Audit

The histopathology of endometrial biopsies performed for abnormal uterine bleeding: an audit in a tertiary care centre in Sri Lanka

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Abstract

Introduction: The main indication for endometrial curettage and pipelle aspiration is abnormal uterine bleeding (AUB). Histological assessment is important in determining the various structural and non-structural aetiologies for AUB.
Objectives: To describe the histomorphology of the endometrium in different age groups of patients presenting with AUB and to determine the percentage having organic causes for AUB in each of these age groups.
Methodology: All the uterine curettage and pipelle aspiration specimens received during a period two years from January 2019 to December 2020 were included in the study. Evacuated products of conception were excluded. The patient characteristics, clinical information and the histopathological findings were obtained. All cases were stratified into age groups 20-39 (reproductive), 40-50 (perimenopausal) and >50 years (postmenopausal). The histological findings were classified as normal pattern (NP), ovulatory dysfunction (OD), exogenous hormonal effects (EHE), endometrial polyp (EP), chronic endometritis (CE), atrophic endometrium (AE), disordered proliferative endometrium (DPE), endometrial hyperplasia (EH) and carcinoma (CA). EP, CE, EH and CA were considered structural/ organic causes.
Results: A total of 778 specimens were analysed. The age range of the patients was 25–80 years (reproductive - 98, perimenopausal - 440, postmenopausal - 240). Structural / organic causes were found in 20.41% (20/98) in the 20–39-year age group (EP-15.31%, CE-4.08%, EH-1.02%), 12.95% (57/440) in the 40–50-year age group (EP-6.36%, CE-2.04%, EH-4.09%, CA-0.45%) and 29.58% (71/240) in the >50 age group (EP-14.17%, CA-10.83%, EH-4.58%). The commonest histological finding for AUB in the >50 age group was AE (22.08%,53/240). NP was the commonest in both the perimenopausal (29.55%, 130/440) and reproductive groups (30.61%,30/98).
Conclusion: There is a variation in the histomorphological findings for AUB among different age groups, and non-structural findings are commoner than structural / organic causes.
Keywords: abnormal uterine bleeding (AUB), organic causes, curettage, pipelle aspiration

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Introduction

Abnormal uterine bleeding (AUB) is one of the commonest complaints among females of all ages, who attend gynaecological units. AUB, although a broad term, is defined as irregularities in the menstrual cycle with regards to four parameters including frequency, regularity, duration and volume of flow occurring in the absence of pregnancy (1). The global incidence of AUB among females in the reproductive age group is estimated to be between 3%-30%. The incidence is higher around menarche and perimenopause (1).

Two layers of the endometrium, the functionalis and the basalis, receive their blood supply via the radial branches of the arcuate arteries. The progesterone level falls at the end of the menstrual cycle leading to breakdown of the functional layer, resulting in menstruation. The blood loss is controlled by vasoconstriction of arteries and the action of platelets and thrombin. Any structural abnormality in the uterus, defects in the clotting pathway or disturbance of the hypothalamic-pituitary-ovarian axis may affect menstruation leading to AUB (2).

The International Federation of Gynecology and Obstetrics (FIGO) has developed an acronym PALM-COEIN to describe both structural and non-structural aetiologies for AUB. The first four letters indicate structural abnormalities; Polyp, Adenomyosis, Leiomyoma and Malignancy. The second set of four letters indicate non-structural aetiologies and represent Coagulopathy, Ovulatory dysfunction, Endometrial and Iatrogenic. The last letter 'N' is reserved for entities which are not yet classified (1,3).

The histological assessment of endometrium is important in determining various structural and non-structural aetiologies in patients with AUB. This also helps in further management of these patients (4).

There are various endometrial sampling techniques, of which, dilatation and curettage (D & C) is considered the gold standard. The other method, the endometrial biopsy, is a limited sampling procedure that does not require anaesthesia as it is a relatively painless procedure. The pipelle endometrial aspirator is a widely utilized device in obtaining endometrial biopsies (5).

