

Histopathological Study of Endometrial Lesions Based on Endometrial Curettage

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Abstract

Background and objectives: To study the histopathological lesions of uterine endometrium based on endometrial curettage and its correlation with hysterectomy findings wherever possible. Also to assess the adequacy of the sample collected with regard to making a diagnosis and to estimate the sensitivity and specificity of endometrial curettage in diagnosing histopathological lesions of endometrium.

Materials and methods: This prospective study included endometrial specimens obtained by D&C from January 2013 to July 2014 in department of pathology, Kannur medical college, Anjarakandy. The specimens were subjected to gross and microscopic examination to arrive at histopathological diagnosis.

Results: A total of 150 cases were analyzed. Histologically, the most common pattern was simple hyperplasia without atypia (29.3%) followed by proliferative phase endometrium (20%). Maximum number of simple hyperplasia was seen in the 40-50 years of age. Out of 150 cases, 2.7% of cases had endometrioid adenocarcinoma. Endometrial curettage

was found highly accurate in diagnosing endometrial carcinoma. Sensitivity of endometrial curettage was found to be 75% whereas specificity and negative predictive value was found to be 96.15% each. Positive predictive value was found to be 75%. In 3.3% cases samples were insufficient with regard to making a diagnosis.

Conclusion: Histopathological examination of endometrial biopsies shows a wide spectrum of changes ranging from normal endometrium in various hormonal cycles to malignancy. Dilatation and curettage of endometrium has relatively same diagnostic accuracy as that of endometrium obtained from hysterectomy except for precancerous lesions and malignancy, where the detection rate was slightly low.

Keywords: Endometrial Dilation and Curettage, Hysterectomy, Endometrium, Endometrioid Adenocarcinoma.

Introduction

Endometrium is constantly engaged in the dynamics of shedding and re-growth during active reproductive life. It is controlled by the rise and fall of pituitary and ovarian

hormones. This control is executed by proper timing of hormonal release in both absolute and relative amounts. Alteration in this fine-tuning mechanism may result in a spectrum of disturbances. Endometrial cycle in women follows a series of morphologic and physiologic events characterized by proliferation, secretory differentiation, degeneration and regeneration of uterine lining. [1] An understanding of the varieties in the normal morphological appearance of the endometrium provides an essential background for the evaluation of endometrial pathology. Endometrial carcinoma is the most common invasive cancer of the female genital tract. [2] It is a biologically and histologically diverse group of neoplasms characterized by a dualistic model of pathogenesis. [3] Abnormal uterine bleeding may be the common presenting complaint in patients with pre-malignant or malignant endometrial lesions. Endometrial biopsy or curettage could be a safe and effective diagnostic step in evaluation of abnormal uterine bleeding after ruling out medical causes. It is the most commonly employed endometrial sampling techniques. Curettage is, in essence, an excisional biopsy of the endometrium. [4, 5] Endometrial curettage is a powerful test for the detection of a wide variety of endometrial lesions ranging from inflammatory changes to infectious organisms and atypia. An initial diagnosis of carcinoma can be made on such specimens. [2] Thus, the technique is now considered as the first line diagnostic tool because of its diagnostic accuracy, safety, quickness and convenience. [6]

Materials And Methods

The present study was undertaken at the department of pathology, Kannur Medical College, Kannur, Kerala; from January 2013 to July 2014.

Source of Data: Patients admitted or managed in Obstetrics and Gynecology department, Kannur Medical

College, Anjarakandy, Kannur. All patients with endometrial biopsy obtained by D&C were included in the study. A total of 150 patients fulfilling the inclusion criteria were selected for the study. Out of 150 patients, 33 patients had subsequent hysterectomy and all these cases were studied for finding the accuracy of EC on endometrial biopsy.

Inclusion Criteria

1. Patients who were willing to enroll in the study.
2. All females in the reproductive age and postmenopausal women
3. All cases in which endometrial curetting were further followed by hysterectomy.

Exclusion Criteria

1. Pre-pubertal age group
2. Patient with hemorrhagic disorders and leukemia.
3. Patients with bleeding associated with pregnancy
4. Patients who underwent dilatation and curettage as a part of medical termination of pregnancy.

