HISTOPATHOLOGICAL SPECTRUM OF ENDOMETRIAL BIOPSIES – A STUDY OF 378 CASES AT AFIP PAKISTAN

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ABSTRACT

Objective: To analyze the histopathological spectrum of endometrial biopsies.

Study Design: Descriptive case series.

Place and Duration of Study: Armed Forces Institute of Pathology (AFIP), Rawalpindi from December 2013 to August 2015.

Material and Methods: All cases of endometrial biopsies were retrieved from AFIP data base. Age and histopathological diagnosis was noted, irrespective of the clinical presentation of the patients. The data was analysed by using computer software program SPSS version 19. Descriptive statistics like mean ± SD, percentages and frequencies were calculated for age and histopathological diagnosis. The data collected for study was statistically analysed using chi-square test.

Results: A total of 378 cases of endometrial biopsies were included in the study. The age at presentation ranged from 13 to 75 years with median age of 40.73 ± 9 years. A total of 73.5% of the cases (n=278) were from 4th to 5th decade of life. The most common histopathological diagnosis was secretory endometrium; present in 117 cases (31%) followed by proliferative endometrium; 78 cases (20.6%). Disordered proliferative endometrium, chronic endometritis and endometrium with hormone induced changes were observed in 62 (16.4%), 41 (10.8%) and 36 (9.5%) cases respectively. Atrophic endometrium was diagnosed in 8 cases (2.1%) and there were 3 cases (0.8%) of endometrial polyp. Among endometrial hyperplasia, 23 cases (6.1%) were of simple cystic hyperplasia, 5 cases (1.3%) were complex hyperplasia without atypia and 4 cases (1.1%) were complex hyperplasia with atypia. Adenocarcinoma in situ (ACIS) was reported in only one case (0.3%). Comparison with other studies revealed the results matching with some and differing with others. Association of age with histopathological pattern was statistically significant with p value <0.05.

Conclusion: Endometrial biopsies revealed a wide variety of age specific histopathological diagnoses. Secretory endometrium is the commonest diagnosis in women of reproductive age group whereas hyperplasia and malignancy are common in premenopausal and postmenopausal age groups. Detailed analysis of endometrial biopsies is therefore necessary for accurate diagnosis, appropriate treatment and favorable outcome.

Keywords: Endometrial biopsy, Histopathological spectrum.

INTRODUCTION

Endometrium forms the innermost linning of the uterine wall, it is glandular in structure and dynamic in function as it passes through a series of changes including proliferation, secretion and menstruation during the menstrual cycle of a woman. These cyclic phases are under the influence of two female sex hormones, estrogen and progesterone. Estrogen affects the proliferative phase whereas progesterone is responsible for the secretory phase of menstrual cycle. An intricate process regulates the equilibrium between endometrial proliferation and apoptosis, influenced by a number of factors like age, environment, hormonal balance, molecular mechanisms, and so forth; likewise endometrium is subjected to a wide variety of disturbances leading to several abnormalities. Microsatellite instability, phosphatase and tensin

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(PTEN) mutations, K-ras mutation, beta-catenin mutation and PIK3CA mutation are the most common genetic alterations in endometrial defects[1].

Endometrial biopsy is a preferred procedure for accurate diagnosis of endometrial pathology. This procedure is now considered as the first line diagnostic tool owing to its safety, accuracy, rapidity, convenience and cost-effectiveness[2].

Patients with premalignant or malignant endometrial lesions may have the common presenting complaint of abnormal uterine bleeding[2]. Abnormal uterine bleeding accounts for more than 70% of all gynaecological visits in the peri- and postmenopausal years[3]. Main causes of abnormal uterine bleeding include fibroids, polyps, hyperplasia, malignancy and atrophy[4]. Endometrial biopsy is the most effective diagnostic approach towards abnormal uterine bleeding[5]. It not only detects the local lesions[6] but also prevents the women from undergoing unwanted hysterectomy procedure[7].

The main aim of this minimally invasive procedure is to exclude serious pathological intrauterine conditions[8]. Endometrial biopsy should be performed in all women over 35 years of age with menorrhagia to rule out malignant or premalignant lesions of the endometrium. It should also be considered in women between 18 to 35 years of age with abnormal uterine bleeding who have risk factors for endometrial cancer[9].

This study was conducted to analyse the histpathological spectrum of endometrial biopsies, their relative frequencies and to compare the results with other similar studies.

