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ORIGINAL ARTICLE

Endometrial Hyperplasia: A Clinicopathological Study in a Tertiary Care Hospital

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Abstract

Objective To evaluate the clinical as well as histomorphologic features in different cases of endometrial hyperplasia along with its relative occurrence.

Materials and Methods A one-and-a-half-year prospective study was conducted on histopathologically diagnosed cases of endometrial hyperplasia in a tertiary care hospital. Apart from relevant clinical findings, histomorphologic details were noted and statistically analyzed.

Observations Maximum number (46.5 %) of endometrial hyperplasia occurred in patients of 41–50 years age group. Majority (55.2 %) of the patients were found to be premenopausal. Menorrhagia was the most common (49.6 %) clinical presentation followed by postmenopausal bleeding (30.8 %). Simple hyperplasia without atypia was the most common type (95.6 %) followed by complex hyperplasia without atypia (3.6 %) and complex hyperplasia with atypia (0.8 %), respectively. The study of gland–stroma ratio revealed 65:35 to be the most frequent (34 %) ratio; variable-sized glands with cystic dilatation (60.4 %) was the commonest gland architecture and most of the cases (99.2 %) showed the absence of atypia. Associated histopathological findings included a case each of endometrial adenocarcinoma and undifferentiated endometrial stromal sarcoma along with the common leiomyoma and progesterone effects.

Conclusion Menorrhagia was the most common presenting complaint in cases of endometrial hyperplasia. The cases were mostly in the premenopausal age group. Simple endometrial hyperplasia without atypia was the commonest type diagnosed histopathologically. Histopathological examination along with clinical details is essential to give the final opinion regarding the diagnosis.

Keywords Endometrium · Hyperplasia · Menorrhagia

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Introduction

Abnormal uterine bleeding is considered to be a common gynecological complaint. The endometrium undergoes cyclical changes by the complex interplay of endogenous

sex steroids and other factors. After excluding organic causes, the remaining so-called dysfunctional uterine bleeding (DUB) is preferably treated medically. Only after the failed trial of appropriate treatment, especially hormonal, hysterectomies are considered. The diagnostic goal in abnormal uterine bleeding is to exclude cancer and to identify the underlying pathology to allow for optimal treatment [1].

Recamier in 1850 first recognized the condition of endometrial hyperplasia. Attempts have been made to define and classify endometrial hyperplasia in many ways since then [2]. The revised WHO classification in 1994 is still being followed now which comprises simple hyperplasia, complex hyperplasia, simple atypical hyperplasia, and complex atypical hyperplasia. Recently, Mutter [3] suggested a new classification of endometrial precursor lesions based on a combination of molecular, morphometric, and morphologic data. They recommended that clonal, noninvasive lesions which lack the histological features diagnostic of adenocarcinoma be classified as endometrial intraepithelial neoplasia, while all of the polyclonal lesions be grouped together simply as hyperplasia.

The probability of progression of endometrial hyperplasia to adenocarcinoma is related to the degree of architectural or cytological atypia. Depending on epidemiology, presentation, and prognosis, there are two fundamentally different pathogenic types of endometrial carcinoma: type I (estrogen related, endometrioid type) and type II (non-estrogen related, non-endometrioid type). Untreated hyperplasia can develop into an endometrioid type of adenocarcinoma; hence, it is important to recognize the precursor lesions. Till date, there are limited studies with respect to the biology of hyperplastic lesions of endometrium documented from India [4].

The present study was conducted to study the clinical profile in cases of endometrial hyperplasia, to study the relative occurrence of endometrial hyperplasia and to evaluate the histomorphologic features of different types of endometrial hyperplasia.

Materials and Methods

The present prospective study was conducted on 250 cases ($n = 250$) in the department of Pathology in association with the department of Gynaecology and Obstetrics in our institution for a study period of 1.5 years (August 1, 2009–January 31, 2011) after taking permission and clearance from the Ethical Committee of the institution and after taking informed consent from the patients. All unequivocally diagnosed cases of endometrial hyperplasia reported from the specimens of endometrial curettage and hysterectomy, received in the department of Pathology for histopathological examination during the study period, were included in the study after conventional tissue processing, standard staining by haematoxylin and eosin (H and E), and examination by light microscopy. Inadequate specimen, improperly processed specimen, and cases with insufficient clinical data and more than one differential diagnoses were excluded from the study. An account of clinical data regarding the age, menstrual history, presenting complaints, and radiological findings were obtained. Histological typing of endometrial hyperplasia was done depending on the criteria used in WHO classification [5]. All cases of endometrial hyperplasia were studied for degree of glandular crowding (gland–stroma ratio), architectural complexity, and cytological atypia. All the accumulated data were analyzed for descriptive statistics.

