"MORPHOMETRIC EVALUATION OF ENDOMETRIAL BLOOD VESSELS IN PATIENTS PRESENTING WITH ABNORMAL UTERINE BLEEDING"

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ABSTRACT

Background – Abnormal uterine bleeding (AUB) is one of the commonest problem encountered in gynaecological practice. The incidence of AUB in perimenopausal and postmenopausal women is more than 70% of all gynaecological problems. Various benign and malignant disorders of endometrial tissue show vascular changes such as congestion, dilatation, and vessel wall irregularities. Hence the present study was done to evaluate the role of vascular morphometry in patients presented with AUB.

Objectives of the study:

To evaluate morphometry of endometrial blood vessels and morphological pattern of endometrium in various endometrial lesions in patients presenting with history of AUB.

Materials and Methods:

A prospective cross sectional study of endometrial blood vessels in patients presented with AUB was undertaken for morphometric analysis. This study was carried out for a duration of 18 months from 1st December 2018 - 30thMay 2020.

Endometrial tissue samples such as dilatation and curettage (D and C) sample, endometrial biopsy, fractional curettage and endometrial tissue processed from hysterectomy specimen were included in the study. Paraffin blocks were prepared and tissue section of 3-6 µ thickness were cut, H and E staining was done and were evaluated for vascular morphometry. Evaluation of vascular morphometry was done under the following headings stating as average number of blood vessels/HPFs, vessel size, contour of blood vessels, degree of dilatation and congestion.

Results:-

Total 150 cases of endometrial tissue in patients presented with AUB were studied. Out of it, 80 cases were reported as proliferative phase, 41 as secretory phase, 15 as disordered proliferative endometrium (DPE), 6 as atrophic phase, 4 as simple hyperplasia without atypia and 4 as endometrial carcinoma. Average number of endometrial blood vessels/HPF in endometrial carcinoma and simple hyperplasia without atypia were more as compared to proliferative, secretory, atrophic and DPE. Endometrial carcinoma and simple hyperplasia without atypia showed large sized blood vessel. Vessel shape irregularities and vascular congestion was observed in all the cases of atrophic phase endometrium, endometrial carcinoma and simple hyperplasia without atypia. Endometrial carcinoma showed significant severe dilatation of endometrial blood vessels. Vascular dilatation was statistically significant with p value less than 0.001.

Conclusion: -

Vascular morphometry plays an important role in various endometrial lesions and can be used to plan the anti-angiogenic therapy in patients presenting with abnormal uterine bleeding.

Key words: - Abnormal uterine bleeding, Blood vessels, Endometrium, Morphometry.

LIST OF ABBREVIATIONS USED

AUB	Abnormal Uterine Bleeding
DUB	Dysfunctional Uterine Bleeding
FIGO	International Federation of Gynaecology and Obstetrics
VEGF	Vascular Endothelial Growth Factor
OPD	Out Patient Department
PID	Pelvic Inflammatory Disease
ECs	Endothelial Cells
ECM	Extracellular matrix
D and C	Dilatation and Curettage
HPF	High Power Field
PPE	Proliferative Phase Endometrium
SPE	Secretory Phase Endometrium
APE	Atrophic Phase Endometrium
DPE	Disordered Proliferative Endometrium
SH	Simple Hyperplasia
MVD	Microvascular Density
H & E	Haematoxylin & Eosin
SD	Standard Deviation
Fig	Figure
SL No	Serial Number
Yrs	Years
HPR	Histopathology Resection

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INTRODUCTION

Abnormal uterine bleeding (AUB) is considered as one of the most common and challenging presentation amongst the women of all age groups attending the Gynaecology Out Patient Department.[1,2] AUB is defined as the bleeding pattern which varies in frequency, duration and amount from that of the normal pattern noticed during a normal menstrual cycle or after menopause.[2-4] The incidence of AUB in perimenopausal and postmenopausal women is more than 70% of all gynaecological problems.[5] It is also observed in reproductive age group and in this age group it accounts for 15-20% cases.[5]

Abnormal uterine bleeding include both dysfunctional uterine bleeding and bleeding from causes like fibroids, adenomyosis, endometrial polyps, endometrial hyperplasia, endometrial carcinoma and oral contraceptive use.[5,6] However majority of cases of AUB have unknown pathology. Poor understanding of the pathogenetic mechanisms leading to AUB has hampered the progress of non-surgical treatments for patients of AUB. Hence few authors did studies to assess the morphometry of endometrial blood vessels in various gynaecological conditions in patients of AUB.[6]

Endometrial tissue has unique feature of angiogenesis which is one of the vital process of the normal endometrial cycle. Angiogenesis is the development of new blood vessels from pre-existing vessels and proliferation of newly formed blood vessels. Increased angiogenesis occurs in many pathologic conditions like cancer, ischemic heart disease, rheumatoid arthritis, and diabetes mellitus. Angiogenesis varies from vasculogenesis. Vasculogenesis means the formation of blood vessels de novo from angioblasts during embryogenesis. [7]

Endometrial angiogenesis is normally characterized by proliferation of vascular endothelial cells during proliferative phase, coiling of arterial system in secretory phase and repair of vascular bed during menstruation. In few studies, it was observed that various benign and malignant disorders of endometrium show excessive or insufficient vascular growth. There is defective remodeling of vascular bed and alteration in vascular fragility in various angiogenesis related diseases of endometrium.[6]

In the recent years of newer anti-angiogenic treatments, awareness of endometrial angiogenesis and changes in vascular morphology certainly has predictive value and thus assists in planning and improvement of medical line of treatment modalities and patient care in patients presented with AUB.[6]

Hence, the present study was undertaken to evaluate the role of vascular morphometry in patients presented with AUB.

OBJECTIVES OF THE STUDY

1. To study the morphologic spectrum of endometrial pathology in patients presenting with AUB.

2. To evaluate morphometry of endometrial blood vessels in various endometrial lesions in patients presenting from AUB.

REVIEW OF LITERATURE

Anatomy - The uterus is hollow muscular organ which is pyriform in shape and is situated in the pelvis, in front of the bladder and behind the rectum. It is formed by Body/Corpus, Isthmus and Cervix. The body/Corpus is further divided into fundus and body proper.[8-10]

The wall of the uterus is comprised of three layers. The outer serous coat is called as perimetrium, middle thickest layer is the myometrium. Myometrium is formed by tightly interwoven bundles of smooth muscle fibres held by connective tissues arranged in different directions. The innermost layer is the mucous lining of the uterine cavity that is endometrium.[8, 9]

Endometrium of the uterus lies above the level of internal os.[8] The functions of the uterine endometrium are to prepare for implantation, to maintain pregnancy if implantation occurs, and to menstruate in the absence of pregnancy.[11] It is comprised of single layer of columnar epithelium and lamina propria. Lamina propria is formed by endometrial glands, stroma, vessels and nerves. The endometrial glands are simple tubular glands which are lined by non-ciliated columnar epithelium. Stroma is comprised of cell rich connective tissue. The endometrium is divided into superficial and deep zones as functional and basal layer respectively. [8, 9,12,13] The functional layer is subdivided into two strata, the compactum and the spongiosum. [8]

The endometrium and the myometrium are of mesodermal origin and are formed secondary to fusion of the mullerian (paramesonephric) ducts between 8th and 9th postovulatory weeks. [14]

Historical aspect

The term "menstruation" is derived from the Latin word "menstruus" meaning monthly.[15] Sir John Williams stated that menstruation is a cyclical process, which begins at cessation of menstrual flow, passes through the developmental changes of mucus membrane of the uterus and ends with the cessation of the next following menstruation.[16]

Hippocrates described AUB for the first time around 460 BC. Until 1800, the description mostly reflected abnormal bleeding symptoms as excessive bleeding described as heavy evacuations of the menses, an overflowing of courses, menstruation to be too profuse, excessive flooding and uterine haemorrhage.[17] The description of AUB in early writings also includes phrases such as "the flux is immoderate, either when the periods return too often, when they continue too long, or when too much blood is discharged at one time." Irregular and often light bleeding was referred to as "the weeping of the womb".[17]

In the middle part of the seventeenth century, William Heberlen, a gynaecologist and successful physician provided earliest and best description of AUB available till then . None of the early writers used terms like menorrhagia or metrorrhagia until the later parts of seventeenth century. [15]

The term "menorrhagia" appears to have been used for the first time in the late 1700s in the lectures of Professor Cullen, physician at the University of Edinburgh. The term "metrorrhagia" probably came into use at the same time, with Cullen using the spelling "maetrorhagia" [15]. Most authors used ''menorrhagia'' to describe a symptom or sign, but few used it to indicate a diagnosis or cause of abnormal bleeding.[15]

The introduction of the confusing modern term "dysfunctional uterine bleeding" did not occur until the 1930s. Graves used the term "dysfunctional uterine bleeding" to try and explain "impairment of endocrine factors," which normally controlled menstrual function. [17]

''Abnormal uterine bleeding'' is a term of relatively recent but widespread use, appearing in numerous publications from 1950 onwards. The actual origin of the term is unclear, but it was used erratically in the 20th century before 1950 although most publications in the first half of the century tended to use terms such as ''abnormal haemorrhage from the genital organs''. Widespread use generally acknowledges AUB as a consistent ''umbrella'' term for a wide range of uterine and menstrual bleeding symptoms and signs.[15]

In 1907, Hitschmann and Adler established the variations in the histological structure of the endometrium during the menstrual cycle.[13] In 1950, Noyes, Hertig and Rock published their sentinel paper on dating the endometrium in which they correlated the morphology with clinical cycles, and developed histologic criteria for endometrial dating.[14]

Histology/ Dating of endometrium

In the reproductive age, the endometrium go through physiologic and morphologic changes in response to sex hormones produced in the ovary.[18] It is characterized by cyclical proliferation, differentiation, and shedding in response to hormones secreted by ovaries namely oestrogen and progesterone.[14]

It is important to study regarding the dating of the endometrium as its histologic appearance can be used to evaluate hormonal status & to assess ovulation which may help in deciding causes of endometrial bleeding and infertility.[14] The typical endometrial cycle is of 28 days, although the length differs in individual female to female.[14] The phases of endometrium namely are menstruation phase, proliferative and secretory phase.[14]

Menstruation Phase – The menstrual phase is usually considered to be the first 4 days. The first day of the menstrual cycle is the onset of menstruation and results in glandular and stromal breakdown. "Menstrual endometrium is characterized by an infiltration of inflammatory cells into the endometrium, necrotic debris, thrombi in stromal vessels, apoptotic bodies, interstitial haemorrhage and gland–stromal dissociation."[12,19] The stroma is condensed and collapsed and the dissociation of the glands from the stroma leads to the formation of darker appearing stromal aggregates called as "blue balls".[19] There is decrease in production of oestrogen and progesterone due to regressed corpus luteum, which leads to sloughing of the secretory endometrium leading to menses. Increasing oestrogen production by recruited follicles of the new cycle permits regeneration and development of proliferative endometrium again. [19]

Proliferative Phase - At the end of menstruation phase, the uterus is lined by thin basal layer of endometrium and deeper part of functionalis.[14] On the third or fourth day of the menstrual cycle, the endometrium starts to proliferate and it increases its thickness up to 4 or 5 mm during the proliferative phase. [14] There is glandular, stromal, and vascular growth occurring between the 5th and 14th days of the cycle, with the endometrium gradually increasing in thickness until it reaches ovulation.[14]

The proliferative phase normally lasts 14 days, but can vary under certain physiologic conditions.[20] It is divided into early and late proliferative phases.[14]

In early proliferative phase, the endometrial glands are uniform, uncoiled and evenly distributed in the loose stroma of spindle shaped cells. The glandular epithelial cells are pseudostratified cuboidal or low columnar cells and they contain small, round to oval shaped nuclei, having dense chromatin with small nucleoli and moderate amount of basophilic cytoplasm. Mitotic activity in the gland is a remarkable feature of proliferative phase.[14]

The stromal cells are uniform in size, poorly differentiated with small, dense nuclei in a scanty cytoplasm. Nucleoli are inconspicuous and mitoses are very rare. The cells are surrounded by a firm reticulin network. Spiral arterioles are immature. The surface epithelium is flat and still regenerating. [20]

Estrogenic activity during the proliferative phase often results in focal ciliation of the surface epithelial cells. Thus, surface ciliated cells are a feature of normal proliferative endometrium. [14]

Between the 8th and 10th days of the cycle, proliferative activity is maximum. In this phase, as the size of gland increases, tortuosity begins to occur and it leads to increase in thickness of endometrium. Also there is increased coiling of glands, and increased mitotic activity in both glands and stroma.[20]

The spindle-shaped stromal cells are still poorly differentiated, with occasional mitoses and are separated by interstitial oedema. Spiral arterioles are not seen. The surface epithelium has increased in height and is now low columnar.[14]

In the late proliferative phase, the glands become more tortuous, convoluted and are variable in size and shape. They are lined by tall columnar epithelial cells piled up against one another with their nuclei at different levels, giving a pseudostratified appearance. The nuclei are enlarged elongated or oval shaped. Nucleoli are prominent, and mitoses are frequent. The cytoplasm is still sparse and poorly differentiated, but rich in RNA.[19,20]

In late proliferative phase, densely cellular endometrial stroma is seen and the stromal cells are enlarged and oval with hyperchromatic nuclei and indistinct cytoplasm and cell borders. The mitotic activity goes on reducing in glands and stroma in late proliferative phase. Spiral arterioles are not noticed. Scanty thin-walled stromal blood vessels are present. The surface epithelium is distinctly columnar. [19,20]

Interval endometrium has features of both proliferative and secretory endometrium. The first day after ovulation shows no morphological change in the endometrium. Hence it is labelled as interphase endometrium. Subnuclear vacuoles are seen approximately in 50% of the glands after second day of ovulation. Mitoses persist in early secretory phase & disappear in the late secretory phase. The gland persists to have a proliferative architecture. However, the features of interval endometrium can be seen even in absence of ovulation hence the pathologist cannot confirm on the basis of this morphology that ovulation has occurred or not. [19,20]

Secretory Phase - The secretory phase of the endometrium begins on the 15th day and continues till the onset of menstruation. The secretory phase is divided into three stages as early, mid-secretory and late-secretory phase. [14] These phases are continuous and not sharply defined. Post-ovulatory corpus luteum secretes the progesterone which is responsible for glandular secretion, stromal maturation, and vascular differentiation in secretory endometrium. The thickness of the endometrium rises upto 7or 8 mm.[14]

In Early secretory phase (16^{th} to 18^{th} day) the glands are tubular and mitotic activity may be seen. Subnuclear vacuoles within the glandular epithelium is the morphological feature of ovulation. It occurs on the 16th day. The number and distribution of subnuclear vacuoles increases gradually till they involve almost all cells within most glands in the functionalis. On the17thand 18th day of the cycle, subnuclear vacuoles are maximum in number.[14]

In Mid-secretory phase (19^{th} day to 23rd day), the amount of glandular secretion increases and is seen within the glandular lumina. Cytoplasmic vacuoles become supranuclear. The endometrial glands have angular shape, and mitotic activity is not seen. The glands in the superficial layers of the functionalis tend to show less secretory activity, and thus superficial biopsies may give a false impression of poorly developed secretory activity.[14]

On day 22nd and 23rd, Stromal oedema gradually increases and becomes more apparent. Spiral arteries become obvious. At this stage, the stromal cells are called as predecidual cells as surrounding spiral arteries acquire a more conspicuous eosinophilic cytoplasm.[14]

In Late-secretory phase (24th to 28th day), glands are seen closely packed and serrated due to decrease in the glandular secretory activity. Predecidual stromal change increases, initially being most obvious in the cells surrounding the spiral arteries. Beneath the surface epithelium, the predecidual change results in the formation of the compact layer (stratum compactum). Occasional mitoses may reappear on day 26 or 27, in the predecidual stromal cells. A stromal infiltrate of granulated lymphocytes can be seen and occasional neutrophils may appear in the premenstrual phase.[14]

Regenerative Phase - During regenerative phase, the endometrium is very thin and is mainly composed of basal remnants of glands and stroma which are partly re-epithelialized, while adjacent areas are still denuded. Stromal cells take a minor part in the regeneration. In the epithelial cells, the nuclear DNA and cytoplasmic RNA are again increasing, but mitoses are still absent. [20]

Atrophic endometrium - In post-menopausal women, endometrial atrophy occurs due to the lack of hormonal stimulation.[19] The endometrium is thin and atrophic. The glands are small with round or oval compressed nuclei. No mitotic activity is seen. Proliferative activity is not seen. The stroma in postmenopausal endometrium is densely cellular and fibrous, composed of ovoid to spindle shaped cells with scant cytoplasm. As the age advances, the stroma becomes more hypocellular and fibrous.[14]

Abnormal uterine bleeding (AUB)

The normal menstrual cycle is of 28 days and ranges from 21 to 35 days with menstrual flow from 4 to 5 day and total blood loss ranges from 20 to 80 ml.[9]

AUB is defined as any uterine bleeding that is abnormal in volume, duration, regularity or frequency.[9,21,22] It is the commonest gynaecological disorder affecting all age groups.[21] Almost 30% of patients attending gynaecology OPD present with complaints of AUB.[9, 23] It includes both organic and nonorganic causes of uterine bleeding. [23]

Dysfunctional Uterine Bleeding (DUB) is a clinical term used for uterine bleeding with no clinically detectable structural, systemic or iatrogenic abnormality.[9, 24]

Terminologies used for categorisation of AUB are as follows[25]:-

1. Amenorrhea refers to absence of menstruation.
2. Menorrhagia / Hypermenorrhoea refers to excessive cyclic uterine bleeding which is excessive in amount or duration or both occurring at regular intervals.
3. Polymenorrhoea / Epimenorrhoea means cyclic uterine bleeding where the cycle is reduced to less than 21 days.
4. Metrorrhagia is defined as irregular acyclic uterine bleeding.
5. Menometrorrhagia means uterine bleeding is so irregular and excessive that menses cannot be identified at all.
6. Oligomenorrhoea refers to scanty or infrequent uterine bleeding occurring more than 35 days apart.

7. Hypomenorrhoea means scanty uterine bleeding at regular interval which lasts for less than 2 days.
8. Hypermenorrhoea refers to increased uterine bleeding at regular interval.
9. Dysmenorrhea means painful menses.

Causes of AUB according to the age group can be divided as follows:- [18]

1. Pre-puberty:- Precocious puberty (hypothalamic, pituitary or ovarian origin)
2. Adolescence:- Anovulatory cycle, coagulation disorders
3. Reproductive age group:-Complications of pregnancy (abortion, trophoblastic disease, ectopic pregnancy), Anatomic lesions (Leiomyoma, adenomyosis, polyps, endometrial hyperplasia, carcinoma), DUB anovulatory cycle, ovulatory dysfunctional bleeding (e.g. inadequate luteal phase)
4. Peri-menopausal age group:-DUB, anovulatory cycle, Anatomic lesions (Carcinoma, Hyperplasia, Polyps)
5. Post-menopausal agegroup:-Endometrial atrophy, Anatomic lesions (Carcinoma, Hyperplasia, Polyps)

The term AUB was introduced by FIGO in 2011 to include all abnormal uterine bleeding with or without any organic lesion.[26]

Women with AUB can have one or multiple potential causes of abnormal bleeding, and the accuracy of their diagnosis might depend on the degree of sophistication of the facility at which they seek consultation. The PALM-COEIN system allows clinicians and researchers to identify and classify women with abnormal bleeding and provides reliable information on classification. [27, 28]

The newer classification system is introduced for categorisation of causes of AUB was known by the acronym PALM–COEIN.[22,29-31]

Categorization of the causes of AUB According to **PALM-COEIN** Classification was as follows:-

A. Structural causes

1. P – Polyp
2. A - Adenomyosis
3. L - Leiomyoma
4. M - Malignancy and hyperplasia

B. Non-structural causes

1. C – Coagulopathy
2. O – Ovulatory dysfunction
3. E - Endometrial
4. I – Iatrogenic
5. N – Not yet classified

A. Structural causes :- [22,29-31]

1) Polyp - Polyp is defined as a confined, disordered proliferation of benign glandular and stromal components which is seen raised above the surface of the adjacent endometrium. The common age group for occurrence of polyp is peri-menopausal. Women usually present as abnormal uterine bleeding. But few can be asymptomatic. However the post-menopausal women having polyp can be at high risk for neoplasia. [29-31]

Macroscopically polyp can be sessile or pedunculated. Pedunculated polyp can bulge through the cervical os. They usually are solitary or multiple and have smooth bosselated surface. On cross section, it is fibrous with tiny cyst like spaces resembling dilated glands.[31]

Microscopically, stromal as well as glandular component is involved. The glands are composed of simple, branched or cystically dilated tubules which are lined by proliferating epithelium. However foci of hyperplasia or carcinoma may be present. The stroma is cellular similar to basal endometrium and has thick walled blood vessels. Polyps having predominantly smooth muscle are called as adenomyomatous polyp.[31]

2) Adenomyosis – It is defined as occurrence of glands and stroma of endometrium into myometrium. The patients usually present as menorrhagia, dysmenorrhea, and pelvic pain. Grossly it is large, globular and asymmetrical due to muscular hypertrophy. On cut section, small cystic lesions are present. They can also be present in nodules. Microscopically endometrial tissue is seen within the myometrium. They coexist with endometriosis. [31]

3) Leiomyoma - Leiomyoma are the most common benign smooth muscle uterine tumour occurring in 4^{th} to 5^{th} decades of life. Most women are asymptomatic, however some may present as menorrhagia, pelvic pain or pressure.[31]

Grossly they can be single or multiple and may be intramural, submucosal or subserosal. They can polypoidal or pedunculated. These tumours are unencapsulated, well circumscribed and on cut section appears as white bulging firm whorled pattern. The submucosal tumours can progress to torsion or prolapse through the cervical os which may get detached from the pedicle and form parasitic leiomyoma. They can be large in size accompanied by haemorrhage or infarction.[31]

Oedematous tumours can manifest as soft, highly cellular with cystic change. Pregnant females with leiomyomas have a beefy red appearance (red degeneration).[31]

Microscopically leiomyomas are well circumscribed and are composed of spindle cells arranged in intersecting fascicles. The cells are spindled shaped with indistinct borders having cigar shaped nuclei with nucleoli. The cytoplasm is eosinophilic. Mitosis is not seen. However hyalinization or calcification can be seen.[31]

Disordered proliferative phase is the term used when the proliferation of the gland goes beyond the normal proliferative endometrium but has no cytological atypia and crowding.[31]

4) Malignancy and Hyperplasia

Endometrial hyperplasia - It is divided into two categories based on the presence of cytologic atypia: hyperplasia without atypia and hyperplasia with atypia. [31]It occurs due to excess stimulation of estrogens as compared to progesterons.[31]

Hyperplasia without atypia- It is increased proliferation of the endometrial glands as compared to the stroma, which results in increased gland to stroma ratio when compared to normal proliferative endometrium but cytological atypia is absent. The variable sized and shaped glands are crowded in back to back fashion separated by little amount of intervening stroma. Stratified columnar epithelium with frequent mitotic figures is noted. [31]

Atypical hyperplasia / endometrioid intraepithelial neoplasm - It is a pre-neoplastic condition of endometrioid adenocarcinoma.[8] The tubular and complex branching glands are seen, intermingled with little amount of intervening stroma. Nuclear atypia consists of increased size, pleomorphism, rounding, loss of polarity and prominent nucleoli. It occurs due to excess stimulation of estrogen.[31]

The well-differentiated endometrioid carcinoma differs from atypical hyperplasia/endometrioid intraepithelial neoplasia by stromal invasion, papillary or glandular, villoglandular or cribriform pattern, loss of intervening stroma and desmoplastic reaction.[31]

Endometrioid carcinoma - About 80% of endometrial carcinomas are endometrioid carcinomas.[31] It presents as tan white nodules or can appear as diffuse and exophytic growth along with necrosis or haemorrhage.[31]

It is a glandular neoplasm which shows acinar, papillary and focal solid areas. It does not have nuclear features of endometrial serous carcinoma. They show squamous, villoglandular and secretory differentiation.[31]

i) Endometrioid carcinoma shows a characteristic glandular or villoglandular pattern which is having stratified columnar lining with tightly packed complex, branching manner. The cells have apical border with neighbouring cells, thus having a smoothly contoured glandular lumen and have eosinophilic, granular cytoplasm. Mild to moderate nuclear atypia is seen along with inconspicuous nucleoli. Variable mitotic index is seen.[31]

Grading of Endometrioid carcinomas:-

Grade I - less than or equal to 5% solid growth pattern.

