# Endometrial Pathology in abnormal uterine bleeding (AUB) & role of different techniques of endometrial sampling in evaluation of AUB : A cross sectional study

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**Abstract**

**Objectives: Primary:** 1. To Analyze prevalence of various endometrial pathologies among patients presenting with abnormal uterine bleeding. **Secondary :** 1. To study age wise distribution of various endometrial pathologies. 2. To study age wise clinical presentation (symptomatology) in patients with AUB. 3. To assess the feasibility and compare different techniques of collecting endometrial sample. **Design and setting:** A single center prospective cross sectional study at teaching institute Population/Sample : 150 females from 18-70 years presenting with abnormal uterine bleeding. Endometrial sample was obtained either by OPD Pipelle brush or Surgical Dilatation and Curettage method or hysteroscopy. Outcome measures : Endometrial sampling methods used, Endometrial Pathology, Age groups wise clinical and pathological correlation, Feasibility of technique used. Statistical Analysis was done by using Epi-Info-7 software. **Results :**Commonest age group presenting with AUB was 41-50 (40%) years ,64 % were para 3 or more, Proliferative and secretary changes, 53(35.3%) and 24(16%) cases while endometrial hyperplasia without atypia 18 (12%) cases and with atypia7cases(4.7% ),endometrial carcinoma 5 cases(3.3%) while endometrial polyp was seen in 8 cases(5.3% ). Heavy menstrual bleeding with normal duration was commonest presentation in 64%. Endometrial sampling technical failure was seen in 2 cases with pipelle biopsy while in 7 cases inadequate sample was obtained with pipelle and dilatation and curettage. Uterine perforation was seen in one case which was managed conservatively. **Conclusion: T**echnical failure and inadequate sample needs to be addressed considering background high risk factors, TVS imaging and repeat sample and use of hysteroscopy may be offered case to case basis.

**Title :Endometrial Pathology in abnormal uterine bleeding (AUB) & role of different techniques of endometrial sampling in evaluation of AUB : A cross sectional study**

**Running Title: Endometrial Pathology in AUB and endometrial sampling techniques.**

**Key Words:** Abnormal uterine bleeding, AUB, Pipelle biopsy, dilatation and curettage, Hysteroscopy, Endometrial sampling, endometrial polyp, endometrial hyperplasia, endometrial carcinoma

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**Design and setting:** A single center prospective cross sectional study at teaching institute

Population/Sample : 150 females from 18-70 years presenting with abnormal uterine bleeding. Endometrial sample was obtained either by OPD Pipelle brush or Surgical Dilatation and Curettage method or hysteroscopy.

Outcome measures : Endometrial sampling methods used, Endometrial Pathology, Age groups wise clinical and pathological correlation, Feasibility of technique used. Statistical Analysis was done by using Epi-Info-7 software.

**Results :** Commonest age group presenting with AUB was 41-50 (40%) years ,64 % were para 3 or more, Proliferative and secretary changes, 53(35.3%) and 24(16%) cases while endometrial hyperplasia without atypia 18 (12%) cases and with atypia7cases(4.7% ),endometrial carcinoma 5 cases(3.3%) while endometrial polyp was seen in 8 cases(5.3% ). Heavy menstrual bleeding with normal duration was commonest presentation in 64%. Endometrial sampling technical failure was seen in 2 cases with pipelle biopsy while in 7 cases inadequate sample was obtained with pipelle and dilatation and curettage. Uterine perforation was seen in one case which was managed conservatively.

**Conclusion: T** echnical failure and inadequate sample needs to be addressed considering background high risk factors, TVS imaging and repeat sample and use of hysteroscopy may be offered case to case basis.

**Introduction :**

Abnormal uterine bleeding (AUB), traditionally defined as uterine bleeding that is abnormal in volume, regularity,and/or timing. Abnormal Uterine Bleeding (AUB) is the most common complaint for which woman reports gynaecologist and clinical presentation varies from heavy flow with normal duration(HMB), heavy flow with prolonged duration, Intermestrual bleeding(IMB) or post-menopausal bleeding and generally it correlates with different age group of presentation as well as underlying endometrial pathology. TransvaginalUltrasonography(TVS),endometrial sampling by pipelle or dilatation and curettage, hysteroscopy etc plays an important role in evaluation and management of AUB.

