ORIGINAL ARTICLE

Endometrial blood vessel morphometry in patients presenting with abnormal uterine bleeding

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ABSTRACT

Background: Abnormal uterine bleeding (AUB) is one of the most common problems encountered in gynecological practice. Various benign and malignant disorders of the endometrial tissue show vascular changes such as congestion, dilatation, and vessel wall irregularities. **Aim:** To evaluate the vascular morphometry of the endometrial tissue in AUB. **Materials and Methods:** A descriptive cross-sectional study of the endometrial tissue in patients presented with AUB was undertaken for vascular morphometric analysis. Histopathological processing of the endometrial tissue samples was done as per the standard format, and the slides were evaluated for vascular morphometry. **Results:** Out of 150 cases of endometrial tissue in patients presented with AUB, 80 cases were reported as proliferative phase, 41 as secretory phase, 15 as disordered proliferative endometrium, 6 as atrophic phase endometrium, and 4 each of endometrial hyperplasia without atypia and endometrial carcinoma. An average number of endometrial blood vessels and large-sized blood vessels were more in endometrial carcinoma and endometrial hyperplasia without atypia as compared to proliferative phase, secretory phase, atrophic endometrium, and disordered proliferative endometrium. Vessel shape irregularities and vascular congestion were observed in all the cases of atrophic endometrium, endometrial carcinoma, and endometrial hyperplasia without atypia. Endometrial carcinoma showed severe dilatation of the endometrial blood vessels. **Conclusion:** Vascular morphometry changes were noted in endometrial hyperplasia, endometrial carcinoma, disordered proliferative endometrium, and atrophic phase endometrium. These findings suggest that studies or trials related to anti-angiogenic therapy may help to plan anti-angiogenic therapy in patients with AUB.

KEY WORDS: Abnormal uterine bleeding, angiogenesis, blood vessels, endometrium, vascular morphometry

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INTRODUCTION

Abnormal uterine bleeding (AUB) is one of the most common and challenging gynecological problems in women of all age groups attending the gynecology department.[1,2] AUB is defined as abnormal uterine bleeding which varies in frequency and duration as compared to that of the usual pattern noticed during a menstrual cycle or abnormal bleeding after menopause.[2-4] The incidence of AUB is more than 70% of all gynecological problems in peri-menopausal and postmenopausal women and 15–20% in the reproductive age group.[5]

AUB includes dysfunctional uterine bleeding (DUB) and AUB in patients having fibroid uterus, adenomyosis, endometrial polyps, endometrial hyperplasia, and endometrial carcinoma. It was also observed in patients who were on oral contraceptive/hormonal therapy.[5,6] In many cases of AUB, the exact etiology is not known.[6] In AUB cases where the exact etiology is unknown, treatment strategies may hamper due to a poor understanding of the pathogenesis.[6]

The endometrial tissue has a unique feature of angiogenesis characterized by new blood vessels from the pre-existing vessels and the proliferation of newly formed blood vessels. Endometrial

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angiogenesis is usually characterized by vascular endothelial cells' proliferation during the proliferative phase, coiling of the arterial system in the secretory phase, and repair of vascular bed during menstruation. Various benign and malignant disorders of the endometrium show excessive or insufficient vascular growth leading to defective remodeling of the vascular bed and alteration in vascular fragility leading to impaired angiogenesis and AUB.[6]

An awareness of endometrial angiogenesis, vascular morphology changes, and anti-angiogenic treatment has unquestionably predictive value in planning and improving the medical line of anti-angiogenic therapy in patients presenting with AUB.[6]

Hence, the present study was undertaken to evaluate the endometrial blood vessels' morphometry in the endometrial tissue in patients presenting with AUB.

MATERIALS AND METHODS

A descriptive cross-sectional study was done on the endometrial tissue samples of clinically suspected cases of AUB received in the histopathology section of the Department of Pathology from December 2018 to May 2020.

