SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, KOLAR, KARNATAKA

ETHICS COMMITTEE CERTIFICATE

This is to certify that the Ethics committee of Sri Devaraj Urs Medical College, Tamaka, Kolar has unanimously approved **Dr. VELICHETI SATYA SREE,** post-graduate student in the subject of **OBSTETRICS AND GYNAECOLOGY** at Sri Devaraj Urs Medical College, Kolar to take up the dissertation work entitled **"ENDOMETRIAL STUDY OF PERIMENOPAUSAL ABNORMAL UTERINE BLEEDING BY TRANSVAGINAL SONOGRAPHY AND ITS CORRELATION WITH HISTOPATHOLOGY**

" to be submitted to **SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCHCENTRE, TAMAKA, KOLAR.**

Member Secretary

Sri Devaraj Urs Medical College,

Kolar–563101

Date :

Place : Kolar

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Dr VELICHETI SATYA SREE

LIST OF ABBREVIATIONS

CA : Carcinoma

CHWOA : Complex hyperplasia without atypia

CHWA : Complex hyperplasia with atypia

DM : Diabetes mellitus

DPE : Disoredered proliferative endometrium

D & C : Dilatation and curettage

EH : Endometrial hyperplasia

ET : Endometrial thickness

HTN : Hypertension

IA : Inadequate

IE : Inactive endometrium

IRE : Irregular endometrium

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ABSTRACT

ENDOMETRIAL STUDY OF PERIMENOPAUSAL ABNORMAL UTERINE BLEEDING BY TRANSVAGINAL SONOGRAPHY AND ITS CORRELATION WITH HISTOPATHOLOGY

INTRODUCTION:

The prevalence of abnormal uterine bleeding is high in kolar region, so we want to estimate the minimum endometrial thickness that needs to be evaluated for biopsy to eliminate unnecessary invasive procedures. Age of onset of perimenopausal transition for 95% is 39-51 years of age.

Abnormal uterine bleeding occurring as heavy cyclical or acyclical flow at perimenopausal age is alarming and needs thorough evaluation, as it could be the only clinical manifestation of genital malignancy. The risk of endometrial cancer is reduced from 5%-10% to under 1% with negative test (endometrial thickness below 10mm) such that no further testing is necessary unless symptoms persist. A positive ultrasound necessitates endometrial biopsy.

This study is conducted to evaluate abnormal uterine bleeding cause for patients coming to R.L.JALAPPA HOSPITAL, KOLAR.

AIMS AND OBJECTIVES:

1. To evaluate endometrial causes of abnormal uterine bleeding in perimenopausal women.

2. To correlate transvaginal sonography findings with histopathology of endometrial biopsy.

METHODS: This is a prospective observational study conducted in R.L.Jallapa Hospital and Research centre, Department of Obstetrics and Gynecology, attached to Sri devaraj urs Medical College, Kolar during June 2017 to July 2018. A total of 80 perimenopausal women with abnormal uterine bleeding were included in the study.

RESULTS:

The present study included 80 women of perimenopausal age group with abnormal uterine bleeding. Among these 54% belonged the age group of 40-44 years. Most perimenopausal women with abnormal uterine bleeding were biparous (58.7%). Maximum number of patients (68%) had endometrial thickness of 10-14mm on TVS. The most common presenting symptom among perimenopausal women with abnormal uterine bleeding is menorrhagia (35%), followed by polymenorrhea (25%). Most of the patients presented with symptoms with duration of <30days (47.5%). Most of the perimenopausal women with abnormal uterine bleeding (45.3%) have no associated comorbidity. Most common histopathological finding was proliferative endometrium (42.5%), followed by secretory endometrium (17.5%). The TVS among perimenopausal women presenting with abnormal uterine bleeding is mostly normal (52.5%). TVS showed good correlation with histopathology findings for submucosal fibroied, endometrial hyperplasia and endometrial polyp. One case was diagnosed with endometrial carcinoma who presented with oligomenorrhea, the TVS showed endometrial hyperplasia and the ET was >20mm. TVS can be taken as a diagnostic tool in settings where hysteroscopy is not available. Out of the 80 histopathology reports 3 samples were reported

as inadequate. Pipelle's aspiration is an office based procedure which is patient friendly, no necessity for anesthesia and no need for dilatation.

CONCLUSION:

The combination of TVS with endometrial sampling by pipelle's aspiration can supplement the shortcomings of dilatation and curettage. Pipelle's aspiration is an office based procedure; without the need for anesthesia. Transvaginal sonogram is a simple and convenient technique to indirectly visualize the endometrial cavity. The incorporation of transvaginal scan into a gynecological office setting along with bimanual pelvic examination can enhance our anatomic diagnosis. This study proves that transvaginal findings correlate well with the histopathological findings.

KEYWORDS: **perimenopausal women, abnormal uterine bleeding, transvaginal scan, pipelle's endometrial biopsy.**

Introduction

INTRODUCTION

Perimenopause is defined by WHO as "the period in time beginning 2-8 years before the final menstrual period (FMP) and lasting up to 12 months after the FMP".[1]The perimenopause is often characterized by irregularities in the menstrual cycle in volume and frequency mostly is due to fluctuating estrogen levels. [2]

Perimenopausal bleeding is the excessive bleeding which occurs near the age when the menopause might be expected. [3]Although irregular bleeding patterns are normal and expected part of perimenopause, incidence of uterine pathology and associated medical complications increase in this age group.[2]

Long anovulatory periods along with unopposed estrogen stimulation may result in endometrial hyperplasia and thus increasing the risk of endometrial cancers. This makes the AUB in the perimenopausal age group assumes great significance.[4]It is better to regard any bleeding which is heavier in amount, longer in duration, or acyclical, occurring in a woman over 40 years of age, as requiring immediate and careful investigation with the possibility of malignant disease ever in mind. [3]

