International Journal of Clinical Trials
Shrivastava K et al. Int J Clin Trials. 2024 Nov;11(4):252-259
http://www.ijclinicaltrials.com
pISSN 2349-3240 | eISSN 2349-3259
DOI: https://dx.doi.org/10.18203/2349-3259.ijct20242672

Original Research Article

Histopathological spectrum of uterine lesions in hysterectomy specimens of patients with abnormal uterine bleeding

Kshama Shrivastava[1], Ranu Tiwari Mishra[2]*, Priyadarshani Tiwari[3], Sanjay Totade[2], Jagmohan Singh Dhakar[4]

[1]Bundelkhand Medical College Sagar, M. P., India
[2]Department of Pathology, Netaji Subhash Chandra Bose Medical College, Jabalpur, M.P. India
[3]Department of Obstetrics and Gynecology, Netaji Subhash Chandra Bose Medical College, Jabalpur, M.P., India
[4]Department of Community Medicine, Virendra Kumar Sakhlecha Govt Medical College, Neemuch, M.P., India

Received: 27 August 2024
Revised: 10 September 2024
Accepted: 11 September 2024

***Correspondence:**
Dr. Ranu Tiwari Mishra,
E-mail: ranu.m7317@gmail.com

ABSTRACT

Background: Abnormal uterine bleeding (AUB) is an overarching term that reflects any departure from normal menstruation or regular menstrual cycle patterns. Treatment depends upon the cause. Hysterectomy being a definite treatment for structural uterine pathology.
Methods: This cross-sectional observational study was conducted in department of pathology, Netaji Subhash Chandra Bose medical college Jabalpur (M.P.). The study comprised of 140 hysterectomy specimens with or without salpingo-oophorectomy obtained from AUB patients and submitted for histopathological examination in our department during study period of 18 months. The relevant data of the patients was collected and analyzed as per designed proforma.
Results: Out of 140 cases, majority of the patients were in 41-50 years age group 63 cases (45%), followed by 31-40 years age group 59 cases (42.14%). Most common clinical presentation was heavy menstrual bleeding in 83 cases (59.28%), followed by intermenstrual bleeding and pain in abdomen in 66 cases (47.14%) each. Commonest lesion found was leiomyoma, 83 cases (59.28%), second being dual pathology of adenomyosis with leiomyoma 23 cases (16.42%) followed by adenomyosis, 19 cases (13.57%). Four cases (2.85%) of benign endometrial polyp and endometrial carcinoma each and 1 case of adenomyoma, simple endometrial hyperplasia and endometrial stromal sarcoma, each, were reported.
Conclusions: A wide spectrum of histopathological findings, ranging from normal cyclic endometrium to benign pathology and malignancy were seen. In some patients, dual pathologies, incidental findings and occult malignant lesions, which were missed clinically or radiologically, was diagnosed on histopathological examination, thus making it a goldstandard for definite diagnosis.

Keywords: AUB, Hysterectomy, Histopathology

INTRODUCTION

The regular cyclical menstruation results from the choreographed relationship between the endometrium and its regulatory factors.[1] Normal menstrual cycle has cycle length of 24-38 days with duration of menstrual blood flow of fewer than eight days, and amount of blood loss is between 5-80 ml/cycle. AUB is defined as any variation in regularity, frequency, heaviness of flow, and duration of menstrual blood flow that occurs in various forms and may be caused by a variety of factors.[2] Causes of AUB may be uterine pathology or secondary to ovulation disorders, coagulation disorders and iatrogenic. Treatment depends upon the cause. Hysterectomy being a

definite treatment for structural uterine pathology.[2] AUB is the major health problem with incidence in reproductive age group 14 to 25%, which further increases up to 50% in peri-menopausal women.[3] In India, reported prevalence is around 17.9% and is an important cause of morbidity and mortality due to its consequences like severe anemia; which may require surgical intervention.[4] For definite diagnosis detailed clinical history, radiological examination and histopathological examination is required.[5] FIGO menstrual disorders group (FMDG) has not only developed a new PALM-COEIN classification for categorization of causes of AUB but also standardized the symptom nomenclature with the abandonment of the terms like menorrhagia, metrorrhagia, and dysfunctional uterine bleeding.[6]

Our study aimed at determining the histopathological spectrum of various uterine lesions in hysterectomy specimens obtained from AUB patients and its association with age, clinical symptoms in AUB patients.

