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Original Research Article

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

Background: Abnormal uterine bleeding (AUB), traditionally defined as uterine bleeding that is abnormal in volume, regularity, and/or timing. It affects 14–25% of women of reproductive age. AUB has a major impact on quality of life of women. Aetiology of AUB may be structural and functional and varies with the age group. Histology of endometrium remains the mainstay in diagnosis of pathology and management of AUB. Various techniques such as endometrial sampling by pipelle, dilatation and curettage (D & C) and hysteroscopy are used to obtain endometrium for histological diagnosis.

Materials and Methods: A single center prospective cross-sectional study at teaching institute was carried out to include 150 females from 18-70 years presenting with abnormal uterine bleeding. Objective of study was to analyse prevalence of various endometrial pathologies in AUB, symptomatology as well as age wise distribution of various endometrial pathologies in AUB and compare feasibility of different techniques of collecting endometrial sample. Endometrial sample was obtained either by OPD Pipelle brush or Surgical Dilatation and Curettage method or hysteroscopy. 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 atypia 7 cases (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 the 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: Technical failure and inadequate sample needs to be addressed considering background high risk factors, TVS imaging, repeat sample and use of hysteroscopy may be offered case to case basis.

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1. Introduction

Traditionally, abnormal uterine bleeding (AUB) is defined as bleeding which is abnormal in volume, regularity, and/or timing¹ is common and affects 14-25% of women of reproductive age.²⁻⁴ AUB has a major impact on quality

of life⁵ and leads to 3.5 million days of work absence,⁶ and generates significant health care costs. FIGO has recommended PALM-COEIN Classification where PALM (Polyp, Adenomyosis, Leiomyoma, Malignancy) denotes the structural causes while COEIN (Coagulopathy, Ovulatory dysfunction, endometrial, iatrogenic and not yet classified) stands for functional causes of AUB. For maintaining the uniformity in terminologies it is recommended to describe

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irregularity of the cycle such as, Heavy flow with normal duration (HMB), Heavy flow with prolonged duration, Inter menstrual bleeding (IMB).^{1,7,8}

Aetiology of AUB may be structural and functional and varies with the age group. Histological pattern of endometrial sampling along with clinical and radiological findings remains the diagnostic standard for clinical diagnosis of endometrial pathology which ultimately helps in deciding the management of patients.⁹

Although transvaginal sonography (TVS) is primarily used for evaluation of AUB however histopathological diagnosis is possible with endometrial sampling by pipelle, dilatation and curettage (D & C) and hysteroscopy guided endometrial biopsy plays an important role in formulating treatment of AUB.

2. Materials and Methods

A single center prospective cross-sectional study at PCMC'S PGI and Y C M Hospital, Pune was carried out from 1st Jan 2020 to 31st May 2021. Total 150 female were (Chart 1) 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 mentioned in the data collection tool (Table 1). Statistical Analysis was done by using Epi-Info-7 software. Informed consent obtained from all participants.

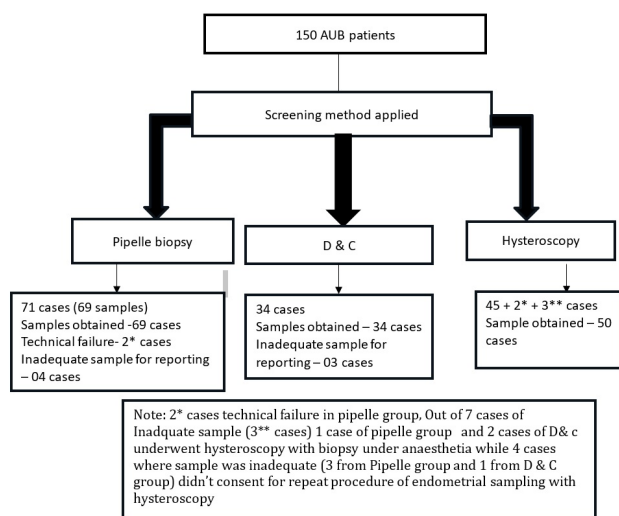


Chart 1:

Table 1: 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

3. Objectives

3.1. Primary

1. To analyze prevalence of various endometrial pathologies among patients presenting with abnormal uterine bleeding.

3.2. 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.

3.3. Inclusion criteria

1. Patients presenting with symptoms of AUB between the age group of 18 and 70 who underwent endometrial biopsy were included in the study.
2. Unmarried patients where sinister pathology (Non benign) is suspected are considered for endometrial sampling.

3.4. Exclusion criteria

1. 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.
2. Patients refusing to consent for participation in the study.

4. Results

Table 2 shows most of our patients are para 3 or more 96 cases (64%) cases and most patients 82 cases (54.6%) belong to lower socio economic class.

