

## Research Article

# Spectrum of uterine lesions presenting as abnormal uterine bleeding in a rural north Indian population: a study from tertiary care center

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## ABSTRACT

**Background:** Abnormal uterine bleeding (AUB) is now a day's one of the commonest complains of female patients attending gynaecological OPD and clinics. The problem is not limited to a particular age group and frequently affects reproductive age group as well as peri and postmenopausal females. Endometrial biopsy or curettage is a well-known safe and effective diagnostic procedure in evaluation of abnormal uterine bleeding and ruling out medical causes.

**Methods:** The study was undertaken to ascertain cause of AUB in all patients presenting at gynecology OPD with complain of abnormal uterine bleeding during the period of January 2013 to January 2014. Relevant clinical data was collected in all cases and endometrial biopsy or hystrectomy specimens were taken for histopathological evaluation.

**Results:** Maximum number of AUB cases (34%) were seen in the age group of 41-50 years of age and predominant histopathological pattern observed was proliferative endometrium seen in 18% cases. Leiomyoma is another important leading cause followed by bleeding in secretory phase and others. Menorrhagia was the most common clinical presentation. Benign conditions and pregnancy related causes occur mostly in the reproductive age group while premalignant and malignant changes occur in premenopausal and postmenopausal age group.

**Conclusions:** A thorough clinical history, etiological factors, ultrasound findings along with clinical presentation are important along with histopathological examination which plays a key role in early and prompt diagnosis of abnormal uterine bleeding.

**Keywords:** Abnormal uterine bleeding, Proliferative endometrium, Menorrhagia, Hystrectomy, Endometrial biopsy

## INTRODUCTION

Abnormal uterine bleeding (AUB) refers to menstrual bleeding of abnormal quantity, duration or schedule. It is a common complaint among one third outpatient visits to gynaecologists. Causes of AUB include both organic and non-organic causes of uterine bleeding covering wide spectrum of diseases of reproductive system and non-gynaecological causes as well. These causes are categorized as disordered proliferative endometrium, benign endometrial polyp endometrial hyperplasia without atypia, endometrial carcinomas and pregnancy associated conditions.

In the absence of any evident systemic and pelvic cause, histopathological examination of endometrial tissue remains the only modality to reach a conclusive diagnosis.

Patients presenting with AUB complain of heavy prolonged flow or spotting at peri and postmenopausal period and these patients require proper evaluation as it may be a clinical manifestation of endometrial carcinoma or its precursor like atypical hyperplasia.<sup>1</sup>

Endometrial biopsy or curettage is a safe and effective diagnostic step in evaluation of abnormal uterine bleeding and ruling out medical causes. This study is

undertaken to evaluate the various causes of abnormal uterine bleeding, to determine specific pathology in different age groups and various types of endometrial malignancies in patients coming to the tertiary care hospital in a rural north Indian population. Endometrial tissue is vulnerable for pathological lesion as it is hormonally sensitive and responsive tissue which constantly undergoes changes throughout the reproductive life. Abnormal uterine bleeding affects one third of female at one or the other time in their life span. It includes bleeding from structures like polyps, endometrial hyperplasia, chronic endometritis, proliferative endometrium, fibroids, carcinoma and pregnancy related complications and dysfunctional uterine bleeding. Most premenopausal women who present with abnormal bleeding have non-specific hormonal disorders. Women with risk factor for endometrial cancer such as polycystic ovarian disease or obesity and women with persistent bleeding should have an endometrial biopsy performed. Dilation and curettage can be a diagnostic as well as therapeutic procedure.<sup>2</sup> The sensitivity of endometrial biopsy for the detection of endometrial abnormalities has been reported to be as high as 96%.<sup>2</sup> Post-menopausal females presenting with abnormal uterine bleeding have an increased risk of hyperplasia and malignancy hence requires immediate evaluation with endometrial biopsy.

## METHODS

Detail history, clinical and relevant diagnostic findings were collected from patients presenting with abnormal uterine bleeding during the period of January 2013 to January 2014 in the gynecology OPD and subsequently endometrial biopsy/ hysterectomy specimens were sent to the department of pathology for histopathological diagnosis. The endometrial curettage material and representative sections from hysterectomy specimens were fixed in 10% formalin and processed routinely to obtain 3 to 4 micrometer thick sections from paraffin embedded tissue. These sections were stained with haematoxylin and eosin (H and E) stain and studied for cause of abnormal uterine bleeding.