Study Design

After obtaining written consent, a detailed history and clinical examination were done including history of menstrual irregularities, date of last menstrual period, parity index, history of drug intake including hormones, and relevant past history. Endometrial curettage samples preserved in 10% formal saline were received in the Department of Pathology, Kannur Medical College from Obstetrics and Gynecology department, Kannur Medical College. Subsequent hysterectomy specimens of the same patient were also received in laboratory in 10% formal saline. Endometrial biopsy and hysterectomy samples were taken, processed and stained. Histopathological study was undertaken on formalin fixed specimens. The results were expressed as histopathological diagnosis with respect to the frequency of various lesions, age distribution, parity, menopausal status and its correlation

with histopathological findings of hysterectomy wherever possible. All data was recorded in a carefully structured preform and data was statistically analyzed by SPSS (Statistical Package for Social Sciences) method.

Statistical Method Applied

Following statistical method were applied in the present study.

- Cross tabs procedure
- Descriptive statistics
- Sensitivity
- Specificity
- Positive predictive value
- Negative predictive value

Crosstabs Procedure

The cross tabs procedure forms two-way and multiway tables and provides a variety of tests and measures of association for two-way tables. The structure of the table and whether categories are ordered determine what test or measure to use. Crosstabs statistics and measures of association are computed for two-way tables only.

Descriptive Statistics

This provides summary, information about the distribution, variability, and central tendency of a variable.

Sensitivity

Sensitivity = True positive/ (True positive + false negative)

Specificity

Specificity = True negative/ (True negative + false positive)

Positive Predictive Value

Positive predictive value = True positive/ (True positive + false positive)

Negative Predictive Value

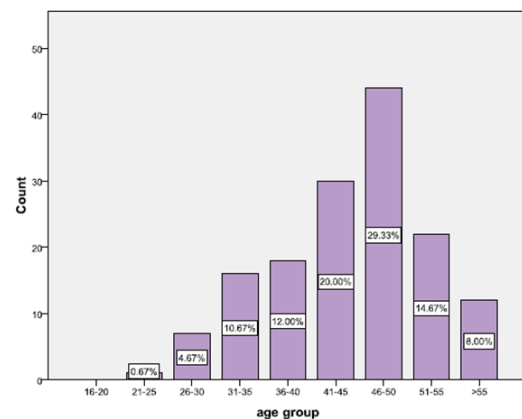
Negative predictive value = True negative/ (True negative + false negative)

Results

In this study, spanning from January 2013 – July 2014; 150 cases of endometrial curetting's from the department of Obstetrics and Gynecology, Kannur Medical College, Anjarakandy, Kannur was included in the study. Out of these, 33 patient's curettage samples were followed up with hysterectomy and these cases were correlated with EC findings. 150 cases of endometrial samples were analyzed in the following ways (table 1):

Among the various endometrial lesions, non-organic endometrial lesions (proliferative phase endometrium, secretory phase endometrium, atrophic endometrium and disordered proliferative endometrium) had an incidence of 54% (81 cases), benign causes (chronic endometritis, endometrial polyp, endometrial hyperplasia) had an incidence of 40% (60 cases) and malignancy (endometrial carcinoma) had an incidence of 2.7% (4 cases) (table 2). The malignant causes were (2.7%) of adenocarcinoma. No cause was found in 3.3% (5 cases) as the material received was not representative of the lesion in the endometrium.

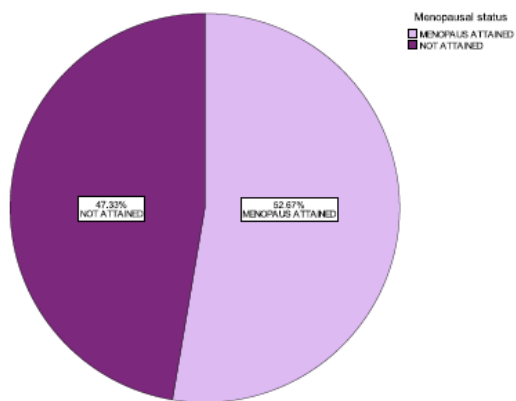
Graph 1: Distribution of 150 Cases of EC According To Various Age Group