The endometrial tissue samples such as dilatation and curettage (D and C), endometrial biopsy, fractional curettage samples, and endometrial tissue samples processed from hysterectomy specimens of clinically diagnosed cases of AUB were included in the study. The endometrial tissue samples were processed as per the standard processing method in the histopathology section. Paraffin blocks were prepared, and tissue sections of 3–6 μ thickness were cut. The sections were stained by H and E stain.

H and E-stained slides were evaluated under light microscopy for the diagnosis of endometrial pathology [Figures 1a, c, 2a and c] and vascular morphometry. The vascular morphometric evaluation was done by using the bright field Zeiss (ScopeA1) microscope with a field number of 23, field diameter 0.57 mm, and field area of 0.255 μm^2 in 400X objective.

Vascular morphometry evaluation was done under the headings of an average number of blood vessels, size of blood vessels, the contour of blood vessels, degree of dilatation, and congestion of blood vessels.

The number of blood vessels viewed in 10 high-power fields (HPFs) per slide was counted, and an average of the count was taken as an average number of vessels per HPFs [Figures 1b, d, 2b and d].

The blood vessel size was measured as follows. A cross-sectional area of 16–150 μm^2 was considered as a small-sized blood vessel and 150–1000 μm^2 as a large-sized blood vessel. The cross-sectional area was calculated using Zeiss (ZEN lite 2012 blue edition version no. 2.5.75.0) and AX10 CAM [Figure 3c].

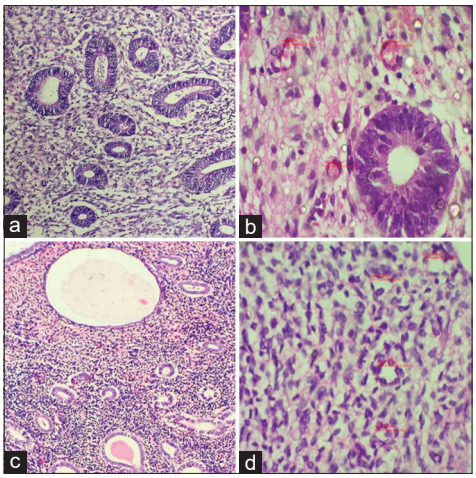

Figure 1: (a) Microphotograph of PPE showing round regular glands with densely cellular stroma (H and E, 100X) (b) Microphotograph of PPE showing the average number of endometrial blood vessels ranged 3–4/HPFS (H and E, 400X, Morphometricanalysis) (c) Microphotograph of APE showing inactive stroma with variable collagenization (H and E, 100X) (d) Microphotograph of APE showing an average number of blood vessels ranged 3–4/HPFs (H and E, 400X, Morphometric analysis)

For contour of blood vessels, vessel shape irregularities were considered and it was categorized as vessel shape irregularity present or absent [Figure 3d].

The degree of dilatation of blood vessels was categorized as mild, moderate, and severe [Figure 3a and d].

The congestion of blood vessels was mentioned as present or absent [Figure 3d].

Inclusion criteria

All histopathological specimens of endometrial tissue of the patients presented with AUB were included in the study.

Exclusion criteria

Endometrial tissue samples containing only blood, inadequate tissue, and autolyzed tissue samples were excluded from the study.

Ethics

All procedures performed in the current study were approved by the Institutional Review Board and Institutional Ethics Committee (IEC No. 286/2018, Date 17/11/2018).

Informed consent was obtained from all the participants.

Statistics

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean ± standard deviation (SD) was used. For categorical data, the number and percentage were used in the data summaries and diagrammatic presentation. Chi-square was used for the association between two categorical variables.