METHODS

Present cross-sectional observational study comprised of 140 hysterectomy specimens with or without salpingo-oophorectomy obtained from AUB patients, andsubmitted for histopathological examination in the department of pathology, NSCB medical college Jabalpur (M.P.) during study period of 18 months. Relevant data of the patients age, clinical presentation, menopausal status, radiological findings collected in designed proforma after obtaining approval from Ethical committee. Hysterectomy specimens were fixed in 10% formalin for 24 h. Detailed gross examination of submitted specimens were carried out. Representative sections were given. Tissue processing done in histokinette and paraffin-embedded blocks were sectioned and stained with hematoxylin and eosin. Microscopic exam of stained slides was done and histopathological diagnosis was made.

Inclusion criteria

All hysterectomy specimens with or without salpingo-oophorectomy, done in a patient of AUB, received in the pathology department for histopathological examination during the study period were included.

Exclusion criteria

Specimens of subtotal hysterectomy, hysterectomies done for tubo-ovarian masses, obstetrical causes, and patients with uterine prolapse will be excluded from the study.

Statistical analysis

Collected data was analyzed by using IBM-SPSS version 23.0. The statistical methods were used to make cross-tabulation, frequencies, percentage, bar diagram and Fisher's exact test was used for comparison of clinical diagnosis and histopathological diagnosis. $P<0.05$ was taken to indicate a statistically significant difference.

RESULTS

Among 140 cases, majority were in 41-50 years age group 63 cases (45%), followed by 31-40 years age group 59 cases (42.14%). Maximum number of the AUB patients were in reproductiveage group 127 cases (90.7%) while 13 cases (9.3%) were presented in postmenopausal age group. Most common clinical presentation was heavy menstrual bleeding 83 cases (59.28%), followed by intermenstrual bleeding and pain in abdomen in 66 cases (47.14%) each. Abdominal lump was seen in 29 cases (20.7%). White discharge and burning in micturition require as seen in 26 cases (18.57%) and 19 cases (13.57%) cases respectively. Only 6 cases (4.28%) patients had a complaintof mass coming out from the vagina while 13 cases (9.28%) had postmenopausal bleeding.

Most common clinical indication for hysterectomy was AUB-L (Leiomyoma) 96 cases (68.57 %), followed by AUB-A (Adenomyosis) 20 cases (14.28%) AUB-P (Polyp) 18 cases (12.85%). In 6 cases (4.28%) the clinical diagnosis of AUB-E (Endometrial malignancy and hyperplasia) was made.

Total abdominal hysterectomy with preservation of both tubes and ovaries was the most commonsurgical method done in 87 cases (62.14%) followed by TAH-BSO in 27 cases (19.28%), TAH-USO in 22 cases (15.71%). Vaginal hysterectomy was done only in 4 cases (2.86%).

On histopathological examination endometrium showed proliferative phase in 93 cases (66.42%), secretory phase in 24 cases (17.85%), cystic atrophic endometrium in 11 cases (7.85%), benign endometrial polyp in 4 cases (2.85%) and endometrial carcinoma in 4 cases (2.85%). One case of adenomyoma, endometritis, simple endometrial hyperplasia and endometrial stromal sarcoma, each, was also reported.

Among the myometrial pathology, commonest lesion was leiomyoma, 83 cases (59.28%), adenomyosis with leiomyoma second largest group of lesions with 23 cases (16.42%) followed by adenomyosis, 19 cases (13.57%). In 10 (7.14%) cases myometrium was unremarkable.

