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Original Article

Pathology Section

Histomorphological Spectrum of Endometrial Tissue in Abnormal Uterine Bleeding

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ABSTRACT

Introduction: Abnormal Uterine Bleeding (AUB) is a very common presenting complaint in patients visiting the gynaecologists all over the world. Though common, AUB can cause tremendous physical as well as emotional distress to the patient.

Aim: To study the histomorphological pattern of endometrium in patients with AUB.

Materials and Methods: This study was a retrospective study conducted during a six month period from October 2021 to March 2022 in the Department of Pathology at Apollo Institute of Medical Sciences and Research, Chittoor, Andhra Pradesh, India, on 210 endometrial tissue samples of women who presented with AUB. Specimens that were received during a one year period between March 2019 and February 2020 were processed routinely and stained using Haematoxylin and Eosin stain. Detailed microscopic evaluation was done and eleven different histopathological diagnoses were made. The data collected was entered into Microsoft Excel sheet and percentages were analysed manually.

Results: Maximum number of cases of AUB were seen in the 41-50 years age group. The most common histopathological pattern in this study was proliferative phase seen in 67 cases (31.90%) followed by endometrial hyperplasia which was seen in 42 cases (20.00%). The other important patterns included pregnancy related complications, 32 (15.24%), secretory phase, 24 (11.43%), disordered proliferative endometrium, 14 (6.67%), chronic endometritis 11 (5.24%) and hormonal/pill endometrium, 8 (3.81%). Endometrial malignancy was diagnosed only in one case (0.48%).

Conclusion: A wide variety of histopathological patterns were found in endometrial samples in AUB across different age groups. Histopathological examination of endometrium is an important tool in the diagnosis and management of AUB.

Keywords: Hyperplasia, Neoplasm, Perimenopausal bleeding, Proliferative phase, Uterus

INTRODUCTION

Abnormal Uterine Bleeding (AUB) is defined as menstrual bleeding that is outside the normal ranges of duration, volume and frequency [1]. It is a very common yet challenging problem seen in the Gynaecological Outpatient Department (OPD) [2]. It affects both the quality of life as well as the psychological condition of women who suffer from it [3].

The AUB can be caused by both organic as well as functional causes [4]. The International Federation of Gynaecology and Obstetrics (FIGO) has developed a system called PALM-COEIN for classifying the etiology of AUB. The acronym PALM-COEIN includes nine categories: Polyp, Adenomyosis, Leiomyoma, Malignancy and Hyperplasia, Coagulopathy, Ovulatory dysfunction, Endometrial, Iatrogenic and not yet classified. Hence, PALM represents the structural causes whereas COEIN represents the functional causes of AUB [5].

Around 10-25% of women experience AUB during their reproductive life. It is commonly seen during extremes of reproductive life i.e., one to two years after onset of menarche and during the premenopausal phase. It is also seen in some women post pregnancy and during lactation. The AUB after onset of menarche is due to the immature hypothalamic-pituitary-ovarian axis that causes anovulatory cycles. Even in perimenopausal women, anovulation can cause menorrhagia. But in this age group, it is important to rule out the presence of endometrial hyperplasia and malignancy [6].

Histopathological evaluation of endometrial tissue remains an important step in the diagnosis and further treatment of AUB [7].

This study was necessary to determine the most common histopathological patterns of endometrium in AUB in patients of Chittoor district, Andhra Pradesh, India. This would be helpful in identifying the endometrial causes of AUB and provide key insight to the clinicians while handling similar cases.

The objectives of this study were to identify the most common histopatholological findings of endometrium in AUB to identify the histopathological spectrum of endometrium in patients across different age groups who had clinically presented with AUB.

MATERIALS AND METHODS

The present retrospective study was conducted between October 2021 and March 2022 on 210 endometrial tissue samples received during a period of one year between March 2019 and February 2020 in the Department of Pathology at Apollo Institute of Medical Sciences and Research, Chittoor, Andhra Pradesh, India. The sample size was determined by including all the samples that were in concurrence with the inclusion criteria. The study was approved by the Institutional Ethical Committee (Reference No-FR016/IEC/AIMSR/2021).

