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HISTOPATHOLOGICAL SPECTRUM OF ENDOMETRIAL LESIONS IN TERTIARY CARE CENTRE- A PROSPECTIVE STUDY

Pathology

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ABSTRACT

Introduction: Endometrial sampling is most often performed for abnormal uterine bleeding. Irregular cycles, abnormal and dysfunctional uterine bleeding is considered to be one of the most common presenting symptom in gynaecological practice amongst all age group of patients. Early detection of precursor lesions and exclusions of malignancy is a diagnostic challenge for pathologist. This study aims at evaluation of the histopathological spectrum of endometrial lesions common for particular age group, presenting complaints and underlying cause for the same. **Materials and methods:** A prospective study for a period of 2 years from January 2021 to December 2022 in the Department of Pathology. Total of 870cases , between 18-80years were included. Histopathological study was done and each sample was categorized on the basis of age, bleeding pattern and histomorphological patterns. **Results:** The mean age was found out to be 42.5±2 years. Most common age group was 3rd and 4th decade with 231 patients (26.55%) of 31-40 years and 226 patients (25.97%) of 41-50 years with lower abdominal pain and menorrhagia [210 cases (24.13%) & 191cases(21.83%) respectively], proliferative phase endometrium was noted in 35.74% cases, disordered proliferative endometrium and endometrial polyps in 10.34% cases , non atypical hyperplasia was seen in 8.39% cases, pill endometrium in 3.33% and endometrial carcinoma contributed to 0.46%. **Conclusion:** Perimenopausal period is a vulnerable age group to a number of endometrial lesions. Lower abdominal pain and menorrhagia were most common clinical presentation and confronted wide spectrum of histomorphological changes in endometrial samples presenting with various patterns of bleeding ranging from normal cyclical changes to malignancy. It is observed that patients with obesity, diabetes mellitus, sedentary lifestyle and low socioeconomic status are more proned to these conditions. Histopathological examination plays a vital role in diagnostic evaluation as a first modality and therapeutic management.

KEYWORDS

Disordered Proliferative Endometrium, Endometrial Polyp, Hyperplasia, Perimenopausal, Atrophy

INTRODUCTION

Endometrial sampling is most often performed for abnormal uterine bleeding. Irregular cycles, abnormal and dysfunctional uterine bleeding is considered to be one of the most common presenting symptom in gynaecological practice amongst all age group of patients. Depending upon the bleeding pattern and age of the patient a biopsy may be performed to monitor therapy for hyperplasia or if there is any suspicion or a need to rule out malignancy such as abnormal endometrial cells on pap smear[1,4]. Abnormal endometrial bleeding may be categorized as pregnancy related, iatrogenic, systemic disease and organic, dysfunctional or neoplastic cause. Abnormal uterine bleeding (AUB) is a term used for any type of bleeding that is not within normal ranges of amount, frequency, duration and cyclycity. It is most common presenting complaint in all age group and is regarded as a sign of uterine disease including acute and chronic AUB. Dysfunctional uterine bleeding (DUB) is defined as abnormal uterine bleeding from uterus unassociated with tumor, inflammation and pregnancy[5,9,15,17,18,]. Due to cost and convenience, endometrial sampling is often the first modality utilized when endometrial sampling is undertaken. It is well tolerated by patients as cervical dilatation is not required[1,4,15]

The aim of this study was to evaluate the histopathological spectrum of endometrial lesions common for particular age group, presenting complaints and underlying cause for the same.

MATERIALS AND METHODS

A prospective study, a total of 870 cases were included. The study was conducted for a period of 2 years from January 2021 to December 2022 in the Department of Pathology, S.Nijalingappa Medical College and HSK Hospital, Bagalkot, Karnataka, India.

All endometrial biopsies, dilatation and curettage and hysterectomy specimens were included in the study. Detailed clinical and menstrual history was obtained from all the patients. Samples were appropriately labeled for name, age, IP/OP number, type of specimen and were fixed in 10% formalin overnight and processed the next day. Paraffin embedded sections were obtained and stained with hematoxylin and eosin for microscopic examination. The samples with leiomyoma, adenomyosis, cervical or vaginal pathology were excluded from the study.