A total of 106 cases of leiomyoma, including those with associated adenomyosis, were identified, out of which 83 cases (59.28%) were showed isolated leiomyoma, and in 23 cases, adenomyosis was additional finding. Among 106 cases, 67.92% presented as solitary lesions, whereas in 32.07% cases, multiple leiomyomata were identified.

Uterine leiomyomata in different locations, like intramural, submucosal and subserosal were seen, with intramural leiomyoma being the most common type. 84 cases (79.24%) of leiomyoma arises in body of uterus involving anterior and posterior wall, 4 (3.77%) cases

were seen in the fundus, 3 cases presented as a pedunculated endometrial mass, four cases from the isthmus, 10 cases arisefrom cervix, and one case of broad ligament leiomyoma was seen.

Chronic nonspecific cervicitis (CNC) was the most common cervical pathology, observed in 90 cases (64.28%), followed by 24 cases (17.14%) showed Nabothian cyst with CNC, 5 cases (3.57%) showed CNC with squamous metaplasia and 3 cases (2.14%) showed cervical intraepithelial neoplasia (CIN), while rest 3 cases (2.14%) showed squamous cell carcinoma of cervix.

Ovaries and fallopian tubes were submitted in 76 specimens of which 2 cases (2.63%) were diagnosed as Serous cystadenoma ovary, 5 cases (6.57%) showed cystic follicles and follicular cysts, each, 2 cases (2.63 %) showed Corpus luteal cyst, and rest 62 specimens (81.57%) were unremarkable.

In 8 cases (10.52%) fallopian tube showed para-tubal cysts and in rest 68 specimens' fallopian tube were unremarkable (89.47%). Among 140 cases, malignancy was seen in 8 cases (5.71%), of which 4 cases (50%) of endometrial carcinoma, 1 case of endometrial stromal sarcoma (ESS) (12.5%), 3 cases (37.5%) of cervical squamous cell carcinoma were diagnosed. Endometrial carcinoma was seen in older age groups, 41-50 and 51-60 years, 2 cases each. ESS and cervical malignancies were seen in slightly younger age group, 31-40 years. Significant association between age and histopathological diagnosis observed with p=0.048.

In our study majority of leiomyoma cases were seen in age group of 41-50 years, followed by 31-40 years. Dual pathology adenomyosis as well as leiomyoma followed by adenomyosis, both of which also showed same age predilection as leiomyoma. Benign endometrial polyp, simple endometrial hyperplasia, adenomyoma, along with cervical polyps, were seen mainly in age groups of 31-40 years, and 41-50 years.

Significant association between clinical diagnosis and histopathological diagnosis was observed with p=0.001, Most clinical cases were of AUB-L and histopathology confirmed diagnosis of leiomyoma. Similarly significant association between radiological diagnosis and histopathological diagnosis was seen with p=0.001. Most of the patients diagnosed radiologically as fibroid uterus was confirmed on histopathology.

Table 1: Histopathological lesions in hysterectomy specimens.

Anatomical site	Types of lesions	N	Percentage (%)
Cervix, (n=140)	CNC	90	64.28
	Nabothian cyst with CNC	24	17.14
	Papillary endocervicitis	1	0.71
	Squamous metaplasia with CNC	5	3.57
	Benign endocervical polyp	3	2.14
	Cervical leiomyoma	10	7.14
	Cervical endometriosis	1	0.71
	CIN	3	2.14
	Squamous cell carcinoma cervix	3	2.14
Endometrium, (n=140)	Proliferative phase	93	66.42
	Secretory phase	24	17.14
	Cystic atrophic endometrium	11	7.85
	Benign endometrial polyp	4	2.85
	Adenomyoma	1	0.71
	Endometritis	1	0.71
	Simple endometrial hyperplasia	1	0.71
	Endometrial carcinoma	4	2.85
	Endometrial stromal sarcoma	1	0.71
Myometrium, (n=140)	Leiomyomas and its subtypes	83	59.28
	Adenomyosis with leiomyoma	23	16.42
	Adenomyosis	19	13.57
	Myometrial invasion by endometrial carcinoma	5	3.57
	Unremarkable	10	7.14
Ovary, (n=76)	Cystic follicles	5	6.57
	Follicular cyst	5	6.57
	Corpus luteal cyst	2	2.63
	Serous cystadenoma ovary	2	2.63
	Unremarkable	62	81.57
Fallopian tubes, (n=76)	Paratubal cysts	8	10.52
	Unremarkable	68	89.47