AUB is defined as bleeding that is excessive or occurs of normal cyclic menstruation. AUB is one of the most common symptoms encountered in gynecology OPD and accounts to about 12% of consultations in any given gynecology OPD.[4]It affects 20-30% of women in the reproductive age group and up to 50% of the perimenopausal age group women.[4]

Cancer of the uterus is found in less than 5% of women complaining of premenopausal bleeding so careful evaluation is required.[3]

Women with abnormal uterine bleeding the incidence of endometrial carcinoma are about 10%. This risk is increased at least five fold in women with a history suggesting of unopposed estrogen use. There is decreased risk of endometrial carcinoma by more than two thirds in women taking a combination of estrogen and progestin.[6]

Malignant precursors such as complex endometrial hyperplasia are seen more commonly during the menopausal transition. As early diagnosis is the most effective way to improve a woman's prognosis, perimenopausal women with abnormal uterine bleeding should undergo an endometrial biopsy to rule out any malignant condition.[6]

46-66 % of all hysterectomies are done for abnormal uterine bleeding. [6]

The diagnosis of the exact cause of AUB can be challenging, because of its wide range of differential diagnosis, in spite of detailed history, various blood tests, and a thorough examination involving transvaginal ultrasonography (TVS), the cause of bleeding is established in only 50 – 60 % of the cases.[6]

The International Federation of Gynecology and Obstetrics, has recently developed a classification system (PALM – COEIN) for the cause of AUB in non – gravid women of reproductive age group. [7]

The categories are arranged according to the acronym PALM – COEIN: polyp, adenomyosis, leiomyoma, malignancy and hyperplasia, coagulopathy, ovulatory dysfunction, endometrial, iatrogenic and not yet classified. [7]

The main concern in perimenopausal bleeding is that it could be the only external manifestation of a hidden serious pathology such as Endometrial carcinoma. Endometrial hyperplasia which is a precursor of endometrial carcinoma and is a common finding in women with perimenopausal bleeding.

Curettage has been considered to be the gold standard for diagnosis of perimenopausal bleeding, but it has many shortcomings. Dilatation and curettage has a failure rate of 12-29% (Arthur etal).

With transvaginal sonogram studying the endometrium for detecting malignant lesions or their precursors at an earlier stage can be done. The thickness and internal echo texture of the endometrium at various phases of the menstrual cycle as seen in Transvaginal Sonogram correlates well with endometrial histology.

The echogenicity of the endometrium is specific characteristics for various phases of the menstrual cycle, thus enabling the histology to be evaluated with precision by examining with TVS.

Endometrial carcinoma can be diagnosed at an earlier stage by loss of sub endometrial halo, later on myometrial invasion is accurately documented.

Other pathologic conditions of the endometrium and myometrium such as myomatous polyps, endometrial polyps and Adenomyosis are also well visualized.

Thus with transvaginal sonogram the endometrial pathology can be visualized whereas dilatation and curettage is a blind procedure. So transvaginal sonogram can be used as an initial diagnostic Procedure.

By this study we want to correlate the findings of the two diagnostic modalities used in the evaluation of women with perimenopausal bleeding namely transvaginal sonogram and Histopathological examination by pipelle's endometrial aspiration.

Objectives

OBJECTIVES

1 To evaluate endometrial causes of abnormal uterine bleeding in perimenopausal women.

2 To correlate transvaginal sonography findings with histopathology of endometrial biopsy.

Review of Literature

REVIEW OF LITERATURE

HISTORY REVIEW:

Abnormal vaginal bleeding after the age of 40 years requires further evaluation to exclude the presence of endometrial polyps, hyperplasia, fibroids or carcinoma.

The invention of dilatation and curettage is generally attributed to Recaimer in the 1840s. He went on to develop a tool for scraping the lining of the uterus and 'fungoides'- the ' subacute curette'.

In 1882, Moriche obtained first endometrial sample using a catheter whereas since 1935 endometrial biopsies have been performed in outpatient setting.

In 1930s endometrial biopsy was performed without cervical dilatation using narrow metal cannula with side opening and syringe attached for suction. This method caused significant cramping during removal.

In 1970, vabra aspirator was introduced. Endometrial sampling with the vabra aspirator requires no anesthesia and has few complications. The difficulty with the vabra aspirator and similar devices, such as the Novak curette, is that they cause discomfort to some women and require a motorized pump with capital outlay.

Pipelle has been extensively studied as an office endometrial sampler. It has been studied in comparison with the Vabra Aspirator, Novak curette, Tis-u-trap, Accurette and Explora.
The Pipelle's is equal to or better than these samplers with regard to histological analysis and patient comfort. Although it samples only 4.2% of the endometrial surface area compared with 41.6% by the Vabra Aspirator, it produces a greater quantity of total tissue.

Endometrial cytology had higher diagnostic accuracy higher than dilatation and curettage.
Endometrial cytology showed sensitivity of 83.3% and specificity of 95.4% and had 95% correlation with cytological and histological findings.

A meta-analysis conducted to assess the accuracy of endometrial sampling devices in detection of endometrial carcinoma and hyperplasia concluded that endometrial biopsy with pipelle's is superior to other endometrial techniques in detection of endometrial carcinoma and atypical hyperplasia and is more accurate in Post-menopausal than pre-menopausal women.
In a recent meta-analysis of methods of endometrial sampling, sensitivity for detection of endometrial carcinoma was in the range of 25–100%.

A study was conducted at Shifa College of Medicine, Islamabad, on 100 patients to compare pipelle's endometrial biopsy to D&C specimens. The adequacy of sample obtained by pipelle's biopsy was 100% with sensitivity, specificity, positive predictive value and negative predictive value of pipelle's 100% for diagnosing secretory endometrium, hyperplasia and carcinoma.