**Methodology:**

A single center prospective cross sectional study at PCMC'S PGI and Y C M Hospital, Pune was carried out from 1$^{st}$ Jan 2020 to 31$^{st}$ May 2021.Total 150 female were enrolled between age group 18 to 70 who presented with Abnormal Uterine bleeding. Endometrial biopsy sample was obtained either by OPD Pipelle brush or by Surgical Dilatation and Curettage method or hysteroscopy along with endometrial biopsy. Histopathological diagnoses were studied for all samples. Data was collected in the standard format as mentioned in the data collection tool. Statistical Analysis was done by using Epi-Info-7 software. Informed consent obtained from all participants.

**Objectives:**

**Primary:** 1. To Analyze prevalence of various endometrial pathologies among patients presenting with abnormal uterine bleeding.

**Secondary :**

1. To study age wise distribution of various endometrial pathologies.
2. To study age wise clinical presentation (symptomatology) in patients with AUB.
3. To assess the feasibility and compare different techniques of collecting endometrial sample.

**Inclusion Criteria:**

Patients presenting with symptoms of AUB between the age group of 18 and 70 who underwent endometrial biopsy were included in the study.

Unmarried patients where sinister pathology (Non benign) is suspected are considered for endometrial sampling.

**Exclusion Criteria:**

Unmarried patients where primary conservative management is done in view of suspected benign pathology are excluded from the study as no endometrial sampling is done in spite of symptoms of AUB

Patients refusing to consent for participation in the study.

**Results :**

Table 1 shows most of our patients are para 3 or more96 cases (64%) cases and most patients 82 cases (54.6%) belong to lower socio economic class.

Table 1 and Table 2 shows age groupwise spectrum of endometrial pathologies in patients with AUB. In age group 21-30 years 7cases(4.5%) underwent endometrial sampling and histological features in this age group were mainly benign changes such as proliferative and pill endometrium 2 cases each, secretary change, chronic endometritis, polyp one case each. Age group 31-40 years 53 cases (35.3%) underwent endometrial sampling and histological changes were mostly benign such as proliferative(23),secretary(11)pill endometrium(2)endometrial hyperplasia without atypia (4), with atypia(2) chronic endometritis and endometrial polyp 3 cases each and inadequate sample in 2 cases. Age group 41-50 contributed to maximum number 60 cases (40%) and endometrial changes were Proliferative(22),secretary(12),endometrial hyperplasia without atypia (7),with atypia(3),carcinoma endometrium (1) ,other changes were chronic endometritis (6),pill endometrium(1),Polyp(2).Age group 51-60 contributed 22 cases 14% of cases and histopathological changes were noted as proliferative(6),disordered proliferative(1), Atrophic endometrium (3)and chronic endometritis 2 cases each, endometrial hyperplasia without atypia(6) with atypia(2),carcinoma endometrium(1),inadequate sample(1) other changes were benign. Age group 61-70 total 8 cases (5.2%) underwent endometrial sampling and pathological changes were endometrial carcinoma(3), atrophic endometrium (3) and endometrial polyp (1),inadequate sample for reporting(1). Repeat endometrial sampling was done in cases after inadequate sample it is reported as chronic endometritis in one case and atrophic endometrium in 2 cases in this age group.

Table 3 shows commonest clinical presentation as heavy menstrual bleeding HMB with normal duration 96 cases (64%), followed by heavy and prolonged bleeding in 23 cases (15.3 %), Post menopausal bleeding 23 cases (15.3%), Intermenstrual bleeding(IMB) was presentation in 8 cases 5.4%.