Morphologic patterns observed in endometrial biopsies vary according to the different age groups, whether premenopausal, perimenopausal or postmenopausal (6. 7). Perimenopause is defined as the period immediately prior to menopause and the first year after menopause. Menopause is defined as spontaneous amenorrhea for a period of 12 months (8).

Published data regarding endometrial biopsy findings in different age groups is sparse in the Sri Lankan population. One of the published studies was a retrospective cross-sectional hospital-study carried out in 2018 at Teaching Hospital Batticaloa for a period of 5 years (9).

The main aim of our study is to describe the histomorphology of the endometrium in different age groups of females presenting with AUB and to determine the percentage of patients having structural causes for AUB in each of these age groups.

Methods

This study was a retrospective, cross-sectional study conducted at the Department of Pathology, North Colombo Teaching Hospital, Ragama for a period of two years from January 2019 to December based 2020.

All the pipelle aspiration and curettage

samples were included in the study. Evacuated products of conception were excluded. These cases were selected from the departmental data base. The request forms and the haematoxylin and eosin-stained slides of all the cases were retrieved. The patient characteristics, clinical information and the histopathological findings were obtained.

The cases were stratified into reproductive (age 20 - 39 years), perimenopausal (age 40-50 years) and postmenopausal groups (above 50 years).

All the slides were reviewed by the principal investigator and when there were diagnostic discrepancies with the initially issued report, these were clarified with the consultant pathologist who reported on the specimen and the research supervisor.

The histological findings were stratified into the following categories after evaluating the haematoxylin and eosin-stained sections.

1. Normal patterns (NP) - This includes endometrium with proliferative phase, secretory phase or menstrual phase.
2. Ovulatory dysfunction (OD) - This includes endometrial glandular and stromal breakdown with features of anovulatory cycles or luteal phase abnormalities
3. Exogenous hormonal effects (EHE)
4. Endometrial polyps (EP)
5. Chronic endometritis (CE)
6. Atrophic endometrium (AE)
7. Disordered proliferative endometrium (DPE)
8. Endometrial hyperplasia (EH)
9. Carcinoma (CA)

Frequencies of these patterns in reproductive, perimenopausal and postmenopausal groups were assessed. EP, CE, EH and CA were considered as structural causes.

Results

A total of 885 samples submitted for histological diagnosis during the period of two years were analyzed. 12% (107/885) of these were inadequate for diagnosis and excluded from the study. The study sample included 778 cases.

The age of the patients ranged from 25-80 years. Most of them were in the 40-50 age group (Table 1).

Table 1. Distribution of cases in different age groups

Age group (years)	Number of cases (%)
20-39	98 (12.6%)
40-50	440 (56.55%)
>50	240 (30.85%)

In our study, 19.02% (148/778) showed structural causes, the commonest was EPs (9.89%,77/778) followed by EH (3.85%, 30/778).

Non-structural pathologies accounted for 80.97% (630/778) of cases, NP was seen in 24.29% (189/778) followed by EHE in 22.24% (173/778). Table 2 shows the various histological patterns observed in patients with AUB.

The commonest non-structural histological finding in both the reproductive group (20-39 years) and the perimenopausal group (40-50 years) were the NP accounting for 30.61% (30/98) and 29.55% (130/440), respectively, while in the postmenopausal age group, this was AE accounting for 22.08% (53/240). In all three groups, EPs were the commonest structural cause (Table 3 and Figure 1). Atypical EH was observed in one EP in a patient in the perimenopausal group.

