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Clinical Profile and Characteristics of Patients with Endometrial Hyperplasia

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ABSTRACT
The purpose of this study is to study the clinical profile in endometrial Hyperplasia. This observational study was conducted at Amrita Institute of Medical Sciences, Kochi, Kerala, India, a tertiary care referral center, over a duration of two years from July 2019-2021. Ethical approval was obtained from the institutional ethical committee. The study included 68 women diagnosed with endometrial hyperplasia, all of whom reported to the gynecological outpatient department (OPD) for evaluation of abnormal uterine bleeding. In this study, the mean age of patients with endometrial hyperplasia was 49 years, with 63.7% of cases showing hyperplasia with atypia. Among the study population, 88% were multiparous and the most common presenting complaint was heavy menstrual bleeding, observed in 50% of patients. Diabetes mellitus and hypertension were prevalent comorbidities, affecting 64% of the participants. Ultrasound findings indicated a mean endometrial thickness of 12 mm for hyperplasia with atypia, with adenomyosis and fibroids present in 30% of cases. This study reveals that endometrial hyperplasia predominantly affects women around the age of 49, with abnormal uterine bleeding as the most common presenting symptom. Diabetes mellitus and hypertension are key risk factors, while ultrasound findings show no significant difference in endometrial thickness between hyperplasia types. The high prevalence of adenomyosis and fibroids suggests a need for careful clinical evaluation in these patients.

INTRODUCTION

Endometrial hyperplasia, characterized by excessive proliferation of endometrial glands, occurs at an incidence rate of approximately 133 per 100,000 women annually. It predominantly affects women in their perimenopausal and menopausal years, with a peak incidence between the ages of 45 and 50 years. Atypical endometrial hyperplasia is most commonly observed in women aged 60-64 years, though incidence estimates may be underestimated due to delayed reporting of symptoms[1].

Endometrial cancer, the most prevalent gynecological malignancy in developed countries and the second most common in developing regions, has seen increasing rates due to an aging population and rising obesity. Despite its significance, awareness of endometrial cancer remains low. Endometrial hyperplasia is a precursor to endometrial cancer, and its incidence is about three times higher than that of endometrial cancer. Some atypical forms of hyperplasia are direct precursors to cancer[2].

Currently, there are no routine screening methods for endometrial hyperplasia or related lesions. Diagnosis is typically made during the evaluation of abnormal uterine bleeding. The American Cancer Society has noted that there is insufficient evidence to support routine screening with transvaginal ultrasound or endometrial biopsy in both general and high-risk populations[3].

Endometrial hyperplasia is diagnosed through histopathological analysis, particularly in women presenting with abnormal uterine bleeding such as heavy menstrual bleeding, intermenstrual bleeding, or irregular cycles. It should be suspected in postmenopausal women with bleeding or those on hormone replacement therapy (HRT) presenting with unscheduled bleeding. In perimenopausal women, hyperplasia should be considered if risk factors are present. Additionally, atypical glandular cells detected on cervical smears or during routine screenings for high-risk conditions like Lynch syndrome may indicate endometrial hyperplasia. Evaluation is recommended for all women with postmenopausal bleeding, those over 45 years of age with abnormal uterine bleeding, and younger women with obesity or other risk factors for endometrial cancer[4].

Ultrasound is a valuable tool in evaluating abnormal uterine bleeding and can serve as an alternative to endometrial sampling, particularly in postmenopausal women. However, in perimenopausal women, ultrasound is mainly useful for identifying structural abnormalities, with limited ability to distinguish between normal endometrial thickness and pathological changes. For premenopausal women, there is no specific cutoff for endometrial thickness on ultrasound that necessitates sampling. The Royal College of Obstetricians and Gynaecologists (RCOG) suggests that endometrial hyperplasia can be excluded when endometrial thickness is less than 7 mm in women with polycystic ovary syndrome (PCOS). In symptomatic postmenopausal women, sampling is indicated if endometrial thickness exceeds 4 mm and up to 11 mm for asymptomatic women. For women on HRT or tamoxifen, the threshold is up to 8 mm, with biopsy recommended if thickness is greater than 5 mm [5-6].

Modern imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) are generally not used for diagnosing endometrial hyperplasia but may play a role in pretreatment assessment. CT can occasionally influence management decisions, although its high cost limits routine use. MRI is useful for evaluating myometrial and cervical involvement and monitoring disease progression, especially in cases of atypical hyperplasia undergoing conservative management. However, the current evidence supporting the use of MRI for endometrial hyperplasia is limited and further research is needed to establish its role and effectiveness[5-7].

MATERIALS AND METHODS

Study Design and Setting:

- **Type of Study:** Observational study.
- **Location:** Conducted at Amrita Institute of Medical Sciences, Kochi, Kerala, India, a tertiary care referral center.
- **Ethical Approval:** Obtained from the institutional ethical committee.
- **Duration:** Study was carried out from July 2019-2021.
- **Participants:** A total of 68 women diagnosed with endometrial hyperplasia, who reported to the gynecological outpatient department (OPD) and were evaluated for abnormal uterine bleeding.