Table 4 shows out of 150 patients out 71 patients subjected to pipelle biopsy only 69 cases sample was obtained while 2 cases technical failure was noted. 34 patients endometrial sample was obtained by traditional dilatation and curettage technique while 47 cases underwent hysteroscopy along with endometrial biopsy and additional 3 cases who consented for repeat sampling by hysteroscopy due to inadequate sample for reporting also underwent hysteroscopy. Inadequate sample was noted in 4 cases in pipelle group and in 3 cases in D & c group . One Uterine perforation was noted in patients undergoing dilatation and curettage. Pipelle biopsy was found to be more feasible for outpatient procedure however dilatation and curettage and hysteroscopy with biopsy were less feasible in our setting

**Discussion :**

Menstrual disorders are more common with advancing age. In our study, below 30 years 7 cases (4.5%) underwent endometrial sampling. Incidence of AUB may be more in this age group however most cases being low risk are managed conservatively and are not subjected to endometrial sampling. Patients with high risk factors such as obesity or family history of endometrial cancer or non response to medical management are generally subjected to endometrial sampling. Most common age group presenting with AUB in our study was 41-50 60 cases (40%) years followed by 53 cases (35.3%) in 31-40 age group and this 31-50 yr age group combined contributed to 75.3% cases . Similar finding have been reported by Doraiswami s et al (1) A similar incidence was reported by Yusuf et al (2) and Muzaffar et al (3) in their study. After the age of 50 that is 51-60 year age group and 61-70 year age group had 22 cases(15% ) and8 cases (5.3%) respectively and this age group(51-70 years) together constituted 30 cases (20%) of our patients. However this age group showed significant changes such as endometrial carcinoma and precursors for endometrial cancer such as endometrial hyperplasia without atypia and with atypia as discussed below.

96 cases out of 150 patients with AUB were para 3 or more and nulliparous were only2.7% in our study. Nulliparous patients less commonly presents with AUB as compared to multiparous patients similar finding is observed in other studies (4,5,6). Patients attending health facilities in public sector are mainly from lower socio economic class contributed to 82 cases (54.6%) in our study.

In our study as per table2, functional endometrium with proliferative and secretary changes were noted

in 53 cases (35.4%) and 24 cases (16%)respectively while Kafle et al (7) in a study of 166 samples noted proliferative and secretary changes in 42.97% and 14.46% cases. Brahmaiah J et al (8) in study of 210 samples noted proliferativeand secretary changes in 31.3% and 11.43% cases respectively. Endometrial hyperplasia without atypia was seen in 18 cases(12%) cases and with atypia was seen in 7 cases (4.66%) in our study while Kafle et al (7) noted hyperplasia of endometrium without atypia in 7.23% cases and atypical hyperplasia in 3.01% cases. Brahmaiah J et al (8) noted endometrial hyperplasia in 20% cases with no specification of features such as atypia or without atypia. Various other authors have noted endometrial hyperplasia 6% to 26% of samples(8). Endometrial hyperplasia with or without hyperplasia should be given immediate attention and patients should be counselled regarding the nature of pathology detected and appropriate treatment to be instituted. Incidence of co-existing endometrial carcinoma ranges 6.4-43% in women undergoing hysterectomy for atypical hyperplasia(9). Natural history of endometrial hyperplasia without atypia suggest that risk of progression to endometrial is 2% if remains untreated and this figure is 23-29% for atypical hyperplasia(10).

In our study endometrial carcinoma is noted in 5 cases (3.3%) while Kafle N et al (7) has reported 2.4% incidence of malignancy which were adenocarcinoma. Brahmaiah J et al (8) reported 0.47% incidence of malignancy in endometrial sample while various authors have mentioned 0.48 to 6.4% incidence of carcinoma endometrium in patients presenting with AUB(8). Incidence of finding carcinoma in endometrial sample varies with the population screened. AUB patients attending general gynaecology outpatient department, all age group patients combined may have lower incidence of detection of carcinoma while screening of patients with high risk factors such as obesity, nulliparity, family history or samples from oncological hospital will report higher detection rate for malignancy.