Russian scientist SergelSokolven in 1929 emphasized the potential importance of sonar and is regarded as ―Father of ultrasound.[7]

The technique of TVS was first introduced in the ultrasound literature in 1984 by Schwimer S.R and lebonce.J, used 5MHz,13mm transducer that was not specifically designed for vaginal work.[8]

Although the comparison of their vaginal and abdominal images was impressive, this form of scanning did not become popular until several years later, when specifically designed vaginal probes were introduced.

PERIMENOPAUSAL BLEEDING

Perimenopausal bleeding is the excessive bleeding which is common at the age when the menopause might be expected.

Cancer of the uterus is found in < 5% of women with premenopausal bleeding.[3]

All bleeding should be cleared within 1 month; if not, or if it recurs afterwards, hysteroscopy and endometrial sampling are essential.

Endometrial cancer should be suspected in any perimenopausal women with abnormal uterine bleeding.

In women with abnormal uterine bleeding the risk is about 10%. [3]

This risk is increased by fivefold in women with history of unopposed estrogen use and decreased by more than two thirds in women on treatment of combination of estrogen and progestin.

Malignant precursors such as complex endometrial hyperplasia become more common during the menopausal transition.

As early diagnosis is the most effective way to for better prognosis, perimenopausal women with abnormal uterine bleeding should undergo an endometrial biopsy to exclude a malignant condition.

CLASSIFICATION OF ABNORMAL UTERINE BLEEDING:

Abnormal uterine bleeding is of two types:

- Anovulatory (80%):
  1. Metropathia haemorrhagica
  2. Threshold bleeding
- Ovulatory (20%):
  1. Idiopathic ovulatory menorrhagia
  2. Luteal phase defect

Anovulatory bleeding [9,10]

Metropathia haemorrhagica

The LH surge in mid-cycle triggers ovulation. But in the perimenopausal age group, the ovarian follicles do not grow into the dominant follicle and this leads to the absence of ovulation. Because of this in the presence of unopposed estrogen the endometrial proliferation is seen followed by profuse, painless, prolonged bleeding that may continue to even 30 days.

The endometrium is mostly associated with cystic, hyperplastic and irregularly dilated glands, tortuous, dilated and thin walled spiral arteries with thrombi formation and increased vascularization. The superficial endometrium undergoes necrosis this leads to histopathological examination finding of the typical „Swiss cheese pattern" appearance.

Threshold bleeding

This is seen in perimenopausal woman due to inadequate follicular development which leads to the low levels of estrogen but almost no progesterone for the endometrium to sustain.

Ovulatory bleeding

It is associated with cyclical abdominal pain with bleeding or premenstrual spotting.

Idiopathic ovulatory menorrhagia

This is due to abnormal ratio of PGE and PGF2α present in the endometrium causing increase in PGE and reduced thromboxane production, this causes increased activity of the fibrinolytic pathway. Since there is ovulation and production of progesterone, the bleeding is painful.

Luteal phase defect

It occurs due to inadequate corpus luteum function. Due to altered prostaglandins production and inadequate production of progesterone, spotting occurs 5 – 6 days prior to the onset of normal menstrual cycle.

Oestrogen withdrawal bleeding

This type of bleeding occurs due to sudden withdrawal of estrogen hormone. This can occur after bilateral oophorectomy or a midcycle bleed that occurs before ovulation due to sudden decrease in the estrogen levels.

Oestrogen breakthrough bleeding

In anovulatory cycles because of continuous estrogen exposure, bleeding may occur, known as estrogen breakthrough bleeding. Low levels of the chronic estrogen exposure causes intermittent staining or spotting, that is prolonged but minimal in volume.

Continuous high levels of estrogen with long period of amenorrhea results in acute episode of profuse bleeding.

Progesterone withdrawal bleeding

Bleeding occurs when treatment with exogenous progesterone or synthetic progesterone supplementation is stopped. It occurs in the endometrium which was previously primed by the estrogen. Bleeding maybe similar to that of normal menstrual cycle.

Progesterone breakthrough bleeding

This type of bleeding occurs when the amount of progesterone is very high as compared to that of estrogen. This results in intermittent bleeding of varying duration and is less in amount.

The PALM – COIEN Classification [6]

It is the classification for the causes of abnormal uterine bleeding in perimenopausal age group.

It is categorized as follows:

P: polyp

A: adenomyosis

L: leiomyoma

M: malignancies and hyperplasia

C: coagulopathy

O: ovulatory disorders

E: endometrial causes

I: iatrogenic

N: Not yet classified

This categorization of the abnormal uterine bleeding causes makes it easier for the clinician for diagnosis and further management.

Polyps (AUB-P)

These are epithelial proliferations that comprise vascular, glandular,
and fibro muscular and connective tissue component. Polyps are noted as either present or absent.64

This causes abnormal vaginal bleeding in 39% of pre-menopausal.

They can be diagnosed by TVS, saline infusion sonography, and hysteroscopy.

Adenomyosis (AUB-A)

Women with adenomyosis present with AUB in 70%, dysmenorrhea in 30% and both in 19% of the cases.

It can be diagnosed by ultrasound or MRI.

Leiomyoma (AUB-LSM or AUB-LO)

It is benign fibro muscular tumor of the myometrium. Lifetime risk in women over age 45 to be more than 60%.

Malignancy and Hyperplasia (AUB-M)

AUB is the primary symptom of endometrial neoplasia. Approximately 50% of women diagnosed with endometrial hyperplasia have concurrent carcinoma. AUB-M includes both premalignant and malignant lesions.65

Coagulopathies (AUB-C)

13% of women with HMB have a systemic disorder of hemostasis that may be overlooked during the differential diagnosis.