Tables 2 and 3 shows age group wise spectrum of endometrial pathologies in patients with AUB. In age group 21-30 years 7 cases (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 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 4 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 5 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 in pipelle group. 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 (total 50 cases) hysteroscopy. Inadequate sample was noted in 4 (5.6%) cases in pipelle group and in 3 (8.8%) cases in D & C group. One Uterine perforation (2.9%) 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.

5. Discussion

AUB may be due to structural or functional causes and histopathological pattern of endometrial sampling along with clinical history and imaging (TVS) remains cornerstone of management of AUB.⁹

Menstrual disorders are more common with advancing age. In our study (Table 2), 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 years 60 cases (40%) followed by 53 cases (35.3%) in 31-40 age group and this 31-50yr age group combined contributed to 75.3% cases. Similar finding have been reported by Doraiswami S et al.¹⁰ A similar incidence was reported by Yusuf et al¹¹ and Muzaffar et al.¹² 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%) and 8 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 (Table 2) out of 150 patients with AUB were para 3 or more and nulliparous were only 2.7% in our study. Nulliparous patients less commonly presents with AUB as compared to multiparous patients similar finding is observed in other studies.¹³⁻¹⁵ Patients attending health facilities in public sector are mainly from lower socio economic class contributed to 82 cases (54.6%) in our study.

Table 3 shows functional endometrium with proliferative and secretary changes were noted in 53 cases (35.4%) and 24 cases (16%) respectively while Kafle et al⁹ in a study of 166 samples noted proliferative and secretary changes in 42.97% and 14.46% cases. Brahmaiah J et al.¹⁶ in study of 210 samples noted proliferative and 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 al⁹ noted hyperplasia of endometrium without atypia in 7.23% cases and atypical hyperplasia in 3.01% cases. Brahmaiah J et al¹⁶ 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.¹⁶ 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

Table 2: 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
61-70 years	08	05.2
Parity		
Zero	04	02.7
1	05	03.3
2	45	30.0
>3	96	64.0
Socioeconomic status		
Upper	25	16.7
Middle	43	28.7
Lower	82	54.6

Table 3: Histopathological features and age group

Histological pattern of endometrium	Age (in years)										Total	
	21-30		31-40		41-50		51-60		61-70		N	%
	n	%	n	%	n	%	n	%	n	%		
Proliferative endometrium	2	1.3	23	15.3	22	14.6	6	4	0	0	53	35.4
Disordered proliferative endometrium	0	0	3	2	4	2.6	1	0.66	0	0	8	5.3
Secretory endometrium	1	0.66	11	7.3	12	8	0	0	0	0	24	16
EH without atypia #	0	0	4	2.6	7	4.6	6	4	1	0.66	18	12
EH with atypia #	0	0	2	1.33	3	2	2	1.33	0	0	7	4.7
Atrophic endometrium	0	0	0	0	0	0	2	2	2	2	4	4
							(+1*)		(+1*)		(+2*)	
Endometrial carcinoma	0	0	0	0	1	0.66	1	0.66	3	2	5	3.3
Chronic endometritis	1	0.66	3	2	5	4	2	1.33	0	0	11	8
					(+1*)						(+1*)	
Pill endometrium	2	1.33	2	1.33	1	0.66	0	0	0	0	5	3.3
Endometrial polyp	1	0.66	3	2	2	1.3	1	0.66	1	0.66	8	5.3
Inadequate sample	0	0	2	1.3	3	1.3	1	0	1	0	7	2.6
					(-1*)		1*)		(-1*)		(-3*)	
Total/ Percentage (%)	7	4.5	53	35.3	60	40	22	15	8	5.3	150	100

EH – Endometrial hyperplasia

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

Table 4: Age group and clinical presentation

Clinical presentation	Age (in years)										Total	
	21-30		31-40		41-50		51-60		61-70		N	%
	n	%	n	%	n	%	n	%	n	%		
Heavy and prolonged menstrual bleeding	0	0	13	8.6	8	5.3	2	1.33	0	0	23	15.3
Heavy menstrual bleeding with normal duration	6	4	36	24	45	30	9	6	0	0	96	64
Intermenstrual bleeding	1	0.66	4	2.66	3	2	0	0	0	0	8	5.4
Postmenopausal bleeding	0	0	0	0	4	2.66	11	7.33	8	5.33	23	15.3
Total	7	4.5	53	35.4	60	40	22	14.7	8	5.4	150	100

Table 5: Comparison of different methods used for endometrial biopsy

Technique of endo. Biopsy	Pipelle Biopsy N1 = 69#		D & C N2 =34		Hscopy with biopsyN3 =50 (45+2*+3**)		TotalN=150 (153**)	
	n 1	% (of n 1)	n 2	% (of n 2)	n 3	% (of n 3)	n	% (of N)
Technical failure	02	2.8	—	—	—	—	02 *	1.33
Inadequate sample	04	5.6	03	8.8	—	—	07	4.6
Repeat Sample By Hysteroscopy	01	1.4	02	5.8	—	—	03**	2
Feasibility of procedure	More	-	Less	-	Less	—	-	—
Rare Complication Perforation	0	0	1	2.9	0	0	1	.66

out of 71 cases 2 cases of technical failure excluded.