Subdivision of endometrial hyperplasia cases was based on the degree of glandular complexity and crowding. Thus, a proliferative lesion displaying no evidence of cytologic atypia and minimal to moderate glandular crowding was termed "simple hyperplasia" whereas one with marked glandular crowding and complex glandular architecture was termed "complex hyperplasia." An endometrial proliferation displaying cytologic atypia without back-to back crowding was designated "simple atypical hyperplasia" and one accompanied by marked crowding and complexity was designated "complex atypical hyperplasia" [6].

Results

The present study included 250 cases ($n = 250$) cases of endometrial hyperplasia diagnosed by histopathological examination on endometrial curettage samples and hysterectomy specimens. When the study population was distributed according to age (Fig. 1), maximum frequency (46.4 %, 116 out of 250) was observed in the range of 41–50 years followed by that of 31–40 years (36.4 %, 91

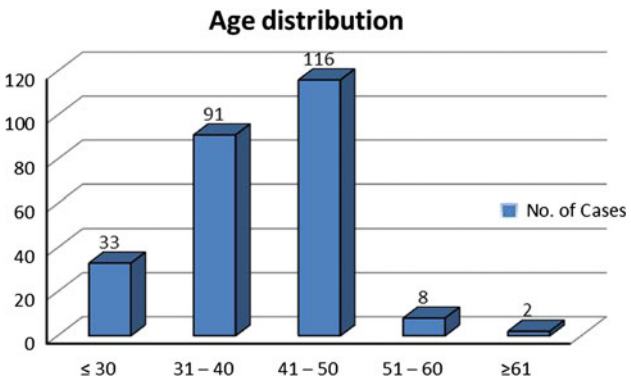

Fig. 1 Age distribution of the study group

out of 250). The most frequent clinical diagnosis was menorrhagia (49.6 %, 124 out of 250). Postmenopausal bleeding came out as the next common complaint (30.8 %, 77 out of 250). Mode of presentation and clinical diagnosis are presented in Table 1. In our study group, 55.2 % patients (138 out of 250) were premenopausal.

The leading pathology was identified as simple endometrial hyperplasia without atypia (95.6 %, 239 out of 250 cases) (Table 2; Fig. 2a). We observed only 9 cases (3.6 %) of complex endometrial hyperplasia without atypia and only 2 cases (0.8 %) of complex atypical endometrial hyperplasia (Fig. 2b). Well differentiated endometrioid adenocarcinoma (Fig. 2c) was associated with one case of complex atypical endometrial hyperplasia.

Distribution of the study population according to gland–stroma ratio, gland architecture, and the presence and extent of cytological atypia are depicted in Tables 3, 4, and 5, respectively.

Among significant pathological findings associated with endometrial hyperplasia, the most frequent lesion observed was leiomyoma (17 cases), followed by progesterone effect (13 cases), endometrial polyp (7 cases) and adenomyosis (7 cases), respectively. In addition, we found two cases of benign granulosa cell tumor of ovary and a case each of endometrial stromal sarcoma and well differentiated endometrial adenocarcinoma.

Table 1 Distribution of the study population depending on mode of presentation and clinical diagnosis

Clinical diagnosis	No. of cases	Percentage (%)
Malignancy	1	0.4
Cervical polyp	2	0.8
Cyst	1	0.4
Endometrial polyp	7	2.8
Fibroid	16	6.4
Menorrhagia	124	49.6
Ovarian cyst	2	0.8
Ovarian mass	2	0.8
Polymenorrhoea	7	2.8
Postmenopausal bleeding	77	30.8
Prolapse	8	3.2
Endometritis	1	0.4
Endometrial hyperplasia	1	0.4
Total	250	100

Table 2 Distribution of the study population according to histological type of endometrial hyperplasia

Histological Type	No. of cases	Percentage (%)
Simple without atypia	239	95.6
Complex without atypia	9	3.6
Simple atypical	0	0
Complex atypical	2	0.8
Total	250	100