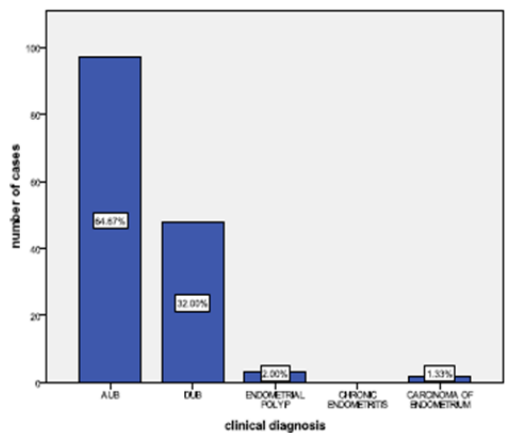
Majority of cases (135 cases) were seen in the parity range of 1-3. Out of which 40 patients had simple hyperplasia, 29 had proliferative phase, 19 had secretory phase, 08 had atrophic phase, 04 had chronic

endometritis, 05 had complex hyperplasia, 01 had complex hyperplasia with atypia, 06 had endometrial polyp, 16 had disordered proliferative endometrium and 04 had endometrial adenocarcinoma. Four (04) cases were inadequate, hence no diagnosis were made. In the parity range of 4-6; there were 14 cases. Majority had simple hyperplasia 04 cases. 03 cases each had endometrial atrophy and disordered proliferative endometrium, 01 each had complex hyperplasia, proliferative endometrium and secretory endometrium. 01 case was inadequate for the diagnosis. There was 1 nulliparous woman with a case of malignancy (table 3)

Graph 2: Distribution of Cases According to Menopausal Status

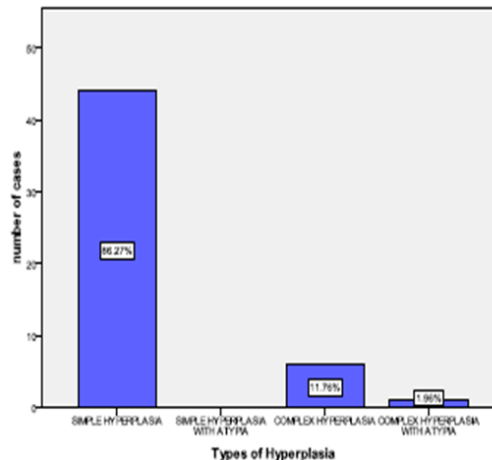


Graph 3: Distribution of Cases According to Clinical Diagnosis

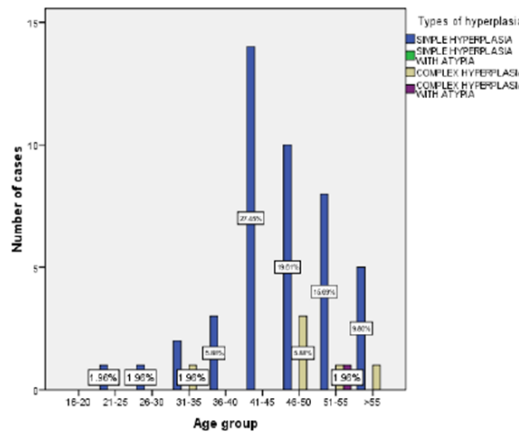


Out of 150 cases, majority of the patients, 97 cases (64.7%) presented with AUB followed by 48(32%) cases of DUB, 3 (2%) cases of endometrial polyp and 02 (1.3%) cases of endometrial carcinoma.