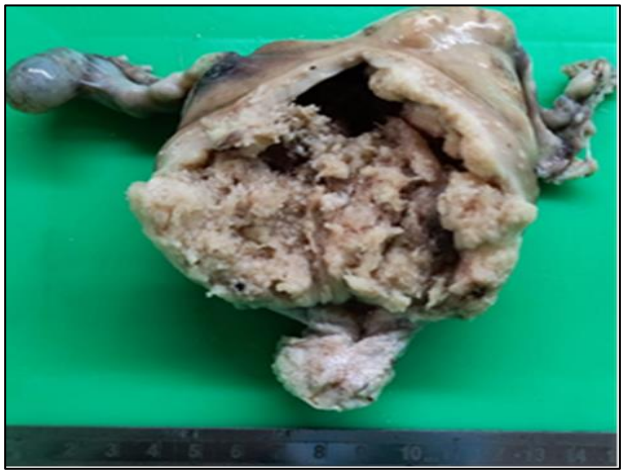

Figure 1: Endometrial carcinoma: gross specimens showing friable, necrotic, exophytic growth in the endometrial cavity with myometrial invasion.

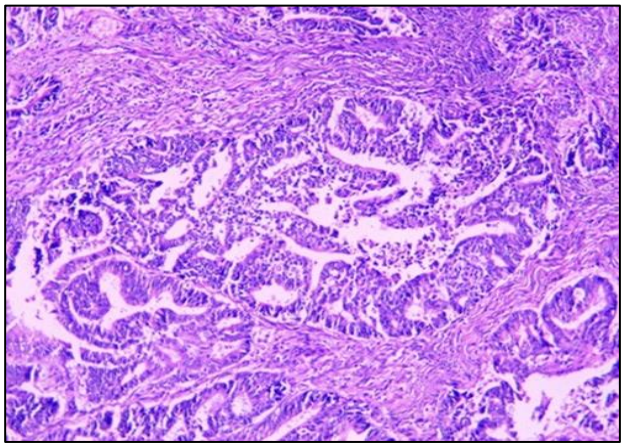

Figure 2: H and E section shows endometrioid carcinoma with myometrial invasion and dirty necrosis, in the gland lumina (100×).

Figure 3: Leiomyoma-gross.