## RESULTS

A total of 250 samples were included in the study of which 155 were endometrial biopsies and 95 were hysterectomy specimen. Age group of the patients ranged from 21 years to 70 years in our study thus including both reproductive and postmenopausal age group patients. Maximum number of cases were seen in the age group of 41 to 50 years.

Majority of the patients having complaints of AUB were multiparous females. Maximum number of cases (34%) were seen in the age group of 41 -50 years of age and predominant histopathological pattern observed was proliferative endometrium seen in 18% cases. Second commonest cause in our set up was uterine leiomyoma

(Figure 1) which accounted for bleeding in 16.4 % of cases.

**Table 1: Age wise distribution of AUB.**

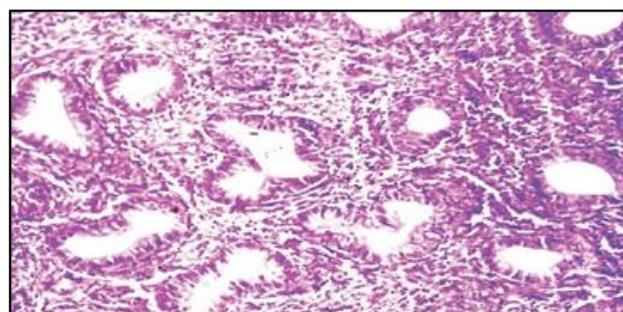
Age in years	Number of cases	Percentage
21-30 years	32	12.8 %
31-40 years	67	26.8 %
41-50 years	85	34 %
51-60 years	48	19.2 %
>60 years	18	7.2 %

**Table 2: Clinical pattern of bleeding in patients presenting with AUB.**

Types	Number of cases	Percentage
Menorrhagia	74	29.6%
Metrorrhagia	50	20%
Polymenorrhoea	56	22.4%
Continuous bleeding	40	16%
Post-menopausal bleeding	30	12%

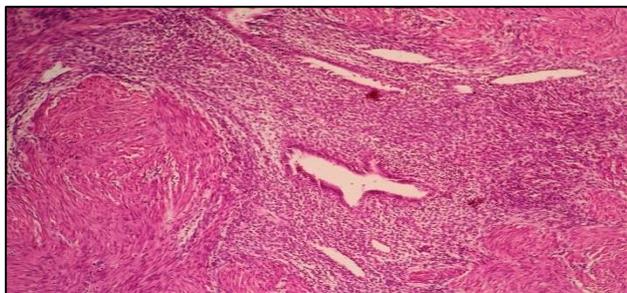
**Table 3: Histopathological diagnosis in cases of AUB.**

Histopathological diagnosis	Number of cases	Percentage
Proliferative phase	45	18%
Secretory phase	35	14%
Disordered proliferative endometrium	20	8%
Endometrial polyp	12	4.8%
Leiomyoma	41	16.4%
Chronic endometritis	31	12.4%
Pregnancy associated conditions	26	10.4%
Adenomyosis	30	12%
Endometrial hyperplasia	08 (05 without atypia, 03 with atypia)	3.2%
Endometrial carcinoma	02	0.8%



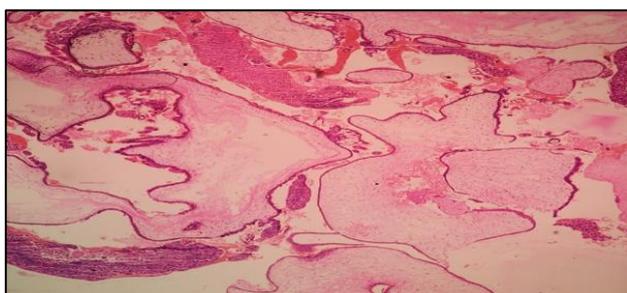
**Figure 1: Photomicrograph showing simple hyperplasia without atypia of uterus (H and E, x40).**

Clinically most of the patients of leiomyomas presented with abdominal pain, dysmenorrhoea and menorrhagia. Most of the patients having leiomyoma were of the reproductive age group. Secretory phase endometrium was the third commonest pattern followed by chronic endometritis. Majority of the chronic endometritis patients presented with infertility, abdominal pain and bleeding. Disordered proliferation was present in 20 (8%) patients.



