

# Analysis of Histopathological Findings in Endometrium of Peri-Menopausal Women Presenting with Dysfunctional Uterine Bleeding

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## ABSTRACT

**Objective:** To analyze histopathological findings in endometrium of peri-menopausal women presenting with dysfunctional uterine bleeding at a tertiary care hospital of South Punjab, Pakistan.

**Study Design:** Cross sectional study.

**Place and Duration of the Study:** The Department of Obstetrics & Gynecology, Bakhtawar Amin Trust Teaching Hospital, Multan, Pakistan from April 2021 to March 2022.

**Material Methods:** During the study period, a total of 141 peri-menopausal women (aged 41 to 55 years) who presented with abnormal vaginal bleeding and underwent diagnostic endometrial curettage for histological analysis were included. A detailed history and careful systemic and pelvic examinations were performed. Endometrial tissue was obtained during dilatation & curettage (D&C) and preserved in 10% formaline and subjected for histopathologic analysis. Clinical and histological information of all subjects were recorded.

**Results:** In a total of 141 women, mean age was calculated to be 47±7 years. Except 24 (17.0%) patients who were already menopausal, 67 (47.5%) patients had normal length of menstrual cycle. Nearly half of the patients had normal histology of the endometrium. Simple hyperplasia was present in 18 (12.8%) and complex hyperplasia was in 10 (7.1%). Only 2 cases (1.4%) each of atypical endometrial hyperplasia and endometrial carcinoma were reported on the histology. Five patients (3.5%) had decidual change in the endometrium, which was mostly due to the prior intake of progestogens as part of medical therapy. Inflammation of endometrium was not uncommon and 19 (13.5%) had presence of inflammatory cells in the endometrium.

**Conclusion:** Peri-menopausal women with abnormal uterine bleeding should undergo diagnostic endometrial curettage to rule out the possibility of malignant or pre-malignant pathology. In perimenopausal patients, endometrial biopsy and other methods of detecting endometrial hyperplasia or carcinoma must be considered early in the investigation.

**Keywords:** Dysfunctional uterine bleeding endometrium, histopathology, peri-menopausal,

## INTRODUCTION

Menstrual dysfunction is a major public health issue among women of reproductive age.<sup>1</sup> The quality of life in women with menstrual dysfunction is disrupted and becomes a reason to seek some kind of medical assistance. Abnormal vaginal bleeding is known to be a frequent issue especially in women belonging to extreme reproductive age groups.<sup>2</sup> According to the data available, the prevalence of the females reporting with abnormal vaginal bleeding ranges between 10-30%.<sup>3,4</sup>

Menorrhagia has always been a common issue with females of reproductive age affecting around 16% of women of reproductive age groups.<sup>5</sup> Researchers in the recent decades have pointed out lactational amenorrhea as well as invention of efficient contraception modes to be common contributors to menstrual dysfunction.<sup>6</sup> Moreover, women of our generation also seem to have more willingness to bear difficulties associated with menstrual period.

Dysfunctional uterine bleeding (DUB) is described as "abnormal uterine bleeding not caused by pelvic pathology, medications, systemic disease or pregnancy".<sup>7</sup> DUB is commonly considered to be a diagnosis of exclusion helping clinicians exclude neoplastic abnormalities. Prior to medical or invasive treatment of abnormal vaginal bleeding, the patient is examined carefully along with general and medical history. Many of the women with DUB have no other presenting complaints while endometrial biopsy is a commonly performed procedure in these women.<sup>8</sup> Cervical dilatation & uterine curettage (D&C) under general anesthesia has been a commonly adopted approach in the past.<sup>9</sup> Last couple of decades has seen huge advancements regarding methods of examining the endometrium like high-resolution trans-vaginal sonography (TVS), outpatient endometrial biopsy, hysteroscopy.<sup>10</sup> The present study was conducted to analyze histopathological findings in endometrium of perimenopausal women presenting with dysfunctional uterine bleeding at a tertiary care hospital of South Punjab, Pakistan.

## MATERIAL AND METHODS

This cross-sectional observational study was conducted at The Department of Obstetrics & Gynecology, Bakhtawar Amin Trust Teaching Hospital, Multan, Pakistan from April 2021 to March 2022. Approval from "institutional ethical committee" was acquired. Informed and written consent was taken from all women enrolled.

During the study period, a total of 141 peri-menopausal women (aged 41 to 55 years) who presented with abnormal vaginal bleeding and underwent diagnostic endometrial curettage for histological analysis were included. Women with apparent anatomical cause of vaginal bleeding were excluded. A detailed history and careful systemic and pelvic examinations were performed. Endometrial tissue was obtained during D&C and preserved in 10% formaline and subjected for histopathologic analysis. Clinical and histological information of all subjects were recorded. A special format was designed to record study data. For data analysis, Statistical Package for Social Sciences version 26.0 was employed.