Grade II - 6 to 50% of solid growth

Grade III - more than 50% of growth is solid along with aggressive nature.

The length of endomyometrial junction to the point of deep invasion is the depth of the myometrial invasion.[31]

ii) The squamous differentiation of endometrioid carcinoma has 10 to 25% of features showing keratin pearl, intercellular bridges, polygonal cells with regular cell membrane and dense eosinophilic cytoplasm.[31]

iii) The secretory differentiation of endometrioid carcinoma have less than 2% features of columnar cells having single, huge, sub/supranuclear glycogen vacuoles.[31]

Serous carcinoma - It is type II endometrial carcinoma. It usually arises from the surface of polyp or in case of atrophic endometrium. [31] It is recognised by complex papillary pattern. However glandular pattern or solid pattern may be present. The papillae can be short, hyalinised, branching to thin, long and delicate. The epithelial lining of each fibrovascular core shows large atypical nuclei, prominent nucleoli and scant amount of cytoplasm.[31]

Serous carcinoma is characterized by a complex papillary and/or glandular architecture with diffuse, marked nuclear pleomorphism. As the shared apical border is missing, the lumina look scalloped or frayed. Gaping glands are seen if it invades the myometrium.[31]

Clear cell carcinoma- It is type II endometrial carcinoma. It is characterised by the presence of papillary, tubulocystic or solid architecture having hobnail or polygonal cells with nuclear atypia and clear eosinophilic cytoplasm. The nuclei show pleomorphism with marked atypia and prominent nucleoli. Occasional mitotic figures can be seen. Dense eosinophilic hyaline bodies can be seen in few cases.[31]

Mixed carcinomas - Mixed carcinoma is comprised of two or more than two different histological category of endometrial carcinoma, out of which one should be type II category. The two components should be easily identified on H and E section. Endometrioid and serous carcinoma combination is the most often observed. Atleast 5% of the second component should be present.[31]

Inflammation of the endometrium is known as endometritis and is classified as acute or chronic. The presence of plasma cells and lymphocytes confirms the diagnosis of chronic endometritis. Pelvic Inflammatory Disease (PID) is a component of endometritis. [8,9]

PID is infection and inflammation of the upper genital tract organs typically involving the uterus (endometrium), fallopian tubes, ovaries, pelvic peritoneum and surrounding structures.[9] The patients suffering from PID mainly present as abdominal pain. AUB can also occur with endometriosis in such patients. It occurs due Neisseria gonorrhoeae, Chlamydia trachomatis and Mycoplasma hominis. It can also occur in post pregnancy period. [8]

B. Non-structural Causes of Abnormal Uterine Bleeding[22,28,29]:

Acronym used for Non-structural Causes of Abnormal Uterine Bleeding is COIEN which include following conditions. [22,13]

1) Coagulopathy: Coagulopathies can be an essential cause of AUB in 13 to 20% of reproductive age group women. Coagulopathy can be congenital or acquired. Von Willebrand disease is the most common cause and can be diagnosed at any age. However additional history of bruising, epistaxis and anemia should be asked to the patients of AUB. Also women having thrombocytopenia or myelosuppression also suffer from AUB. [13,32]

2) Ovulatory dysfunction: Ovulatory disorders can cause AUB in 20% of the cases. If the menses are irregular in length, volume and duration for about 4 to 6 months, ovulatory dysfunction should be suspected. Unpredictable ovulation or anovulation brings about overstimulation of the endometrium from endogenous oestrogen presentation. Hypothyroidism, hyperprolactinemia, mental stress, anorexia, weight loss can lead to disturbances in ovulation. [13,32]

3) Endometrial causes: Endometrium secretes prostaglandins and thromboxanes. AUB can occur whenever the production of prostaglandin is insufficient. Prostaglandin act as a local vasoconstrictor. [13,32]

Increased secretion of plasminogen activator can also lead to lysis of endometrium. AUB can also occur due to defective regeneration of endometrial tissue and increased inflammatory response.[13,32]

Infectious conditions such as Tuberculous endometritis and chlamydial infections are the rare causes of AUB.[13,32]

4) Iatrogenic: Women consuming oral contraceptive pills, steroids, tricyclic anti-depressants, digitalis, phenytoin, anticoagulants and phenothiazines can cause AUB. Cooper T insertion can also lead to "break-through bleeding" or menorrhagia. However, AUB resolves on discontinuing the medication in these patients. [13,32]

5) Not Classified: The non-classified causes of AUB are rare.

Arteriovenous malformations, varicose veins of uterine vessels, myohyperplasia are some of the rare causes leading to AUB.[13,32]

Blood supply of endometrium

The blood supply of endometrium is from the arcuate arteries, which branch out radially and their terminal branches divide into straight and spiral arterioles. The straight arterioles supply the basal layer of endometrium. The functional layer is pierced by the spiral arterioles and supplies the endometrial glands and stroma. They have the ability to change functionally in response to ovarian steroids. In other words, the endometrial artery bed, unlike those in many other tissues, grows and shrinks during different stages of the menstrual cycle and thus provides a robust model of physical angiogenesis.[9,10]

Vascular changes in endometrium –

Endometrial angiogenesis depends on a delicate balance between factors that promote and inhibit blood vessel formation.[33]

New vessel growth or angiogenesis is classified into four stages.[34]

(1) "Degradation of vascular basement membrane and activation of quiescent endothelial cells (ECs).

(2) Sprouting and proliferation of ECs within temporary Extracellular matrix (ECM).

(3) Lumen formation within the vascular sprouts, thereby creating vascular tubes.

(4) Coverage of vascular tubes with mature vascular basement membrane in association with supporting pericytes."[34]

During the earliest stages of angiogenesis, injury due to wounds and ischemia causes release of angiogenic cytokine called as vascular endothelial growth factor (VEGF) leading to basement membrane breakdown around an existing vessel.[34] Succeeding the degradation of basement membrane, the resulting stage is known as vascular sprouting. There is migration of endothelial cells towards a stimulus and also proliferation of the endothelial cells. Vessels become leaky and hyperpermeable causing leakage of the ECM proteins fibrinogen,

vitronectin and fibronectin from the blood. Fibrinogen is consequently converted to fibrin through enzymatic coagulation, and along with extravasated vitronectin and fibronectin instantly transform the interstitial collagen matrix to provisional ECM to form a new patent tube or vessel. Thus, "the early stages of sprouting angiogenesis are generally believed to proceed in an environment rich in pre-existing interstitial collagens in combination with fibrin, vitronectin and fibronectin derived from the blood plasma. As vascular morphogenesis proceeds and vascular sprouts acquire lumens and mature, neovessels are again exposed in vascular basement membrane with associated pericytes and thereby achieve stability."[34]

By providing mechanical stability and cell adhesion, ECM has been shown to be essential for all stages of angiogenesis. In addition to providing basic support for EC proliferation, survival, and migration, ECM also regulates key stages of blood vessel morphogenesis and maturation. Although angiogenic cytokines such as VEGF are often represented as the key mediators of neovascularization, there is a growing body of evidence that ECM and dynamic changes in the composition of ECM are equally important, particularly in regulating vascular morphogenesis and the stabilization of new blood vessels. Thus, at a minimum, angiogenesis should be viewed as a collaboration between cytokines and ECM, wherein ECM actively controls, rather than merely supports, the formation, architecture, and maturation of new blood vessels. [35]

Jacques *et al*.[36] in their study on endometrial angiogenesis concluded that endometrium is angiogenic throughout the menstrual cycle. This angiogenicity has cyclic variation with physiological changes of endometrium and endometrial vasculature during the cycle. They also stated that the endometrial fragments, which are angiogenic are able to generate their own blood supply leading to the progression of endometriotic lesion.

Withdrawal of oestrogen and progesterone hormones releases proteolytic enzymes into the extracellular matrix. These enzymes degrade the matrix including vessels resulting in menstrual shedding.[37]

Menstrual bleeding usually commences from the wall of an arteriole or capillary. Once a previously constricted spiral arteriole relaxes, blood flow recommences. Some blood cells also leave the capillary circulation by diapedesis, as well as by reflux from veins through previously formed breaks in the vasculature. During menstruation, blood loss from a break in the endometrial vasculature normally lasts only for 1–2 min and then ceases due to spiral arteriole vasoconstriction. Throughout the normal menstrual process, the vascular bed is showing signs of constant attempts to repair itself. A number of other mechanisms and factors that influence haemostasis and vascular breakdown are also modified during menstruation, including plasminogen activator and plasminogen activator inhibitor type 1, matrix metalloproteinases and tissue factor.[34]

Clinically, it is well established that both prostaglandin synthesis inhibitors and anti-fibrinolytic agents can act to reduce menstrual blood loss in women suffering from menorrhagia, that they presumably play a central role in controlling menstruation.[34]

In proliferative phase, estradiol and progesterone hormones control the angiogenesis by stimulating or inhibiting the growth factors. These hormones stimulate the production of VEGF, which helps in proliferation of endometrial vessels.[37]

Lara *et al.* [38] their study stated that vessel elongation is the basic mechanism through which angiogenesis occurs in the proliferative phase. The blood vessel density is at the maximum in mid-proliferative phase.

In Secretory Phase progesterone stimulates thrombospondin-1, which is responsible for the inhibition of blood vessel proliferation during the secretory phase.[39]

It is well-established that the spiral arterioles reach their maximum tortuosity towards the end of the secretory phase, during that period endometrial tissue is undergoing regression.

Thus it seems that, the process of endometrial regression plays role in increasing the coiling of the spiral arterioles by forcing them to shorten as the endometrium becomes thinner.[34]

VEGF is an important regulator of angiogenesis and its role has been revealed in developmental, physiological and pathological angiogenesis.[17] In some studies it was mentioned that VEGF-encoding mRNA levels are greatly increased in menstrual endometrium, possibly in part induced by endometrial hypoxia due to spiral artery vasoconstriction, although absolute evidence of endometrial hypoxia at menses does not exist.[40]

In the study done by Khan *et al.* [41] on Morphometric Evaluation of Endometrial Blood Vessels and Its Clinico-pathological Relation in Patients with DUB observed that, ovulatory dysfunctional uterine bleeding was predominantly associated with decreased endometrial vasoconstriction and defective vascular plug formation, leading to excessive bleeding. This could explain the abnormal bleeding encountered in secretory phase.

In anovulatory bleeding, unopposed estrogen leads to excessive endometrial proliferation and hyperplasia. Large thin walled tortuous and fragile superficial blood vessel could lead to increased blood loss is suggested by Livingstone and Fraser.[42] They also stated that menorrhagia may also be due to the local effects of prostaglandin (PGE2 and PGI2), low levels of PGF2α, Nitric oxide (both secreted from vascular endothelium) and reduces levels of endothelin-1 secreted from vascular endothelium, increased tissue plasminogen activator and subsequent increased fibrinolytic activity. [42]

Mints *et al.*[43] in study of microvascular density, vascular endothelial growth factor A, and its receptors in endometrial blood vessels in patients with menorrhagia observed that the up regulation of VEGF-A and its receptors for e.g. VEGFR-1 and VEGFR-2 in capillaries which enhance the proliferation of vascular endothelial cells, augments vascular permeability and induce fenestration in capillaries and venules could be reason for menorrhagia in such patients. They concluded that upregulation of VEGF-A and its receptors VEGFR-1 and VEGFR-2 in capillaries may be involved in abnormal endometrial vascular structure and permeability.[43] Thus various biochemical and molecular factors play an important role in menorrhagia apart from vascular morphological changes in different endometrial patterns.

Nayha *et al*.[7] in their study of angiogenesis in endometrium in preneoplastic and neoplastic lesions observed that, there is close association of angiogenesis in endometrial tumour tissue with other prognostic parameters such as stage of tumour and lymph nodes involved by the tumour. They observed that microvessel count in endometrial adenocarcinoma was correlated significantly with grade, myometrial invasion and lymphatic space involvement. They also opined that high intratumoural microvessel count is associated with poor survival. In poorly differentiated adenocarcinomas, total vessel volume and vessel number was very high, pointing to increased vessel formation.[7]

Blood vessels in neoplasms have been recognized as clinically important therapeutic targets in many types of tumor. [44] Folkman proposed that every increase in a tumor cell population is preceded by an increase in the number of new capillaries. Tumor vessels are dynamic, forming new vessels by means of angiogenesis and remodeling of existing vessels.[45]

Nijkang *et al*.[46] in their study done on blood microvasculature and lymphatic densities in endometrial polyp concluded that, there was numerical increase in blood vessel densities in endometrial polyps as compared to control group endometrial tissue.

In the study done on Morphometric Analysis of Endometrium in Patients with Menorrhagia by Anusha & Annamala[47] revealed an increase in gland to stroma ratio, number of capillaries/mm^2 stroma, mitotic index and lumen/gland relative volume in endometrial hyperplasias and endometrial carcinomas.

Dunton C *et al*.[48] in their study on use of computerized morphometric analyses of endometrial hyperplasias in the prediction of coexistent cancer concluded that, simple endometrial hyperplasias have an increase in glands to stroma ratio but only a few mitoses while in complex endometrial hyperplasias glands to stroma ratio is higher than simple endometrial hyperplasia with an increase in mitoses.

In a study done by Desai and Satpara[49] on evaluation of angiogenesis in various menstrual disorders observed a positive correlation between angiogenesis and menstrual disorders.

In study done on pattern and characteristic of microvascular density (MVD) in neoplastic lesions of endometrium, it was observed that microvascular density is correlated with distinct patterns of changes in various stages of endometrial vessels and it was concluded in these studies that endometrial hyperplasia, degree of hyperplasia and atypia are remarkably associated with changes in vascular density, vessel size and shape. Thus the analysis of vessel size, density, shape plays an important role in predicting or determining endometrial preneoplastic and neoplastic conditions and also it has got potential clinical applications.[7]

MATERIALS AND METHODS

Source of data

A Prospective cross-sectional study was done on endometrial tissue sent for evaluation of AUB to histopathology section in The Department of Pathology, BLDE (Deemed to be University) Shri B.M.Patil Medical College, Hospital and Research Centre, Vijayapura.

Study period: 1st December 2018- 30thMay 2020

Type of study

Prospective cross-sectional study.

Method of collection of data

Endometrial tissue samples such as dilatation and curettage (D and C) sample, endometrial biopsy, fractional curettage and endometrial tissue processed from hysterectomy specimen of clinically diagnosed cases of AUB received for evaluation at the histopathology section of Department of Pathology BLDE (Deemed to be University) Shri B.M.Patil Medical College, Hospital and Research Centre, Vijayapura were included in study. Detailed clinical history and examination findings of the patients presented with AUB were collected from the patients records.

Tissues received were processed as per the routine processing done in the histopathology section. Paraffin blocks were prepared and tissue section of 3-6 µ thickness were cut. Sections were stained by H and E stain.

H and E stained slides were evaluated under the light microscopy for diagnosis of endometrial pathology. Vascular morphometric evaluation was done using the bright field Zeiss (Scope A1) Microscope with a field number of 23, field diameter 0.57mm and field area of 0.255 μm^2 in 400x objective. In vascular morphometry, average number of blood vessels, area of blood vessels, contour of blood vessels, degree of dilatation and congestion of blood vessels were evaluated.

Number of blood vessels viewed in 10 high-power fields (HPFs) per slide were counted and average of count was taken as number of vessels per HPFs.[6]

Cross sectional area of 16-150 μm^2 was considered as small, 150-1000 μm^2 as large vessels. The cross sectional areas was calculated using Ziess (ZEN lite 2012 blue edition version no. 2.5.75.0) and AX10 CAM.

Contour of blood vessels was categorised as present or absent based on vessel shape irregularities.

Degree of dilatation of blood vessels was classified as mild, moderate and severe.

Congestion of blood vessels were categorised as presence or absence.

Inclusion criteria:

All histopathological specimen of endometrial tissue (endometrial curettage/endometrial tissue of hysterectomy specimen) of patients presented with AUB were included in the study.

Exclusion criteria:

1. Tissue specimen of Dilatation and Curettage and suction evacuation containing only blood or inadequate tissue were excluded from the study.
2. Autolysed tissue specimens were excluded from the study.

Sample Size:

Sample size calculation

With 95% confidence level and margin of error of ±7.5% [6], a sample size of 146 subjects was studied to determine the morphometric evaluation of endometrial blood vessels in patients presenting with AUB with finite population correction.

By using the formula:

$$n = \frac{z^2 p(1-p)}{d^2}$$

where

Z= z statistic at 5% level of significance

d is margin of error

p is anticipated prevalence rate (50%)

Statistical analysis

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean± standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries and diagrammatic presentation. Chi-square (χ^2) test was used for association between two categorical variables.

The formula for the chi-square statistic used in the chi square test is:

$$\chi_c^2 = \sum \frac{(O_i - E_i)^2}{E_i}$$

The subscript "c" are the degrees of freedom. "O" is observed value and E is expected value.

C= (number of rows-1)* (number of columns-1)

The difference of the means of analysis variables between two independent groups was tested by unpaired t test.

The t statistic to test whether the means are different can be calculated as follows:

$$t = \frac{(\overline{x_1} - \overline{x_2}) - (\mu_1 - \mu_2)}{\sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}}$$

where $\bar{x}_1$ = mean of sample 1

$\bar{x}_2$ = mean of sample 2

n_1 = number of subjects in sample 1

n_2 = number of subjects in sample 2

s_1^2 = variance of sample 1 = $\frac{\Sigma(x_1 - \bar{x}_1)^2}{n_1}$

s_2^2 = variance of sample 2 = $\frac{\Sigma(x_2 - \bar{x}_2)^2}{n_2}$

The difference of the means of analysis variables between more than two independent groups was tested by ANOVA and F test of testing of equality of Variance.

ANOVA

Source	d.f.	SS	MS	F
Treatment	$a-1$	SS_{treat}	$\frac{SS_{treat}}{a-1}$	$\frac{MS_{treat}}{MS_{error(a)}}$
Error (a)	$N-a$	$SS_{error(a)}$	$\frac{SS_{error(a)}}{N-a}$	
Time	$t-1$	SS_{time}	$\frac{SS_{time}}{t-1}$	$\frac{MS_{time}}{MS_{error(b)}}$
Treat x Time	$(a-1)(t-1)$	$SS_{treat\ x\ time}$	$\frac{SS_{treat\ x\ time}}{(a-1)(t-1)}$	$\frac{MS_{treat\ x\ time}}{MS_{error(b)}}$
Error (b)	$(N-a)(t-1)$	$SS_{error(b)}$	$\frac{SS_{error(b)}}{(N-a)(t-1)}$	
Total	$Nt-1$	SS_{total}		

The sources of the variation include treatment; Error (a); the effect of Time; the interaction between time and treatment; and Error (b). Error (a) is the effect of subjects within treatments and Error (b) is the individual error in the model. All these add up to the total.

If the p-value was < 0.05, then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analysed using SPSS software v.23 (IBM Statistics, Chicago, USA) and Microsoft office 2007.

RESULT AND ANALYSIS

Total 150 cases of endometrial tissue of patients presented with AUB from 1st December 2018 to 30th May 2020 were studied for morphometric analysis of endometrial blood vessels.

Out of 150 cases, in 120 cases endometrial tissue were from hysterectomy specimens and 30 cases were endometrial biopsy/curettage specimens.