Atrophic endometrium is noted in 6cases (4%) in our study which is similar to rate 3.35% reported by Brahmaiah J et al (8) and various authors reported rate of atrophic endometrium from 2-7.38% (8)Rupture of dilated blood capillaries beneath the surface of atrophic endometrium may be responsible for the bleeding in these patients. Study by Doraiswami et al (1) documented 2.4% incidence of atrophic endometrium while Dwivedi et al (11) has reported 11% atrophic endometrium which is higher than our present reported incidence.

Endometrial polyp was reported in 8cases (5.3%) cases in our study while Kafle N et al (7) has reported 2.41% incidence of polyp. Brahmaiah J. et al (8) has reported 0.95% incidence of endometrial polyp in AUB patients. Prevalence of endometrial polyp increase with age, endometrial polyp in postmenopausal women (11.8%) and premenopausal women in (5.8%) have been reported.(12)Sometimes cervical polyp may be seen on speculum examination which may be symptomatic or asymptomatic. Symptomatic cervical polyp may be associated with endometrial polyps and hyperplasia more commonly in perimenopausal and post menopausal women. Endometrial abnormalities are noted in upto 55% of postmenopausal women with cervical polyp and these women should be offered endometrial sampling with hysteroscopy in addition to avulsion of polyp.(13)

Heavy menstrual bleeding with normal duration was commonest presentation 96 cases (64%) in our study. Vijayraghavan et al (14) has reported menorrhagia in 71.25% as the commonest presenting complaint in AUB patients while Kafle N et al (7) has reported 58.43% of AUB cases with menorrhagia as presenting complaint. Postmenopausal bleeding was presentation in 23 cases (15.3 %) cases in our study while Kafle N et al (7) has reported 19.27% incidence of postmenopausal bleeding and Vijayraghavan et al (14) has reported 12.5% incidence of postmenopausal bleeding in patients with AUB. Postmenopausal bleeding should be evaluated properly to rule out sinister pathology as 90% of women with EC present with PMB, but over 90% of women with PMB have a benign benign underlying cause for their symptom(15,16).Heavy and prolonged bleeding was noted in 23 cases (15.4%) cases in our study, while inter menstrual bleeding (IMB) was seen in 8 cases (5.4%).Kafle N et al (7) and Vijayrghavan et al (14) have reported 15.1% and 15% incidence of metrorrhagia in AUB patients respectively.

Table 4 & 2 shows inadequate sample was reported in 7 cases (4.6%) with pipelle and dilation and curettage. These patients were offered endometrial sampling by hysteroscopy for which 3 out of 7 patients consented and underwent repeat sampling by hysteroscopy. Technical failure was noted 2 cases (1.3%) cases where

endometrial sampling was attempted by pipelle. These 2 cases were also underwent repeat sampling by hysteroscopy. Failed endometrial sampling is usually associated with pain or cervical stenosis, which is more common in nulliparous women(17). Pipelle endometrial biopsy is an opd procedure and quick to perform however failure of the procedure in 11% cases and inadequate sample 31%, pain, bleeding, infection and very rarely perforation have been reported(18), while failure rate for operative hysteroscopy 3.4 % and ambulatory procedure 4.2% have been reported in the literature(18). Previously it was thought that women with an inadequate sample can be reassured safely regarding non sinister pathology however study has shown 4.5% of women who were diagnosed with endometrial carcinoma had initial inadequate sample(19) hence it is not appropriate to reassure the patient on the ground of inadequacy of the sample however preoperative high risks factors such as obesity, family history and supporting investigations such as endometrial thickness on TVS, irregularity of the endometrium are to be taken into account before reassuring, As a blind procedure endometrial sampling (pipelle or dilatation and curettage) has potential to miss small, localised cancers (20),women with benign or inconclusive histology, but persistent symptoms or suspicious ultrasound finding should be offered hysteroscopy.