RESULTS

A total of 870 cases were received of which 398 were endometrial biopsies, 369 were from hysterectomy specimens and 103 endometrial curettage (Table 1). The age of the patients ranged from 18years to 80years of age. The mean age was found out to be 42.5±2 years. Minimum age of presentation was 18years and maximum was found out to be 76years. Most common age group affected was 3rd and 4th decade, with 231 patients (26.55%) in the age range of 31-40years and 226 patients (25.97%) in the age range of 41-50 years (Table 2). Amongst these maximum number of cases with menstrual disturbances fell in a range of 38 to 48years which is perimenopausal period.

Table 1: Most Common Specimen Type Received.

Specimen Type	Number	Percentage
Endometrial Biopsy	398	45.74%
Endometrial Curettage	103	11.83%
Hysterectomy	369	42.41%
Total	870	

Table 2 : Age Distribution Of Patients With Menstrual Complaints

Age Range	Number	Percentage
18-20	105	12.06%
21-30	210	24.13%
31-40	231	26.55%
41-50	226	25.97%
51-60	75	8.62%
61-70	19	2.18%
71-80	04	0.46%
Total Cases	870	

The most common clinical presentation/bleeding pattern was lower abdominal pain and menorrhagia [210 cases (24.13%) & 191cases (21.83%) respectively] followed by dysmenorrhea [103 cases(11.83%)], poly menorrhagia [97cases (11.14%)] and the least common presentation was menometrorrhagia [28cases (3.21%)]. Postmenopausal bleeding was observed in 4.45% cases (n-39). (Table 3)

Table 3: Clinical presentation and bleeding pattern in different age groups

Age (In Years) Clinical Presentation And Bleeding Pattern	18-20	21-30	31-40	41-50	51-60	61-70	71-80	Total	Percentage
Lower Abdominal Pain	24	43	36	52	44	10	01	210	24.13%
Menorrhagia	09	30	81	59	12	-	-	191	21.95%
Polymenorrhoea	03	06	09	28	01	-	-	47	5.40%
Dysmenorrhoea	61	19	08	15	-	-	-	103	11.83%
Metrorrhagia	03	36	15	02	-	-	-	56	6.43%
Menometrorhagia	-	17	09	02	-	-	-	28	3.21%
Oligomenorrhoea	-	08	23	33	03	-	-	67	7.70%
Post Menopausal Bleeding	-	-	01	12	14	09	03	39	4.48%
Polymenorrhagia	01	31	47	17	01	-	-	97	11.14%
Amenorrhoea	04	20	02	06	-	-	-	32	3.67%
Total	105	210	231	226	75	19	04	870	

A detailed microscopic examination was done and the histopathological findings of the endometrial samples were categorized into 16 groups as stated in table 4.

Normal cyclical pattern of endometrium amongst which proliferative phase endometrium was noted in majority of the cases forming 35.74% (n-311), most common in age group 21-30years followed by 31-40years. Atrophic endometrium in 10% cases (n-87) mainly observed in the age group 51-60years followed by 41-50years and secretory phase in 8.16% cases (n-71) maximum cases in the age group 31-40 years followed by 21-30years.

The most common pathological endometrial finding was disordered proliferative endometrium forming 10.34%(n-90) commonly observed in the age group 41-50years followed by 51-60years and endometrial polyps inclusive of its subtypes a total of 10.34%(n-90) with most common age group being 41-50 followed by 31-40years.

Non atypical hyperplasia was seen in 8.39% cases (n-73) with most common age group being 41-50years, products of conception was found in 7.24% cases (n-63) with maximum cases falling under the age group 21-30years. Pill endometrium was found in 3.33% cases (n-29) most common age group was found to be 31-40years , molar pregnancy in 2.41% cases (n-21) maximum cases in 31-40years age group. Irregular shedding of endometrium was observed in 2.29% cases (n-20) most common age group being 21-30years, endometritis in 1.03% cases (n-09) with 41-50 years age group, atypical hyperplasia was seen in 0.23% (n-02) and endometrial carcinoma contributed to 0.46% cases (n-04) mainly observed above 50years of age (Table 4) .

Amongst 870 cases, 231 cases were under 31-40 years age group making it most age group for endometrial sampling, followed by 41-50years age group with 226 cases. Least number of cases we noted in 71-80years age group which accounted to only 04 cases.