Table 1. Distribution of Cases according to Age in patients presented with AUB

Age(years)	Number	Percentage (%)
21-30	22	14.7
31-40	69	46
41-50	44	29.3
51-60	10	6.7
61-70	5	3.3
Total	150	100

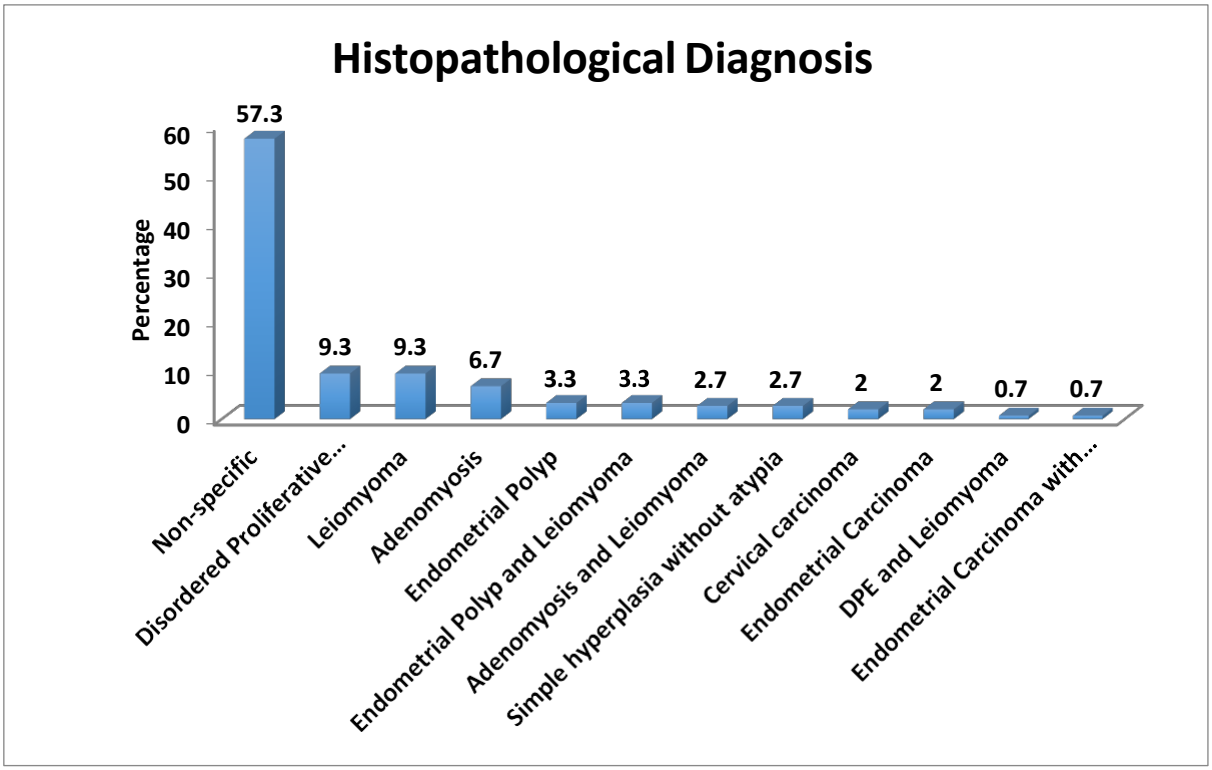
Age group of patients ranged from 20 to 70 years, with the youngest patient aged 22 years and the oldest 70 years with a mean age 40.2 years. Most of the cases were seen in the age group of 31- 40 years (46%).

Table 2. Distribution of Clinical Diagnosis in patients presented with AUB

Clinical Diagnosis	Number	Percentage (%)
DUB	72	48
Fibroid	32	21.3
DUB WITH PID	14	9.3
Endometrial hyperplasia	13	8.7
PID	7	4.7
Endometrial Polyp	5	3.3
Endometrial Carcinoma	4	2.7
Cervical Carcinoma	3	2
Total	150	100

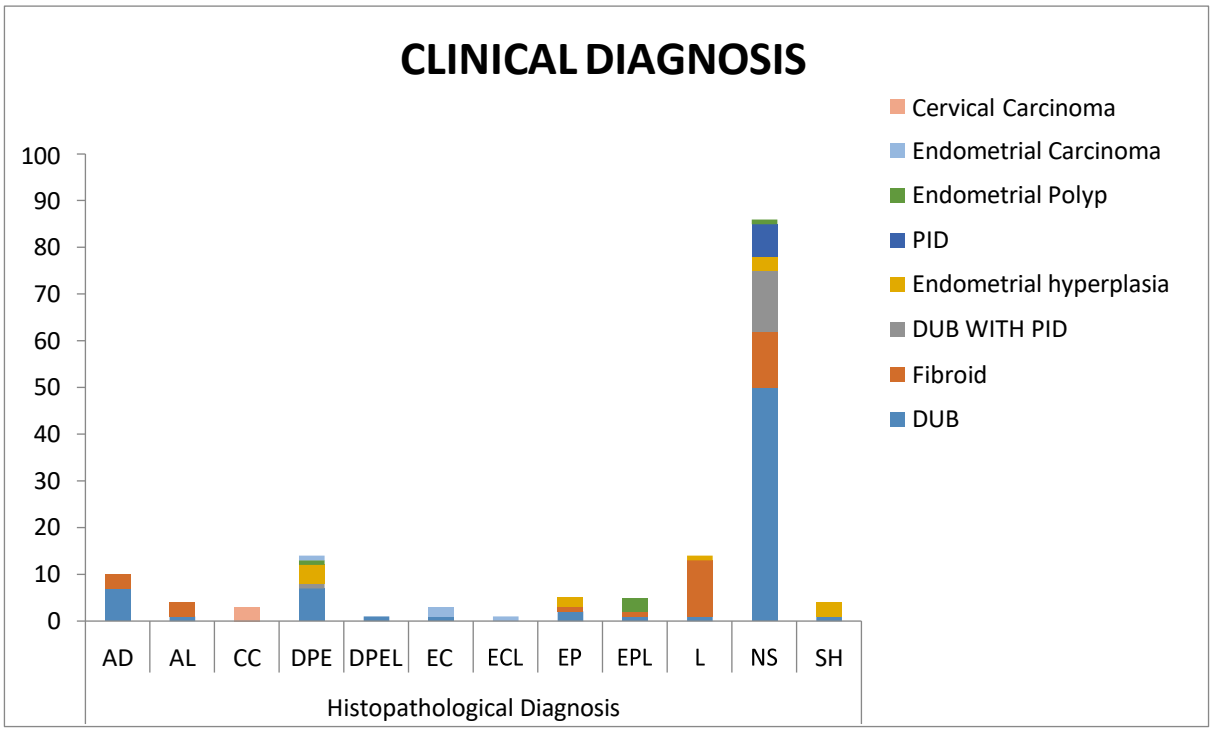
Out of 150 cases of AUB, majority of the cases were clinically diagnosed as DUB accounting for 48 %

Figure 1: Bar diagram showing distribution of Histopathological Diagnosis in patients presented with AUB. (n=64)



Out of 150 cases, specific histopathological diagnosis was possible in 64 cases. Maximum number of cases were DPE, followed by leiomyoma, adenomyosis and endometrial polyp. 86 cases were diagnosed as non-specific lesions such as chronic non-specific cervicitis.

Figure 2: Bar diagram showing association of Clinical Diagnosis and Histopathological Diagnosis in patients presented with AUB



[Abbreviation details in Bar diagram - 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.]

Out of 150 cases, specific histopathological diagnosis was given in 64 cases. In 22 clinically diagnosed DUB cases, maximum cases were diagnosed as adenomyosis and DPE on histopathology amounting to 7 cases each. In 20 clinically diagnosed fibroid cases, maximum cases were interpreted as leiomyoma, followed by adenomyosis on histopathology.

Table 3. Distribution of Histopathological Diagnosis of endometrial tissue in patients presented with AUB

Endometrial tissue	**Number**	**Percentage (%)**
Proliferative phase	80	53.3
Secretory phase	41	27.3
Disordered Proliferative endometrium	15	10
Atrophic Phase	6	4
Endometrial Carcinoma	4	2.7
Simple hyperplasia without atypia	4	2.7
Total	150	100

Out of total 150 cases, majority of the cases were interpreted as proliferative phase 53.3%, followed by secretory phase (27.3%), DPE (10%), atrophic phase (4%), endometrial carcinoma (2.7%) and simple hyperplasia without atypia (2.7%).

Table 4: Average number of blood vessels per HPF in various endometrial lesions of patients presented with AUB.

Endometrial Tissue	Minimum number of blood vessels/HPFs	Maximum number of blood vessels/HPFs	Average number of blood vessels/HPFs	SD	p value
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	

Average number of blood vessels/HPF was high in endometrial carcinoma followed by simple hyperplasia without atypia as compared to other lesions such as DPE, proliferative, secretory, and atrophic phase. However the difference is statistically not significant.

Table 5: Average number of blood vessels/HPFs in endometrial tissue of various histopathological lesions in patients presented with AUB.

Histopathological Diagnosis	Minimum number of blood vessels/HPFs	Maximum number of blood vessels/HPFs	Average number of blood vessels/HPFs	SD	p value
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	

Average number of blood vessels/HPF was high in endometrial carcinoma followed by simple hyperplasia without atypia as compared to other lesions such as adenomyosis, leiomyoma, cervical carcinoma, DPE, endometrial polyp. However the difference is statistically not significant.

Table 6: Size of the blood vessels in various endometrial lesions in patients presented with AUB

Endometrial tissue	Size of blood vessel				p value
	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%	
Total	45	30.0%	105	70.0%	

Note: * significant at 5% level of significance ($p<0.05$)

All cases of endometrial carcinoma and simple hyperplasia without atypia showed large sized blood vessels. Out of 80 proliferative phase endometrium cases, 55 cases showed small sized and 25 cases showed large sized blood vessels. Number of large sized blood vessel was more in endometrial carcinoma and simple hyperplasia without atypia as compared to other lesions such as DPE, proliferative, secretory and atrophic phase. The difference is statistically significant.

Table 7: Size of the blood vessel in endometrial tissue in various histopathological lesions in patients presented with AUB

Histopathological Diagnosis	Size of blood vessel				p value
	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%	
Total	45	30.0%	105	70.0%	

Note: * significant at 5% level of significance ($p<0.05$)

Table 8: Vessel shape irregularities in various endometrial lesions in patients presented with AUB

Endometrial tissue	Vessel shape irregularities				p value
	Absent		Present		
	N	%	N	%	
Atrophic Phase	0	0.0%	6	100.0%	0.124
Disordered Proliferative endometrium	2	13.3%	13	86.7%	
Endometrial Carcinoma	0	0.0%	4	100.0%	
Proliferative phase	22	27.5%	58	72.5%	
Secretory phase	15	36.6%	26	63.4%	
Simple hyperplasia without atypia	0	0.0%	4	100.0%	
Total	39	26.0%	111	74.0%	

In all the cases of atrophic phase endometrium, endometrial carcinoma and simple hyperplasia without atypia, vessel shape irregularities were noted. On the other hand, 22 cases of proliferative phase endometrium, 15 cases of secretory phase endometrium and 2 cases of DPE showed no vessel shape irregularities. However the difference is statistically not significant.

Table 9: Vessel shape irregularities in endometrial tissue in various histopathological lesions in patients presented with AUB

Histopathological Diagnosis	Vessel shape irregularities				p value
	Absent		Present		
	N	%	N	%	
Adenomyosis	2	20.0%	8	80.0%	0.585
Adenomyosis with Leiomyoma	0	0.0%	4	100.0%	
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	0	0.0%	3	100.0%	
Endometrial Carcinoma with Leiomyoma	0	0.0%	1	100.0%	
Endometrial Polyp	2	40.0%	3	60.0%	
Endometrial Polyp with Leiomyoma	1	20.0%	4	80.0%	
Leiomyoma	5	35.7%	9	64.3%	
Non-specific	27	31.4%	59	68.6%	
Simple hyperplasia without atypia	0	0.0%	4	100.0%	
Total	39	26.0%	111	74.0%	

Vessel shape irregularities were observed in all cases of adenomyosis with leiomyoma, cervical carcinoma, DPE and Leiomyoma, Endometrial Carcinoma, Endometrial Carcinoma with Leiomyoma and simple hyperplasia without atypia. However, vessel shape irregularity was statistically not significant.

Table 10: Degree of dilatation in various endometrial lesions in patients presented with AUB

Endometrial tissue	Degree of dilatation						p value
	Mild		Moderate		Severe		
	N	%	N	%	N	%	
Atrophic Phase	6	100.0%	0	0.0%	0	0.0%	<0.001*
Disordered Proliferative endometrium	5	33.3%	10	66.7%	0	0.0%	
Endometrial Carcinoma	0	0.0%	0	0.0%	4	100.0%	
Proliferative phase	58	72.5%	21	26.3%	1	1.3%	
Secretory phase	34	82.9%	7	17.1%	0	0.0%	
Simple hyperplasia without atypia	0	0.0%	2	50.0%	2	50.0%	
Total	103	68.7%	40	26.7%	7	4.7%	

Note: * significant at 5% level of significance ($p<0.05$)

In endometrial carcinoma, severe degree of dilatation of endometrial blood vessels was observed. While all the cases of atrophic phase endometrium showed mild degree of dilatation of endometrial blood vessels. Out of total 41 cases of secretory phase endometrium, 34 cases showed mild and 7 cases showed moderate degree of dilatation of endometrial blood vessels. In simple hyperplasia without atypia, 50% cases showed moderate and 50% showed severe degree of dilatation. For degree of dilatation, significant statistical difference was noted in between various endometrial lesions with p value of less than 0.001.

Table 11: Degree of dilatation in endometrial tissue in various histopathological lesions in patients presented with AUB

Histopathological Diagnosis	Degree of dilatation						p value
	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%	

Note: * significant at 5% level of significance ($p<0.05$)

In endometrial polyp and DPE with leiomyoma severe degree of dilatation of endometrial blood vessels was noted as compared to other lesions. Out of 3 cases of cervical carcinoma, 2 cases showed mild and 1 case showed severe degree of dilatation of endometrial blood vessels. For degree of dilatation, significant statistical difference was noted in between various histopathological lesions with p value of less than 0.001.

Table 12: Vascular congestion in various endometrial lesions in patients presented with AUB

Endometrial tissue	Vascular congestion				p value
	Absent		Present		
	N	%	N	%	
Atrophic Phase	0	0.0%	6	100.0%	0.273
Disordered Proliferative endometrium	3	20.0%	12	80.0%	
Endometrial Carcinoma	0	0.0%	4	100.0%	
Proliferative phase	25	31.3%	55	68.8%	
Secretory phase	11	26.8%	30	73.2%	
Simple hyperplasia without atypia	0	0.0%	4	100.0%	
Total	39	26.0%	111	74.0%	

In atrophic phase, endometrial carcinoma and simple hyperplasia without atypia vascular congestion of endometrial blood vessels was noted. In DPE, in 12 cases vascular congestion was present. While in 3 cases there was no vascular congestion of endometrial blood vessels.

Table 13: Vascular congestion in various histopathological lesions in patients presented with AUB

Histopathological Diagnosis	Vascular congestion				p value
	Absent		Present		
	N	%	N	%	
Adenomyosis	4	40.0%	6	60.0%	0.006*
Adenomyosis and Leiomyoma	0	0.0%	4	100.0%	
Cervical carcinoma	0	0.0%	3	100.0%	
Disordered Proliferative endometrium	2	14.3%	12	85.7%	
DPE and Leiomyoma	1	100.0%	0	0.0%	
Endometrial Carcinoma	0	0.0%	3	100.0%	
Endometrial Carcinoma with Leiomyoma	0	0.0%	1	100.0%	
Endometrial Polyp	4	80.0%	1	20.0%	
Endometrial Polyp and Leiomyoma	3	60.0%	2	40.0%	
Leiomyoma	7	50.0%	7	50.0%	
Non-specific	18	20.9%	68	79.1%	
Simple hyperplasia without atypia	0	0.0%	4	100.0%	
Total	39	26.0%	111	74.0%	

Note: * significant at 5% level of significance ($p<0.05$)

All cases of adenomyosis with leiomyoma, cervical carcinoma and endometrial carcinoma with leiomyoma, vascular congestion in endometrial blood vessels was noted and the difference was statistically significant as compared to other cases.

PHOTOMICROGRAPHS

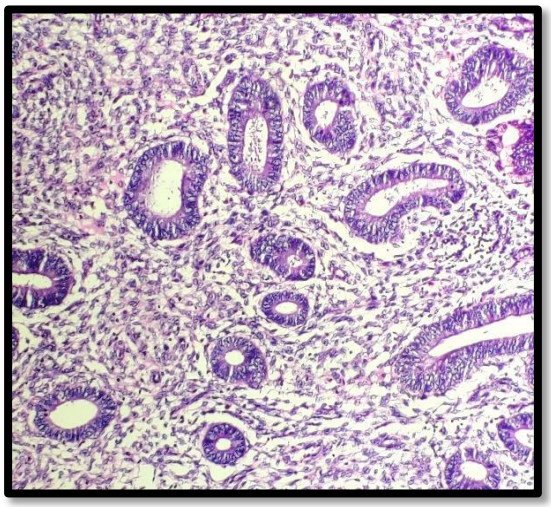


Fig 3 - Microphotograph of PPE showing round regular glands with densely cellular stroma. (H&E, 100X)

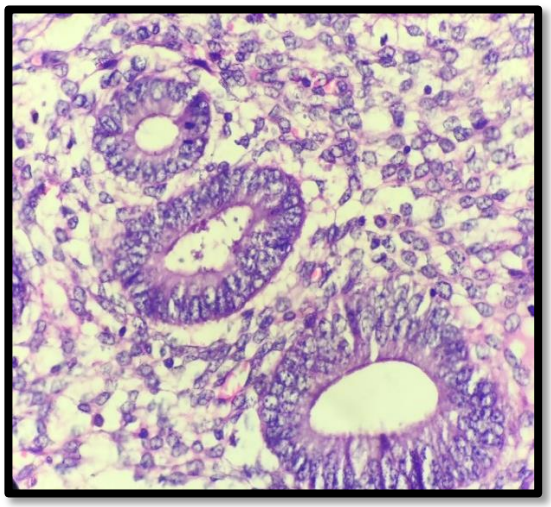


Fig 4 - Microphotograph of PPE showing glands lined by tall, pseudostratified columnar epithelium. (H&E, 400X)

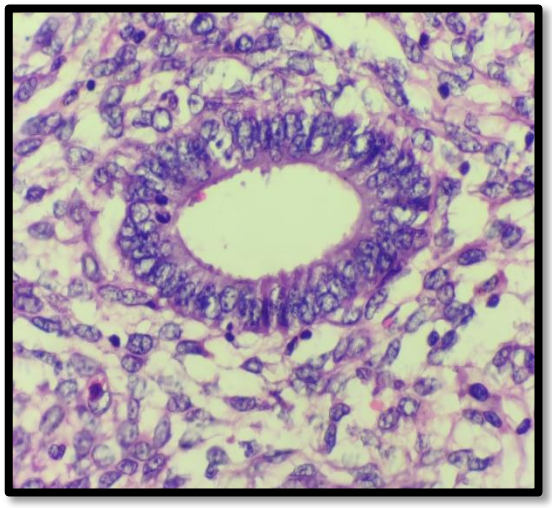


Fig 5 - Microphotograph of PPE showing mitotic activity in endometrial glands.

(H&E, 400X)

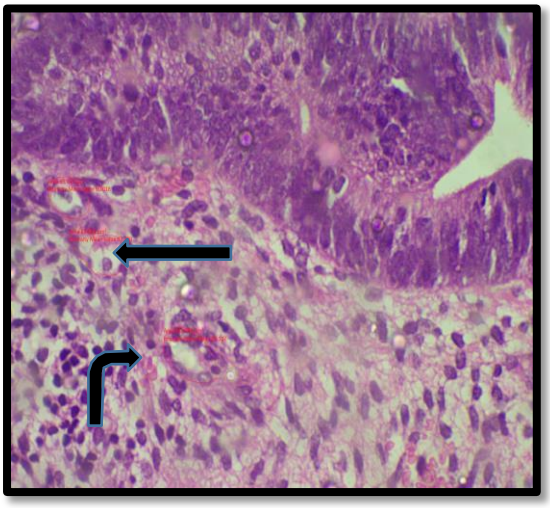


Fig 6 - Microphotograph of PPE showing average number of endometrial blood vessels ranged 3 to 4/HPFS. (H&E, 400X, Morphometric analysis)

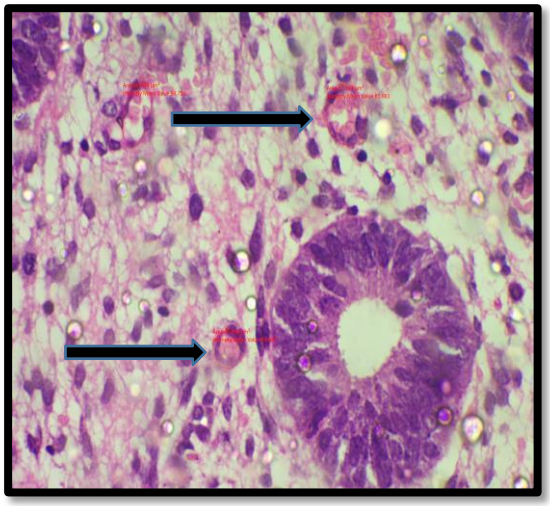


Fig 7 - Microphotograph of PPE showing maximum number of small sized vessels.