Table 2. Distribution of histological findings in AUB

Histological finding	Number of cases	Percentage
Non-structural causes	**630**	(80.98%)
Normal pattern	189	24.29%
Ovulatory dysfunction	69	8.87%
Exogenous hormonal effect	173	22.24%
Atrophic endometrium	129	16.58%
Disordered proliferative endometrium	70	8.99%
Structural causes	**148**	(19.02%)
Chronic endometritis	13	1.67%
Endometrial polyp	77	9.89%
Endometrial hyperplasia (simple/atypical)	30	3.85%
Carcinoma (endometrial/other)	28	3.59%
Total	**778**	**100**

Table 3. Histological findings according to the age group

Histological finding	Reproductive group (20-39 years) (%)	Perimenopausal group (40-50 years) (%)	Postmenopausal group (>50 years) (%)
Normal pattern	30.61% (30)	29.55% (130)	12.08 (29)
Ovulatory dysfunction	5.10% (05)	9.77% (43)	8.75% (21)
Exogenous hormonal effects	24.5% (24)	23.64% (104)	18.75% (45)
Atrophic endometrium	12.24% (12)	14.55% (64)	22.08% (53)
Disordered proliferative endometrium	7.14% (7)	9.55% (42)	8.75% (21)
Chronic endometritis	4.08% (4)	2.04% (9)	None
Endometrial polyp	15.31% (15)	6.36% (28)	14.17% (34)
Endometrial hyperplasia (Simple /atypical)	1.02% (1)	4.09% (18)	4.58% (11)
Carcinoma (endometrial/other)	None	0.45% (2)	10.83% (26)
Total (778)	**98**	**440**	**240**

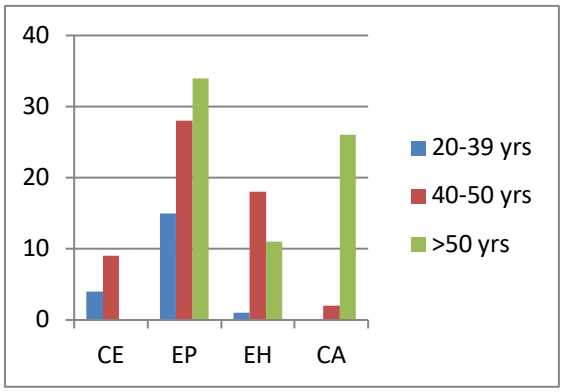

Figure 1. Distribution of structural causes for AUB in the different age groups

In this study, EH was observed in 4.09% (18/440) of patients in the perimenopausal group and 4.58% (11/240) of patients in the postmenopausal group.

A total of 28 malignancies were identified in the study group; 17 were adenocarcinomas, nine were squamous cell carcinomas of the cervix and two were poorly differentiated carcinomas. Of the adenocarcinomas, 10 were endometrioid type endometrial adenocarcinomas, one was a serous

carcinoma, two were endocervical adenocarcinoma-usual type and two were diagnosed as adenocarcinoma without further typing. The remaining two were adenocarcinomas in which the site of origin of the tumour could not be specified.

Discussion

Being a common and a relatively simple procedure, endometrial curettage and especially pipelle aspiration provides valuable information regarding the underlying endometrial pathologies and help to guide the patient management and follow up. It is useful to document the likely pathologies encountered in such biopsies at different stages of life (i.e., reproductive, perimenopausal and postmenopausal) in the local setting.

In our study, most endometrial biopsies were from the perimenopausal (40-50 year) group, which is comparable with other studies, where the perimenopausal group was the most frequently investigated (10-12).

According to this study, non-structural pathologies were commoner than structural causes in all three age groups, accounting for a total of 80.97% (630/778) of cases. In a hospital-based study carried out at Teaching Hospital Batticaloa, Sri Lanka, non-structural causes accounted for 67% of cases of AUB (9).

Of the non-structural causes, NP was the commonest finding in the reproductive and perimenopausal groups, accounting for 30.61% and 29.55% respectively. A higher incidence of NP was observed in several studies, including those of Vani et al. (56.27%), Vaidya et al. (40.94%) and Sajitha et al. (38.99%) (10,13,14).