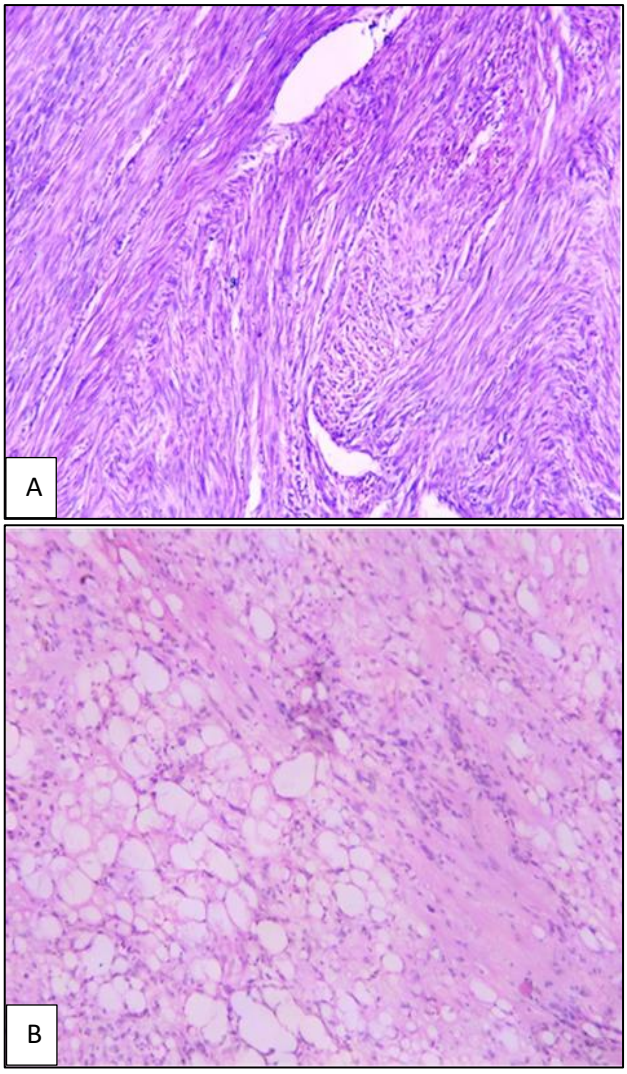

Figure 4: (A) Leiomyoma-microscopy (100x), (B) Lipoleiomyoma H and E section shows mature adipocytes admixed with smooth muscle fibres (100x).

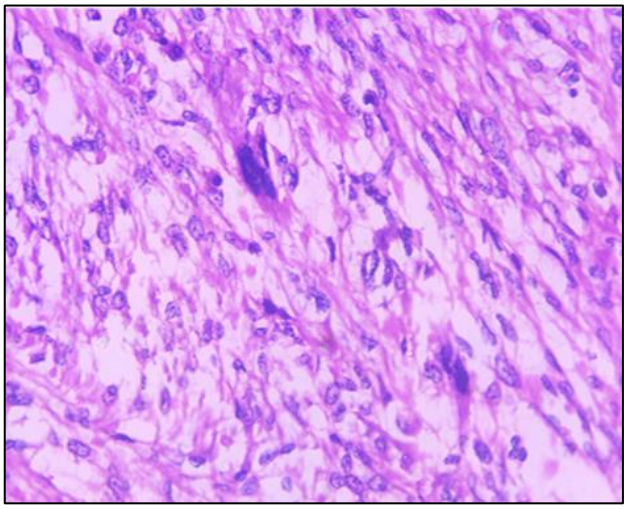

Figure 5: Symplastic leiomyoma with few bizarre cells having pleomorphic nuclei with smudgy chromatin in a background of typical leiomyoma (400x).

Figure 6: Endometrial stromal sarcoma: gross specimen shows pedunculated intra-cavitary mass.

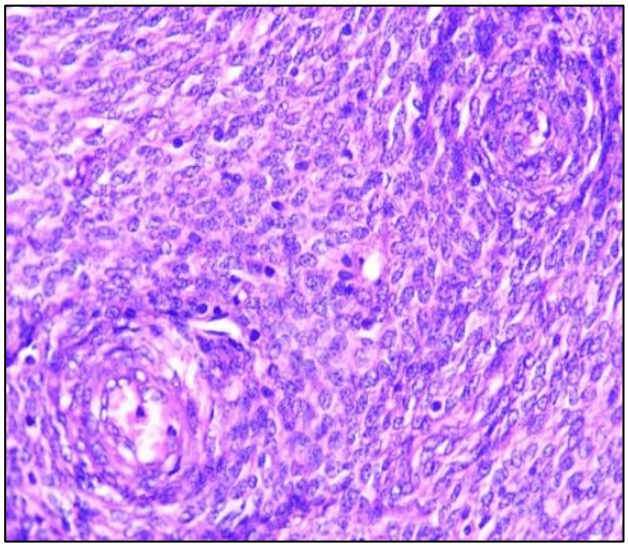

Figure 7: Endometrial stromal sarcoma: H and E section shows tumor cells with small, uniform, oval nuclei and scanty cytoplasm, along with spiral arterioles.