(H&E, 400X, Morphometric analysis)

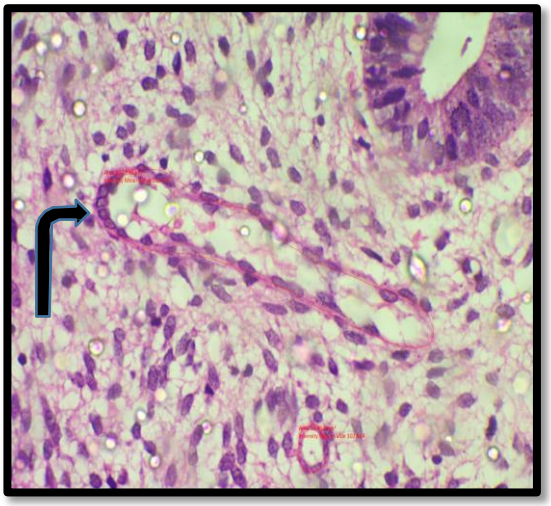


Fig 8 - Microphotograph of PPE showing vessel shape irregularities.

(H&E, 400X, Morphometric analysis)

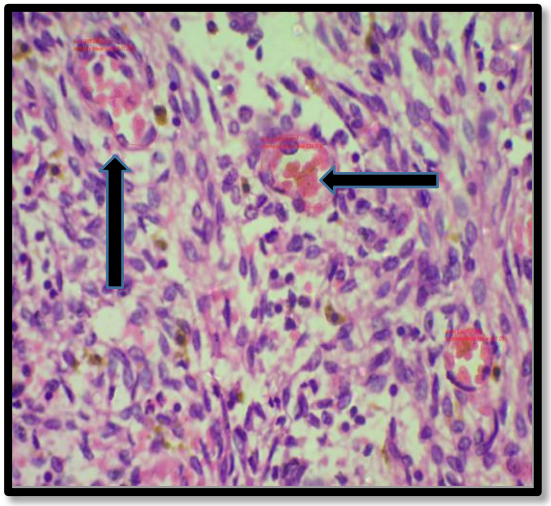


Fig 9 - Microphotograph of PPE showing mild degree of dilatation in endometrial blood vessels.

(H&E, 400X, Morphometric analysis)

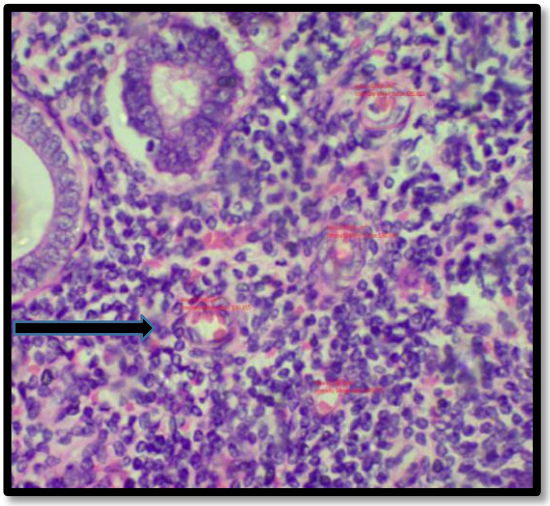


Fig 10 - Microphotograph of PPE showing mild degree of dilatation in endometrial blood vessels.

(H&E, 400X, Morphometric analysis)

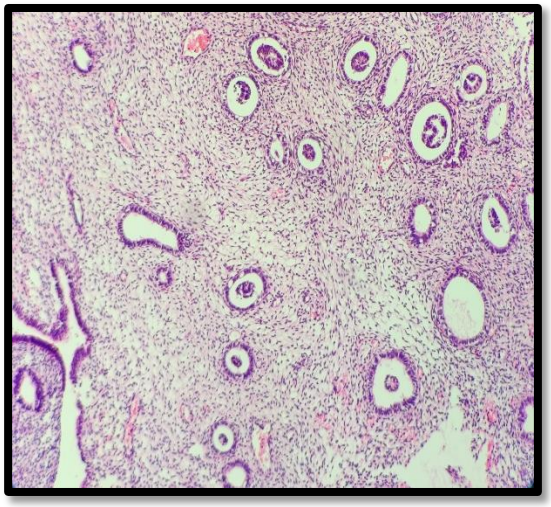


Fig 11 - Microphotograph of SPE showing tortuous endometrial glands and loose edematous stroma (H&E, 100X)

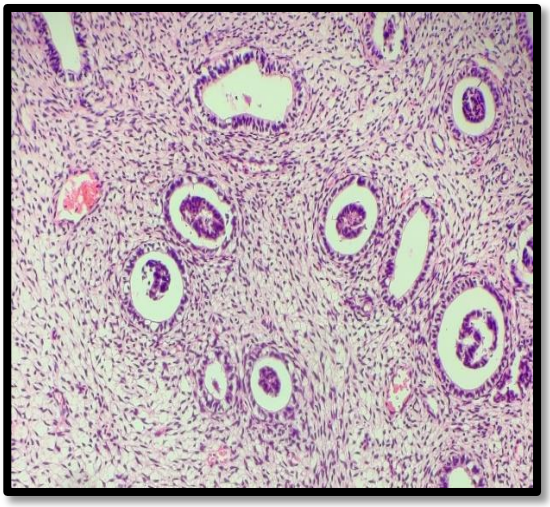


Fig 12 - Microphotograph of SPE showing glands lined by tall columnar epithelium. (H&E, 100X)

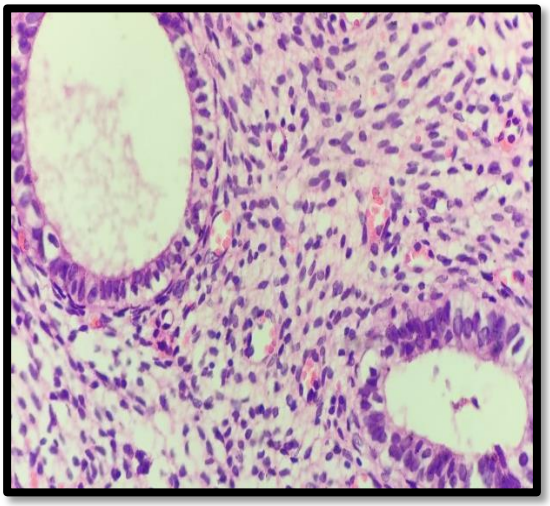


Fig 13 - Microphotograph of SPE showing supranuclear and subnuclear vacuoles.

(H&E, 400X)

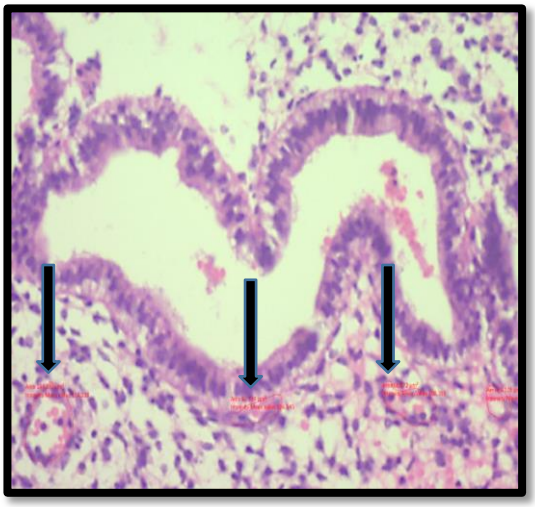


Fig 14 - Microphotograph of SPE showing average number of blood vessels ranged 4 to 5/HPFs.

(H&E, 400X, Morphometric analysis)

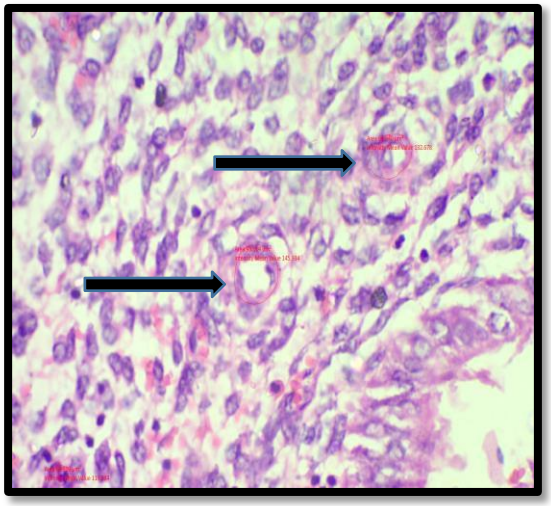


Fig 15 - Microphotograph of SPE showing small sized endometrial blood vessels. (H&E, 400X, Morphometric analysis)

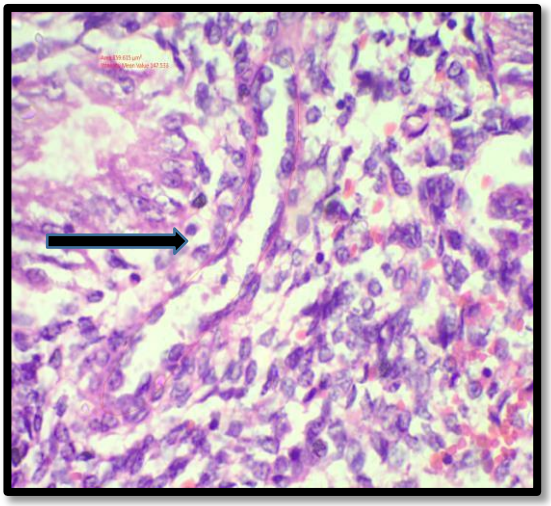


Fig 16 - Microphotograph of SPE showing vascular irregularity.

(H&E, 400X, Morphometric analysis)

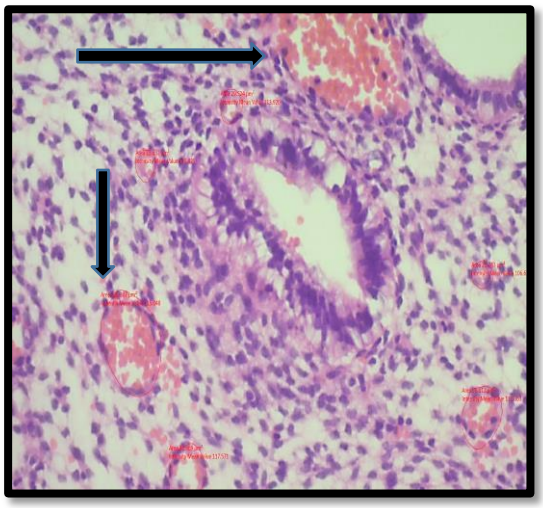


Fig 17 - Microphotograph of SPE showing mild to moderate dilatation of blood vessels.

(H&E, 400X, Morphometric analysis)

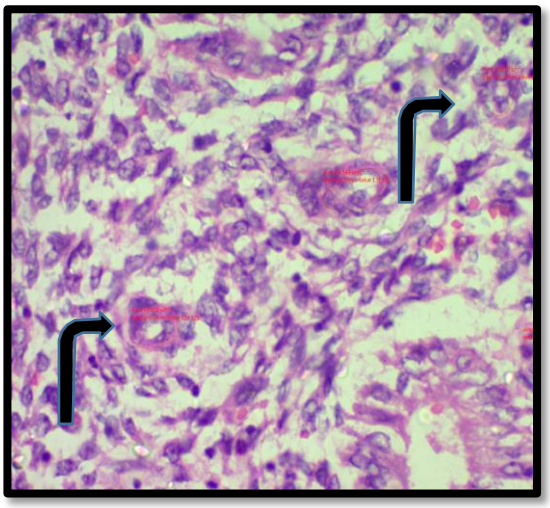


Fig 18 - Microphotograph of SPE showing vascular congestion of blood vessels.

(H&E, 400X, Morphometric analysis)

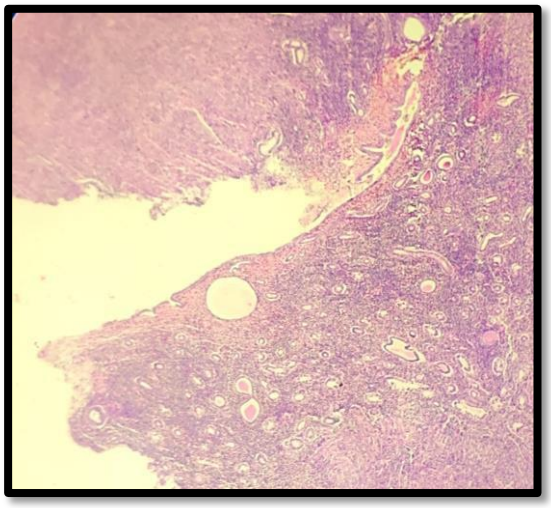


Fig 19 - Microphotograph of APE showing closely packed tubular and cystic glands. Glands are lined by low cuboidal to columnar epithelium. (H&E, 40X)

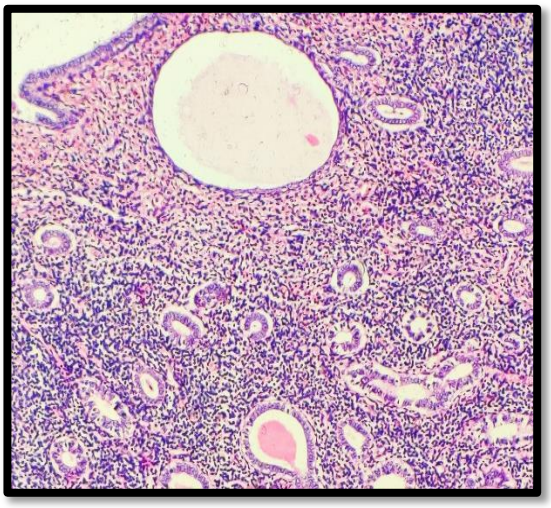


Fig 20 - Microphotograph of APE showing inactive stroma with variable collagenization.

(H&E, 100X)

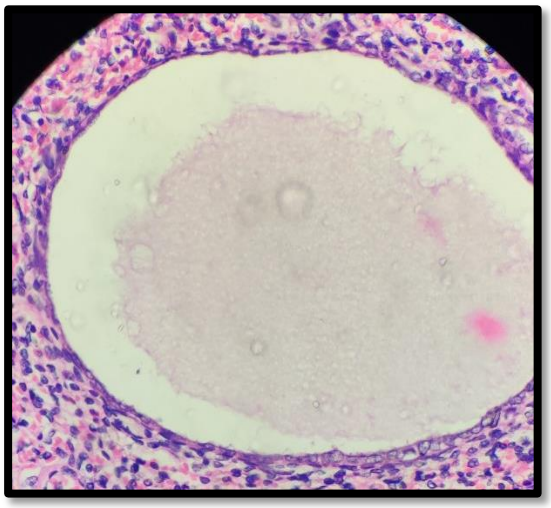


Fig 21 - Microphotograph of APE showing cystically dilated gland lined by flattened to cuboidal epithelium. (H&E, 400X)

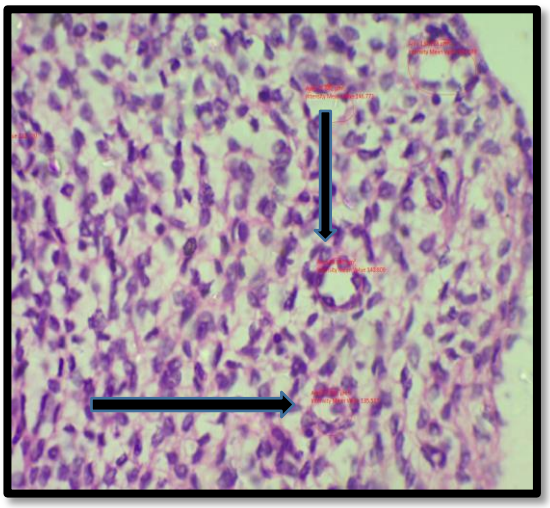


Fig 22 - Microphotograph of APE showing average number of blood vessels ranged 3 to 4/HPFs.

(H&E, 400X, Morphometric analysis)

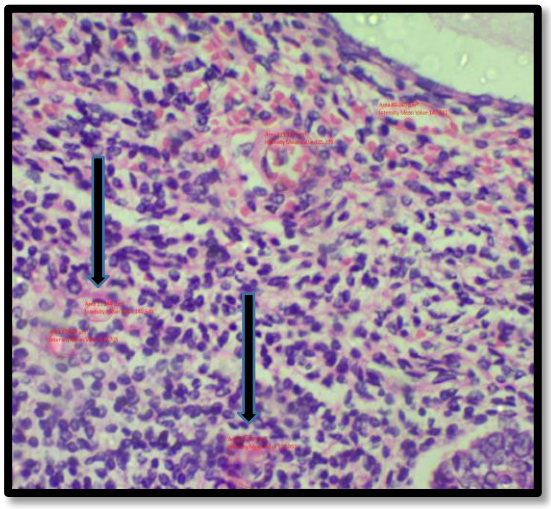


Fig 23 - Microphotograph of APE showing small sized blood vessels.

(H&E, 400X, Morphometric analysis)

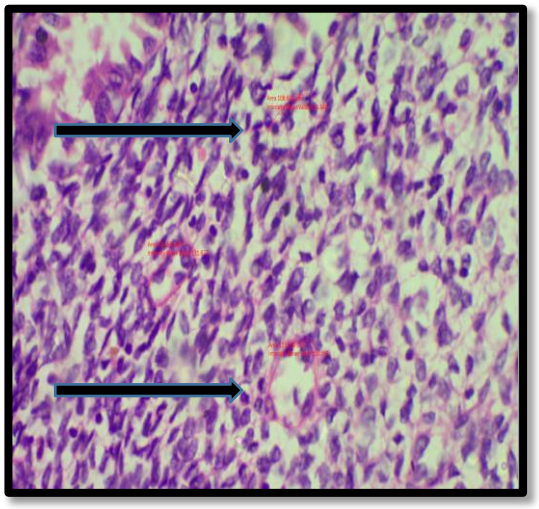


Fig 24 - Microphotograph of APE showing vascular irregularities.

(H&E, 400X, Morphometric analysis)

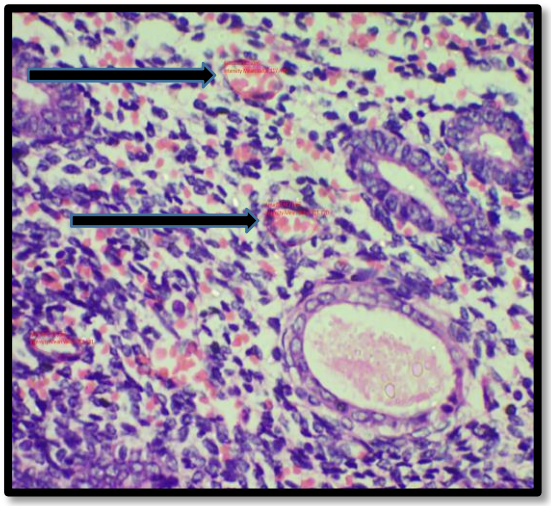


Fig 25 - Microphotograph of APE showing mild degree of dilatation of blood vessels.

(H&E, 400X, Morphometric analysis)

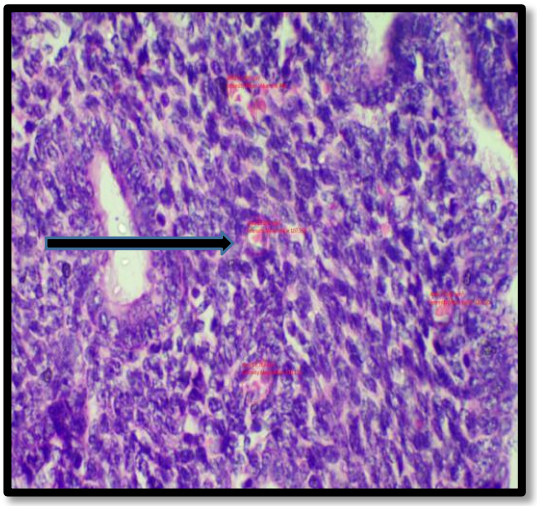


Fig 26 - Microphotograph of APE showing congested blood vessels.

(H&E, 400X, Morphometric analysis)

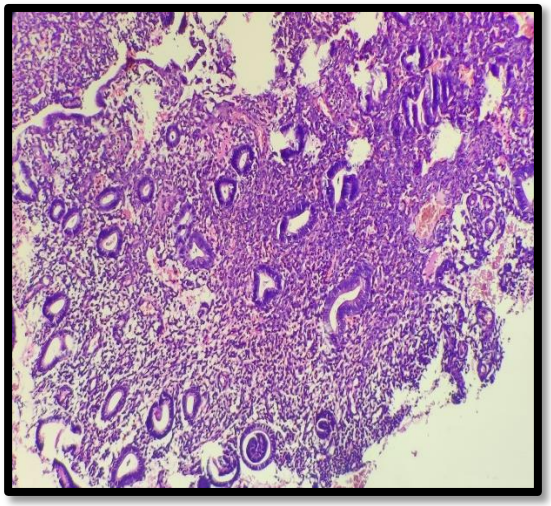


Fig 27 - Microphotograph of DPE showing tubular to tortuous glands with compact stroma.