In the current study, AE was the predominant pattern observed (22.08%, 53/240) in the postmenopausal group. The morphology of AE displays widely spaced tubular to cystically dilated glands. In contrast to hysterectomy specimens, the cystic glands may not be seen in curettage specimens due to fragmentation of the tissue during the procedure. The lining cells are low columnar or attenuated and devoid of proliferative activity. The stroma may be densely cellular or may have a fibrous appearance with advancing age (15). The suggested possible causes for postmenopausal bleeding in AE are degenerative changes or other changes related to endometrial blood vessels (16). A lower incidence of AE (5.62%), with the majority (53.84%) occurring after 50 years of age was observed in the study carried out by Vani et al. (13). A similar lower incidence of 5.13% and 7% was reported in several other studies (10,17).

EP was the commonest structural cause of AUB observed in the present study (9.89%). The morphology of EPs shows polypoidal fragments lined by epithelium on three sides, glandular architectural abnormality, fibrous stroma and thick-walled stromal blood vessels. The endometrium of the lower uterine segment (LUS) can be mistaken for an EP because it displays irregular glandular architecture and fibrous stroma. However, the LUS lacks thick-walled stromal blood vessels (15). In this study, there was one case of an EP with atypical EH in a 43-year-old patient. One study showed a higher incidence (32%) of EPs associated with malignancies in the >65 years age group, with its frequency increasing with age and reaching a statistically significant level in the age group >65 years (18).

EH was observed in 3.85% of patients. It accounted for 4.09% and 4.58% of the cases in perimenopausal and postmenopausal groups, respectively. However, even higher incidences of 19.47%, 10% and 6% were reported in several studies (10,13,19). EH is characterized by irregular size and shape of

the glands with associated increased gland to stroma ratio. EH is classified as EH without atypia and atypical hyperplasia. In atypical hyperplasia, the nuclei of the cells show rounding, enlargement, pleomorphism, loss of polarity and prominent nucleoli. Unopposed oestrogen stimulation plays a role in the development of EH. It is vital to identify EH as this can progress to endometrioid type endometrial carcinoma (20).

Malignancies were identified in 3.39% (28/778) cases in this study, the majority being observed in the postmenopausal group (26/28). This study revealed 13 adenocarcinomas of endometrial origin, the most common type being endometrioid type adenocarcinoma which accounted for 10 cases.

Primary cervical carcinoma involving the endometrium was observed in 1.41% (11/778) of cases, nine of which were cervical squamous cell carcinoma. Two cases were endocervical adenocarcinoma-usual type. A similar incidence was reported in two other studies carried out by Sajitha et al. and Ara et al. in which the incidence of cervical carcinoma was 1.28% and 1.24%, respectively (10,17).

As this was a retrospective study, the investigators categorized the postmenopausal and perimenopausal groups broadly by considering only the age and not as per the definition of spontaneous amenorrhea for a period of 12 months. This is a limitation of this study and may have contributed to the variations seen in the incidence of the different pathologies when comparing with other studies. However, the general variation seen among these groups is similar.

Conclusion

In conclusion, there is a variation in the histomorphological findings in AUB among the different age groups, and non-structural findings are commoner than structural causes. Of the latter, EPs are the commonest and occur in all three age groups. However, the frequency of malignancies increases in the postmenopausal group, hence, the histological assessment of the endometrium in this group is crucial when indicated.

