

Endometrial Hyperplasia: a 5 - Years Retrospective Study

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Abstract

Background: The 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. Alterations in the fine tuning mechanism may result in a spectrum of disturbances and Endometrial Hyperplasia is most important among them.

Objective: To study the histopathology of endometrial hyperplasia

Methods: The present retrospective study on Endometrial Hyperplasia was undertaken over a period of 5 years. Specimens for the study consisted of Endometrial curetting, fractional Curettage and Hysterectomy specimen with history of abnormal uterine bleeding sent for histopathology examination to the pathology department from Gynecology department. The specimen was received in 10% formation. After adequate fixation bits were taken for tissue processing and H&E staining. Wherever necessary, special stain such as reticulin staining, and PAS were done.

Results: Incidence of Endometrial Hyperplasia found to be more in the 4th decade of life followed by 3rd decade. Majority of the Patients with endometrial Hyperplasia are of para 1. Simple Hyperplasia was most common in 788 (86.21%).

Conclusion: Among the cases of endometrial hyperplasia, simple hyperplasia was the commonest lesion found followed by complex hyperplasia. Most cases were seen in 4th decade.

Key words: Endometrial hyperplasia, Lesion, cases

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Introduction

The 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. Alterations in the fine tuning mechanism may result in a spectrum of disturbances and Endometrial Hyperplasia is most important among them.¹

Endometrial Hyperplasia is defined as abnormal proliferation of Endometrium under the influence of prolonged estrogen stimulation unopposed by progesterone. Endometrial Hyperplasia exhibits a spectrum of architectural and cytological abnormalities ranging from disordered proliferative endometrium (an ovulatory cycles) to proliferation so complex and atypical it resembles well differentiated adenocarcinoma of Endometrium.²

Endometrial Hyperplasia has gained importance because of its relationship with endometrial Carcinoma.

Various studies proved that the different types of Endometrial Hyperplasia have got variable incidence in the progression to carcinoma.³

Progression from Hyperplasia to carcinoma occurs in less than 5% of patients with hyperplasia without cytological atypia, 5 to 15 with complex hyperplasia without atypia and 30% or more with Atypical Hyperplasia.³

Relationship between Endometrial Hyperplasia and cancer was first suspected in 1900 by Cullen and Taylor in 1932.⁴ Endometrial Hyperplasia has been the subject or investigation, discussion and controversies. The stumbling block towards the acceptance of these transitional lesions are, first, they have been generally categorised as hyperplasia which often denotes a benign status. Secondly more convincing data may be necessary to illustrate the prospective progression of the defined lesions towards malignancy.⁵

Materials and Methods

The present study included retrospective study from January 2009 to 2014 September on Endometrial Hyperplasia undertaken in the Department of Pathology, over a period of 5 years.

Specimens for the study consisted of Endometrial curetting, fractional Curettage and Hysterectomy specimen with history of abnormal uterine bleeding sent for histopathology examination to the pathology department from Gynecology department.

Relevant clinical history was recorded in proforma from patients. The specimen was received in 10%

formation. After adequate fixation bits were taken for tissue processing and H&E staining. Wherever necessary, special stain such as reticulin staining, and PAS were done.

Prior consent was taken from the patient & there attenders for the study. Ethical approval was taken from the college ethical committee with permission of the dean.

Hematoxylin – Eosin stain

Procedure

Deparaffinize the fresh section by heating to 56°C.
Clear with xylene two changes 10 minutes each.
Dehydrate by change in alcohol 1 minute each.
Rinse with distilled water.
Transfer the section to Ehrlich's hematoxylin.
Wash with distilled water – 2 minutes.
Differentiate in 1% acid alcohol – 30 seconds.
Transfer to running tap water for blueing.
Transfer to 1% eosin yellow – 30 seconds.
Wash with distilled water.
Dehydrate with 95% alcohol.
Clean in Xylene and mount with D.P.X

Result

Nucleus - Purple
Cytoplasm - Pink

PAS stain

Procedure

Deparaffinize & hydrate to Dist. H₂O.
1% periodic acid for 10 minutes
Wash with distilled water for 10 minutes
Schiff's reagent 20-30 minutes
Transfer to running water for minutes.