Ovulatory Dysfunction (AUB-O)

It may be present as a spectrum of menstrual abnormalities that range from amenorrhea, extremely infrequent light bleeding, to extreme HMB requiring intervention to stop further blood loss. These patients usually are associated with endocrinopathies, such as polycystic ovary syndrome, hypothyroidism, Hyperprolactinemia, stress, obesity, extreme exercises and anorexia nervosa.

Endometrial Causes (AUB-E)

These patients have predictable cyclical menses which indicates normal ovulation without any definite cause of AUB.

It may be secondary to endometrial inflammation, infection, or abnormal response to local inflammatory reactions or due to failure of endometrial hemostasis.

Iatrogenic (AUB-I)

Causes include medicated or inert IUD, gonadal steroidal therapy and other systemic pharmacological drugs that affect blood coagulation or ovulation.

Not Yet Classified (AUB-N)

It is for other uterine factors that are poorly defined, not adequately examined and/or both, such as arteriovenous malformation, chronic endometritis and myometrial hypertrophy.

DIAGNOSTIC EVALUATION OF AUB[11,12]

History

- Age of menarche and menopause, Parity
- Menstrual bleeding patterns
- Severity of bleeding (clots or flooding)
- Pain (severity and treatment)
- Medical conditions
- Surgical history
- Use of medications
- Symptoms and signs of possible hemostatic disorder

Physical Examination

- General physical
- Pelvic Examination

1. External
2. Speculum with Pap test, if needed.
3. Bimanual

Laboratory Tests

- Pregnancy test (blood or urine)
- Complete blood count70
- Renal and liver function tests
- TSH
- Targeted screening for bleeding disorders (when indicated, based on history): PT, PTT, specific tests for von Will brand's disease, von Willebrandristocetin cofactor activity, von Will brand's factor antigen, and factor VIII

Available Diagnostic or Imaging Tests (when indicated)

- Abdomino-pelvic scan

- Saline infusion sonohysterography
- Transvaginal ultrasonography
- Magnetic resonance imaging
- Hysteroscopy

Available Tissue Sampling Methods (when indicated)

- Office endometrial biopsy
- Hysteroscopy directed endometrial sampling (office or operating room)

EVALUATION OF ENDOMETRIUM BY DIFFERENT MODALITIES

I. NON INVASIVE METHODS:

1. Abdomino- pelvic ultrasound scans:

•Gives a panoramic view of the pelvis

• Endometrial thickness can be measured

• Other abdominal organs can be evaluated

• Lymph nodes may be visualized

• Free fluid in the peritoneal cavity may be visualized.

2. TVS (Transvaginal sonography):

This can be used as a screening tool in patients with perimenopausal bleeding. Vaginal ultrasound appears to play a major role as a non-Invasive method for evaluating the perimenopausal bleeding. TVS can also diagnose other pathology in the pelvis with more accuracy.

3 .Three-Dimensional TVS:

Three-dimensional sonography can be a useful addition to TVS and hysterosonography in the characterization of abnormalities within the endometrial cavity, including localization of focal abnormalities prior to directed biopsy. It allows the ability to reconstruct any plane of section.[13]

4. MRI (Magnetic Resonance Imaging):

This has the high sensitivity for diagnosing submucosal myomas and in staging endometrial malignancies. But it has a relatively poor sensitivity for other intrauterine pathology. But the main drawback is its high cost.

5. Saline infusion sonohysterography (SIS):

This is a semi-invasive method of evaluation. It is to improve the visualization of the endometrial cavity during a TVS examination. SIS is also less invasive than hysteroscopy and much less expensive than MRI.

II. INVASIVE METHODS:

A. Endometrial Biopsy

This is a minimally invasive method where a Novak's curette is used. It is office based procedure.

B. Fractional or modified fractional curettage

This has been very useful especially while an endocervical study is indicated. Endocervical curettage precedes a thorough curettage of the endometrial cavity.

C. Dilatation and Curettage (D and C):

• Dilatation and curettage provides a more complete method of endometrial sampling than routine endometrial biopsy alone in cases of diffuse endometrial lesions or abnormalities of the endometrial-myometrial interface.

• It was the gold standard in the evaluation of endometrium in abnormal uterine bleeding patients, now being taken over by hysteroscopy & directed biopsy. It is indicated even for therapeutic purposes.

In our institution this is still the most commonly done procedure. In this study histopathological correlation was done with sample obtained through pipelle's endometrial aspirator.

D) HYSTEROSCOPY:

Hysteroscopy is a procedure in which a telescope-like device is introduced Through the vagina into the cervical canal and uterine cavity for visualization of Endocervical canal and uterine cavity.

Hysteroscopy with biopsy provides the most comprehensive evaluation of the Endometrium and is recommended for use in any woman with equivocal findings on Biopsy or ultrasonography.

TRANSVAGINAL SONOGRAPHY (TVS):

- The first report of TVS is attributed to Kratochwit in 1969.

- TVS transducer: It is a small curved array high frequency transducer with convex curved surface which produces an image that combines a larger surface field of view with a sector display format. It has a handle, a shaft (this enters the vagina), a tip or head or the foot print (this houses the ultrasound crystal). Higher frequency transducer is better to depict the endometrium and improves the lateral resolution.