Inclusion criteria: All the endometrial tissue samples (endometrial biopsy, dilatation and curettage and pipelle biopsy samples) that were received with a clinical diagnosis of AUB were included in the study.

Exclusion criteria: Samples that were inadequate for interpretation were excluded from the study.

Study procedure

Samples received in 10% formalin fixative were processed using automated tissue processor. Tissue sections of 3-5 µ thickness were stained using Hematoxylin and Eosin stains. Careful microscopic evaluation of the tissue sections was done under light microscopy and histopathological diagnoses were made. The histopathological diagnoses included eleven categories namely proliferative phase, secretory phase, pregnancy related complications, disordered

proliferative endometrium, chronic endometritis, endometrial polyp, pill endometrium, atrophic endometrium, shedding endometrium, endometrial hyperplasias and endometrial carcinoma. Then age wise distribution of all the cases were analysed as mentioned below.

STATISTICAL ANALYSIS

The collected data were entered and analysed in Microsoft Excel sheet 2010 and expressed as percentages.

RESULTS

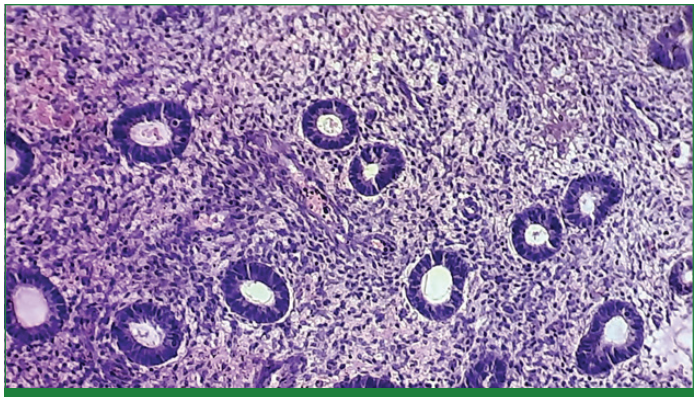
In this study, a total of 210 endometrial samples with the clinical diagnosis of AUB were studied.

Maximum number of cases of AUB were seen in the 41-50 years age group accounting for 75 cases (35.71%).This was followed closely by 31-40 years age group that constituted 73 cases (34.76%) as shown in [Table/Fig-1].

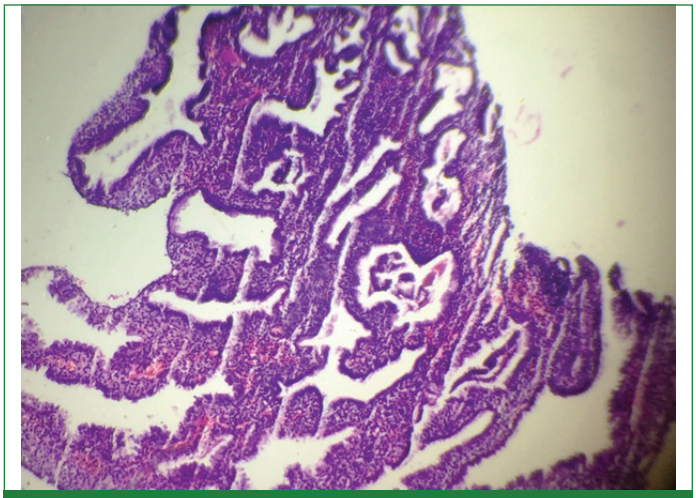
Age group (In years)	Number of cases	Percentage
≤20	09	4.29%
21-30	35	16.67%
31-40	73	34.76%
41-50	75	35.71%
51-60	13	6.19%
61-70	04	1.90%
>70	01	0.48%
Total	210	100.00%

[Table/Fig-1]: Distribution of cases of AUB according to different age groups.

Based on meticulous histopathological examination, all the cases were classified into 11 histopathological categories and the distribution of the histopathological patterns across different age groups is shown in [Table/Fig-2].



[Table/Fig-3]: Proliferative phase endometrium showing small tubular endometrial glands in compact stroma (H&E 10X).



[Table/Fig-4]: Simple hyperplasia without atypia showing increased glands to stroma ratio with endometrial glands of variable sizes and shapes (H&E 10X).

