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# Evaluation and histopathological correlation of abnormal uterine bleeding in menopausal transition in a tertiary care centre at Cheluvamba hospital, Mysore

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**Abstract**
**Introduction:** AUB at menopausal transition is alarming and needs thorough evaluation, as it could be the only clinical manifestation of cancer.
**Methodology:** This prostective study was done to evaluate the gynaecological causes of AUB in menopausal transition in OBG Department, MMC&RI, Mysore. These women were evaluated; clinical, ultrasound and histopathological findings were correlated.
**Results:** In the present study, heavy menstrual bleeding (66.7%) was the commonest type of bleeding pattern. Leiomyoma, DUB and Adenomyosis were the principle causes of AUB. Leiomyoma accounts for the 60.6% of cases, DUB accounts for 15.9%, Adenomyosis accounts for 9.09% and Leiomyoma with Adenomyosis accounts for the 14.39% of cases.
**Conclusion:** Endometrial biopsy and its interpretation play a pivotal role in the management of AUB cases in menopausal transition. It emphasizes the role of health care professionals to encourage teaching and implementation of alternative procedures to ensure that women receive the maximum benefits with least morbidity.

**Keywords:** AUB (Abnormal uterine bleeding), menopausal transition, histopathology

## Introduction

Menopause is the permanent cessation of menstruation which occurs following loss of ovarian activity. It is derived from Greek word 'mens'- month, 'pausis'- cessation [1]. Perimenopause is a period 3-4 years before menopause and followed by 1 year of amenorrhea. It encompasses the change from normal ovulatory cycles to cessation of menses, marked by irregularity of menstrual cycles [2].

The Perimenopausal Transition: Age of onset for 95% of women is 39-51 years. Average age of onset is 46 years. Duration for 95% of women is 2-8years. Average duration is 5 years [1].

While significant awareness has been raised about menopause, less attention has been focused on the perimenopausal or "menopausal transition" period. Many women and their physicians remain unaware of the impact of this transitional phase into menopause [1]. Specifically, heavy and unpredictable perimenopausal bleeding is extremely common [3].

The purpose of this review is to focus on the hormonal and physiologic changes that are associated with perimenopausal heavy vaginal bleeding, to present the essential evaluation of causes for this heavy flow, and to outline the evidence for effective medical and surgical treatments. Advances in the understanding of the normal physiology of perimenopause have led to medical therapies that may lead to fewer surgical procedures and hysterectomies and should be of interest to health care practitioners focusing on women's health [3].

Abnormal uterine bleeding (AUB) refers to a symptom of excessive, prolonged, unexpected or acyclic bleeding regardless of diagnosis or cause. AUB not only affects quality of life such as intimate relationships, day to day living but can have serious adverse consequences as anaemia or malignancy [4].

The diagnostic goal with perimenopausal bleeding is to exclude carcinoma and to identify the underlying pathology to allow optimal treatment [5].

Ultrasonography may reveal an obvious cavitary lesion or an abnormally thin or thick endometrium. In perimenopausal and postmenopausal women with abnormal bleeding, endometrial biopsy is generally considered unnecessary when the endometrial thickness is less

than 4 or 5 mm because the risk of endometrial hyperplasia or cancer is remote. Biopsy is indicated when clinical history suggests long term unopposed estrogen exposure. An endometrial stripe of 5 mm thickness has been shown to be associated with an extremely low risk of endometrial hyperplasia or carcinoma [2]. Women with endometrial thickness >5 mm warrant additional evaluation with saline infusion sonography or endometrial biopsy [3].

An accurate method of determining whether AUB is functional or structural, one needs a minimally invasive accurate method. D&C under general anaesthesia was once considered as gold standard investigation in the evaluation of AUB. It can however miss 2-6% of cases of cancer or hyperplasia.[5] Uterine cancer, the most serious cause of uterine bleeding is diagnosed in fewer than 10% of endometrial biopsies in women presenting with AUB, indicating that more than 90% of endometrial biopsies revealed benign findings [6].

The older terms perimenopause or climacteric generally refer to the time period in the late reproductive years usually late 40s to early 50s. The more correct terminology for this term is menopausal transition [7].

The present study is designed to evaluate the causes of abnormal uterine bleeding in Menopausal Transition & to correlate the clinical evaluation with ultrasonographic & histopathological examination.