References

1. Davis E, Sparzak PB. Abnormal uterine bleeding. [Updated 2022 Feb 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532913/
2. Whitaker L, Critchley HO. Abnormal uterine bleeding. Best Pract Res Clin Obstet Gynaecol. 2016;34:54-65. https://doi:10.1016/j.bpobgyn.2015.11.012
3. Munro MG, Critchley HOD, Fraser IS; FIGO Menstrual Disorders Committee. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. Int J Gynaecol Obstet. 2018;143(3):393-408. https://doi:10.1002/ijgo.12666
4. Sharma S, Makaju R, Shrestha S, Shrestha A. Histopathological findings of endometrial samples and its correlation between the premenopausal and postmenopausal women in abnormal uterine bleeding. Kathmandu Univ Med J (KUMJ). 2014;12(48):275-278. https://doi:10.3126/kumj.v12i4.13734
5. Mazur MT, Kurman RJ. Diagnosis of endometrial biopsies and curettings: A practical approach, 2nd ed. New York: Springer; 2005 USA. p. 275-276.
6. Rizvi S, Wajid R, Saeed G, Jafri A, Haider R. Clinicopathological spectrum of endometrium in abnormal uterine bleeding: Study in a tertiary care hospital in Lahore. Pak J Med Health Sci 2017;11(1):227–9. https://doi.org/10.33279/2307-3934.2020.0113

7. Dahlenbach-Hellweg G. Histopathology of endometrium. New York: Springer-Verlag; 1993.
8. WHO Scientific Group on Research on the Menopause & World Health Organization. (1981). Research on the menopause: report of a WHO scientific group [meeting held in Geneva from 8 to 12 December 1980]. World Health Organization.
https://apps.who.int/iris/handle/10665/41526
9. Thirukumar, M. Ahilan, S. Histopathological pattern of endometrium: Hospital based study in Teaching Hospital, Batticaloa, Sri Lanka. Open Journal of Obstetrics and Gynecology 2018;8:1015-1022.
https://10.4236/ojog.2018.811102
10. Sajitha K, Padma SK, Shetty KJ, Kishan Prasad HL, Permi HS, Hegde P. Study of histopathological patterns of endometrium in abnormal uterine bleeding. CHRISMED J Health Res 2014; 1:76-81.
https://10.4103/2348-3334.134265
11. Jyotsana, Manhas K, Sharma S. Role of hysteroscopy and laparoscopy in evaluation of abnormal uterine bleeding. JK Sci 2004;6:23-7.
12. Azim P, Khan MM, Sharif N, Khattak EG. Evaluation of abnormal uterine bleeding on endometrial biopsies. ISRA Med J 2011;3:84-8.
13. Vani BS, Vani R, Jijiya BP. Histopathological evaluation of endometrial biopsies and curetting's in abnormal uterine bleeding. Trop J Path Micro 2019;5(4):190-197.
https://doi.org/10.17511/jopm.2019.i04.02
14. Vaidya S, Lakhey M, Vaidya S, et al. Histopathological pattern of abnormal uterine bleeding in endometrial biopsies. Nepal Med Coll J. 2013;15(1):74-77.
15. McCluggage WG. Benign diseases of the endometrium. In Kurman RJ, Ellenson LH, Ronnett BM (Eds). Blaustein's Pathology of female genital tract, 6th edition. New York:Springer;2019.p.307-354.
16. Gilks B. Uterus:corpus. In Goldblum JR, Lamps LW, Mckenney JK, Myers JL (Eds.) Rosai and Ackerman's Surgical Pathology, 11th edition. Philadelphia: Elsevier; 2018. p.1294-1338.
17. Ara S, Roohi M. Abnormal uterine bleeding: Histopathological diagnosis by conventional dilatation and curettage. Prof Med J 2011;18:587-91.
18. Hileeto D, Fadare O, Martel M, Zheng W. Age dependent association of endometrial polyps with increased risk of cancer involvement. World J Surg Oncol. 2005;3(1):8.
https://doi:10.1186/1477-7819-3-8
19. Doraiswami S, Johnson T, Rao S, Rajkumar A, Vijayaraghavan J, Panicker VK. Study of endometrial pathology in abnormal uterine bleeding. J Obstet Gynaecol India. 2011;61(4):426-430.
https://doi:10.1007/s13224-011-0047-2
20. Ellenson LH, Ronnett BM, Kurman RJ. Precursor lesions of the endometrium In Kurman RJ, Ellenson LH, Ronnett BM (Eds). Blaustein's Pathology of female genital tract, 6th edition. New York:sSpringer;2019.p 360-389.