Histopathological pattern of endometrium	Age groups (years)							
	≤20	21-30	31-40	41-50	51-60	61-70	>70	Total, n (%)
Proliferative phase	-	09	29	25	03	01		67 (31.90%)
Secretory phase	-	03	16	05	-	-	-	24 (11.43%)
Pregnancy related complications	09	19	04	-	-	-	-	32 (15.24%)
Disordered proliferative endometrium	-	-	03	11	-	-	-	14 (6.67%)
Chronic endometritis	-	01	05	04	01	-	-	11 (5.24%)
Endometrial polyp	-	-	-	02	-	-	-	02 (0.95%)
Pill endometrium	-	02	04	01	01	-	-	08 (3.81%)
Atrophic endometrium	-	-	-	02	02	02	01	07 (3.33%)
Shedding endometrium	-	-	-	01	01	-	-	02 (0.95%)
Endometrial hyperplasia	-	01	12	23	05	01	-	42 (20.00%)
Endometrial carcinoma	-	-	-	01	-	-	-	01 (0.48%)
TOTAL	09	35	73	75	13	04	01	210 (100.00%)

[Table/Fig-2]: Endometrial histopathological patterns in AUB in different age groups.

The normal cyclical endometrial patterns, proliferative and secretory phase together accounted for the maximum number of cases. Proliferative phase [Table/Fig-3] was diagnosed in 67 cases (31.90%) and Secretory phase in 24 cases (11.43%). Endometrial hyperplasia was the second commonest category and it was observed in 42 cases (20%). Among all the 42 cases of endometrial hyperplasia, 41 cases showed simple hyperplasia without atypia [Table/Fig-4]. One sample showed features of complex hyperplasia with atypia. Majority of the patients with endometrial hyperplasia belonged to the 41-50 years age group followed by 31-40 years age group.

Pregnancy related complications were seen in 15.24% of all cases included in the study.

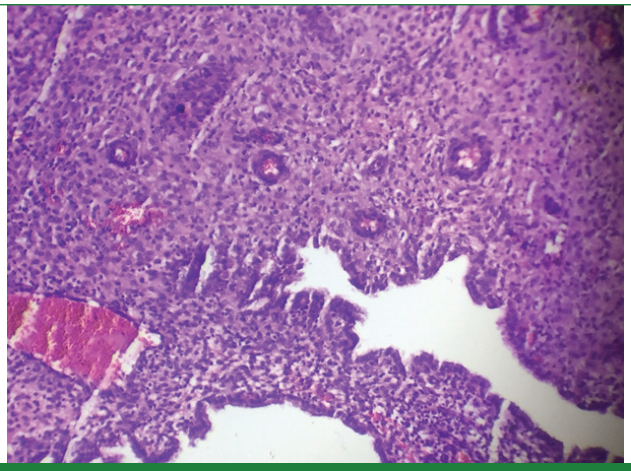
Disordered proliferative endometrium was observed in 14 cases (6.67%) and its incidence was the highest in patients between 41-50 years.

Total 11 cases (5.24%) showed features of endometritis while hormonal/pill endometrium [Table/Fig-5] was seen in 8 cases (3.81%).

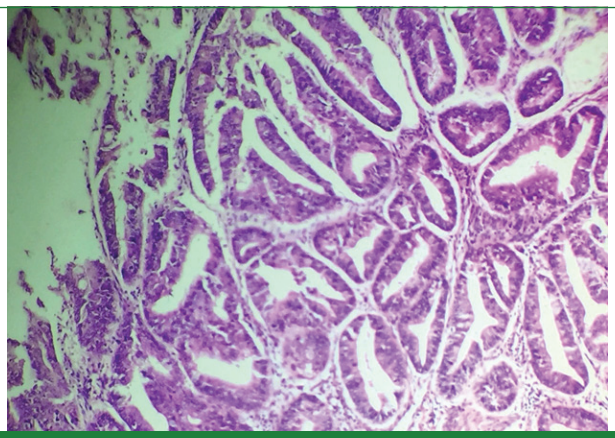
Seven cases (3.33%) of atrophic endometrium were observed in the present study and these were mostly seen in the post menopausal patients.

Two cases of endometrial polyp also were seen that accounted for 0.95% of all the cases. Both were Hyperplastic polyps of the endometrium.