Figure 8: Adenomyosis: cut surface of thickened myometrium is coarsely trabeculated with haemorrhagic foci and tiny, blood filled, cystic spaces.

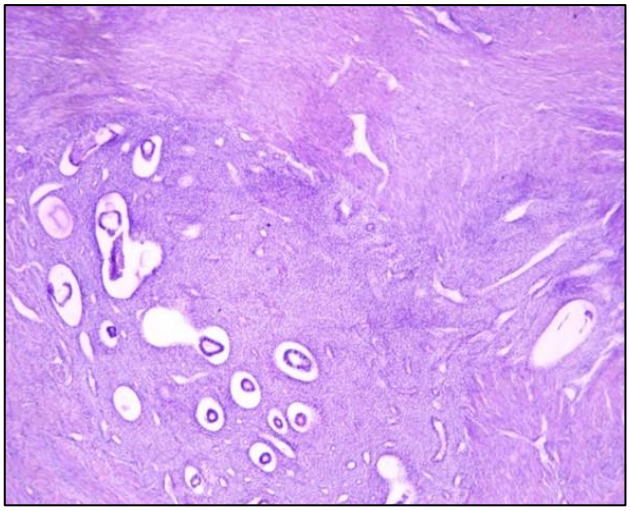

Figure 9: Adenomyosis: H and E section shows endometrial gland and stroma, deep inthe myometrium (100x).

DISCUSSION

In our study, maximum number of patients were in the age group 41-50 years. The 63 cases (45%), followed by 31-40 years. The 59 cases (42.14 %). Chaware et al, Sujatha et al also reported the majority cases in 41-50 years of age 44.02% and 38.91% respectively.[7,8] Sawke et al in study of 100 cases found maximum number of cases in the age group of 41-50 years (n=35) followed by 31-40 years, (n=30).[9]

In present study, patients presented with multiple complaints of which majority cases (57.85%) had complaints of heavy menstrual bleeding. Intermenstrual bleeding and abdominal pain were seen in 45.71% of cases each. 20% of the patients had an abdominal lump, and white discharge and postmenopausal bleeding were seen in 17.14% and 9.28% cases, respectively. Mass coming out from the vagina was the least common clinical complaint, seen in only 4.2% of cases. The findings of this study were found to be in concordance with the various studies. Bobde et al also found heavy menstrual bleeding as the most common symptom accounting for 49.36% of cases, followed by intermenstrual bleeding accounting for 11.39% cases, oligomenorrhea 6.32% cases, and postmenopausal bleeding comprised 9.49% of cases.[10] The studies done by Sujatha et al, Ticku et al and Kaur et al also revealed that patients presented with multiple complaints, of which menorrhagia (heavy menstrual bleeding) was the most common clinical presentation.[8,11,12]

Total abdominal hysterectomy with preservation of both tubes and ovaries was the most commonsurgical method, done in 62.14% cases, followed by TAH-USO in 19.28% cases, and vaginal hysterectomy was done only in 2.86% cases. Sujatha et al observed similar findings in their study with commonest type of hysterectomy was a total

abdominal hysterectomy, done in 66 (42.7%) cases.[8]

The most common clinical indication for hysterectomy was AUB-L in 96 cases (68.57%), followed by AUB-A in 20 cases (14.28%), AUB-P in 18 cases (12.14%). In 6 cases (4.2%), the clinical diagnosis of AUB-E was made. Leiomyoma and Adenomyosis were the most common clinical indications for hysterectomy. Chaware et al and Khunte et al also found leiomyoma as the most common clinical indication for hysterectomy in (38.04%) and (41.5%) respectively.[7,13]

