Evaluation and histopathological correlation of abnormal uterine bleeding in perimenopausal women

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Abstract
Objectives: To study the causes of abnormal uterine bleeding in perimenopausal women and to correlate their clinical evaluation with ultrasonographic and histopathological examination.
Method: This is a retrospective study of 100 perimenopausal women with complaint of abnormal bleeding in the age group ranging from 40 years till 1 year within the menopause, who underwent hysterectomy at Lok Nayak Hospital. The age, parity, menstrual complaints of these patients were noted & clinical diagnosis and ultrasonography were analysed. Finally, histopathology report of the hysterectomy specimen was correlated with the clinical profile of the patient and ultrasonographic findings.
Results: Maximum frequency of abnormal uterine bleeding was seen in the age group 40–45 years. Most of the patients were para 3. Menorrhagia was the commonest complaint & fibroid uterus was responsible for abnormal uterine bleeding in 53% of women. Out of 39 women labelled clinically as dysfunctional uterine bleeding, 8 patients were diagnosed with fibroid uterus on ultrasound & in rest of the 31 patients, no organic cause was found. Out of these 31 patients, 4 patients were diagnosed to have adenomyosis on histopathology & in rest, no gross pathology was detected. Suspected malignancy in all the 3 patients was confirmed on histopathology. Simple endometrial hyperplasia without atypia was present in 19% patients.
Conclusion: Clinical, radiological & pathological evaluation correlated well to diagnose fibroids, however clinically as well as ultrasound proved to be of little help in diagnosing adenomyosis.
Keywords: Abnormal uterine bleeding; histopathology; adenomyosis

1. Introduction
The endometrium represents a plethora of changes ushered in by the complex interplay of endogenous sex steroids & other factors. World Health Organisation defines perimenopause as the period 2-8 years preceding menopause and 1 year after the final menses1. However, a better practical definition is the phase preceding the menopause, generally occurring around 40–50 years (average 45.5 - 47.5 years)2. Perimenopausal period usually last for around 4 years3. Follicular development at this time has been demonstrated to be erratic, with consequent variability in estrogen levels and an increased percentage of anovulatory cycles4. Menorrhagia is defined as excessive uterine bleeding i.e more than 80 mL in a month or prolonged in duration i.e more than seven days. Polymenorrhagia, intermenstrual bleeding, metrorrhagia are other common disorders at perimenopause. The manifestations of various disease patterns can be detected by histological variations of endometrium, taking into account the age of the woman, the phase of her menstrual cycles.
The objectives of this study were:
1. To know the causes of abnormal uterine bleeding in perimenopausal women.
2. To correlate clinical evaluation with ultrasonographic & histopathological examination.

2. Material & Methods

This is a retrospective study conducted on 100 perimenopausal women with abnormal uterine bleeding in the age group of 40 years till 1 year within menopause who underwent hysterectomy at Lok Nayak Hospital, a tertiary care teaching hospital in Delhi. We analysed these women by recording their age, parity, menstrual symptoms and associated symptoms for clinical evaluation. Ultrasonographic evaluation of all these women was done. Clinical impression and ultrasonography reports were correlated. These women underwent endometrial sampling & the histopathology report of the specimen was analysed. Histopathology reports of the hysterectomy specimens were correlated with clinical diagnosis and ultrasonographic findings.

3. Results

The basic characteristics of the patients have been described in table 1. The menstrual complaints presented by the patients have been shown in figure 1.