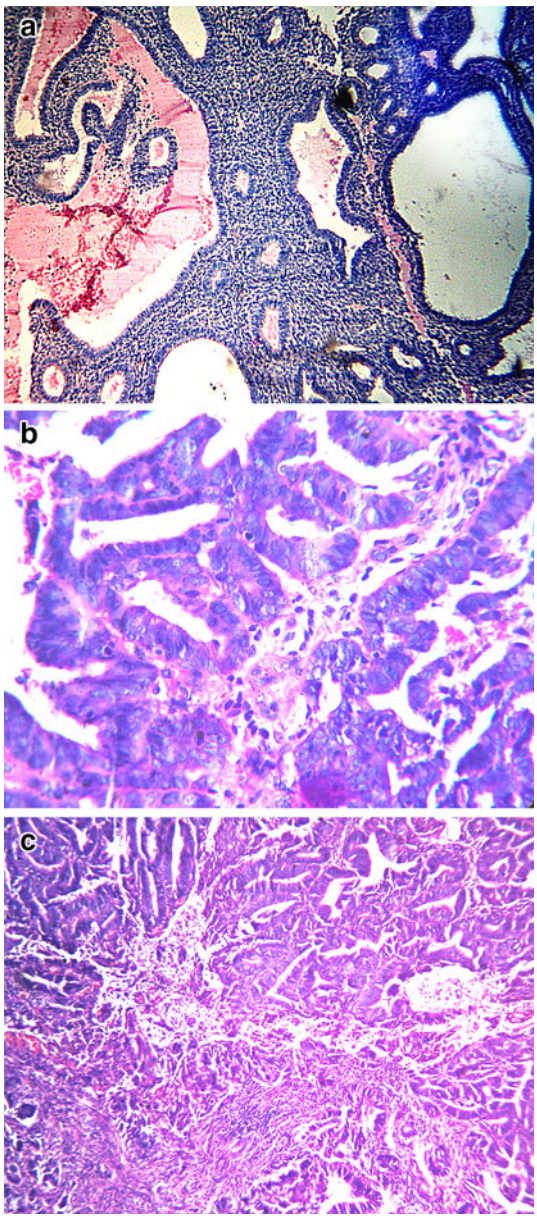

Fig. 2 **a** Photomicrograph of simple endometrial hyperplasia without atypia (H and E, ×100). **b** Photomicrograph showing features of complex endometrial hyperplasia with atypia (H and E, ×400). **c** Photomicrograph of endometrioid adenocarcinoma (H and E, ×100)

Discussion

Muzaffar et al. [7] found that endometrial hyperplasia was one of the leading pathology in women suffering from abnormal uterine bleeding. Their study revealed that

Table 3 Distribution of cases according to gland–stroma ratio

Gland:stroma ratio	No. of cases	Percentage (%)
60:40	77	30.8
65:35	85	34.0
70:30	60	24.0
75:25	17	6.8
80:20	07	2.8
85:15	02	0.8
90:10	02	0.8
Total	250	100

Table 4 Distribution of cases according to gland architecture

Gland architecture	No. of cases	Percentage (%)
Complex with branching	11	4.4
Variable size	28	11.2
Variable size with outpouching	60	24.0
Variable size with cystic dilatation	151	60.4
Total	250	100

Table 5 Distribution of cases according to the presence and extent of atypia

Atypia	No. of cases	Percentage (%)
Absent	248	99.2
Mild	1	0.4
Moderate	1	0.4
Severe	0	0
Total	250	100

24.7 % of such cases were caused by endometrial hyperplasia. They also found that menometrorrhagia was the commonest presenting complaint in endometrial hyperplasia followed by polymenorrhoea. Similarly in our study, 49.6 % patients presented with menorrhagia. Takreem et al. [8] also found out that menorrhagia is the commonest complaint in endometrial hyperplasia (53.3 %). They found that simple hyperplasia was the commonest (66.6 %) which compares favorably with our study. We also found that the commonest age group to be 41–50 years which was previously indicated by Kurman et al. [6] in their study.

The relationship between hyperplasia and carcinoma has been an actively debated subject. Several studies have demonstrated a close relationship of endometrial hyperplasia and carcinoma.