Out of 71 cases (table 4 ) which were subjected to endometrial sampling by pipelle among 2 cases there was technical failure in nulliparous and postmenopausal patients due pinpoint os or stenosed cervix and patients subsequently subjected to hysteroscopy with biopsy under anaesthetia for obtaining the sample. Technical failure was not observed with D & C (34 cases) as well as hysteroscopy procedure (47 cases) for obtaining the endometrial sample. The efficacy of Dilatation and Curettage as a sampling tool has been questioned(21). Obtaining scant tissue and not covering the entire endometrium are the drawbacks of D & C. Hence histopathological report needs to be interpreted keeping patients history in mind to avoid under or overtreatment of patient. Pipelle biopsy was more feasible to use for outpatient services while Dilatation and curettage as well as Hysteroscopy with biopsy required of admission of patient, use of anaesthetia and prolonged stay and hence these methods were less feasible as compared to pipelle biopsy. Though outpatient hysteroscopy with biopsy is possible with miniature 2.9mm scope due non availability of same patients were subjected to procedure under anaesthetia with 4.9 mm hysteroscope. In our study one case of uterine perforation while performing dilatation and curettage which was managed conservatively, however uterine perforation can occur with during hysteroscopy or pipelle biopsy. Average incidence of uterine perforation has been reported as 0.002-1.7% during hysteroscopy(22). Postmenopausal, pregnancy, peurperieum, Acutely anteverted and retroverted uterus, or septic conditions are high risk factors for peforation. Perforations are more likely to happen when junior staff is performing the procedure. Experienced surgeon performing the procedure especially in presence of high risk factors will not only reduce the risk of perforation but can reduce the morbidity by early detection and prompt management.

**Main Findings :** AUB is commonly in Age group 41-50 followed by in the age group of 31-40. Higher parity (para 3 more) with AUB. Functional endometrium with proliferative (35.4%) and secretary changes (16%) were commonly seen in AUB patients. Endometrial polyp was noted in 5.3% cases and precursor lesions for malignancy such as endometrial hyperplasia without atypia 12% and with atypia 4.7% and endometrial cancer was reported in 3.3% cases. In 7 (4.3%) cases endometrial sample obtained was inadequate for reporting and technical failure was noted in 2 (0.66%) cases, uterine perforation was noted in one case. (0.33%)

**Strength and Limitations :** Strength of study include prospective data collection in systematic manner for enrolled cases however study was limited to clinical and histopathological diagnoses while inclusion of treatment and comparison of histopathology after surgical management with the preoperative findings would have given more information about sensitivity and specificity about the endometrial sampling technique.

**Interpretation:** Study is conducted in tertiary teaching hospital in gynaecology department and results of study may be generalised to all age group patients similar population with complaints suggestive of AUB however incidences of pathology may vary if the age group of population post menopausal) differs or patients have high risk factors such as patients attending oncological OPD

**Conclusion** : Pipelle biopsy is feasible as quick and outpatient procedure however possibility of technical

failure should be born in mind. Cases of inadequate sample should be analysed carefully with reference to background history, high risk factors, TVS imaging (endometrial thickness, irregularity of endometrium) and need for repeat sample and use of hysteroscopy to be considered case to case basis.This will help in case management as well as avoid over treatment or under treatment of underlying pathology.

## DECLARATIONS

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Conflict of interest: None to declare

Ethical approval: Yes Letter no. YCMH/PG/ETHICS/11/2019 dated 01/11/2019

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### Authors Contributions

MA,IR, MS, ST, SR involved in all processes of this research work.. All authors read and

approved the final manuscript. Conceived and designed the experiments: MA, MS.

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DATA COLLECTION TOOL

| | |
|---|---|
| Demographic data | Age , parity , socio economic status |
| Clinical presentation | Heavy and prolonged menstrual bleeding, heavy menstrual bleeding and normal duration, intermenstrual bleeding, post menopausal bleeding, Any other menstrual abnormality |
| Method of endometrial Sampling and any technical difficulty | Pipelle Biopsy, Dilatation and Curettage, Hysteroscopy along with endometrial biopsy. Any technical difficulty and feasibility of procedure noted. |
| Histopathology report | As obtained from pathology dept |

Flow chart

(Figure 1)

Tables:

Table 1 : Sociodemographic parameters of patients with AUB

| **Age group** | Frequency | Percentage |
|---|---|---|
| 21-30 years | 07 | 04.5 |
| 31-40 years | 53 | 35.3 |
| 41-50 years | 60 | 40.0 |
| 51-60 years | 22 | 15.0 |

| **Age group** | Frequency | Percentage |
|---|---|---|
| 61-70 years | 08 | 05.2 |
| **Parity** | **Parity** | **Parity** |
| Zero | 4 | 02.7 |
| 1 | 5 | 03.3 |
| 2 | 45 | 30.0 |
| >3 | 96 | 64.0 |
| **Socioeconomic status** | **Socioeconomic status** | **Socioeconomic status** |
| Upper | 25 | 16.7 |
| Middle | 43 | 28.7 |
| Lower | 82 | 54.6 |

Table 2: Histopathological Features and Age group

| Histological pattern of endometrium | Age (in years) | Age (in years) | Age (in years) | Age (in years) | Age (in years) |
|---|---|---|---|---|---|
| | 21-30 | 31-40 | 41-50 | 51-60 | 61-70 |
| Proliferative endometrium | 2 | 23 | 22 | 6 | 0 |
| Disordered proliferative endometrium | 0 | 3 | 4 | 1 | 0 |
| Secretory endometrium | 1 | 11 | 12 | 0 | 0 |
| Endometrial hyperplasia without atypia | 0 | 4 | 7 | 6 | 1 |
| Endometrial hyperplasia with atypia | 0 | 2 | 3 | 2 | 0 |
| Atrophic endometrium | 0 | 0 | 0 | 2 (+1*) | 2 (+1*) |
| Endometrial carcinoma | 0 | 0 | 1 | 1 | 3 |
| Chronic endometritis | 1 | 3 | 5 (+1*) | 2 | 0 |
| Pill endometrium | 2 | 2 | 1 | 0 | 0 |
| Endometrial polyp | 1 | 3 | 2 | 1 | 1 |
| Inadequate sample | 0 | 2 | 3 (-1) | 1(-1) | 1(-1) |
| Total | 7 | 53 | 60 | 22 | 8 |
| Percentage (%) | 4.5 | 35.3 | 40.0 | 15 | 5.3 |

Figures in bracket indicate repeat procedure due to inadequate sample (Refer to footnote in methodology flow chart)

Table 3: Age group and Clinical Presentation

| Clinical presentation | Age (in years) | Age (in years) | Age (in years) | Age (in years) | Age ( |
|---|---|---|---|---|---|
| | 21-30 | 31-40 | 41-50 | 51-60 | 61-70 |
| Heavy and prolonged menstrual bleeding | 0 | 13 | 8 | 2 | 0 |
| Heavy menstrual bleeding with normal duration | 6 | 36 | 45 | 9 | 0 |
| Intermenstrual bleeding | 1 | 4 | 3 | 0 | 0 |
| Postmenopausal bleeding | 0 | 0 | 4 | 11 | 8 |
| Total | 7 | 53 | 60 | 22 | 08 |
| Percentage(%) | 4.5 | 35.4 | 40 | 14.7 | 5.4 |

Table 4: Comparison of different methods Used for Endometrial Biopsy

| | Pipelle Biopsy | D & c | Hscopy with biopsy | Total |
|---|---|---|---|---|
| Total cases | 69# | 34 | 45+2*+3** | 150 (153**) |
| Technical failure | 02 | — | — | 02 * |
| Inadequate sample | 04 | 03 | — | 07 |
| Repeat Sample By Hysteroscopy | 01 | 02 | — | 03** |
| Feasibility of procedure | More | Less | Less | – |
| Rare Complication Perforation | 0 | 1 | 0 | 1 |

# out of 71 cases 2 cases of technical failure excluded

* 2cases of technical failure by biopsy underwent hysteroscopy with biopsy (Ref footnote in flowchart)

** out of 7 inadequate sample 3 patients opted for repeat endometrial sampling with hysteroscopy hence last column total shows 153 in bracket. (Ref footnote in flowchart)

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