Table 4: Histomorphological pattern common for particular age group

Age (In Years) Histomorphological Patterns	18-20	21-30	31-40	41-50	51-60	61-70	71-80	Total	Percentage
Proliferative Phase	73	89	77	68	04	-	-	311	35.74%
Secretory Phase	13	23	32	03	-	-	-	71	8.16%
Irregular Shedding Of Endometrium	04	10	04	02	-	-	-	20	2.29%
Disordered Proliferative Endometrium	03	10	17	42	18	-	-	90	10.34%
Pill Endometrium	02	04	13	09	01	-	-	29	3.33%
Hyperplasia Without Atypia	-	07	30	33	02	01	-	73	8.39%
Atypical Hyperplasia	-	-	-	-	01	01	-	02	0.23%
Atrophy	-	-	03	22	43	16	03	87	10%
Endometritis	-	01	02	05	01	-	-	09	1.03%
Endometrial Polyp	-	02	16	17	01	-	-	36	4.13%
Hyperplastic Polyp	-	04	08	14	02	-	-	28	3.12%
Leiomyomatous Polyp	-	01	05	05	-	-	-	11	1.26%
Adenomyomatous Polyp	-	02	07	06	-	-	-	15	1.72%
Products Of Conception	09	50	04	-	-	-	-	63	7.24%
Molar Pregnancy	01	07	13	-	-	-	-	21	2.41%
Endometrial Carcinoma	-	-	-	-	02	01	01	04	0.46%
Total	105	210	231	226	75	19	04	870	

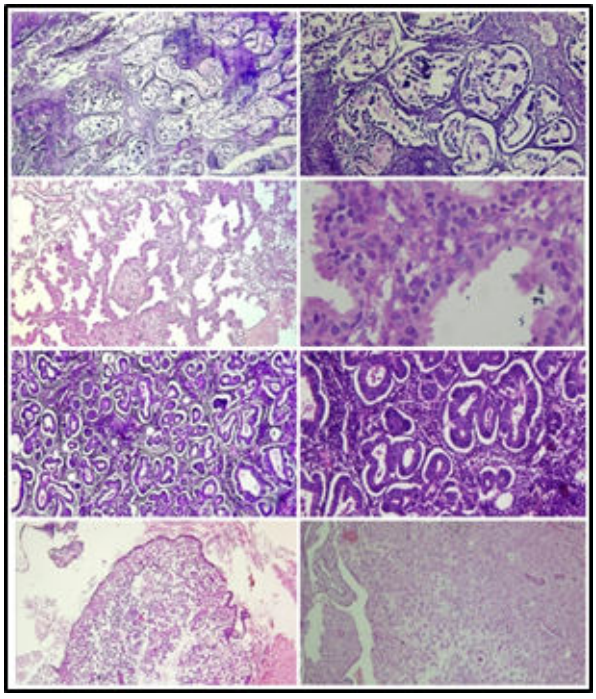

Image 1(H&E) : A(4x), B(40x) Non atypical hyperplasia (complex hyperplasia without atypia); **C(4x),D(40x)** Pill endometrium; **E(4x),F(40x)** Atypical Hyperplasia; **G(4x),H(40x)** Endometrial polypd.

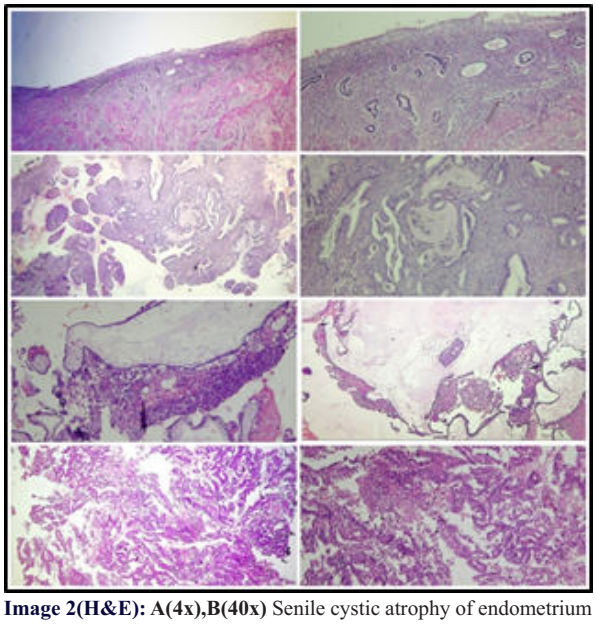

Image 2(H&E): A(4x),B(40x) Senile cystic atrophy of endometrium **C(4x),D(40x)** Disordered proliferative endometrium **E(4x),F(40x)** Hydatidiform mole with cytotrophoblastic proliferation; prominent hydropic change of villi; **G(4x),H(40x)** Endometrial carcinoma-villoglandular type.