Inclusion and Exclusion Criteria:

- **Inclusion Criteria:**
- Women diagnosed with endometrial hyperplasia based on endometrial biopsy.
- Patients planned for hysterectomy, with both biopsy and hysterectomy histopathological analyses conducted at our institute.
- **Exclusion Criteria:**
- Patients diagnosed with endometrial hyperplasia based on endometrial biopsy performed outside our institute.
- Women who were receiving tamoxifen or hormone replacement therapy (HRT).

Methodology:

- **Patient Selection:** Participants included women reporting to the Department of Obstetrics and Gynecology during the study period, who

underwent endometrial sampling for the evaluation of abnormal uterine bleeding.

- **Histopathological Review:**
- Histopathological diagnoses were classified according to the World Health Organization (WHO) criteria into two categories: endometrial hyperplasia with atypia and without atypia.
- **Data Collection:**
- Collected data included patient age, menopausal status, the time interval between endometrial biopsy and hysterectomy, type of endometrial hyperplasia on curettage specimens and the pathological diagnosis at hysterectomy.
- **Pathological Review:** All preoperative and postoperative specimens were reviewed by a single pathologist to ensure consistency.
- **Sample Size:**
- **Calculation Basis:** The sample size was based on a consistency rate of 45% between curettage and hysterectomy specimens, as observed in a previous study.
- **Sample Size:** A minimum of 43 participants was required, considering a 99% confidence level and a 20% allowable error (8).
- Statistical Analysis
- **Software Used:** IBM SPSS version 20 (SPSS Inc., Chicago, USA).
- **Descriptive Statistics:**
- Mean±SD and median (Q1-Q3) for continuous variables.
- Frequency and percentage for categorical variables.
- **Statistical Tests:**
- **Categorical Variables:** Chi-square test with Fisher's exact test to determine statistical significance of differences in proportions.
- **Numerical Variables**:
- Independent sample t-test for parametric data.
- Mann-Whitney U test for non-parametric data.
- **Significance Level:** All tests were two-sided, with a significance level set at $p<0.05$, conducted in an exploratory manner.

RESULTS AND DISCUSSIONS

Objective 2: To Analyze the Clinical and Pathological Characteristics of Patients with Endometrial Hyperplasia:

Demographic Characteristics: Age and Menstrual Status in Endometrial Hyperplasia: The study population had a mean age of 49.87±6.089 years. Patients diagnosed with hyperplasia with atypia had a mean age of 49.20±5.4 years, while those with hyperplasia without atypia had a mean age of 50.95±6.8 years. Although there was a difference in mean age between the two groups, it was not statistically significant (p=0.265).

Regarding menstrual status, the study included 53 perimenopausal and 15 postmenopausal women. Among perimenopausal women, 32 (60.4%) had hyperplasia with atypia and 21 (39.6%) had hyperplasia without atypia. In the postmenopausal group, 9 (60.0%) had hyperplasia with atypia, and 6 (40.0%) had hyperplasia without atypia, with no significant difference between the groups.(Table 1).

Clinical Characteristics: Indications for Hysterectomy in Hyperplasia Without Atypia: In patients diagnosed with hyperplasia without atypia (n=27), the most common indications for hysterectomy were fibroids (37%), followed by adenomyosis (29.6%), a combination of adenomyosis with fibroids (18.5%), and a family history of malignancy (14.8%).

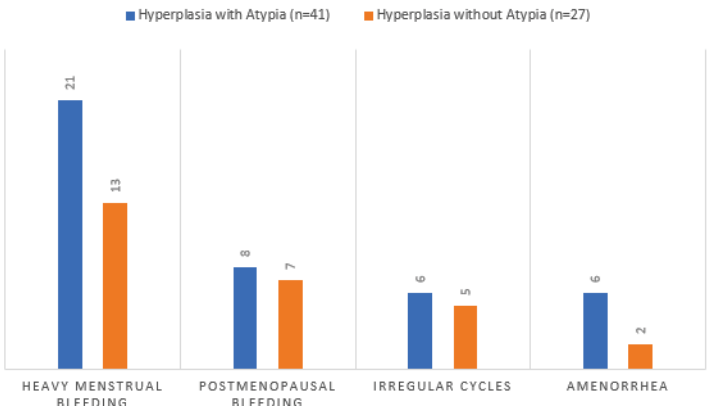
The time interval between endometrial biopsy and hysterectomy was compared between consistent (n=37) and inconsistent (n=31) groups. The consistent group had a mean duration of 1.89±1.468 years with a median of 2.0 years, while the inconsistent group had a slightly longer mean duration of 2.71±2.020 years, also with a median of 2.0 years. This difference was not statistically significant (p=0.060).(Table 2).