Counter stain with Harris Hematoxylin – 10 minutes.
Wash with water for 10 minutes.
Dehydrate in 95% alcohol – absolute alcohol.
Mount with DPX

Result

Positive reaction – rose to purple red.
Nuclei - Blue
Fungi - Red
Background - Pale green

Results

The present study of Endometrial Hyperplasia is done in the Department of Pathology, Dr. V. R. K. Women's Medical College in Collaboration with Department of Gynecology.

The study period is 5 years which include retrospective study (January 2009 to 2014 September).

The total number of cases studied is 1589. The nature of specimen analysed are endometrial curetting, Hysterectomy and fractional specimen with history of abnormal uterine bleeding. All specimens are collected from the Department of Gynecology and Obstetrics. The collected specimens are allowed to fixed in formalin for 24 hrs processed and stained with Hematoxylin & Eosin. Special stains like PAS, Reticulin, wherever required are done.

Analysis of 1589 cases revealed 914 case of Endometrial Hyperplasia. They are classified according to WHO classification 1994. Type of Specimen: 914 cases analysed in the present study among which D&C specimen are 630 & 258 specimens are of total abdominal Hysterectomy. 26 cases of fractional curettage are analysed. (Shown in Table 1)

Table 1: Specimen Studied

Year	D&C	TAH	F&C	Total
1999	131	29	02	162
2000	75	37	05	117
2001	129	63	07	199
2002	167	82	05	254
2003	128	47	07	182
Total	630	258	26	914
Percentage	68.93	28.22	2.84	

D&C – Dilation and Curettage, TAH – Total Abdominal Hysterectomy, F&C Fractional & Curettage

Table 2: Age Distribution in Patients with Endometrial Hyperplasia

Years of study	Age of Patients				Total
	21-30 yrs	31-40 yrs	41-50 yrs	51-60 yrs	
1999	15	60	85	02	162
2000	19	40	52	06	117
2001	21	64	101	13	199
2002	47	89	95	13	254
2003	14	65	88	23	182
Total	116	318	421	59	914
Percentage	12.69%	34.79%	46.06%	6.46%	

Incidence of Endometrial Hyperplasia found to be more in the 4th decade of life followed by 3rd decade. All the 914 cases are married females. Among them 131 cases are nulliparous 405 cases are having only one child. 226 cases are with 2 children, 130 cases are with 3 children and 42 cases are having 4 children (Table 3)

Table 3: Parity in 914 cases of endometrial hyperplasia

Year of Study	Parity of the Patients					Total
	0	1	2	3	4	
1999	13	85	38	21	05	162
2000	21	9	25	17	05	117
2001	17	107	45	20	10	199
2002	27	93	70	51	13	254
2003	33	71	48	20	09	182
Total	111	405	226	130	42	914
Percentage	12.14%	44.31%	24.75%	14.22%	4.60%	

Majority of the Patients with endometrial Hyperplasia are of para 1.

Table 4: Analysis of cases of Endometrial Hyperplasia

Years	Total	Types of Endometrial Hyperplasia			
		Simple Hyperplasia	Complex Hyperplasia	Simple Hyperplasia with Atypia	Complex Hyperplasia with Atypia
1999	162	142	13	4	3
2000	117	89	20	3	5
2001	199	165	26	2	6
2002	254	232	15	2	5
2003	182	160	12	3	7
Total	914	788	86	14	26
Percentage		86.21%	9.41%	1.53%	2.84%

Simple Hyperplasia	788	(86.21%)
Complex Hyperplasia	86	(9.41%)
Simple Hyperplasia with Atypia	14	(1.53%)
Complex Hyperplasia with Atypia	26	(2.84%)

1589 cases with history of abnormal uterine bleeding are analyzed from January 1999 to December 2003. 914 cases of Endometrial Hyperplasia are documented. Remaining 675 cases constitute normal endometrium.