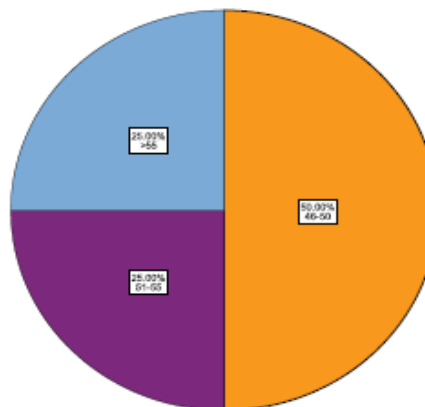
Graph 4: Types of Hyperplasia



Graph 5: Age Distribution of Endometrial Hyperplasias



Graph 6: Age Incidence of Endometrial carcinoma



The incidence of endometrial carcinoma in this study was 2.7% (4 out of 150 cases). It was higher in the age group of 46-50 years, 02 cases (50%). 1 case (25%) of endometrial carcinoma was also seen in the age group of 51-55 years and >55 years. Of 150 patients with endometrial curettage, 33 patients had hysterectomy (table 4). Out of which, 12 cases (36.4%) of proliferative phase, 04 cases (12.1%) of secretory phase, 02 cases (6.1%) of atrophic phase, 04 case (12.1%) of simple hyperplasia, 05 cases (15.1%) complex hyperplasia, 02 case (6.1%) of disordered proliferative endometrium, 04 cases (12.1%) of endometrioid endometrial adenocarcinoma were seen.

Table 5 shows diagnostic accuracy of D&C for detection of histopathological lesions of endometrium by correlating with hysterectomy specimen. Regarding proliferative phase, D&C showed 77.77% sensitivity, 100% specificity and positive predictive value and 91.30% negative predictive value. Secretory phase showed 100% sensitivity, specificity, positive and negative predictive value. Atrophic phase had 100% sensitivity, 96.42% specificity and 66.66% positive predictive value and 100% negative predictive value. Considering hyperplasia, simple hyperplasia had 75% sensitivity, 88.46% specificity and 50% positive predictive value and 95.83% negative predictive value. Complex hyperplasia showed 60% sensitivity, 96% specificity and 75% positive predictive value and 92.30% negative predictive value. Like secretory phase, disordered proliferative endometrium also showed 100% sensitivity, specificity, positive and negative predictive value. This might be due to less number of cases for correlation and hormonal treatment. For detection of endometrial carcinoma D&C showed 75% sensitivity, 96.15% specificity and 75% positive predictive value and 96.15% negative predictive value.

Discussion

Dilatation and curettage (D&C) has been widely considered to be the method of choice for obtaining endometrial samples for histopathological evaluation.[7] Endometrial curettage for the evaluation of abnormal uterine bleeding, dysfunctional uterine bleeding, or other related symptoms and the diagnosis of endometrial hyperplasia, carcinoma and other indications remains one of the most commonly performed gynecological procedures. In present study, the histopathological diagnosis established on endometrial biopsy was evaluated and correlated with that found on hysterectomy wherever possible. Microscopic study of the endometrial specimen is imperative for proper diagnosis and therapy of benign as well as malignant lesions. [8] In women of any age group especially at childbearing age, who presented with abnormal bleeding per vagina, detail history, thorough physical examination (systemic and gynecological), and appropriate investigations are main the tool to rule out causes such as pregnancy and pregnancy related disorders, medications, iatrogenic causes, systemic conditions, and obvious genital tract pathology. However in women of childbearing age who are at increased risk for endometrial cancer (obese, diabetic, with menstrual cycle irregularity, and diagnosed to have polycystic ovarian disease) the evaluation should include endometrial biopsy; or diagnostic hysteroscopy if initial evaluation is inconclusive. A women at post-menopausal age presented with abnormal uterine bleeding must be offered endometrial biopsy. The main aim of endometrial biopsy is not only to identify cause of abnormal uterine bleeding, but also to exclude malignancy. The most common histopathological finding in the present study was endometrial hyperplasia (34%). Among the hyperplasia simple hyperplasia was seen in 29.3%, complex hyperplasia without atypia in 4% cases