(H&E, 100X)

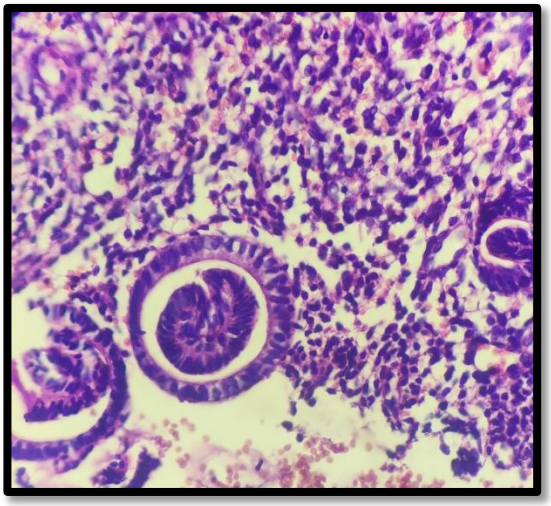


Fig 28 - Microphotograph of DPE showing gland in gland appearance. Glands are lined by columnar epithelium. (H&E, 400X)

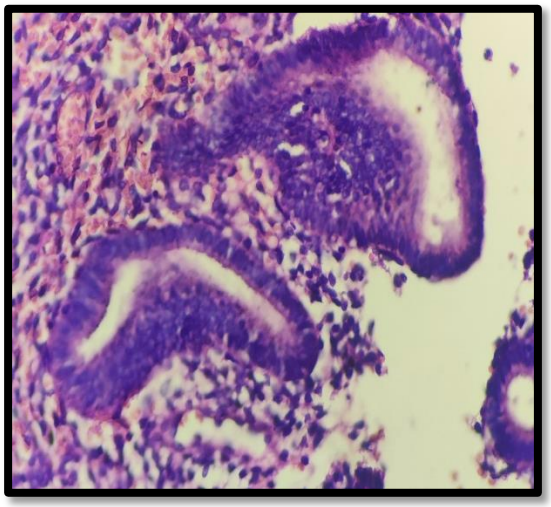


Fig 29 - Microphotograph of DPE showing glands lined by pseudostratified tall columnar epithelium. (H&E, 400X)

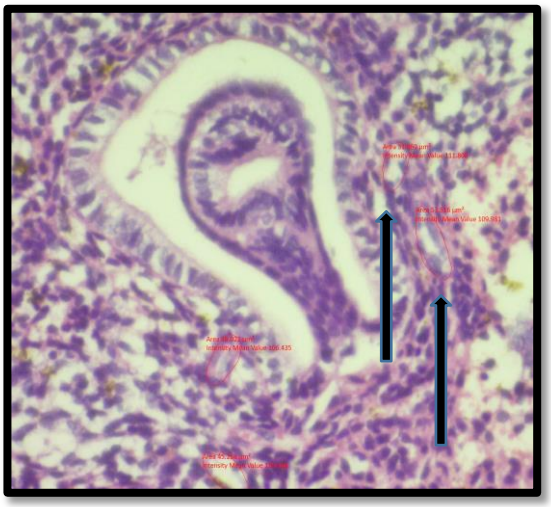


Fig 30 - Microphotograph of DPE showing average number of blood vessels ranged 3 to 4/HPFs.

(H&E, 400X, Morphometric analysis)

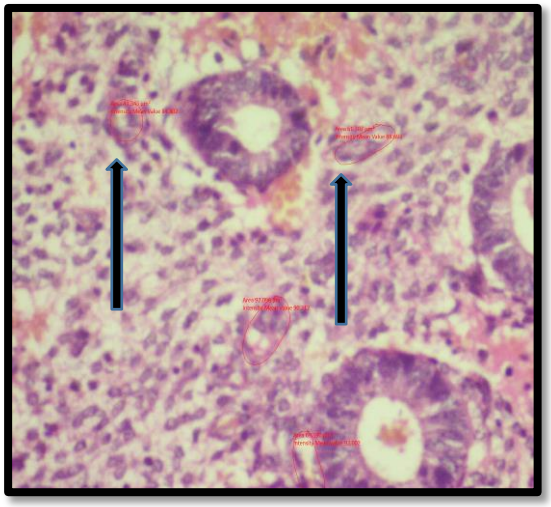


Fig 31 - Microphotograph of DPE showing small sized blood vessels.

(H&E, 400X, Morphometric analysis)

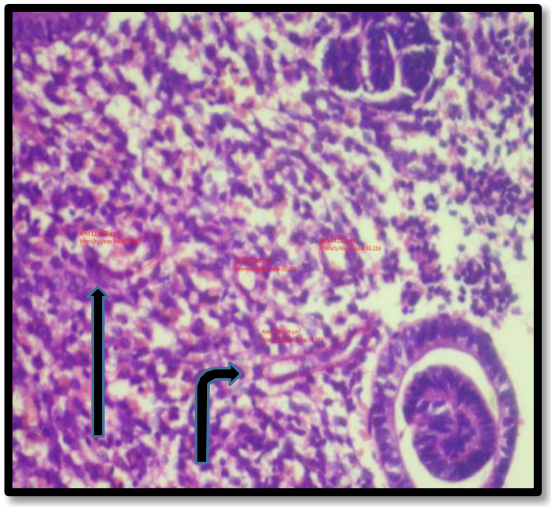


Fig 32 - Microphotograph of DPE showing vascular irregularities.

(H&E, 400X, Morphometric analysis)

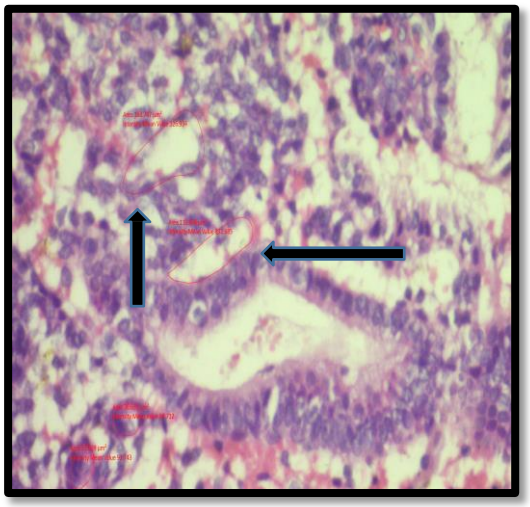


Fig 33 - Microphotograph of DPE showing dilatation of blood vessels.

(H&E, 400X, Morphometric analysis)

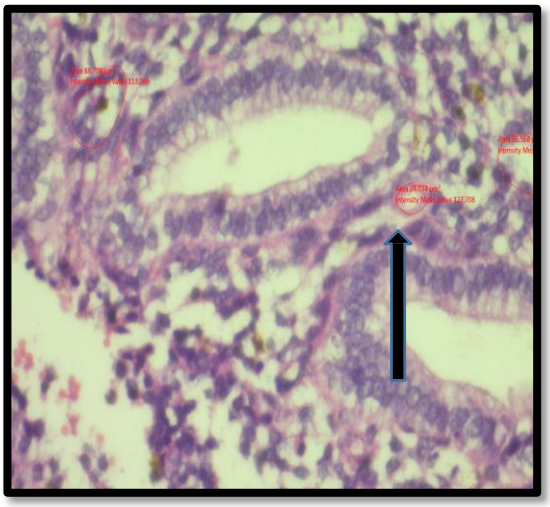


Fig 34 - Microphotograph of DPE showing congestion of blood vessels.

(H&E, 400X, morphometric analysis)

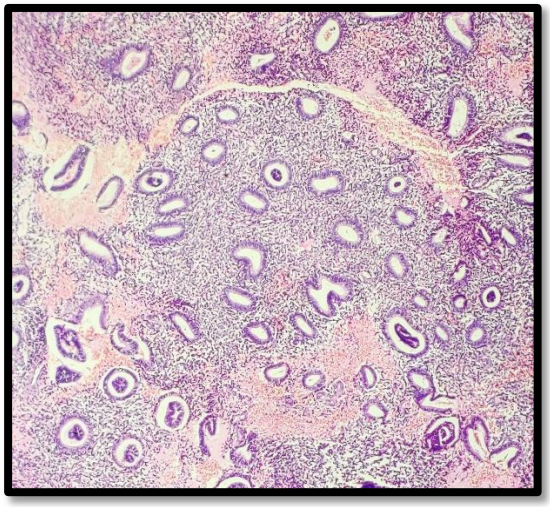


Fig 35 - Microphotograph of SH without atypia showing proliferation of irregular and variable sized endometrial glands. (H&E, 40X)

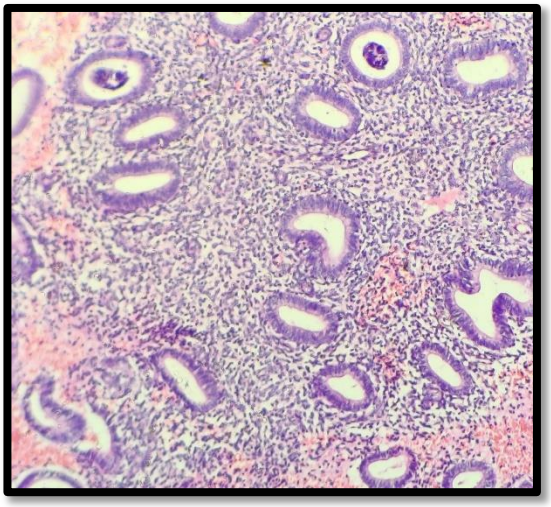


Fig 36 - Microphotograph of SH without atypia showing stromal breakdown. (H&E, 100X)

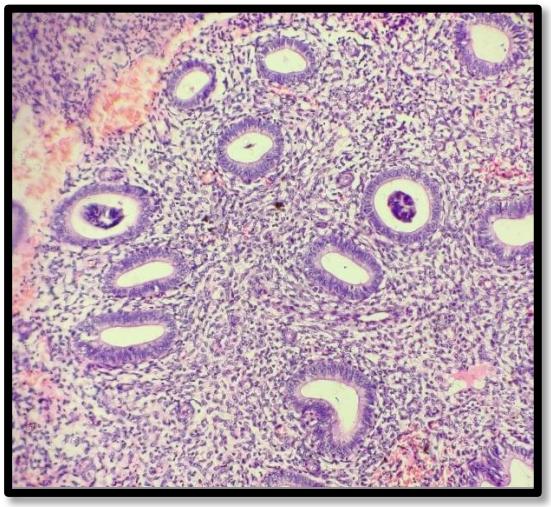


Fig 37 - Microphotograph of SH without atypia showing closely packed glands and increased gland to stroma ratio. Glands are lined by stratified columnar epithelium. (H&E, 400X)

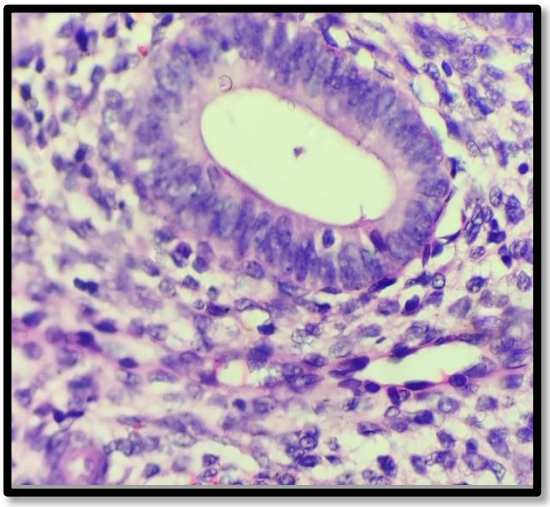


Fig 38 - Microphotograph of SH without atypia showing loss of basal nuclear stratification and variation in nuclear size. (H&E, 400X)

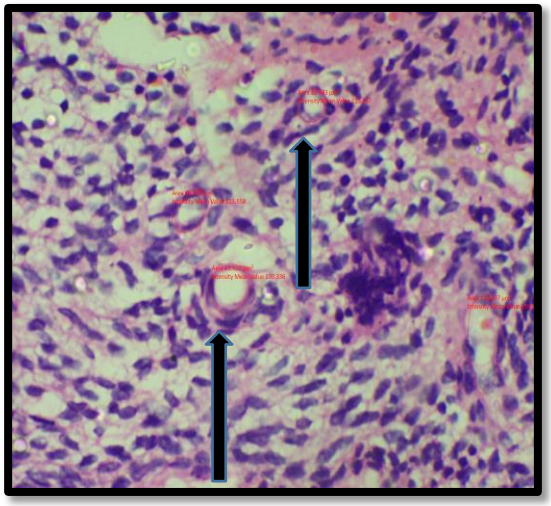


Fig 39 - Microphotograph of SH without atypia showing average number of blood vessels ranged 4 to 5/HPFs.

(H&E, 400X, Morphometric analysis)

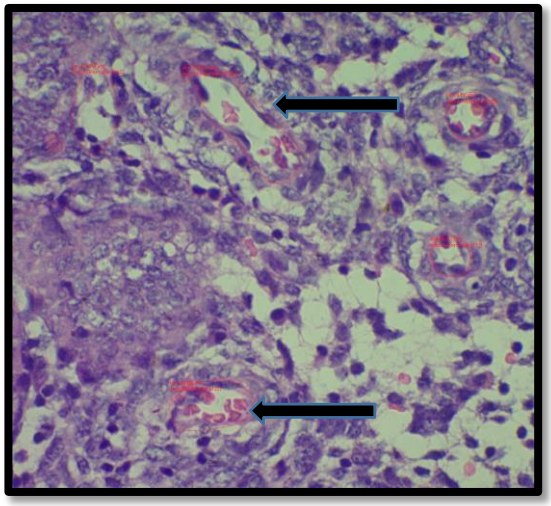


Fig 40 - Microphotograph of SH without atypia showing large sized blood vessels. (H&E, 400X, Morphometric analysis)

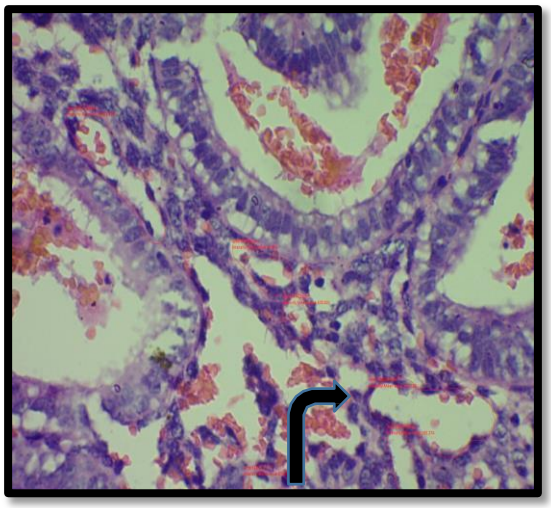


Fig 41 - Microphotograph of SH without atypia showing vessel shape irregularities and moderate to severe degree of dilatation of blood vessels. (H&E, 400X, Morphometric analysis)

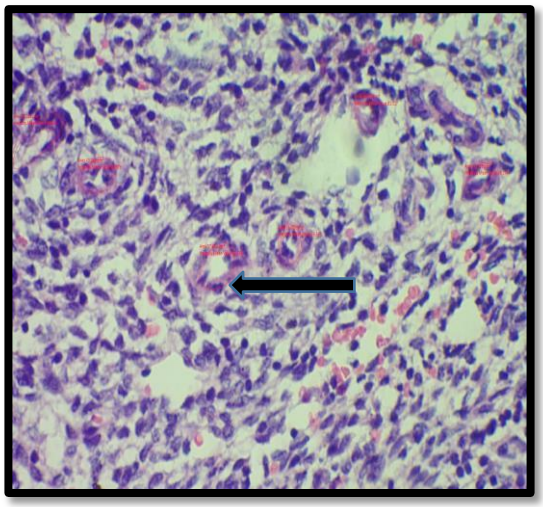


Fig 42 - Microphotograph of SH without atypia showing congestion of blood vessels.

(H&E, 400X, Morphometric analysis)

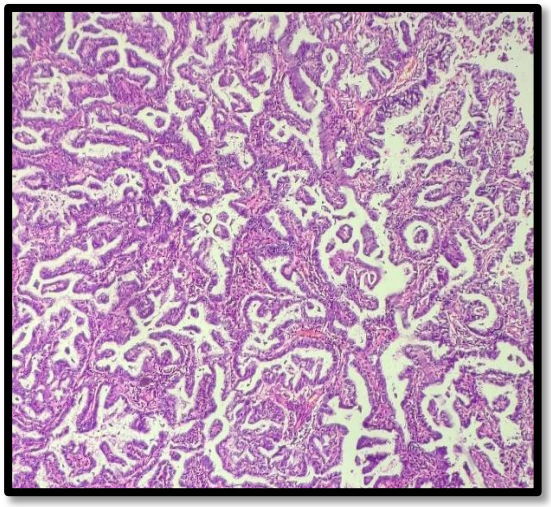


Fig 43 - Microphotograph of Endometrioid carcinoma showing tumour tissue arranged in glandular pattern and complex, branching villous fronds. (H&E, 40X)

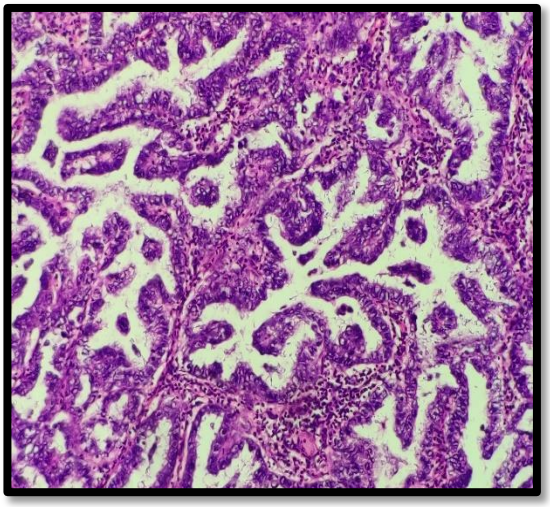


Fig 44 - Microphotograph of Endometrioid carcinoma showing glands and villi lined by tall columnar epithelium showing over crowding and stratification. (H&E, 100X)

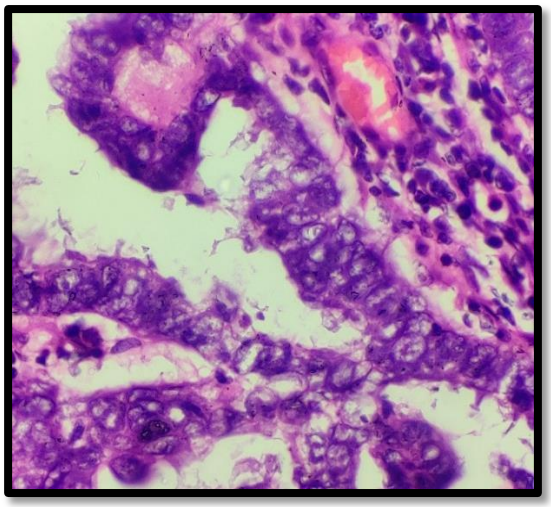


Fig 45 - Microphotograph of Endometrioid carcinoma showing tumour cells having smoothly contoured glandular lumen and have eosinophilic, granular cytoplasm. (H&E, 400X)

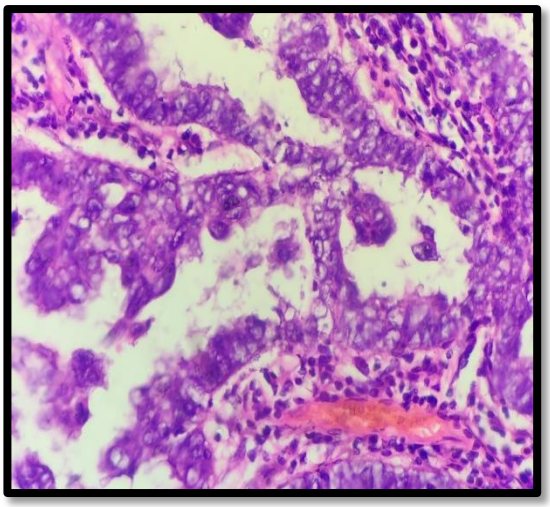


Fig 46 - Microphotograph of Endometrioid carcinoma showing round to oval nuclei showing moderate nuclear pleomorphism with coarse nuclear chromatin and inconspicuous nucleoli. (H&E, 400X)

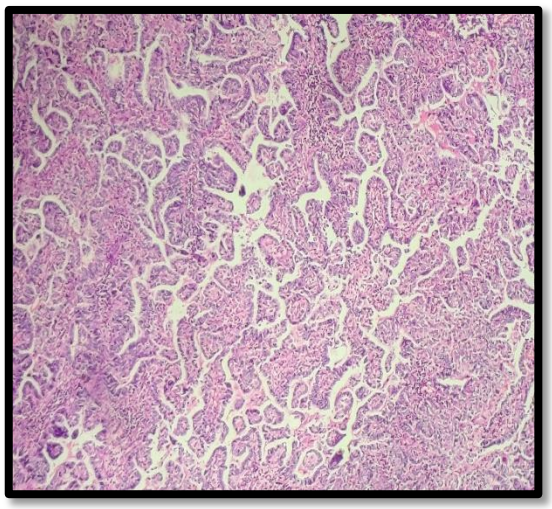


Fig 47 - Microphotograph of Endometrial carcinoma showing tumour tissue arranged in papillary, glandular and solid pattern. (H&E, 40X)

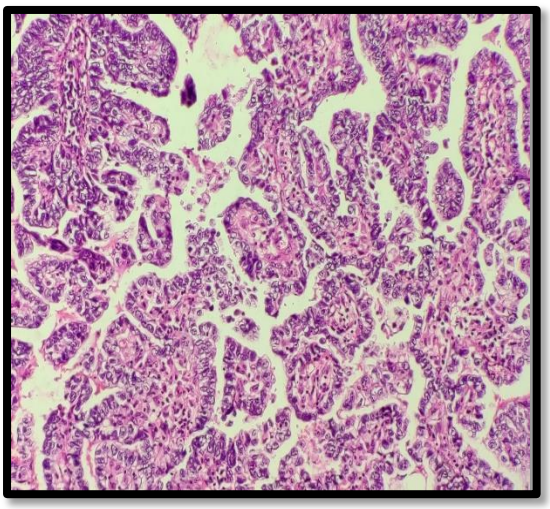


Fig 48 - Microphotograph of Endometrial carcinoma showing glands and villi lined by tall columnar epithelium showing over crowding. (H&E, 100X)

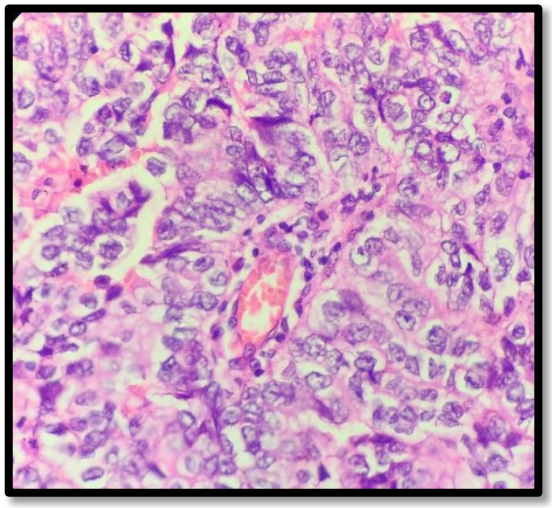


Fig 49 - Microphotograph of Endometrial carcinoma showing large round to oval tumour cells having enlarged pleomorphic nuclei with prominent nucleoli. Cytoplasm is scant in amount and eosinophilic. (H&E, 400X)

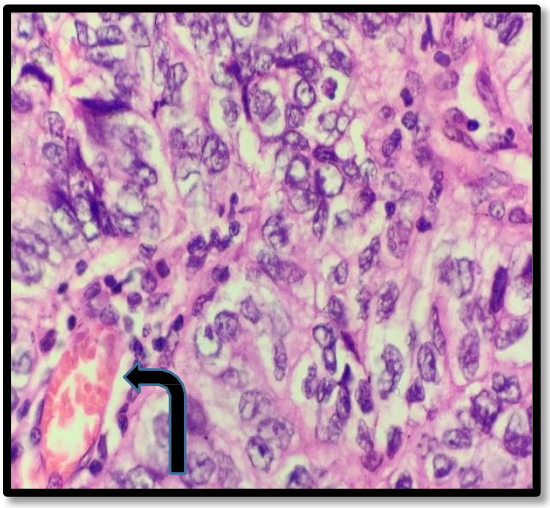


Fig 50 - Microphotograph of Endometrial carcinoma showing large sized blood vessel showing dilatation.