**Aims and objectives**

1. To evaluate clinically the gynaecological causes of abnormal uterine bleeding in Menopausal Transition.
2. To correlate the clinical evaluation with ultrasonographic and histopathological examination.

**Materials and Methods**

**Source of data:** The present study was conducted in the Department of Obstetrics and Gynaecology, Cheluvamba Hospital, attached to Mysore Medical College and Research Institute women who presented with abnormal uterine bleeding in menopausal transition age over a period of one year from November 2013 to October 2014.

**Inclusion criteria**

a. Patients complaining of abnormal uterine bleeding
b. Age 39-51 years

**Exclusion criteria**

**a.** Post menopausal women

**Methods of collection of data**

Ethical committee approval was taken for the study. Before recruiting the patient into the study, an informed consent was taken. Identification of the patient in relation to name, age, address, religion, socio-economic status, marital status, parity and literacy status was done.

Detailed clinical history including onset and duration of bleeding, drug history, past obstetric medical and surgical history was taken. Thorough clinical examination which included general physical examination, per abdomen, per speculum and per vaginal examination was done.

The terms used to categorise the bleeding patterns are as follows:

Acceptable Abbreviations Describing Menstrual Symptoms Established by Popular Usage [8]

AUB: Abnormal uterine bleeding (the overarching symptom)
HMB: Heavy menstrual bleeding
HIMB: Heavy with intermenstrual bleeding
IMB: Inter menstrual bleeding
PMB: Postmenopausal bleeding

Investigations like complete heamogram, ABO Rh, RBS, Thyroid profile, Urine routine, Renal function test, Liver function test, TVS or TAS and endometrial biopsy was done in all patients, irrespective of the endometrial thicknes. The endometrium was imaged in the longitudinal and cross-sectional plane through the body and the fundus of the uterus. The thickest point of the endometrium was measured from the anterior to posterior myometrial-endometrial junction. Both layers of the endometrium were measured, that is the anterior and posterior layers. Morphological changes like appearance of endometrial strip (homogenous/heterogenous), endometrial thickness (diffuse/focal), margins (regular/irregular) are also noted.

Endometrial biopsies were done and the endometrial samples (endometrial curettage / hysterectomy specimens) sent to pathology laboratory, were analysed. These specimens are fixed in 10%formalin and gross morphology were recorded. Histopathological examination of the endometrial pattern as well as that of hysterectomy specimens were done. These bits were placed in cassettes and kept in fixative and processed in the automatic tissue processor. Paraffin tissue blocks were prepared and 3-4micrometer thick sections were cut and stained with routine Haematoxylin and Eosin. A detailed histological study was carried out and the findings were noted.

Evaluation of ultrasound and histopathological findings of clinically diagnosed AUB cases was done with appropriate Statistical analysis was done.

**Results**

The study was conducted in the department of obstetrics and Gynaecology, Cheluvamba Hospital, MMC and RI Mysore. Total number of 132 cases were studied, age ranging from 39-51 years (Mean age=45years).

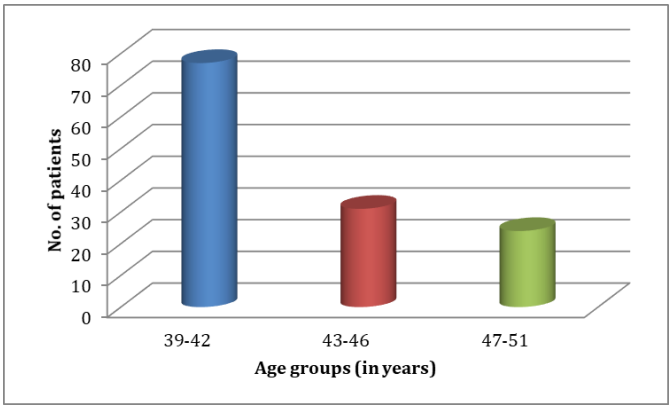


**Fig 1:** Age distribution pattern

In the present study of 132 women in menopausal transition 58.3% belonged to age between 39-42 years, 23.5% belonged to age between 43-46 years, and rest 18.2% belonged to 47-51 year age group (Figure 1).