and complex hyperplasia with atypia was seen in 0.7% cases. There was no case of simple hyperplasia with atypia. In a study done by Khare et al in 2012 also showed similar findings [9] Endometrial hyperplasia is a precursor of endometrial cancer.[10] The classification system used by the World Health Organization (WHO) designates four different types of hyperplasias with varying malignant potential. Hyperplasias are classified as simple or complex based on the presence or absence of architectural abnormalities such as glandular complexity and crowding. Hyperplasias are further designated as atypical if they demonstrate nuclear atypia.[11, 12] Gredmark et al (1995)[13] studied D&C specimens of 457 postmenopausal women and showed atrophy in 50% of cases, varying degrees of hyperplasia in 10 % of cases and adenocarcinoma in 8% of cases. In present study the most common finding in postmenopausal women was simple hyperplasia in 24 cases (30.4%). Atrophic endometrium and disordered proliferative endometrium were other frequent causes. This discrepancy might be due to small sample size of the present study. Dangal G (2003) [14] studied 84 patients of more than 45 years of age who presented with DUB. Out of 84 majority were in the post-menopausal age (45 cases) followed by perimenopausal age (39 cases). In the postmenopausal group, atrophic endometrium was the most common finding (64.4%) followed by endometrial carcinoma (17.7%), but in the present study, most common finding in postmenopausal women was simple hyperplasia. Among perimenopausal women the findings were, proliferative endometrium (38.5%), secretory endometrium and endometrial hyperplasia (23% each), endocervical carcinoma and endometrial adenofibroma (7.7% each), while in the present study, simple hyperplasia was the most frequent finding (32.4%) followed by proliferative endometrium (16.2%) in the

perimenopausal age group(41-50 years).It might be because in this age group , menstrual cycles often become irregular due to decreased number of follicles and their increased resistance to gonadotropic stimulation, resulting in low level of estrogen, which cannot keep the normal endometrium growing.[9] Muzaffar et al (2005)[15] studied endometrial curetting in 260 patients with DUB. Among these 48% patients were seen in the age group of 41-50 yrs. Most common lesions seen were endometrial hyperplasia (24.7%) followed by chronic non-specific endometritis (13%). Present study also showed similar findings in case of hyperplasia (36.5%) in this age group. The incidence of endometrial hyperplasia without and with atypia peaks in the early 50s and early 60s respectively [16]. Next predominant lesion in this age group was disordered proliferative endometrium (18.9%). Abdullah & Bondagji (2011) [17] analyzed 2295 endometrial samples from women presenting with abnormal uterine bleeding from January 1995 to June 2008 and noted that commonest histopathological diagnosis was secretory endometrium in 571 cases(24.9%), followed by proliferative endometrium in 498 (21.7%), endometrial polyp in 227 (9.9%),disordered proliferative endometrium in 200 (8.7%), simple cystic hyperplasia in 160 (7%), chronic endometritis in 134 (5.8%), inactive endometrium in 126 (5.5%), atrophic endometrium in 70 (3.1%), uterine malignancies in 41 (1.8%), complex hyperplasia without atypia in 33 cases (1.4%) and finally complex hyperplasia with atypia in 15 (0.7%) cases. Two hundred twenty (9.6%) samples did not contain endometrial tissue and were considered insufficient for diagnosis. Uterine malignancies and complex hyperplasia with atypia were more common in the age group of 52 years and older, and were seen in 3.3% and 1.2% respectively. In the present study, it was observed that

more number of simple hyperplasia (29.3%) and complex hyperplasia without atypia (4%) were noticed. But uterine malignancy is slightly less (2.7%) compared to this study. But the other histopathological lesions were comparatively similar. In present study, number of cases with insufficient sample was only 3.3%. Baral & Pudasaini (2011) [18] analysed D& C specimens of 300 women and concluded that in patients less than 40 years of age, most frequent finding were normal endometrium (50%). In the age group between 40-55 years, abnormal physiological changes (32%) and in patients above 55 years, malignancy was most the common observations. There were 36% unsatisfactory samples in postmenopausal (above 55) age group. Khan S et al (2011) [19] studied D& C specimens of 500 women presented with AUB and noted that the most common pathological pattern identified was proliferative phase endometrium (46.4%). Secretary phase endometrium was second most common pathology (37.6%). Cystic (5.2%), adenomatous (3.8%), and atypical (3.6%) hyperplasia constituted 12.6% of bulk. In 1.4%, endometritis was identified as a cause of abnormal uterine bleeding followed by atrophic endometrium (1%). Polyp was identified in 0.6% of cases followed by endometrial carcinoma (0.4%). Bhatta S et al (2012)[20] studied 122 patients over 15 years of age with clinical diagnosis of AUB during one year period from June 2004 to May 2005 and showed proliferative phase (26.23%), simple hyperplasia without atypia (18.03%), secretory phase (16.39%), atrophic endometrium (7.38%), disordered proliferative (6.56%), chronic endometritis (6.56%), carcinoma(5.74%),irregular (4.10%), polyp (2.46%) and finally unsatisfactory (6.56%).