Co-Morbidities and Presenting Complaints:

Parity:

The analysis of parity showed that among the 60 multiparous women, 38 (63.3%) had hyperplasia with atypia, and 22 (36.7%) had hyperplasia without atypia. Among the 8 nulliparous women, 3 (37.5%) had hyperplasia with atypia and 5 (62.5%) had hyperplasia without atypia. This difference was not statistically significant (p=0.250).(Table 3).

Co-Morbidities: Co-morbidities such as diabetes mellitus, hypertension and dyslipidemia were evaluated. Although trends were observed, indicating a higher prevalence of certain co-morbidities in one hyperplasia type over the other, none reached statistical significance.(Table 3).



Graph 1: Presting Complaint

Table 1: Comparison of Mean Age and Menstrual Status in Endometrial Hyperplasia

Characteristic	Hyperplasia with Atypia (n=41)	Hyperplasia without Atypia (n=27)	P-Value
Mean Age (years) ± SD	49.20 ± 5.4	50.95 ± 6.8	0.265
Perimenopause	32 (60.4%)	21 (39.6%)	0.979
Postmenopause	9 (60.0%)	6 (40.0%)	

Table 2: Distribution of Indications for Hysterectomy and Time Interval Between Biopsy and Hysterectomy

Indication for Hysterectomy	Frequency (n=27)	Percentage (%)	
Adenomyosis	8	29.6%	
Fibroid	10	37%	
Adenomyosis with Fibroid	5	18.5%	
Family History of Malignancy	4	14.8%	
Time Interval (Years)	**Consistent (n=37)**	**Inconsistent (n=31)**	**P-Value**
Mean ± SD	1.89 ± 1.468	2.71 ± 2.020	0.060
Median (Q1-Q3)	2.0 (1.0-4.0)	2.0 (1.0-2.0)	

Table 3: Association of Parity and Distribution of Presenting Complaints

Parity	Hyperplasia with Atypia (%)	Hyperplasia without Atypia (%)	P-Value
Multipara (n=60)	38 (63.3%)	22 (36.7%)	0.250
Nullipara (n=8)	3 (37.5%)	5 (62.5%)	

Presenting Complaint: The primary presenting complaints were heavy menstrual bleeding, postmenopausal bleeding, irregular cycles and amenorrhea. Heavy menstrual bleeding was the most common complaint, observed in 34 patients, of whom 21(61.8%) had hyperplasia with atypia. Other complaints were distributed relatively evenly between the two hyperplasia types (Graph 1).

The mean age of patients with endometrial hyperplasia in our study was 49±7.3 years, with a slightly younger mean age for hyperplasia with atypia (49±S5.4 years) compared to hyperplasia without atypia (50±6.8 years). This demographic profile is consistent with the findings of Sanderson[9] who noted an increasing incidence of endometrial cancer in women aged 40-44 years, highlighting the shift of endometrial hyperplasia from a predominantly postmenopausal condition to one that is increasingly seen in perimenopausal women .

Most patients in our study were multiparous (88%) and presented with heavy menstrual bleeding (50%) or postmenopausal bleeding (77%). This clinical presentation is typical of endometrial hyperplasia, where abnormal uterine bleeding is the most common symptom. Additionally, 64% of patients had associated comorbidities, with diabetes mellitus and hypertension being the most prevalent. The presence of these comorbidities, particularly in postmenopausal women, is a significant risk factor for the development of endometrial hyperplasia, as noted in other studies.

Ultrasound findings revealed a mean endometrial thickness of 12±4.6 mm for hyperplasia with atypia and 11.9±5 mm for hyperplasia without atypia. Although there was no significant difference in endometrial thickness between the two types of hyperplasia, the presence of adenomyosis and fibroids was more common in our study compared to the literature. For instance, Henderson *et al.* reported an incidence of 6.6% for adenomyosis and 24.3% for fibroids, whereas our study found a prevalence of 30% for each condition. The higher prevalence of these conditions in our study could be due to differences in patient populations or diagnostic criteria.

CONCLUSION

In our study of endometrial hyperplasia, we found that the mean age of patients was 49 years, with a slightly younger age in those with hyperplasia with atypia compared to those without. Despite differences in age and menstrual status between groups, these were not statistically significant. The majority of patients were multiparous and presented with abnormal uterine bleeding, particularly heavy menstrual bleeding and postmenopausal bleeding. Diabetes mellitus and hypertension were identified as significant comorbidities, reinforcing their role as risk factors for endometrial hyperplasia. While ultrasound findings showed similar endometrial thickness between hyperplasia types, adenomyosis and fibroids were more prevalent in our study than reported in previous literature. These findings underscore the importance of considering both demographic and clinical characteristics in the management of endometrial hyperplasia.

Conflict of Interest: Nil.

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