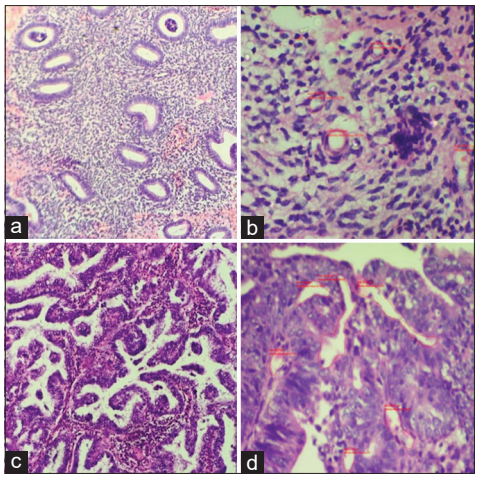

Figure 2: (a) Microphotograph of EH without atypia showing stromal breakdown (H and E, 100X) (b) Microphotograph of EH without atypia showing the average number of blood vessels ranged 4–5/HPFs (H and E, 400X, Morphometric analysis) (c) Microphotograph of endometrioid carcinoma showing glands and villi lined by tall columnar epithelium showing overcrowding and stratification (H and E, 100X) (d) Microphotograph of endometrial carcinoma showing an average number of blood vessels ranged 5–6 blood vessels/HPFs (H and E, 400X, Morphometric analysis)

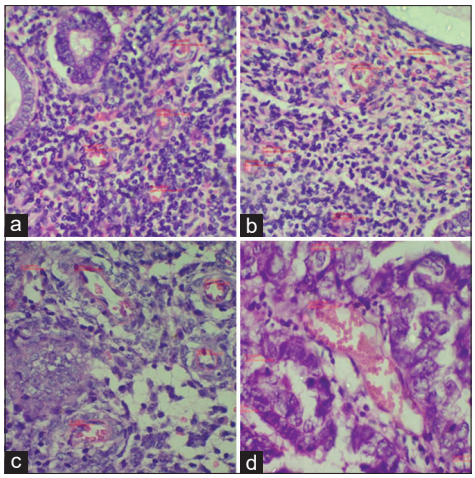

Figure 3: (a) Microphotograph of PPE showing a mild degree of dilatation in endometrial blood vessels. (H and E, 400X, Morphometric analysis) (b) Microphotograph of APE showing small-sized blood vessels. (H and E, 400X, Morphometric analysis) (c) Microphotograph of EH without atypia showing large-sized blood vessels. (H and E, 400X, Morphometric analysis) (d) Microphotograph of Endometrial carcinoma showing vascular irregularities, vessel wall dilation, and congestion (H and E, 400X, Morphometric analysis)

The difference of the means of analysis variables between more than two independent groups was tested by Analysis of Variance (ANOVA) and F test of testing of equality of variance. *P* value less than 0.05 was considered statistically significant. Data were analyzed using the SPSS software v. 23 (IBM Statistics, Chicago, USA) and Microsoft Office 2007.

RESULTS

In the present study, 150 cases of endometrial tissue of patients presented with AUB were included. The age group of the patients in the study varied from 22–70 years, with the youngest patient aged 22 years and the oldest 70 years with a mean age of 40.2 years. Most of the cases amounting to 46% were seen in the age group of 31–40 years.

Out of 150 cases of AUB, the majority of the cases were clinically diagnosed as DUB accounting for 48%. Out of 150 cases, a specific histopathological diagnosis was possible in 64 cases. Out of 64 cases of specific histopathological diagnosis, the maximum number of cases were disordered proliferative endometrium (DPE), amounting to 21.8% of the cases. In 21.8 and 15.6% of the cases, diagnosis of leiomyoma and adenomyosis was noted. In these cases, the endometrial tissue from the hysterectomy specimen was studied. In 7.81% of the cases, a diagnosis of the functional endometrial polyp was rendered. In 86 cases, a specific histopathological diagnosis was not possible [Table 1].