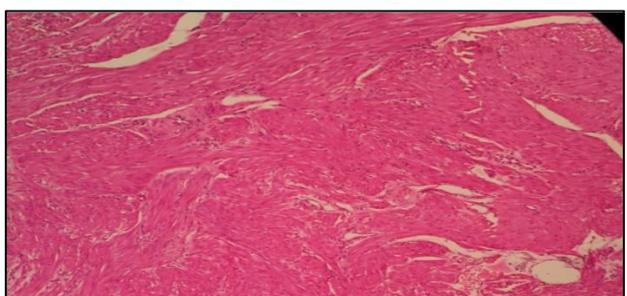
**Figure 2: Photomicrograph showing adenomyosis of uterus (H and E, x40).**

Adenomyosis (Figure 2) was also one of the etiologies of AUB seen in 12% cases affecting 40-50 age group women. Complications of pregnancy were seen in 26 (10.4%) cases in which retained products of conception was the predominant cause followed by ectopic gestation, partial and complete mole (Figure 3).



**Figure 3: Photomicrograph showing H. mole (H and E, x10).**

Benign endometrial polyp was present in 12 cases of AUB. Endometrial hyperplasia was seen in 12 cases while endometrial carcinoma (Figure 4) was diagnosed in 2 cases which were seen in 41-50 year age group only.



**Figure 4: Photomicrograph showing endometrioid adenocarcinoma of uterus (H and E, X 10).**

## DISCUSSION

Endometrium is susceptible to various pathological lesions as it is exposed to various hormonal, environmental and dietary factors. Patients with AUB usually present with bleeding due to various structural causes like fibroid, endometrial polyp, inflammatory causes like chronic endometritis, non-neoplastic causes like adenomyosis, pregnancy related complications and premalignant causes like endometrial hyperplasia along with neoplastic causes like endometrial cancers.

The age distribution of AUB in our study revealed that most of the cases were seen in 41-50 years of age group which is in concordance with study done by Saraswathi et al.<sup>3</sup> In the present study patients presented with different types of AUB and the commonest pattern observed was menorrhagia (36.8%). In the study by Nayak et al menorrhagia was seen in 49.1% of cases, which was a higher percentage compared to our study.

The youngest patient in our study was 21 years old and oldest was 74 years. The commonest age group affected with AUB was 41-50 years similar incidence as reported by Muzaffar et al in their study.<sup>4</sup> Predominant pattern observed in the present study was proliferative endometrium. Anovulatory cycles or inadequate luteal phase are reported as a cause of bleeding in the proliferative phase.<sup>5</sup> Incidence of Uterine leiomyomas was next only to proliferative endometrium with 41 (16.4%) cases. Leiomyoma usually occur during reproductive period as seen in present study also, when pregnancy or hormonal therapy are known to promote its growth similarly its size decreases after treatment with gonadotropin releasing hormone agonist.<sup>6</sup>

Secretory endometrium was observed in 35 (14%) cases. Most of the patients showing this pattern were in perimenopausal age group in the present study similar to the observations made by Damle RP.<sup>7</sup> Bleeding in secretory phase is due to ovulatory dysfunction. Disordered proliferative pattern is characterized by foci of dilated irregularly shaped glands with focal outpouchings and branching as seen in 20 (8%) cases in present study.<sup>8</sup> Disordered proliferative pattern is focal and resembles simple hyperplasia which is a diffuse pattern. It denotes an endometrial appearance that is hyperplastic but without an increase in endometrial volume.<sup>9</sup>

Chronic endometritis was present as a cause of AUB in 31 (12.4%) cases. It represents an intermediate stage of pelvic inflammatory disease from cervicitis to salpingitis.<sup>10</sup> Most patients have menstrual irregularities and about half may have pelvic pain or endometrial biopsy for investigation of irregular bleeding.<sup>11</sup> Patients in our set up also presented with off an on abdominal pain, menstrual irregularities and most of them were having low socioeconomic status.

