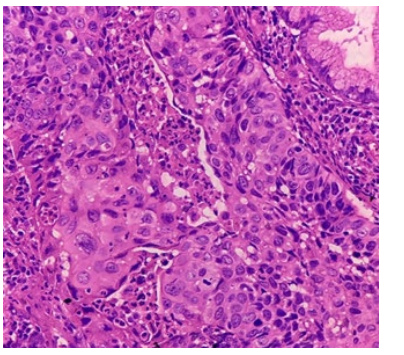

Fig. 7 showing SCC of cervix

DISCUSSION

Postmenopausal bleeding is a common and concerning symptom that could indicate uterine or cervical cancer. It is a common symptom, so patients presenting with it should be worked up on a priority basis for early detection and further management.The mean age of menopause in Nepal, as shown by the study done by Rajbhandari et al., has been reported at 48.7 years[8]. The age range of women with history of postmenopausal bleeding in the study done in Pakistan in 2015 ranged from 38 to 80 years, with a mean age of 57.1 ±8.1 years [3]. The mean age of women with postmenopausal bleeding in our study was 51.9±6.6 years, with a range of 41 to 73 years. Our study identified endometrial hyperplasia without atypia as the major cause of postmenopausal bleeding, followed by atrophic endometrium, disordered

proliferative endometrium, endometritis, leiomyoma, adenomyosis, hormonal changes, endometrial polyps, and endometrial carcinoma. In cases of cervical pathology resulting in postmenopausal bleeding, carcinoma of the cervix is the main entity, followed by endocervical polyps and cervical dysplasia. As per the study done by J Karmakar DP, Wilkinson DA, Rathod DM[9] the main causes of postmenopausal bleeding were as follows: atrophic endometrium, endometrial hyperplasia without atypia, proliferative endometrium, secretory endometrium, endometrial hyperplasia with atypia, benign endometrial polyps, tuberculous endometritis, leiomyoma, Endometrial adenocarcinoma, Malignant mixed mullerian tumor, Cervical carcinoma[9]. Tariq MU, Idrees R, Raheem A, and Kayani N conducted a study in Pakistan that included both endometrial and endocervical biopsies and found that not only endometrial but also endocervical pathologies cause postmenopausal bleeding[3].In our study, 48 cervical biopsy specimens were included, which comprised 17.8 % of the total specimens. Benign pathology was observed in the majority (88.5%) of the cases.Endometrial hyperplasia (EH) was observed in 67(24.8%) cases, which was slightly higher than the incidence reported in various studies (5 - 17%)[10-12]. The incidence of EC has ranged from 9-18% in different studies conducted[13-15] Endometrial carcinoma (EC) is the third most common malignancy of females in Pakistan, with peak incidence in sixth and seventh decades. In Tariq MU's study, EC accounted for 15.9% of the reported histological findings, with 20 (80%) being endometrioid type, and the remaining 5 (20%) consisting of two serous adenocarcinomas, two clear cell adenocarcinomas, and one malignant mixed Mullerian tumor (MMMT). In our study, endometrial carcinoma comprised a lower percentage Endometrioid tissue was found in 2.6% of the reported histological findings. The mean age of endometrioid carcinoma was 61.8[3] whereas the mean age of endometrioid carcinoma in our study was 55 years. Statistical significance was not observeddue to small number of endometrial carcinoma cases. Cervical carcinoma occurs at a rate ranging from 2.5 to 25.5 percent in Pakistan. In the present study, carcinoma of the cervix was observed in 8.9% of these cases, of which 21 were squamous cell carcinoma and 3 were adenocarcinoma. 9 cases of cervical dysplasia were also observed. The most frequent gynecologic cancer in countries with extensive resources is endometrial cancer, which also ranks second in countries with poor resources (cervical cancer is more common). The most typical histologic type of uterine malignancy, including endometrial carcinoma, is endometrioid carcinoma. Atrophic endometrium has been the most common cause of PMB worldwide but we surprisingly noted a single case with atrophic endometrium[16]. However, endometrial hyperplasia, followed by atrophic endometrium, was the most frequent cause of postmenopausal bleeding in both the study conducted by Aravazhi M and the current research.

CONCLUSION

A variety of histopathological findings are seen in PMB. Although benign pathologies were more common but the collective proportion of endometrial and cervical malignancies and pre-malignant conditions is considerably higher in this study.

Histologic examination to find correct benign, premalignant and malignant lesions should be emphasized. An accurate diagnosis will guide the clinician towards the appropriate course of action.

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