(H&E, 400X)

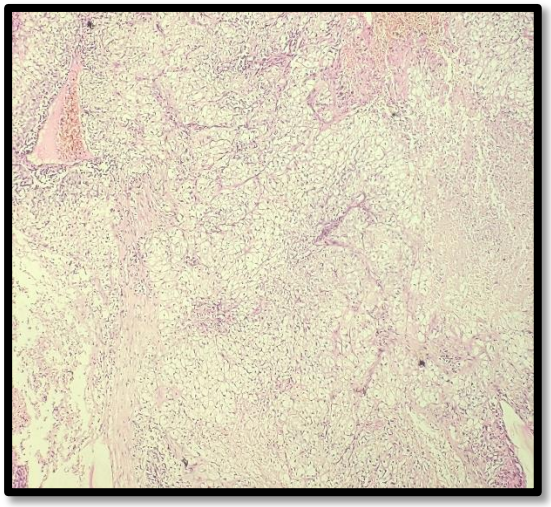


Fig 51 - Microphotograph of Clear cell endometrial carcinoma showing tumour tissue arranged in solid sheets, nests and cords. (H&E, 40X)

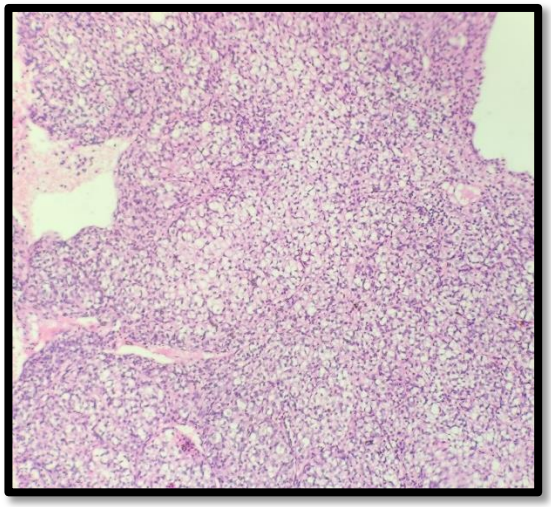


Fig 52 - Microphotograph of Clear cell carcinoma showing signet ring morphology. (H&E, 100X)

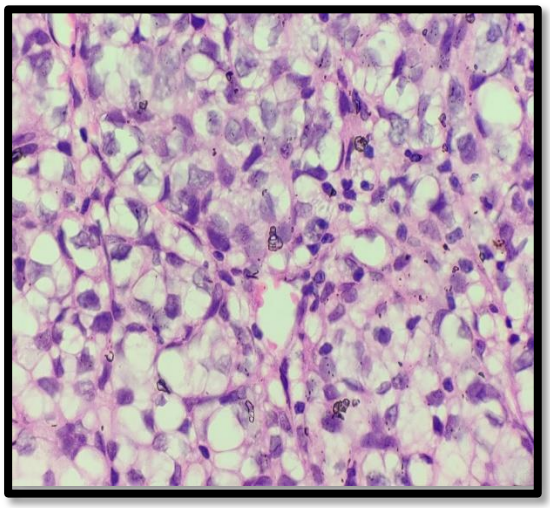


Fig 53 - Microphotograph of Clear cell carcinoma showing tumour cells having enlarged pleomorphic nuclei with prominent nucleoli. Cytoplasm clear to eosinophilic. (H&E, 400X)

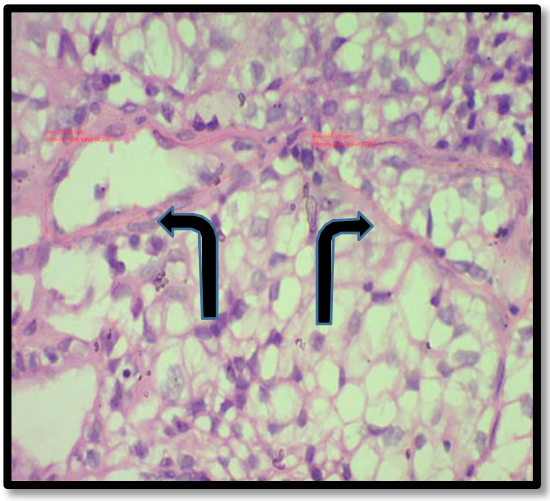


Fig 54 - Microphotograph of clear cell endometrial carcinoma showing vascular irregularities.

(H&E, 400X, Morphometric analysis)

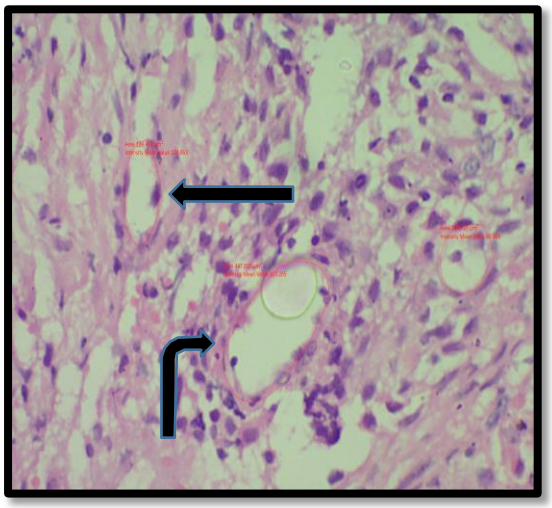


Fig 55 - Microphotograph of clear cell endometrial carcinoma showing large sized blood vessels.

(H&E, 400X, Morphometric analysis)

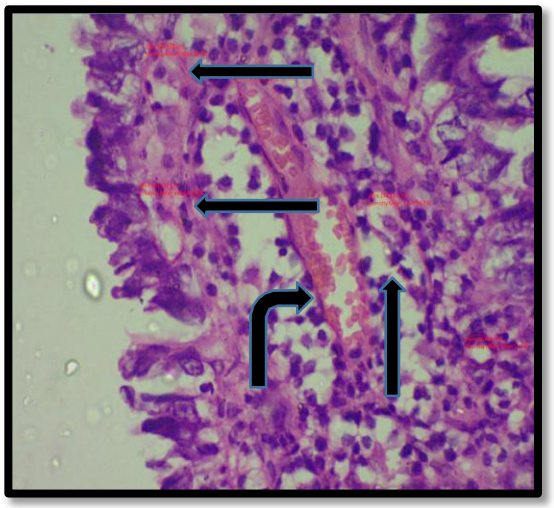


Fig 56 - Microphotograph of Endometrial carcinoma showing average number of blood vessels ranged 5 to 6 blood vessels/HPFs. (H&E, 400X, Morphometric analysis)

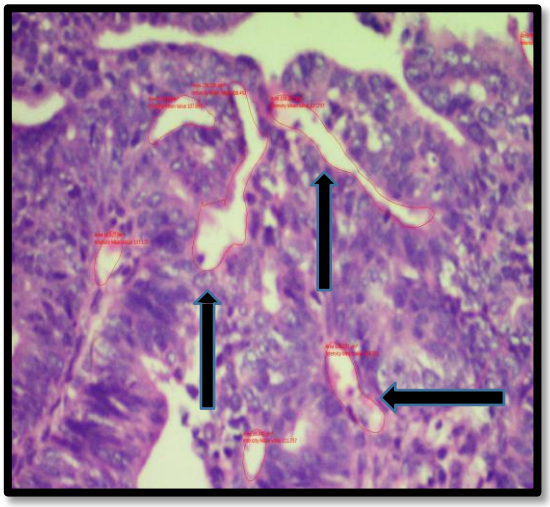


Fig 57 - Microphotograph of Endometrial carcinoma showing large sized blood vessels.

(H&E, 400X, Morphometric analysis)

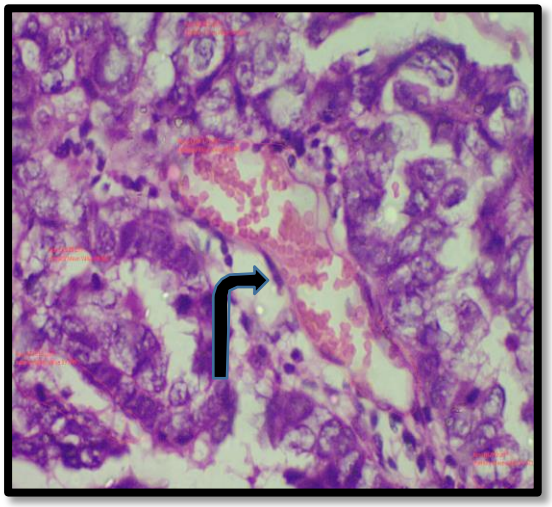


Fig 58 - Microphotograph of Endometrial carcinoma showing vascular irregularities.

(H&E, 400X, Morphometric analysis)

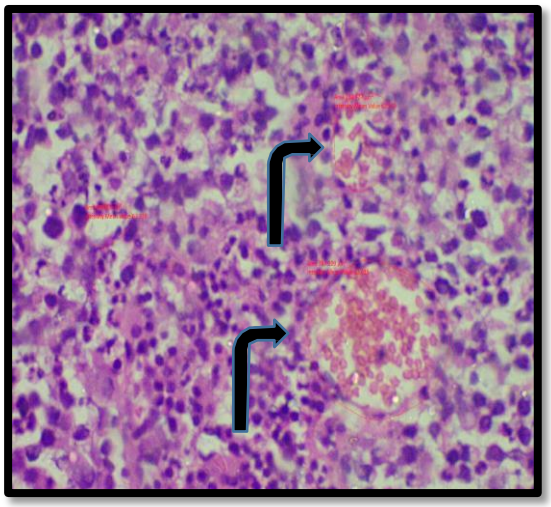


Fig 59 - Microphotograph of Endometrial carcinoma showing severe degree of dilatation.

(H&E, 400X, Morphometric analysis)

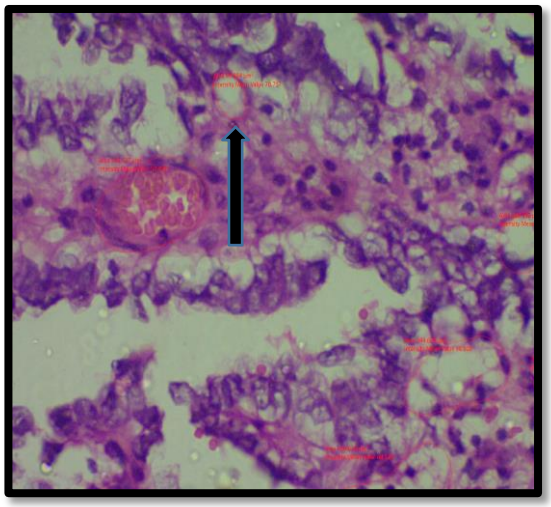


Fig 60 - Microphotograph of Endometrial carcinoma showing vascular congestion.

(H&E, 400X, Morphometric analysis)

DISCUSSION

Endometrial diseases are widespread across whole world, in all age groups and to a great extent are a foremost cause of increased maternal morbidity and mortality. The majority of females with endometrial diseases present with abnormal uterine bleeding. [50]

Histopathological patterns of endometrium in women presenting with AUB is variable.[4] These ranges from simple physiological to much more complex pathological lesions. [50]

In the present study, age group of patients ranged from 20 to 70 years with a mean age of 40.2 years. Similar observations were observed in study done by Behera *et al* [51], Nikethan *et al* [52], Bindroo *et al* [53] , Sajitha *et al* [54].

Table 14: Comparison of Age range and Mean age in different studies and the present study.

Authors	Year	Age range (Yrs)	Mean %
Behera *et al*[51]	2020	17-77	43.25
Nikethan *et al*[52]	2020	20-62	41.2
Bindroo *et al*[53]	2018	19-70	43.3
Sajitha *et al*[54]	2016	23-78	42.95
Present study	2020	20-70	40.2

Table 15: Histopathological categorization of various endometrial lesions in various studies and present study.

Histological findings	Behera et al[51]		Bindroo S *et al*[53]		Bhatt *et al*[55]		Shilpa *et al*[56]		Kumari *et al*[57]		Present study	
	No.	%	No	%	No	%	No.	%	No.	%	No.	%
Proliferative phase	212	38.7	93	37.2	32	26.23	70	35	63	29.03	80	53.3
Secretory phase	121	22.1	85	39.35	20	16.39	53	26.5	27	12.44	41	27.3
DPE	73	13.3	6	2.4	8	6.56	6	3	48	22.12	15	10
Atrophic phase	48	8.7	18	7.2	9	7.38	7	3.5	4	1.84	6	4
SH without atypia	23	4.2	40	16	22	18.03	48	24	32	14.75	4	2.7
Endometrial carcinoma	4	0.7	4	1.6	7	5.74	3	1.5	4	1.84	4	2.7

In the present study, proliferative phase endometrium is the most common histological pattern followed by 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.[51,53,55-57]

In the study done by various authors variety of endometrial patterns were seen in cases of AUB.[51,53,55-57] Blood vessel morphometry study in various conditions such as endometrial polyp, DUB was done by various authors. These authors evaluated average number of blood vessels, area of blood vessels, contour of blood vessels, degree of dilatation and congestion of blood vessels in vascular morphometry.[6,7,41]

Makhija *et al*[6], Hourihan *et al*[58]and Sahasrabudhe *et al*[59] evaluated by counting number of blood vessels viewed in 10 high-power fields (HPFs) per slide and average of count was taken as number of vessels per HPFs. In the present study, similar method was used.

Table 16: Average number of blood vessels per HPF in various studies and present study.

Endometrial lesions	Makhija et al [6]	Khan et al [41]	Present study
Proliferative phase	3.64 ± 0.212	3.4±0.4	3.4±0.4
Secretory phase	3.21 ± 0.141	4.7±0.1	4.3±0.4
DPE	-	3.9±0.8	3.9±0.2
Atrophic phase	3.01 ± 0.50	-	4.0±0.2

In the present study, average number of endometrial blood vessels/HPF in proliferative phase, secretory phase, DPE and atrophic phase was 3.4 ± 0.4 SD, 4.3 ± 0.4 SD 3.9 ± 0.2 SD and 4.0±0.2 SD respectively. Khan *et al* [41] in their study observed similar findings in regards to proliferative and DPE.

In the present study in simple hyperplasia without atypia, average number of blood vessels per HPF was 4.8 ± 0.2 SD. Makhija *et al.*[6] in their study observed that, average number of blood vessels per HPF was 4.47±0.095 in complex hyperplasia.

Khan *et al*[41] in their study observed average number of blood vessels per HPF was 5.0±0.4 in complex hyperplasia without atypia. Our study findings of average number of blood vessels per HPF were co-relating with Makhija *et al*[6] and Khan *et al* [41]. Makhija *et al.*[6] in their study concluded that excessive bleeding in DUB may be related to qualitative changes in the blood vessels[6]. Similar explanation may hold true in the present study.

Nayha *et al.* [7] in their study stated that the number of vessels were increased in well to moderately differentiated endometrial carcinomas as compared to proliferative endometrium and simplex type of hyperplasia. They also observed that vessel number is increased markedly in atypical endometrial hyperplasia as compared to simplex-type of endometrial hyperplasia.[7] Similar results were obtained in the present study.

Table 17: Comparison of mean of size of blood vessels (in μm^2).

Endometrial lesions	Nayha *et al.* [7]	Present study
Proliferative phase	240	133
Atrophic phase	78	99
Simple Hyperplasia without atypia	128	190
Endometrial Carcinoma	258	330

Nayha *et al.* [7] in their study observed that individual vessel size (mean 78 $\mu m^{2)}$ was significantly lower in atrophic endometrium ($p < 0.001$) than in proliferative, hyperplastic or malignant endometrium. Similar results were obtained in the present study.

In the present study, vessel shape irregularities were seen more in endometrial carcinoma, simple hyperplasia without atypia and atrophic phase endometrium as compared to DPE, proliferative and secretory phase endometrium. Similar results were obtained by Nayha *et al.* [7] in their study on angiogenesis in endometrium in preneoplastic and neoplastic lesions. 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 to 50 years in 500 endometrial tissues. In their study, control group included endometrial specimens having normal and regular menstrual cycle and 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 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]

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

Makhija *et al* [6] in his 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, endometrial carcinoma and simple hyperplasia without atypia, 100% vascular congestion of endometrial blood vessels was noted. 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.

Thus, it is possible that the various morphological changes in the endometrial vasculature in DUB and rupture of the dilated and congested vascular channels could be responsible for the abnormal uterine bleeding.[6] Similar explanation can be given 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.[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. Mild degree of dilatation

was observed in 85.7% cases and moderate degree of dilatation in 14.3% of the cases. For degree of dilatation, the difference was statistically significant ($p<0.001$).

Makhija *et al* [6] studied 13 cases of adenomyosis and found no significant difference in the mean of blood vessel concentration as compared to control. Similarly in the present study, 10 cases of adenomyosis were studied and average number of blood vessels/HPF was 4.0 ± 0.6. However the statistical difference was not significant.

Makhija *et al* [6] studied 13 cases of 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. In the present study, 5 cases of endometrial polyp were studied and the average number of blood vessels/HPF was 3.4 ± 0.5.

Khan *et al* [41] studied on morphometric evaluation of endometrial blood vessels and its clinico-pathological relation in patients with dysfunctional uterine bleeding and concluded that the altered vascular morphology in different endometrial patterns in various lesions may be the underlying pathological mechanism for dysfunctional uterine bleeding. Since 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 vascular morphometric evaluation showed significant alteration in endometrial carcinoma and simple hyperplasia without atypia. In these lesions, underlying pathologic mechanisms for AUB may be alteration in the vascular morphology.

Thus many authors mentioned that morphometric analysis of endometrial tissue helps in differentiating various disorders of endometrium. These authors concluded that morphometry can be successfully used to analyse pathological changes in endometrium.[47]

Histopathological examination of vascular morphometry in endometrial tissue is a crucial diagnostic tool in evaluation of AUB and vascular morphometric changes could help in selection of relevant treatment of AUB and this may help to avoid surgical procedure and will also help to reduce the hospital stay and cost of the treatment.[60,61]

SUMMARY

A prospective cross sectional study of endometrial blood vessels in patients presented with AUB was undertaken for morphometric analysis. This study was carried out for a duration of 18 months from 1st December 2018 - 30thMay 2020 in the Department of Pathology, BLDE (Deemed to be University), Shri B. M. Patil Medical College, Hospital & Research Centre, Vijayapura. Paraffin blocks were prepared and tissue section of 3-6 µ thickness were cut as per the standard protocol. H and E staining was done and slides were evaluated for vascular morphometry.

The present study included 150 cases of patients presented with AUB as per the inclusion and exclusion criteria. The mean age of the patients was 40.2 years with most patients in the age group between 31- 40 years (46%).

In the present study, a variety of endometrial patterns were seen in cases of AUB and on blood vessels morphometry various vascular alterations were observed.

Majority of the cases of AUB were clinically diagnosed as DUB accounting for 48%, followed by fibroid (32%).

Out of 150 cases, 64 cases were encountered with specific histopathological diagnosis and 86 cases were diagnosed as non-specific lesions such as chronic non-specific cervicitis.

Out of 64 cases, maximum number of cases were interpreted as DPE, followed by leiomyoma, adenomyosis and endometrial polyp.

Out of 150 cases, majority of the cases showed proliferative phase (53.3%) followed by secretory phase (27.3%), DPE (10%), atrophic phase (6%), endometrial carcinoma (4%) and simple hyperplasia without atypia (4%).

In vascular morphometry, average number of blood vessels, area of blood vessels, contour of blood vessels, degree of dilatation and congestion of blood vessels of endometrial tissue were evaluated. The endometrial blood vessels showed characteristic changes in various lesions of endometrium.

In the present study, Average number of endometrial blood vessels/HPF in endometrial carcinoma, simple hyperplasia without atypia, secretory phase, atrophic phase, DPE and proliferative phase was 5.3 ± 0.2 SD, 4.8 ± 0.2 SD, 4.3 ± 0.4 SD, 4.0 ± 0.2 SD, 3.9 ± 0.2 SD and 3.4 ± 0.4 SD respectively. However, there was no statistically significant difference between the average endometrial blood vessels per HPF in various endometrial lesions.