MATERIAL AND METHODS

This retrospective descriptive case series was carried out at Armed Forces Institute of Pathology, Rawalpindi from December 2013 to August 2015. All cases of endometrial biopsies were retrieved from AFIP data base and included in the study irrespective of the age and clinical presentation of the patient by non probability, consecutive sampling technique. Cases with inadequate biopsy were excluded from the study. Age and histopathologic diagnosis was noted. A total of 378 cases were included in the study. The data was analyzed by using computer software

Table-1: Distribution of 378 cases of endometrial biopsies according to age groups.

Diagnosis	Age Groups							Total
	11-20	21-30	31-40	41-50	1-60	61-70	71-80	
Secretory Endometrium	1	19	50	43	4	0	0	117 (31%)
Proliferative Endometrium	2	15	29	31	1	0	0	78 (20.6%)
Disordered Proliferative Endometrium	0	5	12	36	8	1	0	62 (16.4%)
Chronic Endometritis	0	10	15	14	2	0	0	41 (10.8%)
Hormone Induced Changes	0	4	7	12	3	0	0	36 (9.5%)
Atrophic Endometrium	0	0	0	4	4	0	0	8 (2.1%)
Endometrial Polyp	0	0	0	3	0	0	0	3 (0.8%)
Simple Cystic Hyperplasia	0	2	5	13	3	0	0	2 3(6.1%)
Complex Hyperplasia without Atypia	0	0	1	2	1	1	0	5 (1.3%)
Complex Hyperplasia with Atypia	0	0	1	0	1	2	0	4 (1.1%)
Adenocarcinoma in situ (ACIS)	0	0	0	0	0	0	1	1 (0.3%)
Total	3	65	120	158	27	4	1	378

program SPSS version 19. Descriptive statistics like mean ± SD for age. Percentages and frequencies were calculated for age and histopathological diagnosis. A statistical analysis between age and histopathological diagnosis was done using chi-square test. A *p*-value <0.05 considered as a significant value.

RESULTS

The record from 1st December 2013 to 31st August 2015 showed that a total of 378 endometrial biopsies were evaluated at AFIP, Rawalpindi during this period. A total of 378 cases of endometrial biopsies were included in the study. The age at presentation ranged from 13 to 75 years with median age of 40.73 ± 9 years. 73.5% of the cases (n=278) were from 4th to 5th decade of life. The most common histopathological diagnosis was secretory endometrium; present in 117 cases (31%) followed by proliferative endometrium; 78 cases (20.6%). Disordered proliferative endometrium, chronic endometritis and endometrium showing hormone induced changes were observed in 62 (16.4%), 41 (10.8%) and 36 (9.5%) cases respectively. Atrophic endometrium was diagnosed in 8 cases (2.1%) and there were 3 cases (0.8%) of endometrial polyp. Among 32 cases (8.5%) of endometrial hyperplasia, 23 cases (6.1%) were of simple cystic hyperplasia and 9 cases (2.4%) were diagnosed as complex hyperplasia, out of which 5 cases (1.3%) were complex hyperplasia without atypia and 4 cases (1.1%) were complex hyperplasia with atypia. Adenocarcinoma in situ (ACIS) was reported in only one case (0.3%). The distribution of cases according to different age groups are summarized in Table.1 and shown graphically in fig-1. A significant statistical association was seen between age and histopathological diagnosis with *p* value < 0.001.

Comparison with other studies revealed the results matching with some and differing with others.

DISCUSSION

Endometrial lesions responsible for abnormal uterine bleeding are related to the age of the patient as to whether the patient is premenopausal, perimenopausal or postmenopausal. Abnormal uterine bleeding is defined as a bleeding pattern that differs in frequency, duration, and amount from a pattern observed during a normal menstrual cycle or after menopause[3].

The routine out-patient investigations for abnormal uterine bleeding include blood complete picture, platelet count, prothrombin time (PT), activated partial thromboplastin time (APTT) and liver function tests for ruling out any bleeding disorder or coagulation defect. Serum and urine human chorionic gonadotrophin (HCG) levels are assessed to rule out pregnancy in women of reproductive age group. Endocrine causes will be ruled out by evaluating thyroid function tests, follicle stimulating hormone (FSH), lutenizing hormone (LH) and prolactin levels. Imaging studies are then carried out, such as pelvic and transvaginal ultrasound (USG) followed by endometrial sampling, which can be a diagnostic as well as therapeutic procedure. The reported sensitivity of endometrial biopsy for the detection of endometrial pathology is as high as 96%[5]. Histopathological evaluation of endometrial biopsies is necessary for exact diagnosis of endometrial pathologies in patients of abnormal uterine bleeding[10].