Table 1: Basic characteristics of the patients

| Parameter               | Result                      |
|-------------------------|----------------------------|
| Mean age of the patient | 45.74 ± 2.81 years         |
| Parity                  |                            |
| 1                       | 4                          |
| 2                       | 32                         |
| 3                       | 47                         |
| ≥ 4                     | 17                         |
| Duration of symptoms    |                            |
| Range                   | 3 months to 4 years        |
| Mean                    | 1.5 years                  |

Figure 1: Menstrual complaints in patients
Clinical diagnosis was made on the basis of presenting complaints & clinical examination including per vaginum examination. Hematological investigations included complete blood count & coagulation profile. Thyroid profile was done in most of the patients. Ultrasonography was done to detect any local structural pathology like fibroid & adenomyosis. Endometrial aspiration biopsy was taken in all the patients. The patients who didn’t have any systemic or locally definable structural cause on clinical examination & investigations were labelled as dysfunctional uterine bleeding.

Finally the clinical, radiological & histopathology finding of the hysterectomised specimen were correlated as shown in table 2.

**Table 2 : Clinical, radiological & histopathological correlation**

| Pathology                | Clinical | USG | HPE |
|--------------------------|----------|-----|-----|
| Fibroid                  | 54       | 63  | 53  |
| Adenomyosis              | 4        | 2   | 6   |
| Fibroid with adenomyosis | 0        | 1   | 10  |
| DUB                      | 39       | 31  | 28  |
| Malignancy               | 3        | 3   | 3   |
| Total                    | 100      | 100 | 100 |

In 54% of the patients, a diagnosis of fibroid uterus was made, in 39% dysfunctional uterine bleeding & in only 4% of the patients, provisional diagnosis of adenomyosis was made on the basis of clinical examination & endometrial aspiration biopsy.

The clinical diagnosis was confirmed by ultrasonography. Ultrasound detected fibroid in 100 % of the cases who were suspected to have fibroid on clinical examination. Out of the 4 patients who were clinically suspected to have adenomyosis, two were confirmed on ultrasound. The patients who didn’t have any significant finding on clinical examination were labelled as dysfunctional uterine bleeding. Further, ultrasonography revealed the organic cause in some of these patients. Out of 39 such patients, 8 patients were found to have fibroid uterus & in rest of the 31 patients, no organic cause was found on ultrasound also.

Ultimate diagnosis was made on the basis of histology, so every hysterectomy specimen was sent for histopathological examination. Out of the 63 patients who were diagnosed to have fibroid uterus on ultrasonography, 53 patients were confirmed to have leiomyoma on histopathology & 10 patients had adenomyosis as well as leiomyoma indicating the hyperestrogenic state. Out of the 31 patients who were labelled as dysfunctional uterine bleeding after ultrasound, 4 patients were diagnosed to have adenomyosis on histopathology & in rest 28 patients, no gross pathology was detected. Suspected malignancy in all the three patients was confirmed on histopathology. The ultrasound findings in cases of adenomyosis were heterogenous areas within myometrium & subendometrial cysts. Out of the three cases of malignancies, two patients had a well defined endometrial polypoidal growth & the third case had disruption of endomyometrial junction along with heteroechoic changes in the endometrium.

Endometrial pathology was also studied alongwith. 61% of the patients had normal histology. Simple endometrial hyperplasia without atypia was present in 19% & complex hyperplasia without atypia in 1% of the patients. Hormonal imbalance was present in 7% & chronic non specific endometritis in 9% of the patients (Table 3). The correlation of preoperative endometrial sampling report was correlated with the final histopathology of the specimen & the findings have been shown in table 4.
Table 3: Histopathology findings of endometrium

| Final Pathology       | Normal menstrual phase | Chronic Endometritis | Hormonal Imbalance | Simple Hyperplasia without atypia | Complex Hyperplasia without atypia | Malignancy | Total |
|-----------------------|------------------------|----------------------|--------------------|-----------------------------------|------------------------------------|------------|-------|
| Menorrhagia           | 52                     | 4                    | 0                  | 13                               | 1                                  | 2          | 72    |
| Polymenorrhagia       | 5                      | 2                    | 3                  | 3                                | 0                                  | 0          | 13    |
| Polymenorrhoea        | 4                      | 1                    | 2                  | 0                                | 0                                  | 0          | 7     |
| Metromenorrhagia      | 0                      | 2                    | 2                  | 3                                | 0                                  | 1          | 8     |
| Total                 | 61                     | 9                    | 7                  | 19                               | 1                                  | 3          | 100   |