Endometrial carcinoma and simple hyperplasia without atypia showed more average number of endometrial blood vessels/HPF as compared to proliferative phase, secretory phase, atrophic phase and DPE. Endometrial carcinoma and simple hyperplasia without atypia also showed more number of large sized blood vessels.

Endometrial carcinoma showed significant severe dilatation of endometrial blood vessels. Mild degree of dilatation of endometrial blood vessels was seen in all the cases of atrophic phase endometrium.

Vessel wall irregularities was 100%, 100%, 100%, 86.7%, 72.5% and 63.4% in endometrial carcinoma, simple hyperplasia without atypia, atrophic phase endometrium, DPE, proliferative and secretory phase endometrium respectively. However the difference was statistically not significant.

Vascular congestion of endometrial blood vessels was noted in all cases of atrophic phase, endometrial carcinoma and simple hyperplasia without atypia.

In endometrial polyp, cervical carcinoma and DPE with leiomyoma, small sized blood vessels were more as compared to large sized blood vessels.

Vessel shape irregularities were seen in all cases of adenomyosis with leiomyoma, cervical carcinoma, DPE and Leiomyoma, Endometrial Carcinoma, Endometrial Carcinoma with Leiomyoma and simple hyperplasia without atypia.

In endometrial polyp and DPE with leiomyoma severe degree of dilatation of endometrial blood vessels was observed.

In adenomyosis with leiomyoma and cervical carcinoma, vascular congestion in endometrial blood vessels was observed in all cases. Significant statistical difference was noted as compared to other cases.

In the present study, morphometric parameters like size of blood vessels and vascular dilatation were high in endometrial carcinoma and simple hyperplasia without atypia with statistically significant difference with p value less than 0.001.

CONCLUSION

In cases of Endometrial carcinoma and simple hyperplasia without atypia, average number of endometrial blood vessels/HPF and large sized blood vessels were more as compared to proliferative phase, secretory phase, atrophic phase and DPE. Vessel wall irregularities were seen maximum in endometrial carcinoma, simple hyperplasia without atypia and atrophic phase endometrium as compared to other lesions. However the difference was statistically not significant. Severe dilatation of endometrial blood vessels was significantly high in Endometrial carcinoma. In atrophic phase, endometrial carcinoma and simple hyperplasia without atypia, vascular congestion of endometrial blood vessels was high as compared to other conditions.

Vascular morphometric analysis of endometrial tissue showed varying changes in endometrial blood vessels in different lesions of endometrium and it could be the underlying pathogenetic mechanism of bleeding in patients presented with AUB.

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

However extensive study including control samples of endometrial tissue should be studied to delineate the pathogenesis of abnormal bleeding and role of vascular morphometric assessment.

Limitation of the present study: Less sample size of endometrial lesions such as endometrial carcinoma and simple hyperplasia without atypia. Hence further extensive evaluation with adequate size of endometrial lesions is needed.

Recommendations: Since proliferative and secretory pattern did not show any significant alteration in vascular morphology with regard to mean vascular dilatation and congestion, AUB in these cases may be due to some local molecular mechanism like effects of prostaglandins (PGF2α and PGE2), prostacyclins (PGI2), nitric oxide, reduced levels of endothelin-1 and up regulation of VEGF – A and its receptors e.g. VEGFR-1 and VEGFR-2 which require further studies at molecular level.

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ANNEXURE-I

ETHICAL CLEARANCE

B.L.D.E (Deemed to be University)
SHRI.B.M.PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTRE
VIJAYAPUR – 586103

IEC/NO:286/2018
17-11-2018

INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 13-11-2018 at 03-15 PM scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has accorded Ethical Clearance.

Title : Morphometric evaluation of endometrial blood vessels in patients presenting with abnormal uterine bleeding.

Name of P.G. Student : Dr Neha Mahesh Bhosale.
Department of Pathology.

Name of Guide/Co-investigator: Dr.Surekha.U.Arakeri, Professor of Pathology.

DR RAGHAVENDRA KULKARNI
CHAIRMAN
Institutional Ethical Committee
BLDE(U)'s Shri B.M. Patil
Medical college,BIJAPUR-586103.

Following documents were placed before E.C. for Scrutinization:

1) Copy of Synopsis/Research Project
2) Copy of informed consent form.
3) Any other relevant documents.

ANNEXURE-II

BLDE (DEEMED TO BE UNIVERSITY), SHRI B.M.PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTER, VIJAYAPURAA-586103

INFORMED CONSENT FOR PARTICIPATION IN DISSERTATION/RESEARCH

I, the undersigned,_____, S/O D/O W/O_____, aged_____years, ordinarily resident of_____do hereby state/declare that Dr_____of _____Hospital has examined me thoroughly on _____at_____(place) and it has been explained to me in my own language that I am suffering from _____ disease (condition) and this disease/condition mimic following diseases. Further Doctor informed me that he/she is conducting dissertation/research titled_____under the guidance of

Dr _____ requesting my participation in the study. Apart from routine treatment procedure, the pre-operative, operative, post-operative and follow-up observations will be utilized for the study as reference data.

Doctor has also informed me that during conduct of this procedure adverse results may be encountered. Among the above complications most of them are treatable but are not anticipated hence there is chance of aggravation of my condition and in rare circumstances it may prove fatal in spite of anticipated diagnosis and best treatment made available. Further Doctor has informed me that my participation in this study will help in evaluation of the results of the study which is useful reference to treatment of other similar cases in near future, and also I may be benefited in getting relieved of suffering or cure of the disease I am suffering.

The Doctor has also informed me that information given by me, observations made/ photographs/ video graphs taken upon me by the investigator will be kept secret and not assessed by the person other than me or my legal hirer except for academic purposes.

The Doctor did inform me that though my participation is purely voluntary, based on information given by me, I can ask any clarification during the course of treatment / study related to diagnosis, procedure of treatment, result of treatment or prognosis. At the same time I have been informed that I can withdraw from my participation in this study at any time if I want or the investigator can terminate me from the study at any time from the study but not the procedure of treatment and follow-up unless I request to be discharged.

After understanding the nature of dissertation or research, diagnosis made, mode of treatment, I the undersigned Shri/Smt_____under my full conscious state of mind agree to participate in the said research/dissertation.

Signature of patient:

Signature of doctor:

Witness: 1.

2.

Date:

Place

ANNEXURE-III

PROFORMA

NAME **:** **OP/IP No:**

AGE **:** **HPR No:**

SEX **:** **Lab No:**

Address **:**

Presenting Complaints **:**

Past history **:**

Personal history **:**

Family history **:**

Menstrual history **:**

Obstetric history:

Treatment history **: (Hormonal therapy)**

General physical examination:

Pallor	present/absent
Icterus	present/absent
Clubbing	present/absent
Lymphadenopathy	present/absent
Edema	present/absent
Built	poor/average/well

VITALS: Pulse Rate: Respiratory Rate:

Blood pressure: Temperature:

SYSTEMIC EXAMINATION:

PER SPECULUM AND PER-VAGINAL EXAMINATION:

ULTRASONOGRAPHY FINDINGS:

CLINICAL DIAGNOSIS:

HISTOPATHOLOGICAL STUDY:

i) Morphological diagnosis

ii) Vascular morphometric evaluation.

Table for Vascular Morphometric evaluation:

SL No.	Histopathological diagnosis	Average blood vessels/HPFs	Vessel size: Small/ Large	Vessel Shape irregularities: Present/Absent	Degree of dilatation: Mild/Moderate/ Severe	Vascular congestion Present/Absent

Criteria for morphometric evaluation

Morphometric parameters	Criteria
Average number of blood vessels/HPFs	Calculate average by counting the blood vessels in 10 HPFs (40x)
Size of blood vessel	Small - 16-150 μm^2 Large – 150-1000 μm^2
Vessel shape irregularities	Present Absent
Degree of dilatation	Mild Moderate Severe
Vascular Congestion	Present Absent

KEY TO MASTER CHART

SL NO. - Serial Number

LAB NO. - Laboratory Number

HPR NO. - Histopathology report number

Yrs - Years

HPFs - High Power Fields

EBV - Endometrial Blood Vessels

DUB - Dysfunctional Uterine Bleeding AUB- Abnormal Uterine Bleeding

PID - Pelvic Inflammatory Disease PV- Per vaginal

WDPV - White Discharge Per Vaginally

MASTER CHART

SL NO.	LAB NO.	HPR NO.	NAME	AGE (YRS)	SPECIMEN	COMPLAINTS	CLINICAL DIAGNOSIS	ENDOMETRIAL DIAGNOSIS	HISTOPATHOLOGICAL DIAGNOSIS	AVERAGE NUMBER OF EBV/HPFS	AVERAGE AREA OF E B V	SIZE OF VESSEL	VESSEL SHAPE IRREGULARITIES	DEGREE OF DILATATION OF EBV	VASCULAR CONGESTION
1	36652	1284	Mahirunbi Hainal	30	Hysterectomy without adnexa	WDPV with AUB and Pain in abdomen since 6 years	Fibroid	Secretory phase	Leiomyoma	3.9	349.3375239	Large	Present	Mild	Absent
2	40026	1397	Kalavati Tadalagi	40	Hysterectomy without adnexa	Post menopausal PV bleeding since 1 month	DUB	Proliferative Phase	Endometrial Polyp	3.4	99.04661692	Small	present	Mild	Absent
3	40025	1398	Kashibai Hugimath	40	Hysterectomy without adnexa	Mass per vagina and AUB since 1 year	DUB	Proliferative Phase	Non-specific	3.7	110.412789	Small	present	Mild	present
4	40171	1400	Manjula Gaded	41	Hysterectomy with bilateral adnexa	AUB since 3 months	Endometrial hyperplasia	Proliferative Phase	Leiomyoma	3	101.8359601	Small	present	Mild	present
5	40775	1423	Mainunish Jamadh	52	Biopsy	Menorrhagia since 3 months	DUB	Proliferative Phase	Non-specific	3.5	55.06786249	Small	Absent	Mild	present
6	40813	1425	Jayashree Patil	35	Hysterectomy with bilateral adnexa	AUB since 2 months	Endometrial hyperplasia	Proliferative Phase	Endometrial Polyp	3	127.4161198	Small	present	Mild	Absent
7	40812	1426	Kasturi Kamble	35	Hysterectomy with bilateral adnexa	Per vaginal bleeding since 4 months	Fibroid	Proliferative Phase	Non-specific	4	113.565489	Small	present	Mild	present
8	42212	1480	Laxmibai	58	Hysterectomy with bilateral adnexa	AUB since 2.5 months	DUB	Proliferative Phase	Adenomyosis and Leiomyoma	3.6	124.6399715	Small	present	Mild	present
9	41723	1485	Bhimabai Jadhav	30	Hysterectomy with bilateral adnexa	AUB since 1 month	Endometrial hyperplasia	Proliferative Phase	Non-specific	3.4	135.4327097	Small	present	Mild	present
10	42230	1491	Saraswati Melakari	34	Hysterectomy with bilateral adnexa	WDPV with AUB and Pain in abdomen since 2 years	DUB	Secretory phase	Non-specific	4.2	313.8134013	Large	Absent	Mild	present
11	43804	1517	Davalbi	50	Hysterectomy with bilateral adnexa	Post menopausal PV bleeding since 1 month	Endometrial Cancer	Endometrial Carcinoma	Endometrial Carcinoma with Leiomyoma	5.4	330.8463387	Large	Present	Severe	present
12	42442	1518	Savitribai Madar	32	Hysterectomy with bilateral adnexa	WDPV with AUB and Pain in abdomen since 2 years	DUB	Proliferative Phase	Non-specific	3.5	85.95313482	Small	Absent	Mild	Present
13	43439	1528	Sharada Talwar	37	Hysterectomy without adnexa	per-vaginal bleeding since 2 months	DUB	Proliferative Phase	Non-specific	3	78.83584222	Small	present	Mild	Absent
14	44477	1548	Mahananda Gouri	30	Hysterectomy with bilateral adnexa	AUB since 4 months	Fibroid	Secretory phase	Non-specific	5	188.4709251	Large	present	Mild	present
15	46692	1655	Suhasini Patil	26	Biopsy	Pain in abdomen,menorrhagia since 3 months	Endometrial Polyp	Disordered Proliferative endometrium	Disordered Proliferative endometrium	4	92.79484811	Small	present	Moderate	present
16	46693	1656	Kavita Lamani	38	Hysterectomy with bilateral adnexa	Pain in abdomen,menorrhagia since 1month	DUB	Secretory phase	Adenomyosis	4.9	94.69983324	Small	present	Mild	present
17	48641	1732	Sunita Kagawad	28	Biopsy	Irregular cycles since 3 months	Endometrial hyperplasia	Proliferative Phase	Non-specific	4	68.7602123	Small	present	Moderate	present
18	50099	1792	Shaila Shigubi	37	Hysterectomy with bilateral adnexa	Pain in abdomen,menorrhagia since 3 months	DUB	Proliferative Phase	Non-specific	3.6	305.5055522	Large	Absent	Mild	present

19	51613	1851	Shanta	70	Biopsy	Post menopausal Per vaginal bleeding since 1 year	Endometrial cancer	Endometrial Carcinoma	Endometrial Carcinoma	5.3	361.5102351	Large	present	Severe	present
20	59988	2178	Laxmibai Jadhav	40	Hysterectomy without adnexa	Irregular cycles since 4 months	Fibroid	Proliferative Phase	Non-specific	3	161.2559614	Large	Absent	Mild	present
21	60195	2209	Mahananda Bajantri	29	Hysterectomy without adnexa	Irregular cycles since 3 months	Fibroid	Proliferative Phase	Non-specific	3.4	192.4952223	Large	Present	Moderate	Absent
22	60738	2212	Balabai Karath	45	Hysterectomy with bilateral adnexa	Pain in abdomen,menorrhagia since 1month	DUB	Secretory phase	Adenomyosis	4.1	208.749811	Large	Present	Mild	Present
23	60744	2213	Nasrin Bangi	53	Hysterectomy with bilateral adnexa	WDPV with AUB and Pain in abdomen since 1.5 years	DUB	Proliferative Phase	Non-specific	3.7	207.1661998	Large	Present	Mild	Present
24	60732	2218	Suvarna Maniti B	60	Biopsy	Post menopausal bleeding since 10 days	DUB	Endometrial Carcinoma	Endometrial Carcinoma	5.1	385.2816041	Large	present	Severe	Present
25	61388	2245	Renuka Biradar	38	Hysterectomy with bilateral adnexa	AUB,WDPV with AUB and Pain in abdomen since 6-7months	PID	Secretory phase	Non-specific	4.2	112.7797092	Small	Absent	Mild	present
26	61423	2250	Ningawwa chinamalli	35	Hysterectomy with bilateral fallopian tube	Mass per vagina and AUB since 7 months	PID	Secretory phase	Non-specific	3.9	160.4178015	Large	Present	Mild	Absent
27	63504	2306	Gumabai	38	Hysterectomy with bilateral adnexa	Lower abdominal pain,WDPV,AUB,low backache	DUB	Secretory phase	Non-specific	3.8	103.4280125	Small	Absent	Mild	Present
28	63498	2308	Mahadevi Biradar	56	Hysterectomy with bilateral adnexa	Pain in abdomen and abnormal menses since 1 year	Fibroid	Proliferative Phase	Leiomyoma	3.2	107.2651391	Small	Present	Mild	Absent
29	64835	2344	Shobha chawadikar	48	Hysterectomy without adnexa	Irregular menses since 6 months	DUB	Secretory phase	Adenomyosis	4	81.84028475	Small	Present	Mild	Present
30	64211	2346	Mallamma Biradar	35	Hysterectomy with right sided adnexa	AUB since 4 months	Fibroid	Secretory phase	Leiomyoma	4	130.4848473	Small	Present	Mild	Present
31	68227	2479	Basamma Dalavai	45	Hysterectomy with left sided adnexa	Pain in abdomen with irregular menses since 4 months	DUB WITH PID	Proliferative Phase	Non-specific	3	89.61156697	Small	Present	Mild	Present
32	68913	2517	Gauramma Talikoti	65	Hysterectomy without adnexa	Post menopausal PV bleeding since 6 months	DUB	Atrophic Phase	Non-specific	3.9	85.83352539	Small	Present	Mild	Present
33	69703	2553	Gouramma Hagi	40	Hysterectomy with bilateral adnexa	PV bleeding since 2 months	DUB	Proliferative Phase	Non-specific	3	94.59395067	Small	Present	Mild	Present
34	70379	2585	Ningamma Pujari	35	Hysterectomy with right sided adnexa	Pain in abdomen with irregular menses since 4 months	PID	Proliferative Phase	Non-specific	3.2	115.4248577	Small	Absent	Mild	Present
35	70383	2586	Pandawwa	40	Hysterectomy with bilateral adnexa	PV bleeding since 4 months	DUB	Proliferative Phase	Endometrial Polyp	3.4	54.97144027	Small	Absent	Mild	Absent
36	70384	2589	Tarabai	62	Hysterectomy with bilateral adnexa	Lower abdominal pain and PV bleeding siince 10 months	Fibroid	Proliferative Phase	Leiomyoma	3.4	56.96092713	Small	Absent	Mild	Absent
37	72252	2649	Rukumabai	27	Hysterectomy with right sided adnexa	Pain in abdomen and abnormal menses since 1 year	DUB WITH PID	Secretory phase	Non-specific	3.9	140.5029437	Small	Present	Mild	Absent
38	72250	2654	Bhanath Kalat	45	Biopsy	Menorrhagia since 4 months	Endometrial Polyp	Secretory phase	Non-specific	4.2	75.56366681	Small	Absent	Mild	Present

39	73126	2697	Lalitha Chavan	30	Hysterectomy with bilateral adnexa	WDPV with AUB and Pain in abdomen since 2 months	DUB WITH PID	Proliferative Phase	Non-specific	4	113.3097292	Small	Present	Mild	Absent
40	73201	2704	Sumangla Mallikarjun	40	Hysterectomy with bilateral adnexa	DUB under evaluation	DUB	Proliferative Phase	Non-specific	3	61.96564907	Small	Absent	Mild	Present
41	73867	2715	Anita Patil	40	Hysterectomy with left sided adnexa	DUB/adenomyosis	DUB	Proliferative Phase	adenomyosis	3.5	92.05051072	Small	Present	Moderate	Absent
42	74412	2722	Shantabai Rathod	40	Hysterectomy with bilateral adnexa	Pain in abdomen with irregular menses since 4 months	DUB WITH PID	Secretory phase	Non-specific	4.3	158.644589	Large	Present	Mild	Present
43	74411	2725	Jayashree Shilavanth	40	Hysterectom y without adnexa	Excessive PV bleeding since 6 months	DUB	Proliferative Phase	Non-specific	3.5	46.88766771	Small	Absent	Mild	Present
44	74419	2740	Sonubai Byali	60	Hysterectomy with bilateral adnexa	Mass per abdomen and PV bleeding since 8 days	PID	Proliferative Phase	Non-specific	3.4	236.9237537	Large	Absent	Mild	Absent
45	75129	2757	Sainaj Ainapur	44	Hysterectomy with bilateral adnexa	Menorrhagia since 3 months, mass per vagina	Fibroid	Proliferative Phase	Endometrial Polyp	3.2	65.45639429	Small	Absent	Mild	Absent
46	75656	2770	Mahadevi Talawar	35	Hysterectom y without adnexa	Pain in abdomen with irregular menses since 2months	DUB WITH PID	Proliferative Phase	Non-specific	3	195.3720582	Large	Present	Mild	Absent
47	76717	2790	Sunanda Babanagar	50	Hysterectomy with bilateral adnexa	Excessive PV bleeding,pain in abdomen since 3 months	Fibroid	Secretory phase	Leiomyoma	3.7	97.26280192	Small	Absent	Mild	Present
48	76212	2791	Padma Kulkarni	45	Hysterectom y without adnexa	Menorrhagia since 2 months	Fibroid	Secretory phase	Leiomyoma	4	210.9929059	Large	Absent	Mild	Absent
49	76202	2792	Sugula Bisanal	38	Hysterectom y without adnexa	Excessive bleeding since 8 months	Fibroid	Proliferative Phase	Adenomyosis	4	105.2893435	Small	Present	Moderate	Absent
50	77864	2827	Shantabai Rathod	40	Hysterectomy with bilateral adnexa	Pain in abdomen with irregular menses since 2months	DUB	Secretory phase	Non-specific	4.1	78.41046164	Small	Present	Mild	Present
51	84270	3058	Champavva Madar	40	Hysterectom y without adnexa	Pain in abdomen with abnormal menses since 3 months	Cervical carcinoma	Proliferative phase	Cervical carcinoma	4	127.4682078	Small	Present	Moderate	Present
52	88927	3220	Basamma Gobbur	45	Hysterectomy	Menorrhagia since 5 months	Cervical carcinoma	Proliferative phase	Cervical carcinoma	3	121.613614	Small	Present	Mild	Present
53	94829	3443	Drupati Kakadaki	40	Hysterectomy with bilateral fallopian	Menorrhagia since 2 months	Polyp	Proliferative Phase	Endometrial Polyp and Leiomyoma	3.7	135.53807	Small	Absent	Mild	Present
					bleeding since 3 months	Excessive bleeding since 8 months									
54	95044	3470	Shreedevi Rathod	33	Hysterectomy with bilateral adnexa	PV bleeding since 1 month	DUB	Proliferative Phase	Non-specific	3.2	191.5607256	Large	Present	Mild	Absent
55	99900	3626	Shantamma Hosamani	42	Hysterectomy with bilateral adnexa	Irregular heavy menses since 9 months	PID	Secretory phase	Non-specific	4.5	102.5064074	Small	Absent	Mild	Present
56	102570	3730	Riyanna Shekh	45	Hysterectomy with bilateral adnexa	Lower abdominal pain with PV bleeding since 5 months	Fibroid	Proliferative Phase	Leiomyoma	3.1	76.2618428	Small	Absent	Mild	Absent
57	104901	3827	Gangamma	35	Hysterectomy with left sided adnexa	DUB	Fibroid	Proliferative Phase	Leiomyoma	3.8	165.8507912	Large	Absent	Mild	Absent