Out of 64 cases, in 22 cases, a clinical diagnosis of DUB was rendered. In these cases of DUB, the maximum cases were diagnosed as adenomyosis and DPE on histopathology amounting to 7 cases each. In 20 clinically diagnosed fibroid cases, the maximum cases were interpreted as leiomyoma followed by adenomyosis on histopathology [Table 2].

Table 1: Distribution of histopathological diagnosis in patients presented with AUB (*n*=64)

Histopathological Diagnosis	*Number*	*Percentage (%)*
Disordered proliferative endometrium	14	9.3
Leiomyoma	14	9.3
Adenomyosis	10	6.7
Endometrial polyp	5	3.3
Endometrial polyp and leiomyoma	5	3.3
Adenomyosis and leiomyoma	4	2.7
Simple hyperplasia without atypia	4	2.7
Cervical carcinoma	3	2
Endometrial carcinoma	3	2
DPE and leiomyoma	1	0.7
Endometrial carcinoma with leiomyoma	1	0.7

Out of 150 cases, in 80 cases, the endometrial tissue showed a proliferative phase, followed by a secretory phase in 41 cases. In 15 cases, features of DPE were noted. In six cases, atrophic phase endometrium was observed. Endometrial carcinoma and endometrial hyperplasia without atypia were observed in four cases each.

In the present study, the average number of endometrial blood vessels per High Power Field (HPF) was highest in number in endometrial carcinoma, followed by endometrial hyperplasia without atypia [Figure 1b and d]. The average number of endometrial blood vessels per HPF was the lowest in the proliferative phase endometrium [Figure 1a]. However, there was no statistically significant difference [Table 3].

The average number of blood vessels per HPF was the highest in endometrial carcinoma, followed by endometrial hyperplasia without atypia as compared to other lesions such as adenomyosis, leiomyoma, cervical carcinoma, DPE, and endometrial polyp. However, the difference was statistically not significant [Table 4].

All cases of endometrial carcinoma and endometrial hyperplasia without atypia showed large-sized blood vessels [Figure 3c]. All cases of atrophic phase endometrium showed small-sized blood vessels [Figure 3b]. The number of large-sized blood vessels was more in endometrial carcinoma and endometrial hyperplasia without atypia as compared to DPE, proliferative phase, secretory phase, and atrophic phase endometrium. The difference was statistically significant [Tables 5 and 6].

Vessel wall irregularities were noted in all cases of endometrial carcinoma, endometrial hyperplasia without atypia, and atrophic phase endometrium. In DPE, proliferative and secretory phase endometrium, vessel wall irregularities were present in 86.7, 72.5, and 63.4%, respectively. However, the difference was statistically not significant. Vessel wall irregularities were present in all cases of adenomyosis with leiomyoma, cervical carcinoma, endometrial carcinoma, endometrial carcinoma with leiomyoma, and endometrial hyperplasia without atypia. In adenomyosis, endometrial polyp, endometrial polyp with leiomyoma, leiomyoma, and non-specific inflammatory lesion, vessel wall irregularities were present in 80, 60, 80, 64, and 69%, respectively. However, the difference was statistically not significant.

Table 2: Distribution of clinical diagnosis and histopathological diagnosis in patients presented with AUB (*n*=64)

Clinical Diagnosis	*Histopathological diagnosis*											*Total*
	AD	*AL*	*CC*	*DPE*	*DPEL*	*EC*	*ECL*	*EP*	*EPL*	*L*	*SH*	
DUB	7	1	0	7	1	1	0	2	1	1	1	22
Fibroid	3	3	0	0	0	0	0	1	1	12	0	20
DUB with PID	0	0	0	1	0	0	0	0	0	0	0	1
Endometrial hyperplasia	0	0	0	4	0	0	0	2	0	1	3	10
PID	0	0	0	0	0	0	0	0	0	0	0	0
Endometrial polyp	0	0	0	1	0	0	0	0	3	0	0	4
Endometrial carcinoma	0	0	0	1	0	2	1	0	0	0	0	4
Cervical carcinoma	0	0	3	0	0	0	0	0	0	0	0	3
Total	10	4	3	14	1	3	1	5	5	14	4	64