Atrophic endometrium

In present study there were 11 cases (7.3%) of atrophic endometrium. These findings were relatively similar to a

study done by Usha GD et al. (5.8%). [21]In women with postmenopausal age the finding is compatible with atrophic endometrium. Atrophy of endometrium usually occurs as a consequence of the prolonged absence of endogenous or exogenous estrogenic stimulation. The thin atrophic endometrium is susceptible to minor injury and these may be responsible for postmenopausal bleeding even in the absence of an identifiable lesion. Superficial large, dilated venules are situated under a thin endometrium which may rupture to cause excessive uterine bleeding. [22]

Endometrial carcinoma

In the present study, incidence of endometrial carcinoma was 2.7% (4cases) and all patients were above the age of 45. The cases were mainly endometrioid adenocarcinoma and not a single case of serous adenocarcinoma or clear cell carcinoma. It is same as that reported by Abdullah & Bondagji. [17] In others report it was 0.4% [19] and 5.74%. [20] While these were comparatively higher percentage according to study given by Dangal G (17.6%)[14] and Khare A et al (16.7%).[9]

Unsatisfactory for evaluation

There have been very little publications about the criteria for considering an endometrial specimen as adequate or inadequate. [18] Inadequate samples are reported when no specimen is obtained or the quality or tissue yield of a sample is insufficient for adequate assessment. The present study showed an inadequacy rate of 3.3%. (5cases) Most of these cases showed scanty glands or stroma and large areas of hemorrhage. These were labeled unsatisfactory to report and the clinician was advised to repeat biopsy, if clinically indicated. The rate of inadequacy in the present study is lower than the figures previously reported. [20, 7, 17, 18, 23]

Diagnostic accuracy of the procedure

In the present study, hyperplasia of the endometrium was detected in 51 cases (34%) with the help of endometrial biopsy. Among these 29.3% of simple hyperplasia, 4% complex hyperplasia and 0.7% of complex hyperplasia were seen. Simple hyperplasia showed 75% sensitivity and 88.4% specificity. But Complex hyperplasia showed more specificity (96%) and less sensitivity (60 %). These discrepancy may be due to difference in the number of cases. A study done by Sadia A et al [6] showed 87.5% sensitivity and 82.3% specificity for detection of endometrial hyperplasia with the help of endometrial biopsy. In another study comparing Uterine Explora Device with Conventional Dilatation and Curettage showed higher rate of detection for conventional D&C (68.5%).[7] Disordered proliferative pattern lies at one end of the spectrum of proliferative lesions of the endometrium that includes carcinoma at the other end with intervening stages of hyperplasia.[5] It is an amplification of the normal proliferative phase without noteworthy increase in the overall gland to stroma ratio. [6] Considering disordered proliferative endometrium the present study revealed 100% sensitivity and specificity of endometrial biopsy in picking up the disease. These results were due to the fact that only few cases of disordered proliferative endometrium were included in the study. Normal physiological phases such as proliferative, secretory and atrophic menstrual pattern also showed high detection rate. These were 77.77% and 100%, 100%, 100% and 96.42% sensitivity and specificity respectively. These results are in accordance with the study conducted by Arafah MA et al.[7] In studies comparing endometrial biopsies to hysterectomy specimens, endometrial biopsy had sensitivity ranging 83-96% for recognition of endometrial carcinoma.[24,25] Among diagnostic methods used in patients for detection

of endometrial carcinoma, endometrial biopsy or fractional curettage is considered as a gold standard procedure in preoperative management. [26] In present study there were 4 cases (2.7%) of endometrial carcinoma, out of which 3 cases were later confirmed on hysterectomy. These were found to be 75% sensitive and 96.15% specific. While these were 33 % sensitive and 100% specific according to Sadia A et al. [6] In a study conducted by Clark et al. [27] showed 95% positive predictive value of endometrial biopsy in diagnosing endometrial carcinoma which is comparatively higher compared to present study (75%). In another study by Greiver M found 97.5% sensitivity for detection of endometrial carcinoma by endometrial biopsy (Pipelle).[28] The slight discrepancy might be due to the fact that in our set up patients usually present at advanced stage of the disease. But in developed countries, patients usually present at an earlier stage and will have better screening and diagnostic facilities.