- Transducer selection: Spatial resolution increases with higher frequency transducer but the penetrance of USG diminishes as frequency increases. The attenuation typically increases with increase in ultrasound frequency, so it is better to select the highest ultrasound frequency. When maximum resolution is needed, a higher frequency transducer with excellent lateral and elevation resolution at the depth of the interest is used.[14,15]

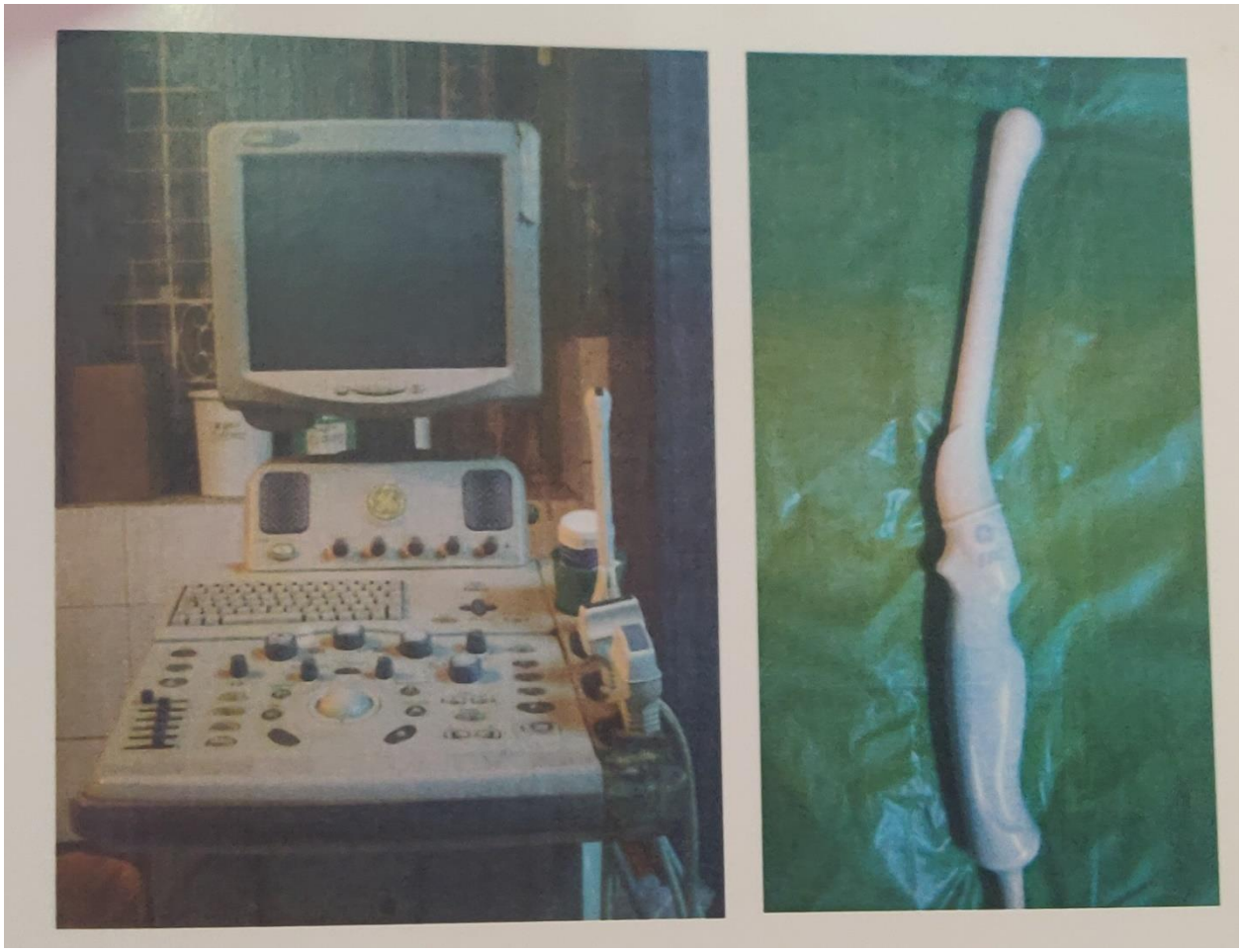


FIGURE:1 Ultrasonography machine and transvaginal probe

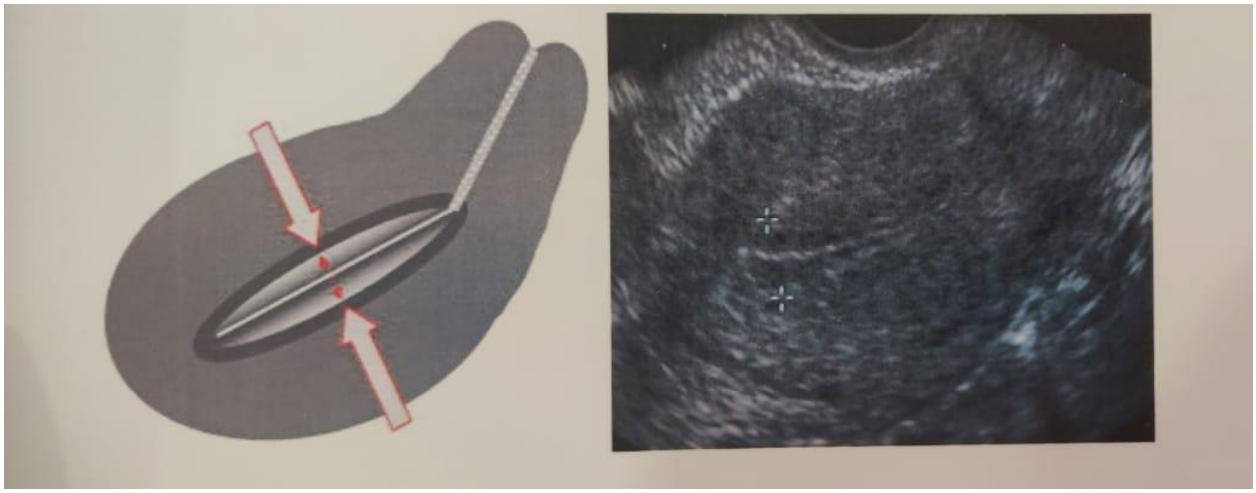


FIGURE: 2 Double layered thickness measurement of endometrium, measured at thickest part in sagittal plane. The surrounding more sonolucent area is considered to be the inner myometrium and is not included.