AD stands for Adenomyosis, AL for Adenomyosis with leiomyoma, CC for Cervical carcinoma, DPE for Disordered proliferative endometrium, DPEL for Disordered proliferative endometrium with leiomyoma, EC stands for Endometrial carcinoma, ECL for Endometrial carcinoma with leiomyoma, EP for Endometrial polyp, EPL for Endometrial polyp with leiomyoma, L for Leiomyoma, NS for Non-specific inflammation, and SH for Simple hyperplasia

Table 3: Average number of blood vessels per HPF in various endometrial lesions of patients presented with AUB (*n*=150)

Endometrial tissue	*Minimum number of blood vessels/HPFs*	*Maximum number of blood vessels/HPFs*	*Average number of blood vessels/HPFs*	*SD*	*P*
Atrophic phase	3.7	4.2	4.0	0.2	0.561
DPE	3.5	4.3	3.9	0.2	
Endometrial carcinoma	5.1	5.5	5.3	0.2	
Proliferative phase	3	4	3.4	0.4	
Secretory phase	3.7	5	4.3	0.4	
Simple hyperplasia without atypia	4.4	4.9	4.8	0.2	

Table 4: Average number of blood vessels/HPFs in the endometrial tissue of various histopathological lesions in patients presented with AUB (*n*=150)

Histopathological diagnosis	*Minimum number of blood vessels/HPFs*	*Maximum number of blood vessels/HPFs*	*Average number of blood vessels/HPFs*	*SD*	*P*
Adenomyosis	3	4.9	4.0	0.6	0.473
Adenomyosis and leiomyoma	3	5	3.7	0.9	
Cervical carcinoma	3	4.2	3.7	0.6	
Disordered proliferative endometrium	3.5	4.2	3.9	0.2	
DPE and leiomyoma	3.7	3.7	3.7	0.0	
Endometrial carcinoma	5.1	5.5	5.3	0.2	
Endometrial carcinoma with leiomyoma	5.4	5.4	5.4	0.0	
Endometrial polyp	3	4.2	3.4	0.5	
Endometrial polyp and leiomyoma	3	4.2	3.5	0.5	
Leiomyoma	3	4.7	3.6	0.5	
Non-specific	3	5	3.8	0.5	
Simple hyperplasia without atypia	4.4	4.9	4.8	0.2	

Table 5: Size of the blood vessels in various endometrial lesions in patients presented with AUB (*n*=150)

Endometrial tissue	*Size of blood vessel*				*P*
	Large size		*Small size*		
	n	*%*	*n*	*%*	
Atrophic phase	0	0.0%	6	100.0%	<0.001
Disordered proliferative endometrium	2	13.3%	13	86.7%	
Endometrial carcinoma	4	100.0%	0	0.0%	
Proliferative phase	25	31.3%	55	68.8%	
Secretory phase	10	24.4%	31	75.6%	
Simple hyperplasia without atypia	4	100.0%	0	0.0%	

Table 6: Size of the blood vessel in the endometrial tissue in various histopathological lesions in patients presented with AUB (*n*=150)

Histopathological diagnosis	*Size of blood vessel*				*P*
	Large		*Small*		
	n	*%*	*n*	*%*	
Adenomyosis	3	30.0%	7	70.0%	<0.001
Adenomyosis and leiomyoma	1	25.0%	3	75.0%	
Cervical carcinoma	0	0.0%	3	100.0%	
Disordered proliferative endometrium	2	14.3%	12	85.7%	
DPE and leiomyoma	0	0.0%	1	100.0%	
Endometrial carcinoma	3	100.0%	0	0.0%	
Endometrial carcinoma with leiomyoma	1	100.0%	0	0.0%	
Endometrial polyp	0	0.0%	5	100.0%	
Endometrial polyp and leiomyoma	2	40.0%	3	60.0%	
Leiomyoma	4	28.6%	10	71.4%	
Non-specific	25	29.1%	61	70.9%	
Simple hyperplasia without atypia	4	100.0%	0	0.0%	