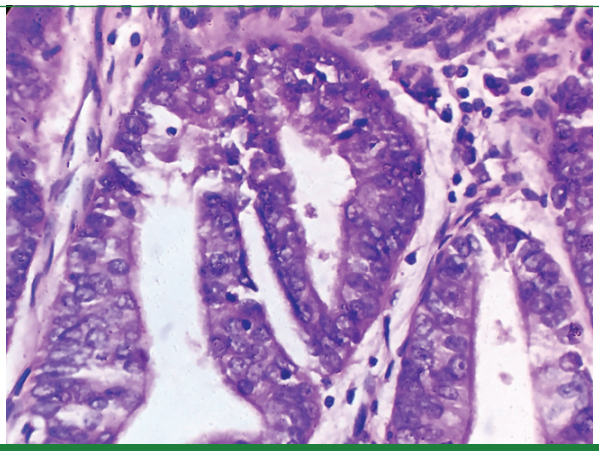
There was one case of endometrial carcinoma (0.48%) and the patient belonged to the 41-50 years age group. The endometrial adenocarcinoma [Table/Fig-6,7] was of endometrioid type.



[Table/Fig-5]: Exogenous progesterone hormone induced change (pseudo-decidualisation of stroma) seen in pill endometrium (H&E 10X).



[Table/Fig-6]: Endometrioid endometrial adenocarcinoma showing back to back glands without intervening stroma (H&E 10x).



[Table/Fig-7]: Endometrioid endometrial adenocarcinoma- cells lining the neoplastic glands show nuclear enlargement, nuclear rounding with nucleoli (H&E 40X).

DISCUSSION

Abnormal uterine bleeding is defined as menstrual flow that does not fulfill the criteria for normal menstruation [7]. A normal menstrual cycle usually lasts between 21 to 35 days. Polymenorrhoea refers to cycles reduced to less than 21 days whereas menstrual cycles more than 35 days apart constitute oligomenorrhoea. Menorrhagia is cyclical bleeding at normal intervals but the bleeding is excessive in amount (>80 mL) or duration (>7 days). Metrorrhagia is irregular and acyclic bleeding from the uterus but the amount of bleeding is variable [8]. Bleeding that occurs at irregular, noncyclical intervals along with heavy flow (>80 mL) or duration (>7days) is menometrorrhagia. Post menopausal bleeding is bleeding that occurs in a lady who has attained menopause (at least one year after the cessation of her cycles) [9].

In this study, endometrial histopathological patterns in 210 patients with AUB were studied.

Most cases (35.71%) of AUB in this study belonged to the age group 41-50 years. This finding is in concordance with the studies by Doraiswami S et al., [7], Kumari SR and Anuradha M [10] and Bhatta S and Sinha A [9]. This may be due to the fact that, the women in this age group were in the perimenopausal phase where anovulatory cycles are common.

In [Table/Fig-8] given below, comparison of findings in the present study with various other studies is shown [3,7,9-11].

Proliferative phase was the most common histopathological pattern identified in this study accounting for 67 cases (31.90%).A similar finding was reported by Sharma R et al., [11], Bhatta S and Sinha A [9] and Kumari SR and Anuradha M [10]. Pregnancy related complications were reported in 32 cases (15.24%) and maximum number of cases was seen in 21-30 years age-group. It was identified as the most important cause of AUB in early reproductive years in this study. Doraiswami S et al., [7] also reported 22.74% cases with complications of pregnancy in their study. However, this finding is in discordance with the data in the study by Sharma R et al., [11] where its incidence was very low (3.3%).A total of 11 cases (5.24%) showed features of endometritis. Similar findings were reported in studies by Doraiswami S et al [7], Bhatta S and Sinha A [9] and Anupama Suresh Y et al., [3]. Most cases of endometritis in this study were identified in the 31-40 years age group.