Our study has clearly revealed that the occurrence of endometrial lesions increases with advancing age. Age group of 41-50 years is the commonest age group that showed the maximum number of cases with proliferative lesions like disordered proliferative pattern, benign endometrial polyp and hyperplasia. These findings are in accordance with the findings reported by Saraswathi et al[5].

Our study shows that the mean age at the time of diagnosis in our population is 40.73 ± 9 years. The mean age reported by Jetley et al[3] 44.8 years and Saadia et al[2] 42.5 years, is in concordance with the mean age of the current study.

The age range in our study is from 13 to 75 years which is in accordance with Vaidya et al[10] (18-70 years) and Saraswathi et al[5] (17-79 years).

In our study, predominant number of cases showed normal physiologic phases such as proliferative and secretory menstrual pattern. The most common histopathological diagnosis was secretory endometrium (31%) followed by proliferative endometrium (20.6%) comparable to the results of Jetley et al[3], 32.4% and 30.6% respectively.

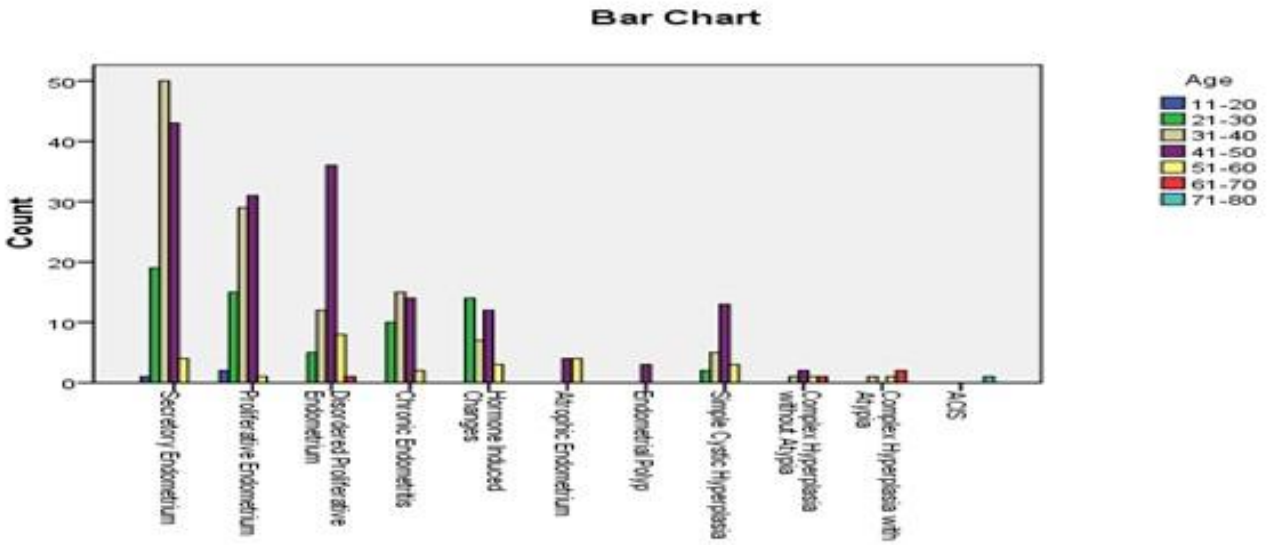

Figure-1: Relative frequency of histopathological diagnosis in Endometrial Biopsies.

A significant number of cases showed disordered proliferative endometrium in the 41-50 years age group. Disordered proliferative pattern occupies a position at one end of the spectrum of proliferative lesions of the endometrium, and carcinoma lies at the other end, with stages of hyperplasia in-between[4]. Disordered proliferative pattern was observed in 16.4% of our cases, which is higher as compared to studies conducted by Vaidya et al[10] (13.40%) and Soleymani et al[11] (15.4%). Increased health awareness leading to an earlier stage of presentation could explain the high incidence of disordered proliferative pattern in our study.

Chronic endometritis and endometrium with hormone induced changes showed a frequency of 10.8% and 9.5% respectively in our study while Jetley et al[3] showed it to be 9.1% and 2.7% respectively. Chronic endometritis was of nonspecific type without any evidence of granulomas. Hormone induced changes were seen in the endometrium of patients of atypical uterine bleeding being managed by exogenous hormone therapy.

According to our study, frequency of endometrial polyp in endometrial biopsies is 0.8% which is lower as compared to Jetley et al[3], 2.7%. It is difficult to recognize polyps in curettage specimens. These are identified by the presence of epithelium on three sides of a polypoidal fragment. Other identifying feature is fibrous stroma and thick walled blood vessels in contrast to the other endometrial fragments, thus suggesting a polyp.

