HISTOPATHOLOGICAL SPECTRUM OF ENDOMETRIUM IN PERI-MENOPAUSAL AND POSTMENOPAUSAL WOMEN IN SOUTHERN PUNJAB; AN EXPERIENCE AT TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: To determine frequency and association of different histopathological diagnoses and symptoms in peri-menopausal and post-menopausal women presenting with abnormal uterine bleeding.

Material and Methods: This comparative cross-sectional study was done from 1st January 2018 to 30th April 2020 in a tertiary care hospital, Southern Punjab. The study included all endometrial biopsies done for abnormal uterine bleeding in peri-menopausal (40-50 years) and post-menopausal age group (above 50 years). Haematoxylin and Eosin stained sections of all cases were examined by the same histopathologist. Descriptive statistics were calculated and Fisher's exact test was used to find an association between symptoms and histological findings.

Results: Out of 194 selected cases, 117 (60.3%) were from the peri-menopausal group, while the remaining 77 (39.7%) were from the post-menopausal age group. Diverse histopathological diagnoses were found on endometrial biopsies. The most frequent histopathological entity was proliferative endometrium in both groups, while endometrial hyperplasia and endometrial carcinoma were among the least common ones. Proliferative endometrium, secretory endometrium, and hormone-induced changes were the commonest of all histopathological entities in the peri-menopausal group and have presented with different symptoms. Fisher's exact test showed (P-value of >0.05) that there is no statistically significant association between symptoms and any particular histopathological entity.

Conclusion: A variety of histopathological diagnoses is found during the evaluation of endometrial biopsies of patients in peri-menopausal and post-menopausal groups. The peri-menopausal group presents with different symptoms, but these symptoms are not associated with any particular histological diagnosis.

Key Words: Endometrium, Biopsy, Menopause, Peri-menopause, Menorrhagia.

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INTRODUCTION

Endometrial biopsy, either as curettage or outpatient biopsy, is one of the commonest samples in any histopathology setup. Now-a-days, the number of specimens has markedly increased as no general anesthesia is required while sampling using pipelle sampling. Endometrial biopsy is done to ascertain underlying pathologies ranging from benign to malignant conditions [1]. Abnormal uterine bleeding is a common symptom which is experienced by almost every third women in her life. Abnormal uterine bleeding is caused by variety of disorders, including benign and malignant conditions [2,3].

Peri-menopause or menopause transition begins several years before the onset of menopause due to gradual decrease in estrogen production from the ovary. It usually lasts for four years but may vary from few months up to ten years. Peri-menopausal period usually ends when there is no menstruation for a period of one year. Peri-menopause causes histological changes in endometrium as well as some behavioral changes [4]. The most important histopathological changes that occur in the endometrium are due to inflammation, metaplasia, hormone imbalance and tumors. These changes in peri-menopusal and post-menopausal women lead to abnormal uterine bleeding. Abnormal uterine bleeding may be of many types like polymenorrhea, metrorrhagia, menometrorrhagia menorrhagia, hypomenorrhea, oligomenorrhoea, dysmenorrhea etc [5]. Histopathological examination of the endometrium is the most common investigation used worldwide to evaluate the causes of abnormal uterine bleeding, and is significant in postmenopausal women to identify premalignant and malignant conditions [6]. Different endometrial pathological entities have different treatment options ranging from simply follow up to staging hysterectomy. Therefore, finding of a particular pathology in these groups associated with any particular symptom will stratify the treatment strategy by clinicians [7].

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MATERIAL AND METHODS

This cross-sectional study was done from 1st January 2018 to 30th April 2020 in the department of pathology, in a tertiary care hospital, Southern Punjab. The study included 194 cases of both peri-menopausal (40-50 years) and post-menopausal age group (above 50 years) whose endometrial biopsies were received for evaluation of abnormal uterine bleeding. Cases with bleeding disorder, having anticoagulant therapy or receiving treatment for malignancy were excluded from the study. All cases without adequate history and having scanty endometrial tissue during microscopic examination were also excluded from the study. Specimens were fixed in 10% formalin overnight and tissue was processed and paraffin embedded blocks were made. Thin slices of 5 microns were made and stained with Haematoxylin and Eosin. Microscopic examination of all cases was done by same histopathologist without knowing demographic details. Descriptive statistics were calculated and Fisher's exact test was used to find association between symptoms and histological findings.