DISCUSSION

Endometrial assessment is performed to evaluate the influence of hormones on endometrium and to diagnose premalignant and malignant conditions of endometrium. The occurrence of menstrual disorders increases with advancing age.[1,2]

In the reproductive age group, pregnancy related causes of bleeding, including intrautrerine pregnancy, ectopic pregnancy and gestational trophoblastic disease must always be considered. Rarely, systemic cause such as coagulation disorder, is the cause of abnormal uterine bleeding. Sometimes bleeding perceived as uterine may not be endometrial origin or may even be nongenital, originating from cervix, vagina, bladder or rectum.[2,4,9]

The more common etiologies of bleeding in the perimenopausal and postmenopausal woman are organic, dysfunctional and neoplastic etiologies. Organic causes of abnormal bleeding are lesions intrinsic to the uterus, such as submucous leiomyomas, adenomyosis or polyps. Abnormalities of angiogenesis are currently thought to be related to the bleeding seen with these lesions. Neoplasia may be hormonally related or hormone independent.[1,2,5,9,11,17]

Irregular cycles, abnormal and dysfunctional uterine bleeding is considered to be one of the most common presenting symptom in gynaecological practice amongst all age group of patients.[2,4] Patients may present with lower abdominal pain, menorrhagia, polymenorrhagia, dysmenorrhea, menometrorrhagia, metrorrhagia, polymenorrhoea, intermenstrual bleeding, oligomenorrhoea and postmenopausal bleeding. It can occur anytime between menarche and menopause, in ovulatory and anovulatory cycles and is known to be associated with almost any type of endometrium ranging from normal endometrium to hyperplasia, irregular ripening, irregular menstrual shedding and atrophy.[2,4,11,12,14,17]

In the present, we have studied the histopathology of endometrium to identify the endometrial causes AUB,DUB and occurrence of various pathologies in different age groups.

In our study a total of 870cases were studied over a period of 2 years.

Age distribution in our study ranged from 18 to 80years with mean age group being 42.5±2 years. Similar observation was seen in studied by Tiwana et al [3]and Rashmikumari T.R et al[4] where age ranged from 22-85years with mean age of 45 years and 21-80years with mean age of 41years respectively.

In our study maximum number of cases fell in the age group of 31-40years (26.55%) which is in concordance with studies by Mariam Abid et al[5], Rajesh Patil et al [6]and Mitra k et al[7], followed by 41-50years (25.97%) which fell in perimenopausal age group and was found to be compatible with studies by Themthingla Zimik et al[8], Devanshi M et al[9], Vaidya S et al[10], Doraiswami S et al[11], Jairajpuri et al[12], Bolde SA et al[13] and Rehana K et al[14].

Cluster of cases in perimenopausal age group could be due dearrangements in the hypothalamo-pituitary-ovarian axis resulting in dearrangements of maturation of ovarian follicles, ovulation or formation of corpus luteum, anovulatory cycles which are more frequent and chronic anovulation which is associated with irregular and unpredictable pattern of bleeding which explains the most common cause of AUB and DUB in perimenopausal age group[9]. A lesser number of patients were noted above 60years of age.

The most common clinical presentation in our study was lower abdominal pain with most common bleeding pattern being menorrhagia which accounted to 21.95% cases. Similar observation was seen as dominant complaint in studies by Rehana K et al[14] (55.8%), M Banyameen Iqbal et al[15] (36.0%). Polymenorrhoea was most common bleeding pattern in study by Marium Abid et al[5] (30%).

Table 5: Histomorphological Patterns Observed In Different Studies.