Patients with AUB showed a wide spectrum of histopathological findings, ranging from normal cyclic endometrium to benign pathology and malignancy. In our study, out of 140 hysterectomy specimens 93 specimens (66.42%) showed endometrium in the Proliferative phase, 24 (17.14%) specimens showed endometrium in the Secretory phase, whereas in 11 (7.85%) specimens, cystic atrophy of the endometrium was seen. A similar order of endometrium in different phases, was observed in the study done by Purandhare et al which also showed proliferative endometrium in 66.3% cases, secretory phase endometrium in 20.6% percent cases, atrophic endometrium in 6.1% cases and 7% cases of simple endometrial hyperplasia.[14]

Similarly, Sujatha et al in their study of 155 hysterectomy specimen also showed proliferative phase endometrium in 83 cases (53.54 %), secretory phase in 10 cases (6.45%) and atrophic endometrium in 9 cases (5.8%).[8] The 31 cases (20%) showed simple endometrial hyperplasia, 3 cases of complex hyperplasia, whereas 7 (4.51%) cases of endometrial Polyps, 4 cases of endometritis, and 6 cases of (3.87%) endometrial carcinoma were identified.

Five cases (3.57%) of uterine malignancies contributed as a cause of AUB. Four cases were diagnosed as endometrioid carcinoma, and one case of low-grade endometrial stromal sarcoma was seen.

Endometrial carcinoma

All four endometrial carcinoma patients were presented between 50-60 years of age. Three patients out of four cases presented with the complaint of postmenopausal bleeding, whereas one patient of 50 years had not attended the Menopause and presented with the complaint of heavy menstrual bleeding and intermenstrual bleeding. The overall occurrence of endometrial carcinoma in our study was 3.57%. These findings are in accordance with the findings of Sujatha et al, Gattu et al and Sreedhar et al, also reported 3.8%, 4% and 3.5%, incidence of endometrial carcinoma as a cause of AUB, respectively.[8,19,20]

Macroscopic appearance

All specimens showed a friable necrotic exophytic growth arising and filling the endometrial cavity. Growth was invading the myometrium. 2 cases out of 4 (50%) showed myometrial invasion more than 50%, and in the remaining two cases myometrial invasion was less than 50%. Specimens were grossed and reported as per the CAP protocol for examination of the specimens of carcinoma and carcinosarcoma of endometrium.

Microscopic examination

Grading was done by using FIGO grading criteria which is based on architectural pattern and nuclear features. Grade 1 had less than 5% solid growth, grade 2 showed 6 to 50% non-glandular and non-squamous solid areas, and grade 3 had more than 50% solid areas which were non-glandular and non-squamous. Squamous differentiation in the form of the squamous morules was seen. Out of 4 cases of endometrial carcinoma, two cases were FIGO grade 2. One case was graded as FIGO grade 1, and 1 case was graded as FIGO grade 3.

Low-grade endometrial stromal sarcoma

One case of low-grade endometrial stromal sarcoma was diagnosed in a 40-year-old patient who presented with the clinical diagnosis of AUB-L. Ultrasound findings were suggestive of fibroid polyp. Total abdominal hysterectomy was done with the primary diagnosis of fibroid polyp. Microscopic examination showed irregular densely cellular nests of the tumor cells showing a permeative tongue-like pattern of myometrial invasion. The characteristic finding was the proliferation of small size spiral arterioles admixed with the tumor cells. The tumor cells resemble the stromal cells of proliferative endometrium, having small, uniform oval nuclei and scanty cytoplasm. The cells were relatively uniform in size and shape, giving a monotonous appearance. Necrosis was absent.