## RESULTS

In a total of 141 women, mean age was calculated to be 47±7 years. Abnormal uterine bleeding was less common in the women of low order parity and was more common in the women of high order parity. A vast majority of the patients (97.2%) had regular menstrual cycle until the recent past, while 4 (2.8%) of the patients complained of irregular cycle for many years. Majority of the patients (83.0%) who presented with abnormal uterine bleeding were in the pre-menopausal status and only 24 (17.0%) of the patients presented with post-menopausal bleeding. Except 24 (17.0%) patients who were already menopausal, 67 (47.5%) patients had normal length of menstrual cycle. However, 44 (31.21%) patients had menstrual cycle duration less than 22 days. Only 23 (16.3%) of the patients consulted at the first episode of abnormal uterine bleeding. One third of the patients, 49 (34.75%)

sought consultation within six months after the onset of the abnormal vaginal bleeding. However another one third of the patients postponed to seek the medical advice for more than a year after the onset of abnormal bleeding. More than half of the patients (n=77, 54.6%) never practiced any form of contraception, while the remaining used various methods of contraception for variable period of time. Twenty eight (19.9%) patients had tubal ligation in the past.

Table-1: Characteristics of Women (n=141)

Characteristics		Number (%)
Age (years)	41-49	111 (78.7%)
	50-55	30 (21.3%)
Parity	Nullipara	4 (2.8%)
	P 1-2	11 (7.8%)
	P 3-4	41 (29.1%)
	P 5-6	38 (27.0%)
	P 7 or above	47 (33.4%)
Previous menstrual Cycle	Regular	137 (97.2%)
	Irregular	4 (2.8%)
Duration of menstrual Cycle	Less than 22 days	44 (31.2%)
	22 – 42 days	67 (47.5%)
	More than 42 days	6 (4.3%)
	Menopausal	24 (17.0%)
Duration Since Onset of Abnormal Vaginal Bleeding	First Episode	23 (16.3%)
	2 – 6 months	49 (34.8%)
	7 – 12 months	20 (14.2%)
	13 – 18 months	12 (8.5%)
	More than 18 months	37 (26.2%)
Contraception Techniques	Never	77 (54.6%)
	Barrier	23 (16.3%)
	Injectable progestational contraceptives	7 (4.9%)
	IUCD	6 (4.3%)
	Sterilization surgery	28 (19.9%)

Majority of the women who sought medical advice, and subsequently underwent endometrial sampling procedure, presented with irregular heavy bleeding (n=53, 37.6%). Menorrhagia 32 (22.7%), post-menopausal bleeding 24 (17.0%), continuous bleeding 13 (9.2%), occasional spotting 9 (6.4%), intermenstrual bleeding 7 (5.0%) and oligomenhorrea 3 (2.1%) were other bleeding patterns observed. Use of hormonal treatment, anti-fibrinolytic agents alone, combination of hormonal treatment and anti-fibrinolytic agents, hormone replacement therapy and use of other drugs was reported in 32 (22.7%), 2 (1.4%), 17 (12.1%), 2 (1.4%) and 8 (5.7%) respectively. There were 80 (56.7%) women who were not taking any medical treatment. Table-2 is showing details of gross appearance of endocurettings.

Table-2: Gross appearance of Endocurettings (n=141)

Gross Appearance of Endocurettings	Number (%)
Normal looking	79 (56.3%)
Profuse	31 (22.0%)
Scanty	17 (12.0%)
Necrotic	7 (5.0%)
Blood clot	5 (3.6%)
POC's	2 (1.4%)

Table-3: Histologic findings in endometrium of peri-menopausal women presenting with dysfunctional uterine Bleeding (n=141)

Histological diagnosis	Number (%)
Proliferative Phase	48 (34.0%)
Secretory Phase	23 (16.3%)
Decidual reaction	5 (3.5%)
Endometritis	19 (13.5%)
Simple hyperplasia	18 (12.8%)
Complex hyperplasia	10 (7.1%)
Atypical hyperplasia	2 (1.4%)
Endometrial Cancer (Grade I-III)	2 (1.4%)
Placental tissue / POCs	3 (2.1%)
Atrophic endometrium	9 (6.4%)
Incorrect / inadequate tissue for histological analysis	2 (1.4%)

Nearly half of the patients had normal histology of the endometrium with proliferative phase (n=48, 4.0%) and secretory phase (n=23, 16.3%). Simple hyperplasia was present in 18 (12.8%) and complex hyperplasia was in 10 (7.1%). Only 2 cases (1.4%) each of atypical endometrial hyperplasia and endometrial carcinoma were reported on the histology. Five patients (3.5%) had decidual change in the endometrium, which was mostly due to the prior intake of progestogens as part of medical therapy. Inflammation of endometrium was not uncommon and 19 (13.5%) had presence of inflammatory cells in the endometrium (table-3).