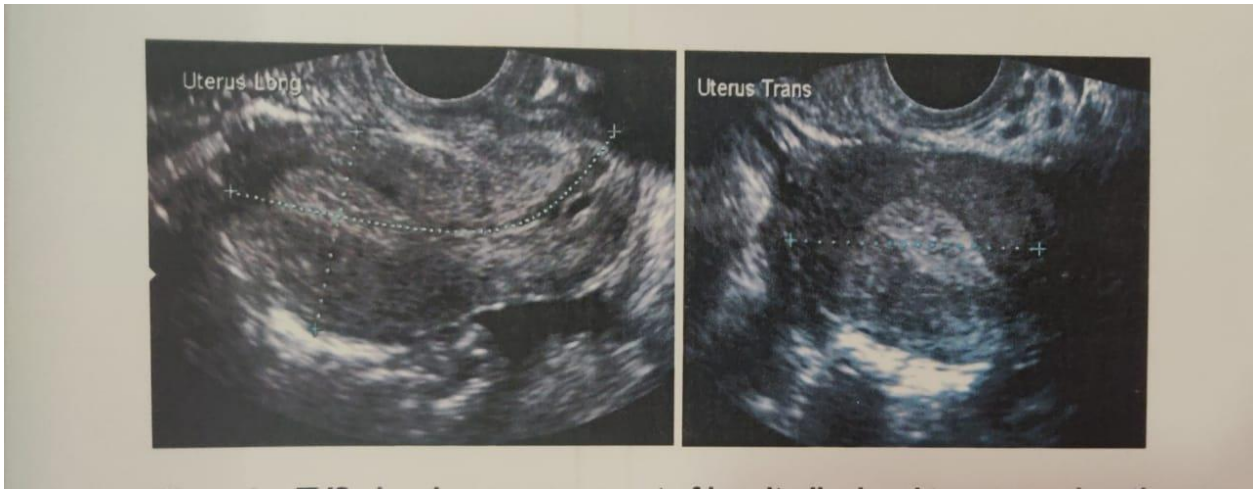


FIGURE:3 TVS showing measurement of longitudinal and transverse length of uterus.

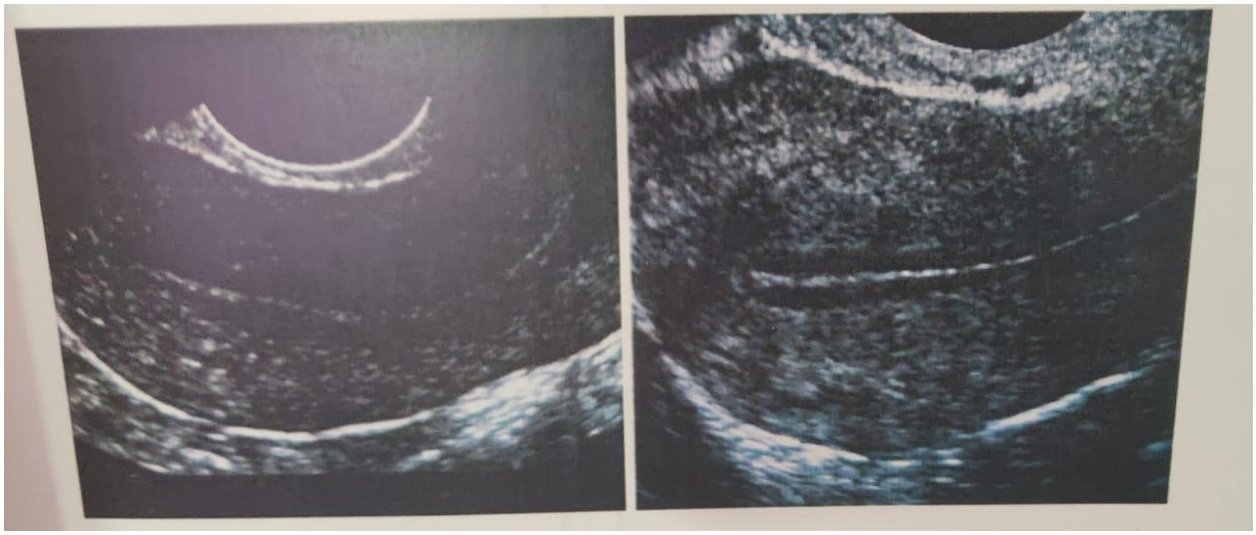


FIGURE:4 normal early proliferative endometrium and "triple layer" appearance of endometrium.

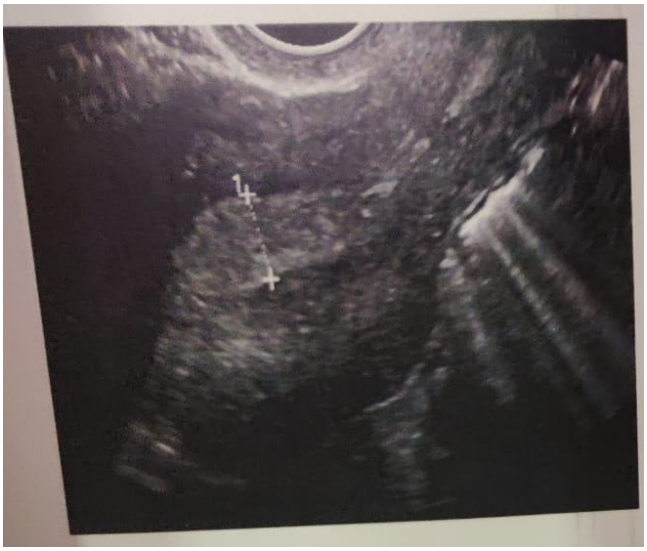


FIGURE: 5 secretory endometrium

ADVANTAGES OF TVS OVER CONVENTIONAL TRANSABDOMINAL SCAN ARE:

- We can place the high frequency transducer nearer to the region of interest.
- Optimal visualization of uterus, cervix and adnexa, pouch of Douglas, urinary bladder and bowel and the characterization is better.
- Helpful in evaluating an obese patient and in patient with retroverted and retro flexed uterus.
- Elimination of blind spots those caused by overlying bone or air filled organ.
- Distance from the probe to the organ of interest is approximately equal in every patient hence examination may be conducted with largely standardized instruments settings, enabling visual comparison of documented findings.
- Bladder distension is not required.