Atrophic endometrium was seen in 3.33% of cases in the present study. This is in concordance with studies by Sharma R et al., [11] and Doraiswami S et al., [7]. This is in slight discordance with the studies by Bhatta S and Sinha A [9] and Anupama Suresh Y et al., [3] which reported a slightly higher incidence of atrophic endomerium. The rupture of dilated blood capillaries beneath the surface of atrophic endometrial epithelium causes AUB in these cases [8]. Only two cases (0.95%) of endometrial polyp were reported in the present study. Both these cases were identified in women between 41-50 years. The studies by Sharma R et al., [11], Kumari SR and Anuradha

Histopathological finding	Doraiswami S et al., [7] (2011)	Bhatta S et al., [9] (2012)	Anupama suresh Y et al., [3] (2014)	Kumari SR et al., [10] (2017)	Sharma R et al., [11] (2018)	Present study, (2022)
Proliferative phase	116 (28.36%)	32 (26.23%)	94 (26.2%)	63 (29.03%)	71 (38.8%)	67 (31.90%)
Secretory phase		20 (16.39%)		27 (12.44%)	30 (16.4%)	24 (11.43%)
Endometrial Hyperplasia	25 (6.11%)	22 (18.03%)	96 (26.7%)	36 (16.59%)	22 (12.0%)	42 (20.00%)
Pregnancy related	93 (22.74%)	--	--	--	6 (3.3%)	32 (15.24%)
Disordered Proliferative endometrium	84 (20.54%)	8 (6.56%)	37 (10.3%)	48 (22.12%)	12 (6.5%)	14 (6.67%)
Endometritis	17 (4.16%)	8 (6.56%)	23(6.4%)	3 (1.38%)	6 (3.3%)	11 (5.24%)
Endometrial polyp	46 (11.25%)	3 (2.46%)	31 (8.6%)	5 (2.3%)	4 (2.2%)	2 (0.95%)
Hormonal change	--	--	--	6 (2.76%)	11 (6.0%)	8 (3.81%)
Atrophic	10 (2.44%)	9 (7.38%)	20 (5.6%)	4 (1.84%)	8 (4.4%)	7 (3.33%)
Shedding endometrium	--	--	--	14 (6.45%)	--	2 (0.95%)
Endometrial Carcinoma	18 (4.40%)	7 (5.74%)	23 (6.4%)	4 (1.84%)	2 (1.1%)	1 (0.48%)

[Table/Fig-8]: Comparison table showing histopathological patterns of Endometrium in AUB in various studies [3,7,9-11].

M [10] and Bhatta S and Sinha A [9] showed an incidence of 2.2%, 2.3% and 2.46% respectively. In contrast, a higher incidence of Endometrial polyp was reported in the studies by Anupama Suresh Y et al., [3] and Doraiswami S et al., [7] accounting for 8.6% and 11.25% respectively. Hormonal/pill endometrium was diagnosed in 8 cases (3.81%) and is similar to the study by Kumari SR and Anuradha M [10], which reported its incidence as 2.76%. Shedding endometrium was reported in 0.95% of cases and is in discordance with the study by Kumari SR and Anuradha M [10] that reported an incidence of 6.45%.

Total 6.67% of cases in the present study showed disordered proliferative endometrium and this finding is similar to the studies by Sharma R et al., [11] and Bhatta S and Sinha A [9]. On the contrary, disordered proliferative endometrium accounted for a higher percentage of cases, 22.12% and 20.54% of cases respectively in studies by Kumari SR and Anuradha M [10] and Doraiswami S et al., [7]. The term disordered proliferative endometrium is difficult to define but is usually used when the endometrial appearance looks hyperplastic but there is no actual increase in endometrial volume [12].

A significant number of cases (20.00%) were diagnosed with endometrial hyperplasia in the present study. This finding is comparable to the data in the study by Bhatta S and Sinha A [9] (18.03%) and is in discordance with the studies by Doraiswami S et al., [7] (6.11%) and Sharma R et al., [11] (12.0%) which reported significantly lower incidence of Endometrial Hyperplasia. The occurrence of endometrial hyperplasia also was highest among women between 41-50 years in the present study. Out of these cases, one case was complex hyperplasia with atypia and the remaining were simple hyperplasia without atypia. This is because anovulatory cycles are common in perimenopausal age group causing unopposed estrogen stimulation and this may lead to endometrial proliferation and hyperplasia [13]. Disordered proliferative endometrium and hyperplasia without atypia are lesions of the same spectrum and is related to prolonged estrogenic stimulation. Continuous unopposed estrogen action can cause progression of hyperplasia without atypia to atypical hyperplasia/ endometrial intraepithelial neoplasia. Hence, histopathological study of endometrium is important to identify endometrial hyperplasia with atypia as it is considered as the precancerous lesion for endometrial Carcinoma [14].