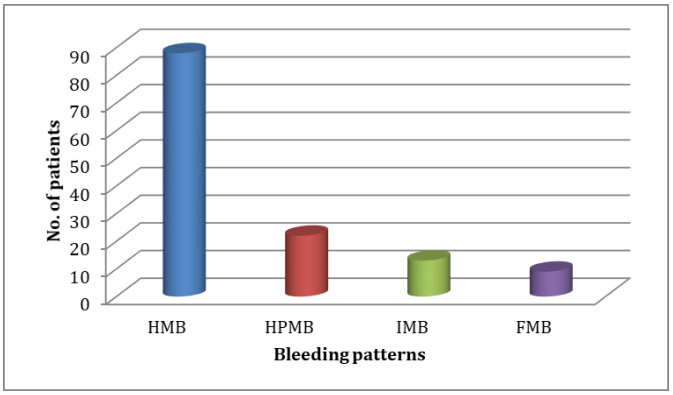


**Fig 2:** Distribution of bleeding patterns

In the present study 66.7% had Heavy Menstrual Bleeding (HMB), 16.7% had Heavy Bleeding with Intermenstrual Bleeding (HPIB), 9.8% had Intermenstrual Bleeding (IMB), and 6.8% had Frequent Menstrual Bleeding (FMB) (Figure 2).

**Table 1:** Histopathology findings of endometrium in relation to symptoms

| Final pathology/ Symptoms | Normal menstrual phase | Disordered proliferative phase | Atrophic endometrium | Chronic endometritis | Simple hyperplasia without atypia | Complex hyperplasia without atypia | Endometrial polyp | Total |
|---|---|---|---|---|---|---|---|---|
| HMB | 55 | 8 | 15 | 2 | 6 | 0 | 2 | 88 |
| | 62.5% | 80.0% | 93.8% | 100.0% | 60.0% | 0.0% | 40.0% | 66.7% |
| HIMB | 17 | 1 | 0 | 0 | 2 | 1 | 1 | 22 |
| | 19.3% | 10.0% | 0.0% | 0.0% | 20.0% | 100.0% | 20.0% | 16.7% |
| IMB | 9 | 1 | 0 | 0 | 1 | 0 | 2 | 13 |
| | 10.2% | 10.0% | 0.0% | 0.0% | 10.0% | 0.0% | 40.0% | 9.8% |
| FMB | 7 | 0 | 1 | 0 | 1 | 0 | 0 | 9 |
| | 8.0% | 0.0% | 6.2% | 0.0% | 10.0% | 0.0% | 0.0% | 6.8% |
| Total | 88 | 10 | 16 | 2 | 10 | 1 | 5 | 132 |
| | 100.0% | 100.0% | 100.0% | 100% | 100.0% | 100.0% | 100.0% | 100% |

Out of 88 patients with Heavy Menstrual Bleeding (HMB), 55 patients had normal menstrual phase of endometrium, 8 patients had disordered proliferative endometrium, 15 patients had atrophic endometrium, 2 patients had endometrial polyp, 6 patients had simple hyperplasia without atypia and 2 patients had chronic endometritis (Table 1).

Out of 22 patients with Heavy with Intermenstrual Bleeding (HIMB), 17 patients had normal menstrual phase of endometrium, 1 patient had disordered proliferative endometrium, 1 patient had endometrial polyp, 2 patients had simple hyperplasia without atypia and 1 patient had complex hyperplasia without atypia (Table 1).

Out of 13 patients with Intermenstrual Bleeding (IMB), 9 patients had normal menstrual phase, 1 patient had disordered proliferative phase, 2 patients had endometrial polyp, 1 patient had simple hyperplasia without atypia (Table 1).

Out of 9 patients with Frequent Menstrual Bleeding (FMB), 7 patients had normal menstrual phase endometrium, 1 patient had atrophic endometrium and 1 patient had simple hyperplasia without atypia (Table 1).