In the atrophic phase, the endometrial carcinoma and endometrial hyperplasia without atypia, vascular congestion of endometrial blood vessels were present in all cases. Out of 15 cases of DPE, in 12 cases, vascular congestion was present. Vascular congestion in proliferative and secretory phase endometrium was 68 and 73%, respectively. Vascular congestion was noted in all cases of adenomyosis with leiomyoma, cervical carcinoma, endometrial carcinoma, endometrial carcinoma with leiomyoma, and endometrial hyperplasia without atypia. Vascular congestion in adenomyosis, endometrial polyp, and endometrial polyp with leiomyoma, leiomyoma, and non-specific inflammation was 60, 20, 40, 50, and 79%, respectively. The difference was statistically significant.

In endometrial carcinoma, a severe degree of dilatation of endometrial blood vessels was observed [Figure 3d]. In contrast, all the cases of atrophic phase endometrium showed a mild degree of dilatation of endometrial blood vessels. Out of 41 cases of secretory phase endometrium, 34 cases showed mild, and 7 cases showed a moderate degree of dilatation of endometrial blood vessels. In endometrial hyperplasia without atypia, 50% of the cases showed moderate, and 50% showed a severe degree of dilatation. In DPE, out of 15 cases, 10 cases showed a moderate degree of dilatation, and 5 cases showed a mild degree of dilatation. In the proliferative phase endometrium, a severe degree of dilatation was noted in 72.5%, moderate in 26% cases, and mild in 1.5% cases. For the degree of dilatation, a significant statistical difference was noted between various endometrial lesions with *P* value less than 0.001.

In endometrial polyp and DPE with severe leiomyoma degree of dilatation of endometrial blood vessels was noted as compared to other lesions. Out of three cases of cervical carcinoma, two cases showed mild, and one case showed a severe degree of dilatation of endometrial blood vessels. For the degree of dilatation, a significant statistical difference was noted between various histopathological lesions with a *P* value of less than 0.001 [Table 7].

In the present study, morphometric parameters like the average number of blood vessels, size of blood vessels, and vascular dilatation were high in endometrial carcinoma and endometrial hyperplasia without atypia [Figures 1-3].

DISCUSSION

Menstrual disturbance is the most common gynecological problem for which endometrial curettage or hysterectomy is done. A majority of the cases of menstrual disturbances have AUB of unknown pathology.[6] In most organs, angiogenesis does not take place in physiological conditions. The female genital tract is an exception to it, where angiogenesis occurs in physiological conditions. In the endometrium, angiogenesis is a vital process of a normal endometrial cycle. Angiogenesis in the endometrium is characterized by a significant growth of spiral arterioles in the secretory phase. Coiling and repair of the vascular bed occur during menstruation. This complex process involves the proteolytic degradation of extracellular matrix, proliferation, and migration of endothelial cells, and ultimately the formation of patent capillary tubules.[7]

Histopathological patterns of endometrium in women presenting with AUB are variable.[4] These changes range from simple physiological changes to much more complex pathological lesions in the endometrium.[8]

In the present study, the proliferative phase endometrium is the most common histological pattern followed by the secretory phase endometrium. Endometrial carcinoma was found to be the least common in our study. In the studies done by other authors also proliferative phase endometrium was the commonest histopathological pattern and endometrial carcinoma was the least common condition.[9-13]

The average number of endometrial blood vessels/HPF in the proliferative phase, secretory phase, DPE, and atrophic phase in the present study were correlating with the Khan *et al.* study.[14] In their study, the average number of blood vessels per HPF in the proliferative phase, secretory phase, and DPE were 3.4 ± 0.4 SD, 4.7 ± 0.1 SD, and 3.9 ± 0.8 SD, respectively.[14]