Our study showed 8.5% cases of endometrial hyperplasia, among these 6.1% were of simple cystic hyperplasia and 2.4% were diagnosed as complex hyperplasia, out of which 1.3% were complex hyperplasia without atypia and 1.1% were complex hyperplasia with atypia. However, according to the studies conducted by Jetley et al[3] and Vaidya et al[10], incidence of endometrial hyperplasia is 10.8% and 10.92% respectively. The

possible explanation for the lower incidence of endometrial hyperplasia in our study could be that most of our patients belong to lower socioeconomic class and the occurrence of risk factors (obesity, diabetes, increased intake of animal fat and sedentary life style) is low.

The incidence of atrophic endometrium in our study is 2.1% which is slightly lower when compared to the results of Saraswathi et al[5] which showed it to be 2.4%.

Malignant pathology (ACIS) was diagnosed in 0.3% of our cases whereas in Soleymani et al[11], it is 0.7%. The lower incidence of malignancy in our patients is most likely attributed to the practice of early childbearing and multiparity. Adenocarcinoma of endometrium is the most common genital cancer in women over 45 years of age and its incidence is increasing with advancing age[9]. Various studies have shown a probable role of human papillomavirus (HPV) in the pathogenesis of endometrial carcinoma, however it has been revealed that HPV does not play any significant role in the pathogenesis of endometrial carcinoma, since endometrium does not appear to be a suitable host for HPV replication[12].

CONCLUSION

Histopathological examination of endometrial biopsies revealed a wide spectrum of age specific diagnoses ranging from normal endometrium to malignancy. Secretory endometrium is the commonest diagnosis in women of reproductive age group whereas hyperplasia and malignancy are common in perimenopausal and postmenopausal age groups. Careful endometrial evaluation with an understanding of the underlying causes is therefore necessary to rule out any preneoplastic or neoplastic condition and hence a way to compelling treatment and ideal result.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

REFERENCES

1. Chandra V, Kim JJ, Benbrook DM, Dwivedi A, Rai R. Therapeutic options for management of endometrial hyperplasia. J Gynecol Oncol. 2016; 27(1): 08.
2. Saadia A, Mubarik A, Zubair A, Jamal S, Zafar A. Diagnostic accuracy of endometrial curettage in endometrial pathology. J Ayub Med Coll Abbottabad. 2011; 23(1): 129-131.
3. Jetley S, Rana S, Jairapuri ZS. Morphological spectrum of endometrial pathology in middle-aged women with atypical uterine bleeding: A study of 219 cases. J Midlife Health. 2013; 4(4): 216-220.
4. Pyari JS, Rekha S, PK S, Goel M, Pandey M. A comparative diagnostic evaluation of hysteroscopy, transvaginal ultrasonography and histopathological examination in cases of abnormal uterine bleeding. J Obstet Gynecol India. 2006; 56: 240-3.
5. Saraswathi D, Thanka J, Shalinee R, Aarthi R, Jaya V, Kumar PV. Study of endometrial pathology in abnormal uterine bleeding. J Obstet Gynecol India. 2011; 61(4): 426-430.
6. Moghal N. Diagnostic value of endometrial curettage in abnormal uterine bleeding - A histopathological study. JPMA. 1997;47:295–9.
7. Sarwar A, Haque A. Types and frequencies of pathologies in endometrial curettings of abnormal uterine bleeding. IJP. 2005; 3(2):65-70.
8. Clark TJ, Voit D, Gupta JK, Hyde C, Song F, Khan KS. Accuracy of hysteroscopy in the diagnosis of endometrial cancer and hyperplasia. JAMA. 2002; 288: 1610-1621.
9. Riaz S, Ibrar F, Dawood NS, Jabeen A. Endometrial pathology by endometrial curettage in menorrhagia in premenopausal age group. J Ayub Med Coll Abbottabad. 2010; 22(3): 161-4.
10. Vaidya S, Lakhey M, Vaidya S, Sharma PK, Hirachand S, Lama S, et al. Histopathological pattern of abnormal uterine bleeding in endometrial biopsies. Nepal Med Coll J. 2013; 15(1): 74–7.
11. Soleymani E, Ziari K, Rahmani O, Dadpay M, Taheri-Dolatabadi M, Alizadeh K, et al. Histopathological findings of endometrial specimens in abnormal uterine bleeding. Arch Gynecol Obstet. 2014; 289(4): 845-9.
12. Karadayi N, Gecer M, Kayahan S, Yamuc E, Onak NK, Korkmaz T, et al. Association between human papillomavirus and endometrial adenocarcinoma. Med Oncol. 2013; 30(3): 597.