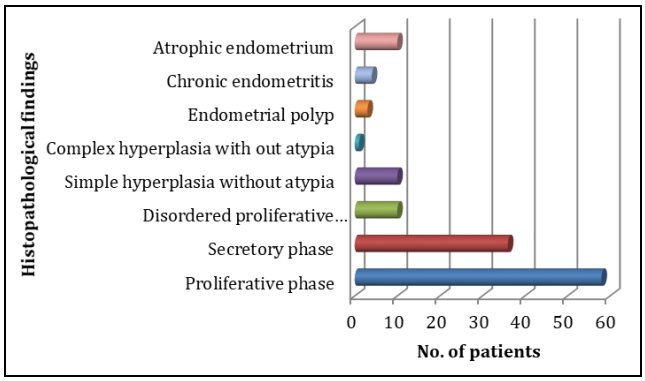


**Fig 3:** Endometrial biopsy reports

In the present study, of endometrial biopsy, proliferative endometrium was found in 43.9% of patients, secretory endometrium in 27.3%, disordered proliferative endometrium in 7.6%, atrophic endometrium in 7.6%, simple hyperplasia without atypia in 7.6%, chronic endometritis in 3%, endometrial polyp in 2.3% and complex hyperplasia without atypia in 0.8% of patients (Fig 3).

**Table 2:** Clinical diagnosis and HPE report correlation

| Clinical | HPE | | | | Total |
|---|---|---|---|---|---|
| | Leiomyoma | Adenomyosis | Leiomyoma+ adenomyosis | DUB | |
| Leiomyoma | 72 | 6 | 18 | 4 | 100 |
| | 72.0% | 6.0% | 18% | 4% | 100% |
| Adenomyosis | 2 | 2 | 0 | 0 | 4 |
| | 50.0% | 50.% | 0% | 0% | 100% |
| DUB | 6 | 4 | 1 | 17 | 28 |

| | | | | | |
|---|---|---|---|---|---|
| | 21.4% | 14.3% | 3.6% | 60.7% | 100% |
| Total | 80 | 12 | 19 | 21 | 132 |
| | 60.6% | 9.1% | 14.4% | 15.9% | 100% |

Out of 132 patients, on clinical examination, 100 patients were diagnosed to be having leiomyomas, finally confirmed by Histopathological examination. 72 cases were to be having leiomyoma, 18 were found to be having leiomyoma and adenomyosis, 6 were found to be having adenomyosis, 4% found to be having normal morphology of uterus. Out of the 4 patients found to be having adenomyosis, on clinical examination 2 were found to be having adenomyosis and 2 were found to be having leiomyoma (Table 2).

Out of the 28 cases diagnosed to be having DUB, on clinical examination, 6 were diagnosed as leiomyoma, 4 were found to be having adenomyosis, One was diagnosed to be having adenomyosis and leiomyoma. 17 cases were correlated with clinical diagnosis since no gross pathology found in the uterus (Table 2).

**Table 3:** USG diagnosis and HPE report correlation

| USG | HPE | | | | Total |
|---|---|---|---|---|---|
| | Leiomyoma | Adenomyosis | Leiomyoma+ adenomyosis | DUB | |
| Leiomyoma | 74 | 3 | 16 | 3 | 96 |
| | 77.1% | 3.1% | 16.7% | 3.1% | 100.0% |
| Adenomyosis | 1 | 1 | 2 | 0 | 4 |
| | 25% | 25% | 50% | 0% | 100.0% |
| Leiomyoma + Adenomyosis | 4 | 0 | 0 | 0 | 4 |
| | 100% | 0.0% | 0.0% | 0.0% | 100.0% |
| DUB | 1 | 8 | 1 | 18 | 28 |
| | 3.57% | 28.5% | 3.57% | 64.2% | 100.0% |
| Total | 80 | 12 | 19 | 21 | 132 |
| | 60.6% | 9.1% | 14.4% | 15.9% | 100.0% |

Out of 132 cases, on Ultrasonography 96 patients were diagnosed as leiomyomas. After histopathological examination, out of 96 patients, 74 were diagnosed as leiomyomas, 3 were diagnosed as adenomyosis, 16 were diagnosed as leiomyomas with adenomyosis and 3 patients were diagnosed as Dysfunctional Uterine Bleeding (Table 3).

Out of the 4 patients diagnosed to be having adenomyosis, histopathological examination diagnosed adenomyosis in one case, leiomyoma in one case and dual pathology of leiomyoma and adenomyosis in 2 cases. Out of 4 patients diagnosed as Adenomyosis + Leiomyoma, confirmed by histopathological examination (Table 3).

Out of 28 patients who were labelled as Dysfunctional Uterine Bleeding by Ultrasonography, 1 patient was diagnosed to be having leiomyoma, 8 patients were diagnosed to be having adenomyosis, one patient was diagnosed to be having adenomyosis with leiomyoma and in the rest of 18 patients no gross pathology was detected on histopathological examination (Table 3).