Leiomyoma

Maximum cases were diagnosed as leiomyoma. Among 106 cases, 67.92% presented as solitary lesions, whereas in 32.07% cases, multiple leiomyomata were identified. Similar findings were also observed by Bhatta et al (80.95% and 19.05%), Khan et al (82.50% and 17.50%), respectively.[15,16] Gawri et al found 71% solitary leiomyoma in their study.[17] Most common location of solitary leiomyoma was intramural in 32.07% cases followed by submucosal leiomyoma in 24.52% and subserosal leiomyoma in 11.32% cases, in the remaining 32.07% cases, leiomyomas were seen at more than one location. Bhatta et al also found intramural leiomyoma in 51.2% cases, submucosal leiomyoma in 16.66% cases, subserosal leiomyoma in 13.1% cases and in 19.04% cases more than 1 location was seen.[15] Study by Khan et al, Ticku et al and Gawri et al also showed intramural leiomyoma as commonest location, followed by subserosal leiomyoma and submucosal leiomyoma.[11,16,17]

Majority of leiomyoma were seen in age group of 41-50

years, 40 cases (48.19%), followed by 31-40 years of age 38 cases (45.78%). Similar findings were seen in a study done by Kaur et al where 78.4% cases of leiomyoma were reported in the age group of 41 to 50 years, and 66.7% of the cases of leiomyoma in the age group of 31 to 40 years were seen by Khan et al and Bhatta et al also observed the majority of cases in 41-50 years of age group 59.16% and 54.76%, respectively.[12,15,16] Six variants of leiomyoma were encountered in the present study constituting cellular leiomyoma, symplastic leiomyoma, hydropic leiomyoma, hemorrhagic leiomyoma, myxoid leiomyoma and lipoleiomyoma. Various degenerative changes and leiomyoma subtypes were seen in 15 cases (14.15%) cases. Khan et al also found that 18.3% cases showed degenerative changes.[16]

Macroscopic appearance

Leiomyoma appeared as a well-circumscribed, unencapsulated lesion with a grey-white cut surface showing whorling.

Microscopic appearance

Leiomyomas are composed of whorled and intersecting fascicles of spindle cells. Cells have eosinophilic fibrillary cytoplasm with uniform cigar-shaped elongated nuclei having blunt ends and small nucleoli. Cytological atypia was absent. Mitosis was not seen and there are no areas of necrosis.

Adenomyosis

It is characterized by the presence of endometrial glands and stroma within the myometrium.

Macroscopic examination

Uterus was enlarged and globular due to thickened myometrium. The cut surface of the myometrium was coarsely trabeculated and showed hemorrhagic foci along with tiny blood-filled cysts.

Microscopic examination

Showed endometrial glands and stroma deep in myometrium at least one low power field from the endo-myometrial junction.

Cervix pathology

In our study overall frequency of chronic non-specific cervicitis, including chronic cervicitis with squamous metaplasia and Nabothian cysts and papillary endocervicitis 85.71%. Results comparable with Kaur et al, Ticku et al, Sujatha et al, Raza and Gattu et al.[8,11,12,18,19]

Limitations

In this study, we have evaluated only the structural uterine pathologies causing AUB (PALM). This study didn't evaluate the other, non-structural causes (COEIN) of AUB.

CONCLUSION

The study concluded that Patients with AUB showed a wide spectrum of histopathological findings, ranging from normal cyclic endometrium to benign pathology and malignancy. Leiomyoma was commonest lesion diagnosed clinically as well as on histopathological examination. In order to avoid inconsistency in nomenclature of symptoms and categorization of causes of AUB, FIGO PALM-COEIN classification should be adopted. In some patients, dual pathologies, incidental findings and occult malignant lesions, which were missed clinically or radiologically, was diagnosed on histopathological examination, thus histopathological examination of submitted hysterectomy specimens is gold standard for definite diagnosis.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Shrivastava K, Mishra RT, Tiwari P, Totade S, Dhakar JS. Histopathological spectrum of uterine lesions in hysterectomy specimens of patients with abnormal uterine bleeding. Int J Clin Trials 2024;11(4):252-9.