Table 5: Total Number 1589 cases studied (1999 January-December 2003)

Endometrial Hyperplasia	914
Proliferative Phase	517
Secretary Phase	95
Hormonal Effects	31
Endometrial Polyp	02
Senile Cystic Atrophy	12
Irregular Shedding	05
Menstrual Phase (Shedding Phase)	13
Total	1589

The following special stains are undertaken in the cases of endometrial hyperplasia with factors of cellular atypia.

1. Periods Acid Schiff's stain
2. Reticulin stain

Analysis of special stain in Atypical Endometrial Hyperplasia shown below

Special Stain: In the present study 87 cases of complex hyperplasia are documented and in 26 cases of complex hyperplasia with Atypia periodic Acid Schiff's – staining are done.

Complex Hyperplasia revealed variable PAS positivity complex Hyperplasia with Atypia revealed PAS negativity for PAS staining.

Reticulin Staining: Revealed staining of basement membrane all around the glandular epithelial elements in both complex hyperplasia and complex hyperplasia with Atypia.

Discussion

Endometrial Hyperplasia is common gynaecological disorder. It is mainly due to prolonged unopposed estrogen stimulation. Microscopic studies show varieties of Endometrial Hyperplasia which ranges from simple hyperplasia to complex hyperplasia and atypical lesion, which has to be differentiated from adeno-carcinoma of endometrium.

As early as in 1900 Cullen described the Inter-relationship of Endometrial Hyperplasia and endometrial carcinoma. He described Endometrial Hyperplasia as pale glands, which coexist with adeno-carcinoma.⁶

Gusberg in 1947 coined the term Adenomatous Hyperplasia of Endometrium. He recognized Endometrial Hyperplasia as precursor lesion of the carcinoma.

Hertig et al – 1949 confirmed the entity Endometrial Hyperplasia as a precursor for endometrial carcinoma.⁷

Gusberg and Kaplan in 1963 graded Adenomatous Hyperplasia into mild, moderate and marked types.⁸

In 1977 Welsch & Scully suggested that atypical cellularity and Atypical architecture hyperplasia should be designed as Atypical Hyperplasia.⁹

Sherman & Brown – 1978 classified adenomatous Hyperplasia as mild dysplastic, moderately dysplastic and sever dysplastic endometrial Hyperplasia.

Fox and Buckley in 1982 have suggested a new terminology based on the biological nature of various endometrial abnormalities and proposed to introduce a new term as intra endometrial neoplasia to all forms of endometrial glandular hyperplasia with cellular Atypia and intra endometrial adeno-carcinoma.¹⁰

Kurman & Norris in 1982 stated that stromal invasion is the predicting prognosis factor of malignant transformation of Atypical Hyperplasia and carcinoma in situ of Endometrium.¹¹

Bergerson et al – 1999 proposed usage of histologically indistinguishable endometrial lesion i.e. Atypical Hyperplasia, intra epithelial adeno-carcinoma and Endometrial Carcinoma with stromal invasion under the uniform term “Endometrial Neoplasia”.¹² This term has already been proposed by Sherman & Brown – 1992 and fox & Buckley in 1982.

Incidence

Age – Gusberg & Kaplan in their study (1963) of 191 cases the peak incidence of Endometrial Hyperplasia was noticed in 4th decade followed by 5th decade. They documented highest incidence in nulliparous compare to parous women.

7 patients had thyroid dysfunctions and Diabetes mellitus.

In the present study 914 cases of Endometrial Hyperplasia are documented. The peak incidence is noticed at 4th decade following by 3rd decade. Highest incidence of Endometrial Hyperplasia noticed in low

parous women 93 patients showed association with diabetes.