## Discussion

Abnormal uterine bleeding is the main reason, woman are referred to gynecologists and accounts for two-thirds of all hysterectomies [9]. Evaluation of patients with abnormal uterine bleeding and identifying those with AUB is achieved with combination of the following: history, physical examination, ultrasound and histopathological evaluation. AUB in women of menopausal transition age group is associated with endometrial carcinoma in 10% of patients [9], so evaluation of woman's risk factors for endometrial hyperplasia or carcinoma is recommended.

Though endometrial sampling can be done by endometrial biopsy, endometrial aspiration and hysteroscopy, hysteroscopic guided biopsy is considered gold standard.

The results from the study were analyzed and compared with results of other published studies.

In the present study, most of the women with AUB belonged to 39-42years age group (58.3%), followed by 23.5% in the age group of 42-46 years, in the range of age distribution between 39-51 years, which is comparable with the study by Archana B *et al*., at LTMMC hospital, Mumbai [10], 76.1% were in the age group of 40-45 years.

**Table 4:** Distribution of bleeding pattern

| Menstrual complaints | Gupta *et al* [11] | | Present study | |
|---|---|---|---|---|
| | Number | Percentage | Number | Percentage |
| HMB | 72 | 72 | 88 | 66.7 |
| HPMB | 13 | 13 | 22 | 16.7 |
| IMB | 08 | 08 | 13 | 9.8 |
| FMB | 07 | 07 | 09 | 6.8 |
| Total | 100 | 100 | 132 | 100 |

In the present study, heavy menstrual bleeding was the commonest type of bleeding pattern (66.7%) followed by heavy and prolonged menstrual bleeding (16.7%), intermenstrual bleeding in 9.8% of patients and frequent menstrual bleeding in 6.8% of patients, is in concordance with the study done by Gupta *et al* [11].

In the present study, endometrial thickness was assessed using ultrasound, 7.6% had thickness of less than 5mm, 56.8% had ET of 5-8mm, 26.5% of women had ET of 9-12mm and 9.1% had ET of >12mm. In the study done by Asma Fared *et al*. [12], recommended a ET of >6mm single layer endometrium as cut off point for the further evaluation of AUB in menopausal

transition.

**Table 5:** comparative study of HPE report of endometrium

| Final Pathology | Gupta *et al*[11] | | Present study | |
|---|---|---|---|---|
| | Number | % | Number | % |
| Normal menstrual phase | 61 | 61 | 88 | 66.7 |
| Disordered proliferative phase | 7 | 7 | 10 | 7.6 |
| Atrophic endometrium | 0 | 0 | 16 | 12.1 |
| Chronic endometritis | 9 | 9 | 2 | 1.5 |
| Simple hyperplasia without atypia | 19 | 19 | 10 | 7.6 |
| Complex hyperplasia without atypia | 1 | 1 | 1 | 0.8 |
| Endometrial polyp | 0 | 0 | 5 | 3.8 |
| Malignancy | 3 | 3 | 0 | 0 |

In the present study, final histopathological examination of endometrium shows normal menstrual phase that is, proliferative and secretory phase (66.7%), which is in concordance with study by Gupta *et al.* [11] (61%), disordered proliferative phase in 7.6%, atrophic endometrium in 16%, chronic endometritis in 1.5%, simple hyperplasia without atypia in 7.6%, endometrial polyp in 3.8% of patients.

No case of malignancy was found in the present study as compared to 3% of cases in Gupta *et al* [11] study. Atrophic endometrium was found in 12.1% of cases compared to Gupta *et al* [11]. The study by Archana *et al* [10] found proliferative endometrium 66.1% of cases, secretory endometrium in 16.1% of cases, which is also comparable to present study.

**Table 6:** Clinical, radiological and HPE correlation

| Pathology | Gupta *et al* | | | Present study | | |
|---|---|---|---|---|---|---|
| | Clinical | Ultrasound | HPR | Clinical | Ultrasound | HPR |
| Leiomyoma | 54 | 63 | 53 | 100 (75.76%) | 96 (72.73%) | 80 (60.60%) |
| Adenomyosis | 4 | 2 | 6 | 4 (3.03%) | 4 (3.03%) | 12 (9.09%) |
| Leiomyoma+ adenomyosis | 0 | 1 | 10 | 0 (0.00%) | 4 (3.03%) | 19 (14.39%) |
| DUB | 39 | 31 | 28 | 28 (21.2%) | 28 (21.2%) | `21 (15.90%) |
| Malignancy | 3 | 3 | 3 | 0 | 0 | 0 |
| Total | 100 | 100 | 100 | 132 | 132 | 132 |

Finally the clinical, radiological and histopathological findings of hysterectomy specimens were correlated.