APPLICATIONS OF TVS:

Uterus

- Uterine anomalies
- Retroverted and retroflexed uterus
- Leiomyomas
- Endometrial fluid
- Neoplastic lesions
- IUCD
- Menorrhagia, peri and post-menopausal bleeding

Cervix

- Diagnosing cysts, myomas and carcinoma.

Adnexa

- Evaluation of adnexal masses in the cases of PID
- Ovarian and other pelvic tumors.
- In cases of obesity ,adhesions .plenty of bowel gas, inability to maintain bladder distention, TVS may be helpful.

- TVS is useful in diagnosing pregnancy & its pathologies

- In IVF(in vitro fertilization) procedures

- Diagnosing some non-gynecologic pelvic pathology.

LIMITATIONS OF TVS :

1. In contrast to transabdominal scan which provides a global view of the pelvis, lesions outside the range of TVS probe may be missed.

2. Field of view & penetration are limited but characterization of a lesion is better accomplished.

3. Maneuverability of the probe within the vagina is limited.

4. Not suitable for prepubertal & virgin patients.

5. Some postmenopausal women & patients with acute pelvic pain may not tolerate the examination

6. Some patients may refuse it for psychological or personal reasons.

7. Extension to upper abdominal structures not possible.

8. Although minimally invasive, TVS use has been hampered by inability to access the vagina or uterus for anatomic or pathologic reasons.

9. Cervical stenosis or unacceptable procedural pain can prevent performance of office-based endometrial biopsy, saline-infusion hysterosonography, or hysteroscopy 4%-10% of the time.[16,17,18]

10. TVS is operator-dependent.

11. It has relatively poor spatial and tissue contrast resolution compared with MRI and CT.

12. Safety of the procedure: After so many years of use, neither clinical nor epidemiological studies have demonstrated adverse side effects of diagnostic ultrasounds

REGULATION OF THE MENSTRUAL CYCLE

The menstrual cycle includes two cycles:

1. ovarian cycle
2. Uterine cycle.

The ovarian cycle has two phases:

1. follicular phase
2. Luteal phase.

The uterine cycle has two phases:

1. proliferative phase
2. Secretory phase.

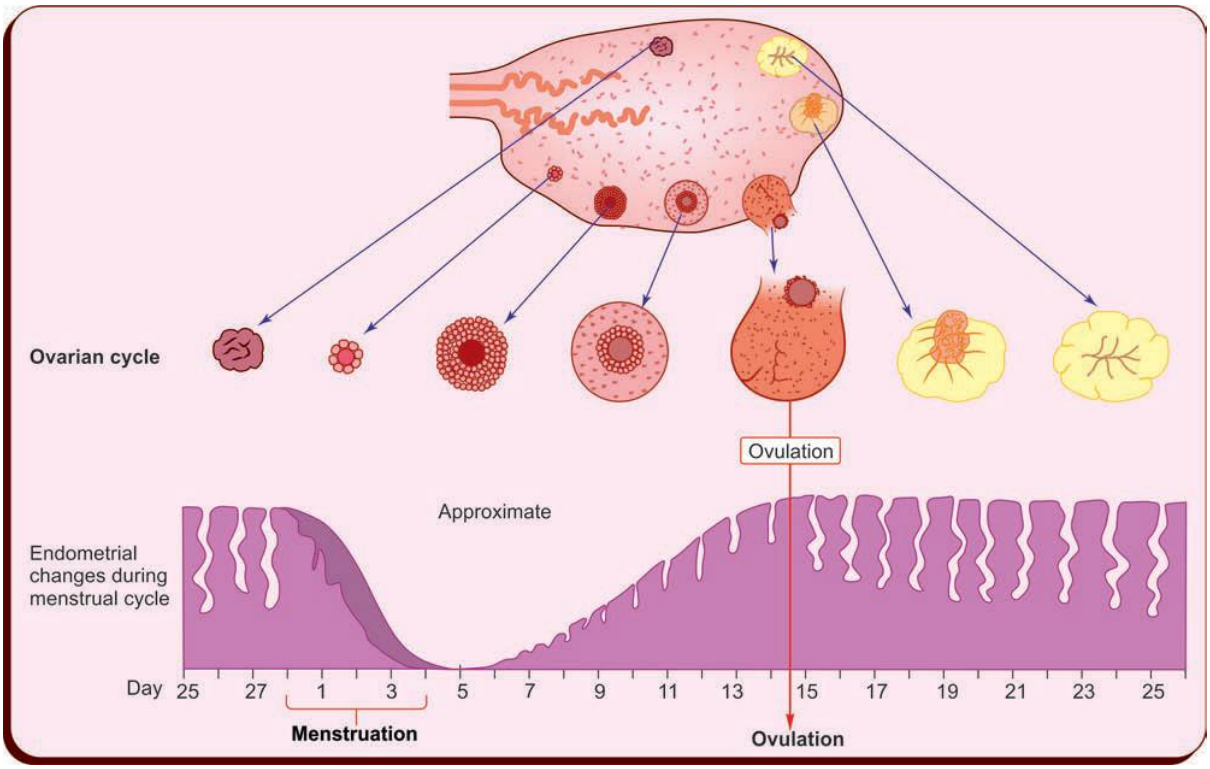


FIGURE 6: NORMAL MENSTRUAL CYCLE

Follicular Phase

It is the phase during which follicular development from the primordial follicle into the fully developed Graafian follicle. The primary follicle is the one in which the granulosa cells are

lined by cuboidal epithelium and undergo pseudo stratification. Also there is an increase in the number of cells resulting in the formation of zona pellucida. From the primary follicle, arises the secondary follicle.