Histological Types:

Simple Hyperplasia – In the present study 788 cases are diagnosed as simple hyperplasia. Gusberg & Kaplan 1963 named simple hyperplasia as mild dysplasia.⁸

In 1975 WHO classification, simple hyperplasia was classified as Cystic Hyperplasia.¹³

In 1977 William & Robert E. Scully described Simple Hyperplasia as cystic Hyperplasia. Cysto glandular Hyperplasia was used by Fox & Buckley – 1982.¹⁰

EIN Group (Mutter et al) 2000 proposed a nomenclature for Simple Hyperplasia as Endometrial Hyperplasia.¹⁴ European expert – two class system – 1999 described simple hyperplasia as Endometrial Hyperplasia.⁶

Complex hyperplasia – Number of cases of complex Hyperplasia diagnosed in the present study are 86.

Cases of complex hyperplasia were documented by Gusberg & Kaplan – 1963 as moderate adenomatous hyperplasia.⁸

William R. Welch & Scully classified Endometrial Hyperplasia as Atypical proliferative hyperplasia. Fox & Buckley in 1982 – described the Adenomatoid Hyperplasia which resembles complex Hyperplasia.¹⁰

Bergeron et al 1999 – European Experts have put complex hyperplasia as Endometrial Hyperplasia.¹²

EIN group 2000(Muller et al) have put along with simple hyperplasia, complex hyperplasia as Endometrial Hyperplasia.¹⁴

Atypical Simple Hyperplasia: In the present study 14 cases with Atypical Simple Hyperplasia are analysed.

Gusberg & Kaplan 1963 – Used marked Adenomatous Hyperplasia to simple Hyperplasia with Atypia.⁸

Fox & Buckley described this entity as glandular hyperplasia with cellular atypia.

Sherman & Brown – 1979 used sever dysplastic endometrium to simple hyperplasia with Atypia.¹⁵

Endometrial Intraepithelial Neoplasia 2000 (Mutter et al) used the terminology as EIN to simple Hyperplasia with Atypia.

European experts Society – 1999 (Bergeron et al) used the endometrial neoplasia to Simple Hyperplasia with Atypia.¹²

Complex Hyperplasia Atypia: In the present study 26 cases diagnosed as Complex Hyperplasia with Atypia.

In 1966 Gore & Hertz¹⁶ & Vellios – 1972⁴ – called this entity as Ca in Situ.

Fox & Buckley – 1982 used the term Glandular Hyperplasia with cellular Atypia to complex Hyperplasia with Atypia.¹⁰

Kurman & Norris 1987 – described this entity into Atypical Hyperplasia with Architectural Atypia.¹¹

European experts – Bergeron et al 1999 – have classified Complex Hyperplasia with Atypia into Endometrial Neoplasia.¹²

Endometrial Intraepithelial Neoplasia group 2000 classified complex Hyperplasia with Atypia as Endometrial Intraepithelial Neoplasia.¹⁴

The increase intra and intra observer variability – the diagnosis of Endometrial Hyperplasia leads to lot of confusion in the diagnosis between pathologist and Clinicians. The current classification of W.H.O., International society of gynecological pathology group did not overcome this difficulty. Two new classifications emerged.

European group of expert (1999) divided Endometrial Hyperplasia into 2 groups.

1. Endometrial Hyperplasia
2. Endometrial Neoplasia

Mutter et al 2000 – Endometrial Intraepithelial Neoplasia group divided endometrial hyperplasia into:

1. Endometrial Hyperplasia
2. Endometrial intra epithelial neoplasia.

Both the classification is based on the semi quality determination of the stromal volume in relation to total volume.

In the present study classification proposed by International society of gynecological pathology (1992) and WHO (1994) is adopted.

Special Stain Study: Periodic Acid Schiff's stain complex hyperplasia revealed variable intensity of PAS stain positivity.

In Complex Hyperplasia with Atypia in noticed in 26 cases. PAS staining was negative.

Conclusion

Among the cases of endometrial hyperplasia, simple hyperplasia was the commonest lesion found followed by complex hyperplasia. Most cases were seen in 4th decade.

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