AUB due to abortion was seen in young reproductive age group patients in present study. They presented with pelvic pain or tenderness and off and on continuous bleeding. Pregnancy associated conditions constituted 10.4% of total cases. The overall histopathological features show presence of shadows of stromal cells and trophoblast as the main identifying criteria. Intermediate trophoblastic shell infiltrate the deciduas surrounding the blastocyst to form trophoblastic shell, invade the spiral arterioles of the placental bed and infiltrate the myometrium beneath the implantation site.<sup>12</sup> Partial moles, complete moles should be distinguished from hydropic villi seen in 15-40% of spontaneous abortions.<sup>13</sup> In histopathology complete mole shows circumferential proliferation of villous trophoblast with villous edema and cellular atypia while partial mole show two population of villi, one enlarged edematous and the other normal type without any cellular atypia. Adenomyosis was also one of the etiologies of AUB seen in 12% cases affecting 40-50 age group women. It is characterized by presence of endometrial glands and stroma within the myometrium. Patients are typically pre or perimenopausal women who present with AUB and dysmenorrhoea.<sup>14</sup> Risk factors causing adenomyosis are age between 40 and 50 years, early menarche, short menstrual cycles, a first birth at an early age, multiparity, sharp curettage during early pregnancy, obesity and tamoxifen use.<sup>14,15</sup> Adenomyosis is also seen with uterine leiomyomas in many cases.

Endometrial hyperplasia accounted for 8 (3.21%) cases in which majority (5 cases) was without atypia and remaining showed atypia. This was more common in perimenopausal age group as also seen in study done by Khare et al.<sup>2</sup> Simple hyperplasia characteristically have cystically dilated glands which are surrounded by abundant cellular stroma whereas in complex hyperplasia glands are crowded and have very little intervening stroma.<sup>16</sup> Pronounced stromal reaction is also a manifestation seen in invasive carcinoma.<sup>17</sup>

On microscopy only very well differentiated endometrial carcinomas pose difficulty in differentiating them from atypical hyperplasia and this dilemma is overcome by applying specific criteria to minimize the subjective variation.

In the present study cases of endometrial hyperplasia were seen mainly in the age group of 41-50 years and majority of cases were of simple hyperplasia without atypia.<sup>18</sup> In a study by Ferenczy A et al it was observed that cases of endometrial hyperplasia treated with progesterone are not at increased risk of developing endometrial carcinoma.<sup>19</sup> Only 2 cases of endometrial carcinomas were encountered in present study. It is typically known to occur in elderly postmenopausal patients.<sup>20</sup> One patient was diagnosed previously as endometrial hyperplasia with atypia. The patient was obese, hypertensive and presented with off and on abnormal vaginal bleeding. On histopathology diagnosis

of endometrioid variant of endometrial adenocarcinoma was made. Other case was diagnosed as clear cell carcinoma of endometrium. This patient was 55 year old female having a family history of her mother and sister suffering from breast carcinoma.

Initial presenting feature of endometrial carcinoma is abnormal vaginal bleeding. Over 80% of endometrial carcinoma is composed of tubular glands lined by stratified non mucin containing epithelium.<sup>21</sup> Known risk factors associated with carcinoma endometrium are prolonged estrogenic stimulation as seen in obesity, hormonal therapy, hypertension, diabetes and presence of endometrial hyperplasia.<sup>22</sup> p53 or PTEN mutations are present in 10-20% of endometrial cancers which are mostly Grade 3. Loss of function mutation or a null mutation in PTEN is observed in 20% of endometrial hyperplasia and 50% of endometrioid carcinoma.<sup>23</sup> Clear cell carcinoma is a rare type of aggressive tumor associated with poor prognosis and accounts for only 5% of all endometrial cancer.<sup>24</sup>

## CONCLUSION

In our study involving 250 patients histopathological evaluation of endometrial tissue was undertaken to ascertain the etiology of AUB. Their percentage along with clinical presentation and age group affected was also studied. It was observed that incidence of AUB is more common in 41-50 years of multiparous women. Proliferative endometrium was the most common observed histopathological pattern in patients presenting with AUB. Leiomyoma was the next important cause of AUB followed by secretory endometrium. Though benign lesions of endometrium account for majority of cases presenting with AUB, in pre and postmenopausal age group other premalignant and malignant causes should also be considered. A comparative clinicopathological study will help in arriving at the cause and correct diagnosis. Histopathological examination is one of the major tools in evaluation of abnormal uterine bleeding and helps us in proper management and treatment of cases.

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