RESULTS

In the present study a total of 194 biopsies were selected which were fulfilling the inclusion and exclusion criteria. Three biopsies having inadequate material were excluded from the study. Histo-pathological diagnosis of all cases was made on routine Haematoxylin and Eosin stained sections. The entities ranged from proliferative endometrium to endometrial carcinoma in both groups.

The peri-menopausal group with abnormal uterine bleeding was having the age from 40 to 50 years with the mean age of 46.3 years and standard deviation of ± 1.46. The post-menopausal group with abnormal uterine bleeding was having the age range of 51 to 85 years with the mean age of 58.3 years and a standard deviation of ± 5.46 years.

Out of 194 cases, 117 were from peri-menopausal group, while 77 were from post-menopausal age group. The most frequent histopathological entity was proliferative endometrium in both groups, while endometrial carcinoma and endometrial hyperplasia were least common (as shown in Table-I). No case of cystic atrophy was seen in peri-menopausal group and similarly no case of interval endometrium was seen in the post-menopausal group.

The patients have presented with different patterns of bleeding in peri-menopausal group, ranging from menorrhagia to polymenorrhea (Shown in Figure-1). In the post-menopausal group, all cases have presented with the common symptom of postmenopausal bleeding. Proliferative endometrium was most frequent (55.6%) followed by endometrium showing hormone induced effects (14.9%), collectively in both groups.

Three histological findings of proliferative endometrium, secretory endometrium and hormone induced changes were most common of all histopathological entities in the peri-menopausal group and were found in cases presenting with different symptoms. (as shown in table-II). Fisher's exact test was applied to determine the association of symptoms with all histological entities which showed (p value of >0.05) that there is no statistically significant association between symptoms and any particular histopathological entity.

Table-I: Showing histopathological diagnosis in peri-menopausal and post-menopausal groups.

Histopathological entities	Peri-menopausal group	Post-menopausal group
Proliferative endometrium	64	44
Secretory Endometrium	23	9
Endometrium showing hormone induced changes	18	11
Benign endometrial polyp	5	4
Chronic endometritis	2	2
Cystic atrophy	-	2
Endometrial hyperplasia without atypia	2	2
Interval phase Endometrium	1	-
Endometrial hyperplasia with atypia	1	1
Endometrioid adenocarcinoma	1	1

Table-II-Showing common histological findings and symptoms in peri-menopausal group.

	Metrorrhagia (n=30)	Polymenorrhea (n=19)	Menotrorrhagia (n=25)	Menorrhagia (n=31)
Proliferative endometrium	15	15	13	21
Secretory phase endometrium	8	4	5	6
Hormone induced changes	7	0	7	4

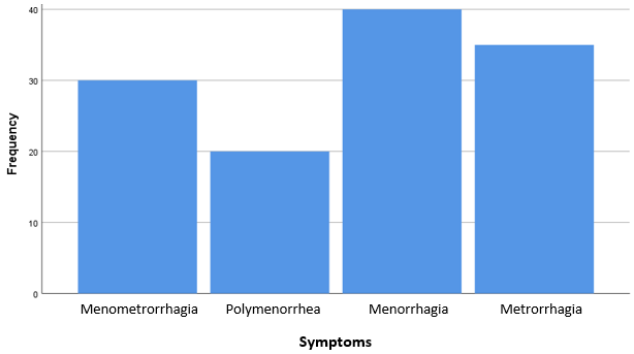

Figure-I: Showing frequency of symptoms in peri-menopausal group

DISCUSSION

Abnormal uterine bleeding is the most common complaint in gynecological department. More than 70% of the patient in the peri-menopausal and postmenopausal period present with abnormal uterine bleeding [8]. Endometrial biopsy is an important method for diagnosing the cause of abnormal uterine bleeding due to indigenous reason or hormonal imbalances without any organic cause [9]. Any abnormality in hypothalamic-pituitary-ovarian axis leads to derangements in follicular maturation, ovulation or corpus luteum formation leads to changes in the hormonal environment. These abnormalities in the hormonal balance may result in abnormal uterine bleeding.

In consort with histology other observations were also made. In the present study, more cases (60.3%) presented with abnormal uterine bleeding in the peri-menopausal group rather than post-menopausal group (39.7%). Despite having a wide range, majority of cases were from peri-menopausal group (ranging from 40-50 years) rather than the post-menopausal group (ranging from 51-85 years). This finding is in concordance with the study done by Husain *et al* [10] in which peri-menopausal age group incidence was also higher i.e. 69.2%. In other studies, conducted by Abid *et al* [11] and Masood *et al* [12], peri-menopausal age group was on top involving 51.3% and 68.0% of cases, respectively.