## DISCUSSION

In order to have assistance in correct treatment, the histopathological examination of endometrium indicates the type of functional disturbance in cases of abnormal uterine bleeding. Number of medical treatments or conservative measures can be taken in a more confident way when pre-malignant or malignant pathology is excluded. In this study, abnormal uterine bleeding in pre-menopausal aged women was observed in 83% patients while 17% had post-menopausal bleeding. Among the group, the patients aged between 41-46 were 60%. Similar age distribution has been reported by Wren BG.<sup>11</sup> Slaneikov et al reported that the mean age of Russian women with abnormal bleeding was 48 years<sup>12</sup> which is very close to what we noted where mean age of women of peri-menopausal women with abnormal vaginal bleeding was 47 ± 7 years.

In this study polymenorrhagia was observed in (37.6%) and menorrhagia in (22.7%) of the patients. The patients with post-menopausal bleeding for at least 1 year after the menopause were (17.0%). On the other hand the pattern of bleeding mentioned by Moughal N was 48% and 41% as metrorrhagia and menorrhagia respectively and 6% were presented with post-menopausal bleeding.<sup>13</sup>

It is increasingly been observed that higher prevalence of abnormal uterine bleeding among the women who had sterilization surgery.<sup>14</sup> Others have also identified this association of abnormal uterine bleeding with tubal ligation, although tendency to seek surgical solution rather than a "post-tubal-ligation syndrome" has been suggested.<sup>15</sup> The relationship with tubal ligation and abnormal uterine bleeding in the subsequent years needs further evaluation. The presentation of anovulatory cycle in 55.3% of the patients and ovulatory cycle in 33.3% of the patients was observed through endometrial curettage.

There were 13.5% cases in which there was predominantly an inflammatory process in the endometrium which may itself be responsible for abnormal bleeding and may be obscuring some underlying serious pathology. Atrophic endometrium was obtained in 6.4% patients and all of them were menopausal. Placental / trophoblastic tissue was obtained in 2.1% cases. In 1.4% specimens, pathologist could not find any endometrial tissue, and mostly comprised of blood clots. Endometrial carcinoma was diagnosed in 1.4% of the cases. The role of endometrial biopsy in the investigation of abnormal uterine bleeding is well established.<sup>16,17</sup> But, the main drawback with conventional D&C for obtaining the endometrial sample is that it is a blind procedure and there are fair chances that the pathology confined to a particular area of endometrial cavity may be missed. Comparing the results with studies, which employed hysteroscope for obtaining the endometrial tissue, the diagnostic accuracy is increased. In a study by Schwarzler et al, on diagnostic accuracy of conventional D&C and hysteroscope guided endometrial biopsy the diagnostic accuracy was increased from 68% to 92%.<sup>18</sup> Hysteroscopy has evolved to replace D&C in the investigation of abnormal uterine bleeding.<sup>19</sup> When endometrial biopsy / D&C result in a positive diagnosis, this diagnosis is generally reliable. The two key issues are the accuracy of histopathologic report based on morphometric study and the natural history of the underlying pathology, both of which remain the focus of intense research effort. However, when these procedures are "negative" this does not exclude significant abnormality and additional testing may be required. The patients,

who presents with DUB and history of menstrual cycle irregularity warrants a careful evaluation particularly in the women over the 40 years of age. The key to the evaluation of abnormal uterine bleeding is a thorough history and physical and pelvic examination. Carefully sampled endometrial tissue helps in establishing a firm diagnosis. Histological analysis of endometrium is a valuable diagnostic aid to determine the pathology behind an abnormal uterine bleeding, and helps in deciding the future management plans.

## CONCLUSION

Peri-menopausal women with abnormal uterine bleeding should undergo diagnostic endometrial curettage to rule out the possibility of malignant or pre-malignant pathology. In perimenopausal patients, endometrial biopsy and other methods of detecting endometrial hyperplasia or carcinoma must be considered early in the investigation. Clinical information, along with the reproductive stage of the patient, narrows the etiologic possibilities. The etiology of abnormal bleeding can be uncovered in a cost-effective way if the physician knows the most common causes of bleeding in each age group and uses a logical diagnostic approach.

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