* 2 cases of technical failure by pipelle biopsy underwent hysteroscopy with biopsy.

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

ranges 6.4-43% in women undergoing hysterectomy for atypical hyperplasia.¹⁷ 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.¹⁸

In our study endometrial carcinoma is noted in 5 cases (3.3%) while Kafle N et al⁹ has reported 2.4% incidence of malignancy which were adenocarcinoma. Brahmaiah J et al.¹⁶ 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.¹⁶ Incidence of finding carcinoma in endometrial sample varies with the population screened. AUB patients attending general gynaecology outpatient department, inclusive of all age group 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 6 cases (4%) in our study which is similar to rate 3.35% reported by Brahmaiah J et al¹⁶ and various authors reported rate of atrophic endometrium from 2-7.38%.¹⁶ Rupture of dilated blood capillaries beneath the surface of atrophic endometrium may be responsible for the bleeding in these patients. Study by Doraiswami et al¹⁰ documented 2.4% incidence of atrophic endometrium while Dwivedi et al¹⁹ has reported 11% atrophic endometrium which is higher than our present reported incidence.

Endometrial polyp was reported in 8 cases (5.3%) cases in our study while Kafle N et al⁹ has reported 2.41% incidence of polyp. Brahmaiah J. et al¹⁶ 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.²⁰ 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.²¹

Heavy menstrual bleeding with normal duration was commonest presentation 96 cases (64%) in our study. Vijayraghavan et al²² has reported menorrhagia in 71.25% as the commonest presenting complaint in AUB patients while Kafle N et al⁹ has reported 58.43% of AUB cases with menorrhagia as presenting complaint. Postmenopausal bleeding (PMB) was presentation in 23 cases (15.3%) cases in our study while Kafle N et al⁹ has reported 19.27% incidence of PMB and Vijayraghavan et al²² has reported 12.5% incidence of PMB in patients with AUB. PMB 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 underlying cause for their symptom.^{23,24} 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 al⁹ and Vijayraghavan et al²² have reported 15.1% and 15% incidence of metrorrhagia in AUB patients respectively.

Tables 3 and 5 Technical failure was noted in 2 cases out of 69 cases (2.8%) of pipelle biopsy group. These 2 cases were also underwent repeat sampling by hysteroscopy. Overall technical failure was seen in 2 cases (1.33%) however technical failure was not seen in D & C and Hysteroscopy group in our study. Failed endometrial sampling is usually associated with pain or cervical stenosis, which is more common in nulliparous women.²⁵ 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,²⁶ while failure rate for operative hysteroscopy 3.4% and ambulatory procedure 4.2% have been reported in the literature.²⁶ In our study inadequate sample was obtained in 7 cases (4.6%) overall and 5.6% (N1= 69) in pipelle group and 8.8%

(N2 =34) in D & C group. These patients were offered endometrial sampling by hysteroscopy for which 3 out of 7 patients consented and underwent repeat sampling by hysteroscopy. 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 sample²⁷ 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,²⁸ women with benign or inconclusive histology, but persistent symptoms or suspicious ultrasound finding should be offered hysteroscopy.

Out of 71 cases (Table 5) 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 anaesthesia for obtaining the sample. Hence, only 69 cases endometrial sample was obtained by pipelle biopsy out of 71 procedures. 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 questioned²⁹ however D & C still remains the choice for clinicians due to lack of availability of hysteroscope or cost factor for the patients.. 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 anaesthesia 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 anaesthesia with 4.9 mm hysteroscope. In our study one case of uterine perforation (out of 34 cases 2.9%) 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.³⁰ In our study hysteroscopy group did not had perforation. Postmenopausal, pregnancy, puerperium, acutely anteverted and retroverted uterus, or septic conditions are high risk factors for perforation. 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.

In summary main findings of our study are, AUB is commonly in age group 41-50 followed by in the age group of 31-40. Higher parity (para 3 more) is associated 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 (4.6%) cases endometrial sample obtained was inadequate for reporting and technical failure was noted in 2 (1.33%) cases out of 150 cases however technical failure was exclusively seen in pipelle group with technical failure rate of 2.8% of all pipelle procedres, uterine perforation was noted in one case out of 150 cases (0.66%).

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

7. 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.

8. 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.

9. Sources of Funding

None.

10. Conflict of Interest

None.

11. Ethical Approval

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


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