58	104597	3836	Parvati Godekar	45	Biopsy	DUB	DUB	Disordered Proliferative endometrium	Disordered Proliferative endometrium	4.2	113.872893	Small	Present	Moderate	Present
59	108008	3917	Sumangla R	22	Biopsy	Menorrhagia since 4 months	DUB WITH PID	Disordered Proliferative endometrium	Disordered Proliferative endometrium	3.9	91.06896654	Small	Present	Moderate	Present
60	198231	3942	Saraswati Hebbal	36	Hysterectomy with right sided adnexa	Polymenorrhoea since 2 years,menorrhagia since 6 months	DUB	Disordered Proliferative endometrium	DPE and Leiomyoma	3.7	100.1485481	Small	Present	Mild	Absent
61	108842	3960	Rajashree	40	Hysterectomy without adnexa	DUB under evaluation	DUB	Proliferative Phase	Leiomyoma	3.9	133.8173942	Small	Present	Moderate	Present
62	108668	3968	Mangalabai	38	Hysterectomy with bilateral adnexa	Pain in abdomen and abnormal menses since 1 year	DUB WITH PID	Proliferative Phase	Non-specific	3.5	91.18073596	Small	Present	Moderate	Present
63	108953	3971	Kamalabai Kori	40	Hysterectomy with bilateral adnexa	Polymenorrhoea ,menorrhagia since 4 months	Endometrial hyperplasia	Secretory phase	Endometrial polyp	4.2	78.3715281	Small	Present	Mild	Present
64	108951	3973	Siddamma Tanakedar	40	Hysterectomy with right sided adnexa	Polymenorrhoea since 2 years,	DUB WITH PID	Secretory phase	Non-specific	5	70.79255419	Small	Present	Moderate	Present
65	110845	4040	Layawwa	25	Hysterectomy with bilateral adnexa	Menorrhagia since 4 months	DUB	Proliferative Phase	Non-specific	3.8	84.02297383	Small	Present	Moderate	Present
66	111718	4057	Sabeena Attar	35	Hysterectomy with right sided adnexa	Irregular menses since 6 months	Fibroid	Proliferative Phase	Non-specific	3.4	133.1330661	Small	Present	Mild	Present
67	111575	4064	Bismilla Nadaf	30	Hysterectomy with bilateral adnexa	Pain in abdomen with irregular menses since 4 months	DUB	Secretory phase	Non-specific	4	135.5867527	Small	Absent	Mild	Present
68	112405	4086	Malabee Balurgi	35	Hysterectomy with bilateral adnexa	Irregular heavy menses since 2 months	DUB	Secretory phase	Non-specific	3.9	86.12219373	Small	Absent	Mild	Absent
69	114009	4160	Bashira Inamdar	29	Biopsy	Menorrhagia since 2 months	Endometrial hyperplasia	Simple hyperplasia without atypia	Simple hyperplasia without atypia	4.9	157.1446983	Large	Present	Moderate	Present
70	115619	4216	Padmawathi siradar	35	Hysterectomy with left sided adnexa	DUB	DUB	Secretory phase	Non-specific	4.5	135.5867527	Small	Absent	Mild	Present
71	115618	4218	Kouraul Rafiq Lati	45	Hysterectomy with bilateral adnexa	Continuous heavy PV bleeding since 2 months	DUB	Secretory phase	Endometrial Polyp and Leiomyoma	4.2	115.3686041	Small	Present	Mild	Absent
72	117725	4307	Laxmibai Hosamani	50	Biopsy	Post menopausal bleeding since 15 days	Fibroid	Proliferative Phase	Non-specific	3	94.17421639	Small	Absent	Mild	Present
73	120758	4407	Vitabai Pujari	42	Biopsy	Continuous menoorhagia since 5 months, Endometrial hyperplasia 1.2x8mm	DUB	Disordered Proliferative endometrium	Disordered Proliferative endometrium	3.8	99.56251614	Small	Present	Moderate	Absent
74	120699	4409	Anusabai Biradar	46	Hysterectomy with right sided adnexaExcessive bleeding since 4 months	Menorrhagia since 4 months	DUB	Proliferative Phase	Non-specific	4	193.3611822	Large	Present	mild	Present
75	121575	4443	Vani H	29	Biopsy	Continuous bleeding since 1 month	DUB	Disordered Proliferative endometrium	Disordered Proliferative endometrium	4.1	113.0490026	Small	Present	Moderate	Present

76	124154	4581	Laxmi	40	Hysterectomy with left sided adnexaExcessive bleeding since 4 months	PV bleeding since 3 months	Endometrial Polyp	Proliferative phase	Endometrial Polyp and Leiomyoma	3	77.15575925	Small	Present	Mild	Absent
77	124155	4582	Sujata	38	Hysterectomy with bilateral adnexa	Frequent menses since 2 months	DUB	Secretory phase	Adenomyosis	3.8	110.4724492	Small	Present	Moderate	Present
78	125996	4611	Sumitra	35	Hysterectomy without adnexa	DUB	DUB	Proliferative phase	Non-specific	3.5	92.52435824	Small	Absent	Moderate	Present
79	126665	4643	Bibifatima Patel	42	Hysterectomy with bilateral adnexa	AUB	DUB	Proliferative Phase	Non-specific	3.5	116.8202571	Small	Present	Mild	Absent
80	126480	4651	Nilavva Bandi	45	Hysterectomy with bilateral adnexa	Post menopausal bleeding since 1 month	DUB WITH PID	Atrophic Phase	Non-specific	3.7	126.7202254	Small	Present	Mild	Present
81	127566	4675	Ambika Koti	38	Hysterectomy without adnexa	DUB	DUB	Proliferative Phase	Non-specific	4	79.1116427	Small	Absent	Mild	Present
82	127900	4709	Shobha Hallur	32	Biopsy	Irregular menses since 3 months	DUB	Disordered Proliferative endometrium	Disordered Proliferative endometrium	3.6	108.3318389	Small	Absent	Mild	Absent
83	129122	4738	Shreedevi Goundi	31	Hysterectomy with bilateral adnexa	Abnormal menses since 4 months	PID	Secretory phase	Non-specific	4	92.20975196	Small	Present	Moderate	Absent
84	129118	4739	Hameda	35	Hysterectomy with right sided adnexaExcessive bleeding since 4 months	Menorrhagia since 40 days	DUB	Secretory phase	Non-specific	4.3	74.91412853	Small	Absent	Moderate	Present
85	129123	4740	Rajashree Pawar	43	Hysterectomy with bilateral adnexa	Dysmenorrhoea, PV bleeding since 2 months	DUB	Proliferative phase	Adenomyosis	4	85.67835622	Small	Absent	Mild	Absent
86	128729	4741	Neelamma Kakkamari	45	Hysterectomy with bilateral adnexa	AUB since 3 months	Fibroid	Proliferative phase	Endometrial Polyp and Leiomyoma	3.4	174.8503254	Large	Present	Mild	Absent
87	129115	4751	Gurudevi Hotti	45	Hysterectomy with right sided adnexaExcessive	bleeding since 4 months	DUB	Proliferative phase	Non-specific	3.2	87.34387416	Small	Absent	Mild	Present
88	130446	4819	Gouravva Biradar	35	Hysterectomy with bilateral adnexa	irregular menses since 3 months	Fibroid	Proliferative Phase	Adenomyosis	3.7	340.4089845	Large	Absent	Mild	Absent
89	131906	4836	Paraveen Asangi	40	Biopsy	DUB	DUB	Secretory phase	Non-specific	4.2	130.6377456	Small	Absent	Mild	Absent
90	132642	4870	Rukmabai	55	Hysterectomy with bilateral adnexa	Abnormal PV bleeding since 1 month	Fibroid	Proliferative Phase	Leiomyoma	3.2	124.9639467	Small	Present	Moderate	Absent
91	132592	4890	Bhuvaneshwari Natikar	32	Biopsy	AUB since 2 months	Fibroid	Secretory phase	Non-specific	4.6	68.73896111	Small	Absent	Mild	Present
92	132877	4904	Lalamba Police	40	Hysterectomy with right sided adnexaExcessive bleeding since 4 months	Menorrhagia since 2 months	DUB	Proliferative Phase	Non-specific	3.2	79.34948098	Small	Present	Severe	Absent
93	132878	4906	Bagamma Naikodi	41	Hysterectomy with right sided adnexaExcessive bleeding since 4 months	AUB since 25 days	DUB	Secretory phase	Non-specific	4.8	111.5129551	Small	Absent	Mild	Present
94	132910	4910	Bebu Rathod	35	Hysterectomy with bilateral adnexa	AUB since 15 days	DUB WITH PID	Secretory phase	Non-specific	4	136.6437358	Small	Present	Moderate	Absent

95	132852	4917	Dawalabi	27	Hysterectomy with right sided adnexaExcessive bleeding since 4 months	Menorrhagia since 2 months	DUB	Secretory phase	Non-specific	4.5	115.5047373	Small	Present	Mild	Present
96	133477	4924	Gangabai	30	Hysterectomy with bilateral adnexa	Pain in abdomen with irregular menses since 3 months	PID	Proliferative Phase	Non-specific	3.7	166.514019	Large	Present	Moderate	Present
97	135134	4979	B.Geeta Pujari	41	Hysterectomy with bilateral adnexa	DUB	DUB	Proliferative Phase	Non-specific	3.2	166.514019	Large	Absent	mild	Present
98	136572	5013	Jyothi Pawar	42	Hysterectomy with bilateral adnexa	AUB	DUB WITH PID	Secretory phase	Non-specific	4.3	87.47060453	Small	Absent	Mild	Absent
99	135739	5022	Jayashree Bansode	26	Biopsy	Pain in abdomen with DUB	DUB	Secretory phase	Non-specific	5	67.74889908	Small	Present	Mild	Absent
100	136958	5046	Kasturibai Hilli	48	Biopsy	Post menopausal bleeding since 1 month	Endometrial carcinoma	Disordered Proliferative endometrium	Disordered Proliferative endometrium	3.5	83.71451533	Small	Present	Moderate	Present
101	137900	5100	Sidamma Kumbhar	31	Biopsy	Continuous PV bleeding since 20 days	DUB	Disordered Proliferative endometrium	Disordered Proliferative endometrium	4	123.339378	Small	Present	Moderate	Present
102	141107	5190	Sunanda Shirabalshetti	45	Biopsy	PV bleeding since 1 week	DUB	Disordered Proliferative endometrium	Disordered Proliferative endometrium	3.7	62.84813872	Small	Absent	Moderate	Present
103	160041	5790	Mangala Patil	40	Hysterectomy with bilateral adnexa	Menorrhagia under evaluation	DUB	Proliferative Phase	Non-specific	4	97.10133171	Small	Present	Mild	Absent
104	185095	6605	Basamma Madar	40	Hysterectomy with bilateral adnexa	Irregular menses since 20 days	Fibroid	Proliferative Phase	Adenomyosis and Leiomyoma	3.2	226.757552	Large	Present	Mild	Present
105	185938	6606	Mangala Rathod	35	Hysterectomy with bilateral adnexa	PV bleeding since 10 days	Endometrial hyperplasia	Secretory phase	Non-specific	4.1	226.757552	Large	Present	Mild	Present
106	186169	6609	Nagamma Geeja	37	Hysterectomy with bilateral adnexa	Lower abdominal pain with menorrhagia since 2 months	DUB	Proliferative Phase	Non-specific	4	149.3727219	Small	Present	Mild	Present
107	186282	6614	Sangeeta Narale	28	Hysterectomy with bilateral adnexa	Lower abdominal pain with menorrhagia since 2 months	DUB	Proliferative Phase	Non-specific	3.7	99.75161081	Small	Present	Moderate	Present
108	186689	6616	Parubai Mane	42	Hysterectomy with bilateral adnexa	Irregular menses since 3 months	Fibroid	Secretory phase	Adenomyosis	4.8	75.56366681	Small	Present	Mild	Present
109	186601	6623	Laxmi Pujari	35	Hysterectomy with bilateral adnexa	PV bleeding since 2 months	Fibroid	Secretory phase	Leiomyoma	4.7	196.132649	Large	Present	Mild	Present
110	186838	6641	Jayashree Vandal	41	Hysterectomy with bilateral adnexa	PV bleeding since 4 months	Fibroid	Secretory phase	Adenomyosis and Leiomyoma	5	111.8463288	Small	Present	Moderate	Present
111	186843	6642	Bharati Hosamani	35	Hysterectomy with bilateral adnexa	Irregular menses since 3 months	Fibroid	Proliferative Phase	Non-specific	4	98.00046693	Small	Present	Mild	Present
112	187569	6645	Manjula Kalaburgi	42	Hysterectomy with bilateral adnexa	PV bleeding since 2.5 months	Fibroid	Proliferative Phase	Leiomyoma	3.5	143.5148556	Small	Present	Mild	Present
113	187516	6659	Kasturibai Tolabaqal	35	Biopsy	Menorrhagia since 2 months	DUB	Proliferative Phase	Non-specific	3	144.1951988	Small	Present	Mild	Present
114	187848	6677	Shantawwa Dombali	32	Hysterectomy with bilateral adnexa	AUB since 3 months	DUB	Secretory Phase	Non-specific	4.2	149.4315171	Small	Present	Mild	Present
115	188408	6687	Yallawwa	35	Hysterectomy with bilateral adnexa	Irregular menses since 6 months	DUB	Proliferative Phase	Non-specific	3	155.2531774	Large	Present	Moderate	Present

116	189294	6725	Shabana Shikeh	35	Hysterectomy with bilateral adnexa	PV bleeding since 4 months	DUB	Atrophic Phase	Non-specific	4.1	99.47493121	Small	Present	Mild	Present
117	189295	6740	Bhuneshwari	30	Hysterectomy with bilateral adnexa	Abdominal pain and PV bleeding since 6 months	DUB	Secretory Phase	Non-specific	4	120.5703026	Small	Present	Mild	Present
118	189279	6748	Sumitra	65	Hysterectomy with bilateral adnexa	Irregular menses since 4 months	DUB	Proliferative Phase	Non-specific	4	127.9466201	Small	Present	Mild	Present
119	189475	6755	Chandabee	42	Hysterectomy with bilateral adnexa	Menorrhagia since 6 months	Fibroid	Proliferative Phase	Non-specific	3.7	107.3540297	Small	Present	Mild	Present
120	190773	6772	Marilingamma Hosamani	50	Hysterectomy with left sided adnexa	Post-menopausal bleeding since 3 months	Fibroid	Atrophic Phase	Non-specific	4	66.70398276	Small	Present	Mild	Present
121	191472	6781	Shreedevi Karadi	29	Biopsy	Polymenorrhagia since 2 months	DUB	Simple Hyperplasia without atypia	Simple Hyperplasia without atypia	4.9	178.3102489	Large	Present	Severe	Present
122	191446	6787	Savita Honakambale	35	Hysterectomy with bilateral adnexa	Lower abdominal pain with menorrhagia since 2 months	PID WITH DUB	Proliferative Phase	Non-specific	3	214.5851157	Large	Present	Moderate	Present
123	192348	6816	Parvati Jalwadi	45	Hysterectomy with bilateral adnexa	Pain in abdomen and irregular menses since 3 months	DUB	Atrophic Phase	Non-specific	4.1	71.19044025	Small	Present	Mild	Present
124	192281	6820	Renuka Sukhadev Shivasharam	40	Hysterectomy without bilateral adnexa	AUB since 20 days	PID WITH DUB	Secretory Phase	Non-specific	4.2	115.8873387	Small	Present	Mild	Present
125	191686	6831	Kavita Hanjagi	45	Hysterectomy without bilateral adnexa	Post-menopausal PV bleeding since 1month	PID WITH DUB	Secretory Phase	Non-specific	4.4	197.1742047	Large	Present	Moderate	Present
126	192464	6835	Mumtaj Begum	55	Hysterectomy with bilateral adnexa	Post menopausal bleeding since 2 months	DUB	Proliferative Phase	Non-specific	4	216.0919116	Large	Present	Moderate	Present
127	192465	6836	Kasturi Bandiwaddar	50	Hysterectomy with Right sided adnexaMenorrhagia and polymenorrhagia since 40 days	Menorrhagia since 3 months	DUB	Proliferative Phase	Non-specific	4	115.1680799	Small	Present	Mild	Present
128	194700	6914	Asmar Daliya	22	Biopsy	Abnormal uterine bleeding since 3 months	DUB	Proliferative Phase	Non-specific	3.9	135.6890722	Small	Present	Mild	Present
129	194595	6938	Kantabai Mainalli	40	Biopsy	Irregular heavy menstrual bleeding since 2 months	DUB	Disordered Proliferative endometrium	Disordered Proliferative endometrium	3.9	132.2435337	Small	Present	Mild	Present
130	195100	6941	Shamshadi Anesur	25	Biopsy	Continuous bleeding since 25 days	Fibroid	Proliferative Phase	Non-specific	3.7	120.3112458	Small	Present	Mild	Present
131	205471	7175	Sugarabi Makandar	67	Hysterectomy with bilateral adnexa	PV bleeding since 6 months	Endometrial Carcinoma	Endometrial Carcinoma	Endometrial Carcinoma	5.5	242.5404724	Large	Present	Severe	Present
132	206982	7212	Suvarna Jagadaskar	35	Biopsy	Menorrhagia since 4 months	Endometrial hyperplasia	Disordered Proliferative endometrium	Disordered Proliferative endometrium	3.6	257.937731	Large	Present	Moderate	Present

133	207977	7234	Shantabai Kumbar	45	Hysterectomy with Left sided adnexaMenorrhagia and polymenorrhagia since 40 days	PV bleeding since 3 months	DUB	Proliferative Phase	Adenomyosis	3	160.4092822	Large	Present	Moderate	Present
134	207981	7238	Siddamma Pujari	45	Hysterectomy with Left sided adnexaMenorrhagia and polymenorrhagia since 40 days	Pain in abdomen and irregular menses since 6 years	DUB	Proliferative Phase	Non-specific	3	99.71757817	Small	Absent	Mild	Present
135	208231	7243	Laxabai Jambagi	45	Hysterectomy with bilateral adnexa	Heavy post-menopausal bleeding since 2 months	DUB	Proliferative Phase	Non-specific	3	179.6802319	Large	Present	Moderate	Absent
136	208747	7276	Meenakshi Jolad	45	Biopsy	PV bleeding since 15 days	Endometrial hyperplasia	Disordered Proliferative endometrium	Disordered Proliferative endometrium	4	167.8506809	Large	Present	Moderate	Present
137	210830	7305	Channamma	38	Hysterectomy with bilateral adnexa	DUB since 1 month	DUB	Proliferative Phase	Non-specific	3	164.3003742	Large	Present	Moderate	Present
138	215051	7399	Seetabai Magaleri	48	Hysterectomy with bilateral adnexa	DUB since 20 days	DUB	Proliferative Phase	Non-specific	3.2	190.1990473	Large	Present	Mild	Present
139	9537	345.2	Shantamma Gudadinni	55	Hysterectomy with bilateral adnexa	PV bleeding since 10 days	Cervical Carcinoma	Atrophic Phase	Cervical carcinoma	4.2	149.4542852	Small	Present	Mild	Present
140	21749	831.2	Mallawwa Dalawai	50	Biopsy	AUB with mild anemia	Endometrial hyperplasia	Disordered Proliferative endometrium	Disordered Proliferative endometrium	3.8	120.3112458	Small	Present	Mild	Present
141	21820	839.2	SumitraTadlagi	45	Hysterectomy with bilateral adnexa	PV bleeding since 1 month	Endometrial polyp	Proliferative phase	Endometrial Polyp and Leiomyoma	3	155.2531774	Large	Present	Moderate	Present
142	23189	900	Sunanda Mokashi	47	Hysterectomy with bilateral adnexa	PV bleeding since 2 months	Fibroid	Proliferative phase	Leiomyoma	3	129.2512496	Small	Present	Mild	Present
143	22754	916	Sunanda Salutgi	35	Hysterectomy with bilateral adnexa	PV bleeding since 2 months	DUB	Proliferative phase	Non-specific	3	118.5131194	Small	Present	Mild	Present
144	23817	930	Laxmi Biradar	45	Hysterectomy with Left sided adnexaMenorrhagia and polymenorrhagia since 40 days	Polymenorrhoea and menorrhagia since 2 years	DUB	Proliferative phase	Non-specific	3.4	167.4294615	Large	Present	Moderate	Present
145	23825	931	Saidabee Jainapure	55	Hysterectomy with bilateral adnexa	Post menopausal bleeding since 3 months	Fibroid	Proliferative phase	Adenomyosis and Leiomyoma	3	115.9531781	Small	Present	Mild	Present
146	24330	942	Chinnamma	30	Biopsy	PV bleeding since 15 days	Endometrial hyperplasia	Simple Hyperplasia without atypia	Simple Hyperplasia without atypia	4.4	245.5897412	Large	Present	Severe	Present
147	58467	955	Sailaja Nigadi	40	Hysterectomy with bilateral adnexa	PV bleeding since 2 months	Fibroid	Proliferative phase	Non-specific	3.4	276.8757329	Large	Present	Moderate	Present
148	47773	1834	Bhavani Gatage	40	Biopsy	Heavy menstrual bleeding since 20 days,pain in abdomen	Endometrial hyperplasia	Simple hyperplasia without atypia	Simple Hyperplasia without atypia	4.8	179.6802319	Large	Present	Moderate	Present

149	48544	1855	Prema mang	38	Hysterectomy with right sided adnexaMenorrhagia and polymenorrhagia since 40 days	Heavy menstrual bleeding since 1 month	DUB	Proliferative phase	Non-specific	3.8	190.1990473	Large	Present	Mild	Present
150	48727	1884	Deepa Patil	40	Biopsy	AUB since 40 days	Endometrial hyperplasia	Disordered Proliferative endometrium	Disordered Proliferative endometrium	4	123.339378	Small	Present	Mild	Present