Table 7: Degree of dilatation in the endometrial tissue in various histopathological lesions in patients presented with AUB (*n*=150)

Histopathological diagnosis	*Degree of dilatation*						*P*
	Mild		*Moderate*		*Severe*		
	n	*%*	*n*	*%*	*n*	*%*	
Adenomyosis	6	60.0%	4	40.0%	0	0.0%	<0.001
Adenomyosis and leiomyoma	3	75.0%	1	25.0%	0	0.0%	
Cervical carcinoma	2	66.7%	1	33.3%	0	0.0%	
Disordered proliferative endometrium	4	28.6%	10	71.4%	0	0.0%	
DPE and leiomyoma	1	100.0%	0	0.0%	0	0.0%	
Endometrial carcinoma	0	0.0%	0	0.0%	3	100.0%	
Endometrial carcinoma with leiomyoma	0	0.0%	0	0.0%	1	100.0%	
Endometrial polyp	5	100.0%	0	0.0%	0	0.0%	
Endometrial polyp and leiomyoma	4	80.0%	1	20.0%	0	0.0%	
Leiomyoma	12	85.7%	2	14.3%	0	0.0%	
Non-specific	66	76.7%	19	22.1%	1	1.2%	
Simple hyperplasia without atypia	0	0.0%	2	50.0%	2	50.0%	
Total	103	68.7%	40	26.7%	7	4.7%	

Makhija *et al*.[6] in their study observed that the average number of blood vessels per HPF was 4.47 ± 0.095 in complex hyperplasia. Khan *et al*.[14] in their study observed that the average number of blood vessels per HPF was 5.0 ± 0.4 in complex hyperplasia without atypia. In the present study, the average number of blood vessels in the endometrial hyperplasia without atypia was 4.8 ± 0.2. Our study findings of the average number of blood vessels per HPF in the endometrial hyperplasia without atypia were corelating with the findings in a study done by Makhija *et al*.[6] and Khan *et al*.[14]

Nayha *et al*.[7] in their study stated that the number of vessels was increased in well to moderately differentiated endometrial carcinomas as compared to proliferative phase endometrium and endometrial hyperplasia. Similar observations were noted in the present study.

Nayha *et al*.[7] in their study observed that the individual vessel size (mean 78 μm^2) was significantly lower in the atrophic endometrium ($P < 0.001$) than in the proliferative endometrium, hyperplastic endometrium, and endometrial carcinoma. Similar results were obtained in the present study. In the present study, the individual vessel size in the atrophic endometrium was 99 μm^2.

In the present study, the vessel shape irregularities were seen more in the endometrial carcinoma, endometrial hyperplasia without atypia, and atrophic phase endometrium as compared to DPE, proliferative and secretory phase endometrium. Similar results were noted in other studies also. They observed that vessel shape abnormalities were noted in atypical or complex-type of endometrial hyperplasia and well-differentiated endometrial adenocarcinoma ($P < 0.001$).[7]

Makhija *et al*.[6] conducted a study on morphometry of endometrial blood vessels of age group between 24 and 50 years in 500 endometrial tissues. In their study, the control group included endometrial specimens having a normal and regular menstrual cycle and the study group included cases of DUB, endometrial polyps, fibroids, adenomyosis, cases of infertility, and atrophic phase. They observed that the number of cases showing mild dilatation in the group endometrium of DUB (proliferative + secretory) was 21.4% and moderate dilatation was 5.4%. Both these figures were significantly higher as compared to control with a *P* value of less than 0.001. In complex hyperplasia, 50% of the cases showed mild dilatation which was significant as compared to control.[6]

In the present study, in endometrial hyperplasia without atypia, 50% of the cases showed a moderate degree of dilatation while 50% of the cases showed a severe degree of dilatation. In the proliferative phase, 72.5% of the cases showed a mild degree of dilatation, 21% of the cases showed a moderate degree of dilatation, and 1.3% of the cases showed a severe degree of dilatation. In the secretory phase, 82.9% showed a mild degree of dilatation and 17.1% showed a moderate degree of dilatation. For the degree of dilatation, a significant statistical difference with a *P* value of less than 0.001 was noted in the present study.