Endometrial carcinoma was diagnosed only in one case (0.48%) in the present study and it was of endometrioid type. This patient had presented with post menopausal bleeding. In concordance with this finding, the studies by Prathipaa R et al., [15] and Sharma R et al., [11] also reported a very low incidence of 0.39% and 1.1% respectively.

The present study showed that normal cyclical endometrial patterns were the most common histopathological findings in AUB. In such cases, other structural non endometrial causes or functional causes might have caused the bleeding. Endometrial hyperplasias have been mostly identified in the perimenopausal age-group. This reiterates the importance of endometrial sampling in this age group so that early detection and appropriate treatment of hyperplasias would be possible. Endometrial malignancy is the least common cause of AUB as suggested by various studies including the present one.

Limitation(s)

The present study is purely a histopathological study of endometrial tissue cases that were clinically diagnosed as AUB. Therefore, the study is lacking in clinic-pathological correlation.

CONCLUSION(S)

Abnormal Uterine Bleeding is a common complaint among women belonging to all the age groups. But the occurrence is more during the perimenopausal age group. The causes for AUB differ across different age groups. Histopathological evaluation of endometrium plays an invaluable role in the accurate diagnosis of AUB.

REFERENCES

[1] 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;1:76-78.
[2] Khare A, Bansal R, Sharma S, Elhence P, Makkar N, Tyagi Y. Morphological spectrum of Endometrium in patients presenting with dysfunctional uterine bleeding. People's J Scient Res. 2012;5(2):13-16.
[3] Anupamasuresh Y, Suresh YV, Jain P. Abnormal uterine bleeding: A clinicohistopathological analysis. Int J Reprod Contracept Obstet Gynecol. 2014;3:656-61.
[4] Verma D, Verma A. Histopathological correlation of abnormal uterine bleeding in perimenopausal women. Int J Reprod Contracept Obstet Gynecol. 2016;5:2343-45.
[5] Mishra D, Sultan S. FIGO's PALM-COEIN classification of abnormal uterine bleeding: A clinico-histopathological correlation in Indian setting. J Obstet Gynaecol India. 2017;67(2):119-25.
[6] Kumar S, Padubidri VG, Daftary SN. Abnormal Uterine Bleeding. In: Kumar S, Padubidri VG, Daftary SN, eds. Shaw's Textbook of Gynecology. 17th ed. New Delhi, India: Elsevier; 2018: pp. 128-40.
[7] 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):426-30.
[8] Konar H. Abnormal Uterine Bleeding. In: Konar H, editor. DC dutta's Textbook of Gynecology. 7th ed. New Delhi, India: Jaypee Brothers Medical; 2016: pp.152-62.
[9] Bhatta S, Sinha A. Histopathological study of endometrium in abnormal uterine bleeding. Journal of Pathology of Nepal. 2012;2(4):297-300.
[10] Kumari SR, Anuradha M. Endometrial patterns in abnormal uterine bleeding: A retrospective study. Int J Reprod Contracept Obstet Gynecol. 2017;6:4966-70.
[11] Sharma R, Mishra P, Kumar N, Srivastava P. Histomorphological spectrum of endometrial lesion in women presenting with abnormal uterine bleeding: A 3-year study at a tertiary care center. Trop J Path Micro. 2018;4(7):525-31.
[12] Silverberg SG. Problems in the differential diagnosis of endometrial hyperplasia and carcinoma. Mod Pathol. 2000;13(3):309-27.
[13] Albers JR, Hull SK, Wesley RM. Abnormal uterine bleeding. Am Fam Physician. 2004;69(8):1915-26.
[14] Vani BS, Vani R, Jijiya Bai P. Histopathological evaluation of endometrial biopsies and curetting's in abnormal uterine bleeding. Trop J Path Micro. 2019;5(4):190-97.
[15] Prathipaa R, Divya J. Histopathological study of endometrial samples in abnormal uterine bleeding. Indian J Pathol Oncol. 2020;7(4):567-70.

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