Conclusion

Abnormal bleeding from the female genital tract should have prompt evaluation with endometrial sampling. It is an alarming symptom and needs thorough evaluation as it could be the only clinical manifestation of endometrial cancer. Histopathological examination of EC tissue in patients with reproductive age and postmenopausal age shows a wide spectrum of changes ranging from normal physiological phase to malignancy. However, frequency of occurrence is quite variable with regard to age, parity and menopausal status. Dilatation and curettage of endometrium has relatively same diagnostic accuracy as that of endometrium obtained from hysterectomy in non-organic lesions. However, in precancerous lesions and malignancy the detection rate was slightly low. Therefore, in conclusion dilatation and curettage is useful

for diagnosis, to assess therapeutic response and to know the pathological incidence of organic lesions in cases of abnormal uterine bleeding prior to surgery.

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Legend Tables

Table 1: Histopathological Patterns of Endometrium Based on Endometrial Curettage

Endometrial lesions	No. of cases	Percentage
Proliferative phase	30	20.0
Secretory phase	20	13.3
Atrophic phase	11	7.3
Chronic endometritis	4	2.7
Simple hyperplasia	44	29.3
Complex hyperplasia	6	4.0
Complex hyperplasia with atypia	1	0.7
Endometrial polyp	6	4.0
Disordered proliferative endometrium	19	12.7
Endometrioid endometrial adenocarcinoma	4	2.7
Inadequate	5	3.3
Total	150	100.0

Table 2: Distribution of 150 Cases of EC According To Nature of Lesion

Nature of lesion	No. of cases	Percentage
Benign	60	40.0
Malignant	4	2.7
Non organic	81	54.0
No cause found	5	3.3
Total	150	100.0

Table 3: Relation of Parity to Endometrial Lesions

Endometrial lesions	PARITY			Total
	Nulliparous	Multiparous (1-3)	Grand multiparous (4-6)	
Proliferative phase	0	29	1	30
Secretory phase	0	19	1	20
Atrophic phase	0	8	3	11
Chronic endometritis	0	4	0	4
Simple hyperplasia	0	40	4	44
Complex hyperplasia	0	5	1	6
Complex hyperplasia with atypia	0	1	0	1
Endometrial polyp	0	6	0	6
Disordered proliferative endometrium	0	16	3	19
Endometrioid endometrial adenocarcinoma	1	3	0	4
Inadequate	0	4	1	5
Total	1	135	14	150

Table 4: Comparison of EC Diagnosis with Hysterectomy Findings

Endometrial lesion	EC (n)	Percentage	Hysterectomy(n)	Percentage
Proliferative phase	7	21.2	12	36.4
Secretory phase	4	12.1	4	12.1
Atrophic phase	3	9.1	2	6.1
Simple hyperplasia	6	18.2	4	12.1
Complex hyperplasia	4	12.1	5	15.1
Disordered proliferative endometrium	2	6.1	2	6.1
Endometrioid endometrial adenocarcinoma	4	12.1	4	12.1
Inadequate	3	9.1	0	0
Total	33	100.0	33	100

Table 5: Diagnostic Accuracy of Endometrial curettage

Endometrial lesion	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Proliferative phase	77.77%	100%	100%	91.30%
Secretory phase	100%	100%	100%	100%
Atrophic phase	100%	96.42%	66.66%	100%
Simple hyperplasia	75%	88.46%	50%	95.83%
Complex hyperplasia	60%	96%	75%	92.30%
Disordered proliferative endometrium	100%	100%	100%	100%
Endometrial carcinoma	75%	96.15%	75%	96.15%