Table 4: Correlation of endometrial biopsy with the final histopathology report

| Endometrial biopsy       | Normal menstrual phase | Chronic endometritis | Hormonal imbalance | Simple hyperplasia without atypia | Complex hyperplasia without atypia | Malignancy | Total |
|--------------------------|------------------------|----------------------|--------------------|-----------------------------------|------------------------------------|------------|-------|
| Normal menstrual phase   | 58                     |                      |                    |                                   |                                    |            |       |
| Chronic endometritis     | 4                      |                      |                    |                                   |                                    |            |       |
| Hormonal imbalance       | 7                      |                      |                    |                                   |                                    |            |       |
| Simple hyperplasia without atypia | 17                   |                      |                    |                                   |                                    |            |       |
| Complex hyperplasia without atypia | 1                  |                      |                    |                                   |                                    |            |       |
| Malignancy               | 3                      |                      |                    |                                   |                                    |            |       |
| Total                    | 100                    |                      |                    |                                   |                                    |            | 100   |

4. Discussion

Abnormal Uterine Bleeding is the main reason women are referred to gynaecologists and accounts for two thirds of all hysterectomies\textsuperscript{5}. Evaluation of patients with abnormal uterine bleeding and identifying those with dysfunctional uterine bleeding is achieved with a combination of the following: history, physical examination, ultrasound & histopathological evaluation. Abnormal uterine bleeding in perimenopausal women is associated with endometrial carcinoma in 10% patients\textsuperscript{5}, so evaluation of women’s risk factors for endometrial hyperplasia or carcinoma is recommended.

Majority of women with uterine fibroid associated with menorrhagia are treated by hysterectomy. In our study, fibroid uterus was responsible for abnormal uterine bleeding in 52% of women comparable with a study of LTMMC hospital Mumbai\textsuperscript{6} & DHQ hospital Multan\textsuperscript{7} in which abnormal uterine bleeding evaluation revealed fibroid in 54% & 54.8% respectively.

We compared our study of endometrial patterns with LTMMC hospital\textsuperscript{6} & Michail et al\textsuperscript{8} study. In these studies, no. of cases were 112 & 84 respectively, where simple hyperplasia without atypia was present in 17.8% & 8.53% respectively as compared to 24% in our study.

Menorrhagia in fibroids is due to increased size of uterine cavity thereby increasing the surface area of the endometrium, hyperestrogenemia causing endometrial hyperplasia, vascular alteration of the endometrium and obstructive effect of fibroid on uterine vasculature leading to endometrial venule ectasia which causes proximal congestion in the myometrium and the endometrium.

In our study, only 4 cases were diagnosed as adenomyosis, ultrasound diagnosed only 2 of them, however, final
histopathology diagnosed 6 cases.

Diagnosis of adenomyosis on clinical findings is usually different. Transabdominal sonography doesn’t allow reliable diagnosis of adenomyosis, even transvaginal ultrasonography has limitation in tissue characterization. MRI is more helpful to diagnose adenomyosis but is expensive.

Ours is a retrospective study done on 100 patients. Larger sample size will have a better correlation of the clinical, radiological & histopathological findings.

5. Conclusion

In our study, fibroids of the uterus were the most common cause of the AUB. Second common cause was DUB followed by adenomyosis. Histopathology revealed majority of endometrium in the proliferative phase. Clinical, radiological & pathological evaluation correlated well to diagnose fibroids, however clinically as well as USG proved to be of little help in diagnosing adenomyosis. Maximum hysterectomies were done for fibroid uterus. AUB occurring as heavy cyclical or acyclical flow at perimenopausal age is alarming and needs thorough evaluation, as it could be the only clinical manifestation of endometrial cancer.

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