Makhija *et al*.[6] in their study observed that the number of cases in the group endometrium (proliferative + secretory) showed congestion in 42.78% as compared to 12.7% cases in the control group which was significantly higher having *P* value less than 0.001; 75% cases of complex hyperplasia showed significant congestion with *P* value of less than 0.001.[6] In the present study, atrophic phase endometrium, endometrial carcinoma, and endometrial hyperplasia without atypia showed vascular congestion of endometrial blood vessels in all the cases. Out of total proliferative and secretory phase endometrium cases, vascular congestion was noted in 68.8 and 73.2%, respectively. However, the difference was not statistically significant in the present study.

Makhija *et al*.[6] studied 55 cases of fibroids and they observed that the mean of the blood vessels in the stratum basalis was 3.34 ± 0.54 and stratum functionalis, 3.53 ± 0.58 which was

not significantly different as compared to the controls. The endometrial blood vessel congestion was 13.2% as compared to control (12.7%) which was not significantly different ($P > 0.05$). No significant difference in dilatation was seen between the two groups. Also, in their study, they noted 13 cases of adenomyosis and found no significant difference in the mean of the blood vessel concentration as compared to the control. These authors studied 13 cases of the endometrial polyp. The mean blood vessel concentration in polyp was 5.96 ± 0.37 which was significantly higher ($P < 0.05$) as compared to control.[6] In the present study, in 14 cases of leiomyoma, the average number of blood vessels/HPF was 3.6 ± 0.5 and endometrial vascular congestion was observed in 50% of the cases. A mild degree of dilatation was observed in 85.7% of the cases and a moderate degree of dilatation in 14.3% of the cases. For a degree of dilatation, the difference was statistically significant ($P < 0.001$). Similarly in the present study, 10 cases of adenomyosis and 5 cases of endometrial polyp were studied having an average number of blood vessels/HPF 4.0 ± 0.6 and 3.4 ± 0.5, respectively.

It was mentioned in some studies that the various morphological changes in the endometrial vasculature in the endometrial tissue of the patients of AUB may lead to the rupture of the vessels. Also, rupture of dilated and congested vascular channels could be responsible for the AUB.[6] A similar explanation may hold in the present study.

Khan *et al*.[14] studied morphometric evaluation of endometrial blood vessels and their clinicopathological relation in patients with DUB and concluded that the altered vascular morphology in different endometrial patterns in various lesions may be the underlying pathological mechanism for DUB. Since the proliferative and secretory pattern did not show any significant alteration in vascular morphology with regard to mean vascular density, dilatation, and congestion. In the present study also, a vascular morphometric evaluation showed significant alteration in endometrial carcinoma and endometrial hyperplasia without atypia. In these lesions, the underlying pathologic mechanisms for AUB may be alterations in the vascular morphology.

Thus, histopathological examination of vascular morphometry in endometrial tissue is crucial in the evaluation of AUB and vascular morphometric changes could help in the planning of relevant medical line of treatment for patients of AUB which may help to avoid surgical procedure and will help to reduce the hospital stay and cost of the treatment.[3,15]

Hence awareness of endometrial angiogenesis and changes in vascular morphology certainly has predictive value and thus can assist in planning newer anti-angiogenic treatment modalities and patient care in patients presented with AUB.

However extensive study including a greater number of samples of endometrial tissue of various endometrial lesions will delineate the pathogenesis of abnormal bleeding, the role of vascular morphometric analysis, and utility of anti-angiogenic treatment.

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Conflicts of interest

There are no conflicts of interest.

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