In 75.76% of patients a diagnosis of leiomyoma was made. In 21.2% of patients a diagnosis of DUB and in only 3.03% of patients, provisional diagnosis of adenomyosis was done on clinical examination.

The clinical examination findings were confirmed by ultrasound which detected leiomyoma in 100% of patients who were suspected to have leiomyoma on clinical examination. Out of 4 patients, who were clinically suspected to have adenomyosis, all the 4 were confirmed by USG. The patients who didn't have any significant finding on clinical examination were labelled as DUB.

Ultimate diagnosis was made on the basis of final histology of the hysterectomy specimen. Out of 96 patients who were diagnosed to have fibroids on USG, 80 patients were confirmed to have leiomyoma and 19 patients had leiomyoma with adenomyosis indicating the hyper estrogenic state.

Out of 28 patients who were labelled as DUB after ultrasound, 8 patients were diagnosed to have adenomyosis, 1 patient is found to be having adenomyosis + leiomyoma and 1 more patient found to be having leiomyoma.

Majority of women with uterine Leiomyoma associated with mennorhagia are treated by hysterectomy. In our study Leiomyoma uterus was responsible for AUB in 60.6% of patients comparable with the study of LTMMC hospital Mumbai [10] 54%, DHQ Hospital, Multan [13] 54.8% and Gupta *et al* [11] 52% Fl Cornitescu *et al* [1] 49.6%, where evaluation of AUB revealed Leiomyoma.

Heavy menstrual bleeding in fibroids is due to increased size of the uterine cavity thereby increasing the surface area of endometrium, hyperestrogenism 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 endometrium.

Diagnosis of adenomyosis on clinical examination is usually different [15]. TAS doesn't allow reliable diagnosis of adenomyosis or consistent differentiation from Leiomyoma, even TVS has limitation in tissue characterization. MRI is more helpful to diagnose Adenomyosis but expensive. In our study clinically, only 4 (3.03%) cases were diagnosed as Adenomyosis, Ultrasound diagnosed 4 (3.03%) cases and histopathological examination diagnosed 12 (9.09%) cases. The reported prevelance of Adenomyosis in hysterectomy specimens varies from 5 to 70 percent.

In the present study DUB was the second most common cause of AUB, accounting for the 21% of cases, which is in concordance with the study by Gupta *et al* [11] (28%). In the present study Adenomyosis with Leimyoma is the third common cause of AUB, accounts for the 19% of cases, which is in concordance with the study by Gupta *et al* (10%). In the present study Adenomyosis is the least common cause of AUB, in 9,09% of cases, which is in concordance with the study by Gupta *et al* (6%). The study by Archana *et al* [10] found Adenomyosis was the second most common cause of AUB in 29.4% of cases.

## Conclusion

AUB is one of the most common problems in women of all age groups affecting 10-30% of reproductive aged women and upto 50% of women in menopausal transition. It is a challenging gynaecological problem caused by various structural abnormalities of the uterus and endometrial pathologies.

Endometrium is the mirror image of hormonal status in women

of different age groups. It is important in detecting the cause, clinching the diagnosis and managing the patients with AUB.

Endometrium can be easily procured in AUB cases by endometrial biopsy which is a simple cost effective and appropriate method that provides accurate diagnostic yield. Endometrial biopsy and its interpretation play a pivotal role in the management of AUB cases in menopausal transition.

In the present study, Leiomyoma uterus was the most common cause of AUB, second common cause was DUB. Histopathology revealed majority of endometrium in normal menstrual phase. Clinical, radiological and pathological evaluation correlated very well to diagnose Leiomyomas. However clinical examination as well as ultrasonography proved to be of little help to diagnose Adenomyosis.

Maximum hysterectomies were done for Leiomyoma uterus, thus hysterectomy remained the commonest method of intervention. However, it is the responsibility of the health care professionals to encourage teaching and implementation of alternative procedures to ensure that women receive the maximum benefits with least morbidity.

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