In peri-menopausal period anovulatory cycles are the main reason related to an abnormal pattern of bleeding. Due to unopposed estrogen production without ovulation, progesterone results in a cascade of endometrial proliferation, rupture and irregular bleeding. This bleeding is usually painless and irregular, but has variable presentations. In perimenopausal group menorrhagia was the commonest symptom (32%) in the present study. In the study by Abid *et al* [11] polymenorrhea (30%) was the commonest symptom rather than menorrhagia. The study published by Abid *et al* [11] menorrhagia was 22%, but with lower percentages as compared to present study. Metrorrhagia followed menorrhagia in the present study (28%), but menometrorrhagia accounted for only 2% of cases in the study by Abid *et al* [11]. In the present study, in post-menopausal age group all 77 cases (100%) presented with postmenopausal bleeding.

In peri-menopausal age group, proliferative endometrium was commonest (54.7%), which is quite higher than the data published by Husain *et al* [10] (15.3%) and Masood *et al* [12] (16.7%). In the present study, secretory endometrium was present in 18.4% of cases in the peri-menopausal group, which was slightly higher than data published by and Masood *et al* [12] (14.7%). However, in the present study, endometrial polyp was 4.2 % in peri-menopausal women which was quite lower than the studies by Husain *et al* [10] (16.6%), Abid *et al* [11] (10.4%) and Masood *et al* [12] (5.3%).

In the present study, among the premalignant and malignant conditions in the peri-menopausal women endometrial hyperplasia without atypia makes 1.7% of total cases, but incidence in other studies are little higher. Similarly, endometrial carcinoma appears in 0.8% of peri-menopausal age group in the present study, which correlates with the data of Hussain *et al* [10] (0.7%), but was found slightly higher in the studies conducted by Abid *et al* [11] (1.2%) and Masood *et al* [12] (2%). These symptoms and histopathological diagnosis do not have any statistically significant relationship and are independent of each other. Therefore, patient should be subjected to endometrial biopsy as treatment depends on pathology of endometrium and cannot be decided solely on symptoms.

At menopause, imbalance of hormones may occur and leading to postmenopausal bleeding. Unpredicted bleeding can also happen when a woman is altering the dose of her hormone replacement therapy. In the present study in the post-menopausal group, the proliferative endometrium was significantly higher (57.14%) when compared with study conducted by the Husain *et al* [10] (4.3%). Similarly, secretory phase endometrium was 11.6% in the present study, which was higher than data published by Husain *et al* [10] (2.2%). However, endometrial polyp appeared in 5.19% cases in the present study, whereas data published by Husain *et al* [10] (21.9%), and Abid *et al* [11] (10.4%) were higher.

Among premalignant and malignant conditions in the post-menopausal group, endometrial hyperplasia without atypia was seen in 2.57% of cases in the present study, which was

significantly lower than the data published by Husain *et al* [10] (21.9%). Endometrial Carcinoma made 1.3% of post-menopausal age group which was found lower than incidence published by Abid *et al* [11] (9.0%) and Husain *et al* [10] (7.0%).

These differences in the incidences of the particular types in different studies might be because of the different selection criteria and use of ancillary studies like radiological modalities and geographic/genetic distribution of particular types. Finding of a particular histological finding on biopsy helps clinician to select most beneficial treatment for the patient, ranging from simple reassurance to staging hysterectomy.

CONCLUSION

Wide spectrum of histopathological diagnosis, ranging from benign to premalignant and malignant conditions, is found on evaluation of endometrial biopsies of patients presenting with abnormal uterine bleeding in the peri-menopausal and post-menopausal age group. Peri-menopausal group presents with different symptoms, but these symptoms are not associated with any particular histological diagnosis. Similarly, postmenopausal group also have a variety of histological diagnosis, although present with the common symptom of postmenopausal bleeding. Therefore, all cases with abnormal bleeding should be subjected to endometrial biopsy for appropriate management.

AUTHOR CONTRIBUTIONS

Sabah Kaleem: Designed the study and helped in critical review
Adeel Arif: Drafting and collection of data.
Syed Naeem Raza Hamdani: Literature review.
Fareeha Naseer Syed: Lab tests performed
Kamran Afzal: Data analysis.
Sana Saddique: Proofreading & discussion writing

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