Lacey et al. [9] studied the absolute risk of endometrial carcinoma during 20-year follow-up among women with endometrial hyperplasia cumulative 20-year progression risk among women who remained at risk for at least 1 year was less than 5 % for non-atypical endometrial hyperplasia but was 28 % for atypical hyperplasia.

Rao et al. [4] carried out a retrospective study in Indian population for 16 years to determine the nature and outcome of proliferative lesions of the endometrium. They reviewed histopathological diagnosis of the endometrial hyperplasia, polyp, and carcinoma, on endometrial biopsy and hysterectomy specimens in the follow-up cases. Hyperplasia cases included 59 cases of simple hyperplasia out of 74, 10 cases of complex hyperplasia without atypia, and five cases with atypia. The predominant age range for patients with all types of hyperplasia was 41–50 years. Progression to a higher grade was seen in 8.10 %, regression to a lower grade was seen in 9.45 %, lesions reverted to a normal pattern in 10.81 % cases, and lesions persisted in 70.27 % of the cases. They concluded that predominant persistence of the lesion possibly resulted from a fluctuating but higher level of estrogenic stimulus. Hence, it was not only the high levels of estrogen that influenced the biology, but its sustenance for a prolonged period.

As our study was of a short duration and only 10 patients had complex hyperplasia, follow-up was beyond our scope. Because our study did not include outcomes, we could not define which features were more predictive of risk of carcinoma. We plan to continue our study later including further follow-up.

Kurman et al. [6] carried out an important study with endometrial curettings from 170 patients with all grades of endometrial hyperplasia, who did not undergo a hysterectomy for at least 1 year and who were evaluated from 1 to 26.7 years to correlate the histopathologic features with behavior. The findings in their study provided a rationale for classifying noninvasive endometrial proliferations primarily on the basis of cytologic atypia since this was the most useful criterion in predicting the likelihood of progression to carcinoma. Chamlian and Taylor [10], in a long-term study, found that 14 % adenomatous and atypical hyperplasias subsequently developed into carcinoma. Other studies have reported the highest risks of progression to carcinoma in the atypical hyperplasia group, as well as the highest risk of persistence of the lesion despite hormonal therapy [11].

The WHO [5] describes nuclear rounding, loss of polarity, prominent nucleoli, irregular nuclear membranes, and cleared or dense chromatin as features of cytologic atypia but acknowledges that atypia may be best observed by comparing with the adjacent normal glands. In fact, the WHO specifically states that "definitions of cytologic atypia are difficult to apply in the endometrium because nuclear cytological changes occur frequently in hormonal imbalance, benign regeneration and metaplasia." The endometrial intraepithelial neoplasia (EIN) scheme used by Mutter [3] is more specific, using a volume percent stroma

of less than 55 % (area of glands > stroma), maximum linear dimension of glands exceeding 1 mm, and exclusion of mimics and cancer as the diagnostic criteria for a diagnosis of EIN. The EIN scheme avoids using a descriptive definition of cytologic atypia and instead uses distinct cytology in the architecturally crowded focus that is different from background.

Endometrial hyperplasia regardless of its type must be considered as a warning sign that an endometrium is non-cycling and therefore susceptible to neoplastic events. The mere presence of hyperplasia is not a basis for hysterectomy. However, in general, the more severe the hyperplasia, the more likely it is to be followed by invasive carcinoma. Timely treatment can help us provide an environment for the lesion to regress and avoid radical surgeries. Endometrial hyperplasia without atypia may be treated medically or surgically with simple hysterectomy, while the atypical endometrial hyperplasia requires a meticulous intraoperative assessment of the gross pathology or frozen section, and the endometrial carcinoma requires a more extensive procedure of surgical staging [1, 4].

Several investigators have found beneficial effects from treating hyperplasia and carcinoma with progesterone. Kistner [12] treated patients with atypical hyperplasia and patients with carcinoma in situ with progesterone and found that the lesions were reversible and none advanced.

Conclusion

Endometrial hyperplasia presented most commonly with menorrhagia and in premenopausal age group in the present study. Histopathological examination along with clinical details is essential to give the final opinion regarding the diagnosis. Though frequency of complex atypical endometrial hyperplasia appeared to be very low in the present study while simple hyperplasia without atypia was the commonest type, we recommend further prospective, long-term, multicentric, and large-scale follow-up study along with hormonal assay for a deeper understanding of the precancerous lesions of endometrium.

Conflict of interest The authors declare that they have no conflict of interest.

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