Histomorphological Pattern	Ritika Et Al (200)	Sharma R Et Al (183)	Sarika Et Al(202)	Vaidya S Et Al(403)	Present Study(870)
Proliferative Phase	35.5%	38.8%	41.6%	18.36%	35.74%
Secretory Phase	7.3%	16.3%	17.3%	22.58%	8.16%
Atrophic Endometrium	-	4.4%	1.98%	4.71%	10%
Disordered Proliferative Endometrium	29%	6.5%	7.4%	13.4%	10.34%
Hyperplasia	9.5%	12.0%	15.3%	10.9%	8.62%
Pill Endometrium	1.3%	6.0%	6.4%	6.20%	3.33%
Polyp	4%	2.2%	1.5%	1.24%	10.34%
Endometritis	-	3.3%	2.97%	3.23%	1.03%
Pregnancy	-	3.3%	0.51%	-	9.65%
Endometrial Carcinoma	3.0%	1.1%	1.98%	2.48%	0.46%

Out of 870 cases, the normal physiologic changes of endometrium were predominant with most common histopathological pattern being proliferative phase in 35.74% cases and secretory phase in 8.16% cases. These were in concordance with studies by Rashmikumari T R et al[4] (37.26% and 16.34%), Vaidya et al[10] (40.94%) and Sarika et al[16] (19.5% and 15%). (Table 5)

The second commonest lesion observed in our study was disordered proliferative endometrium with 10.34% cases, there is abnormal proliferative type of endometrium with architectural changes due to unopposed estrogen stimulation and with normal gland to stromal ratio. This can progress to hyperplasia without atypia. This was comparable to studies by M Banyanmeen Iqbal et al[15] (14.8%) , Sarika et al[16] and Doraiswami et al[11].

Endometrial polyps inclusive of its subtypes a total of 10.34% cases in age group 41-50years were noted in present study; the incidence increased with age and obesity where overall lifetime exposure to estrogen was increased by peripheral aromatization of adrenal androgens. Similar finding was noted in study by Ritika Bhat et al[17] and Sarika et al[16].

10% of atrophic endometrium cases were noted in present study which was more predominant >50years which was similar in studies by Sharma R et al.[18] A higher incidence was noted in study by Themthingla Z et al[8] (27.8%), Anuradha S et al[19](30.7%). It is postulated to be due to vessel wall undergoing sclerotic degeneration or local abnormal hemostatic mechanism as major mechanism of bleeding.

Non atypical hyperplasia was seen in 8.39% cases with most common age group being 41-50years which is comparable with studies by Sharma R et al[18](12%), Sarika et al [16](15%) and Rehana K et al[14] (20.5%) . It is most common in perimenopausal age group due to failure of ovulation. There are persistent unripe follicles which expose the endometrium to excessive and prolonged action of estrogen and cause hyperplasia.

Products of conception and molar pregnancy were found in 7.24% and 2.41% cases in present study with age range being 18-40years. Molar pregnancy is known to occur in extremes of age i.e. <20year or >35yeras due to abnormal gametogenesis and fertilization. This was in concordance with study by Sharma R et al[18] and Bhoomika D et al[20].

In our study, pill endometrium was found in 3.33% cases which was comparatively less when compared to studies by Sarika et al[16] and Sharma R et al[18]. Morphologic changes are secondary to effect of exogenous hormones on estrogen or progesterone receptors in endometrium.

Endometritis was seen 1.03% cases in 41-50 years age group similar findings were noted in studies by Sarika et al[16] and Sharma R et al[18] usually seen post pregnancy, abortion, infections, insertion of intrauterine contraceptive devices and tubercular origin associated with infertility and menorrhagia.

Atypical hyperplasia was seen in 0.23% and endometrial carcinoma contributed to 0.46% cases i.e four cases mainly observed above 50years of age amongst which three were endometrioid type endometrial carcinoma and one was villo glandular type of endometrial carcinoma. Our study was in concordance with studies by Sarika et al[16] and SharmaR et al[18]. Endogenous and exogenous hyperestrogenism is most common risk factor for endometrial carcinoma, with endometrial hyperplasia being the most common precursor.

Depending upon age, parity, lifestyle and ethnicity, the histopathological pattern of endometrium tends to be diversified.

CONCLUSION

Analyzing the results, we concluded that perimenopausal period is a vulnerable age group to a number of endometrial lesions. Lower abdominal pain and menorrhagia were most common clinical presentation and confronted wide spectrum of histomorphological changes in endometrial samples presenting with various patterns of bleeding ranging from normal cyclical changes to malignancy. It is observed that patients with obesity, diabetes mellitus, sedentary lifestyle and low socioecomic status are more proned to these conditions. Histopathological examinations plays a vital role in

diagnostic evaluation as a first modality and therapeutic management.

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