The secondary follicle also known as the preantral follicle consists of the granulosa cells surrounded by theca interna and theca externa. The stroma surrounding the granulosa cells undergoes differentiation into the theca cells.

There is a collection of fluid in the follicle and between the granulose cells, as the FSH levels increases[19]. This is called an antrum. Only 4-5 follicles attain this stage in each cycle. When the FSH levels declines, one follicle which has high number of TSH receptors continue to grow as a Graafian follicle. [20]

The Graafian follicle consists of mural granulosa, which are the cells around the antrum and the cells surrounding the oocyte is called the corona radiata. Cumulus oophorous is the mass of cells formed by the ovum and the granulosa cells[9] .

Ovulation

Ovulation is the process of expulsion of the ovum. It is triggered by the LH surge. During this stage, there is extrusion of the polar body and the first meiotic division of the oocyte is completed[20]

Luteal Phase

It consists of the formation of the corpus luteum to the onset of menses, which is usually constant at about 14 days. Left-over Graafian follicle undergoes luteinisation. Neovascularization of the corpus luteum occurs and the hormones enter the general circulation. If fertilization does not occur, the corpus luteum degenerates, a process known as luteolysis[22] and becomes corpus albicans.

Anatomy and Histology of Normal Endometrium

The endometrium is divided into superficial functional layer and deep basal layer. The functional layer is sensitive to estrogen and progesterone and undergoes cyclical changes according to the phase of menstrual cycle. The basal layer does not undergo changes and serves as a source for endometrial regeneration[23].

The superficial layer (two - third)

- Stratum functionalis
- Consists of two zones:
    1. Superficial – stratum compactum composed of glands and stroma.
    2. Deep – stratum spongiosum containing endometrial glands, increased interstitial tissue and less stroma.

The deep layer (one-third)

- Stratum basalis which is formed by a single layer of cuboidal epithelium which dips into form tubular glands.

UTERINE CYCLE

Proliferative Phase

Day 1 is the start of the vaginal bleeding. The endometrium is seen as a thin echogenic line on completion of menses. After menses there is only stratum Basale and few part of stratum spongiosum. Estrogen increases and causes stimulation of endometrial glands and proliferation of stroma and thickening of stratum functionale[24].

By mid-follicular phase on ultrasound a trilaminar phase of the endometrium is seen and the thickness increases from 1-2 mm to about 6 mm on day 7 and the endometrium thickens further and is usually 8 mm before ovulation. The endometrial glands increase in tortuosity and the stromal and mitotic figures increase in number.

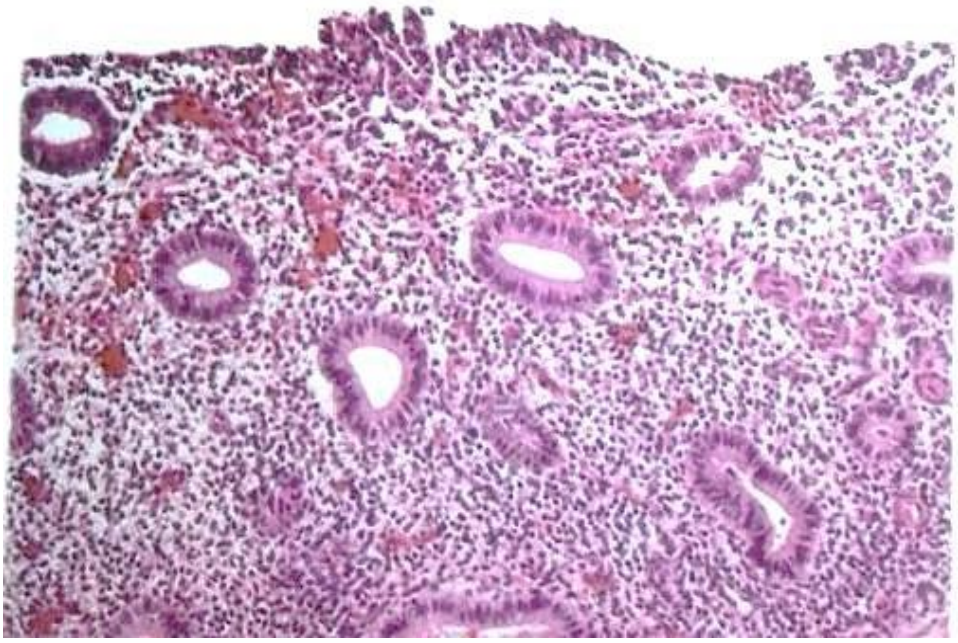


FIGURE 7: Follicular Phase Histopathology

Secretory Phase

Progesterone is the hormone responsible for secretory phase. After ovulation the trilaminar appearance is lost and there is increased and uniform echogenicity of the endometrium. The mean endometrial thickness is 12 mm. The endometrium is vascularized and causes supercoiling of spiral arterioles that secrete clear fluid. The length of the cycle is constant, about 14 days. [25]

Towards the end of the secretory phase the glands become more tortuous and the stroma becomes vascular. If implantation does not take place the glands collapse and the neutrophils and the leukocytes begin to infiltrate to produce inflammatory cytokines. Resulting in release of various enzymatic substances and disruption of the endometrium and tissue necrosis.
Vasoconstriction is also mediated by endothelin and PGF2α. Regeneration begins after 36 hours of menses. Bleeding stops generally with complete reepithelialisation of the endometrium usually by day 5.

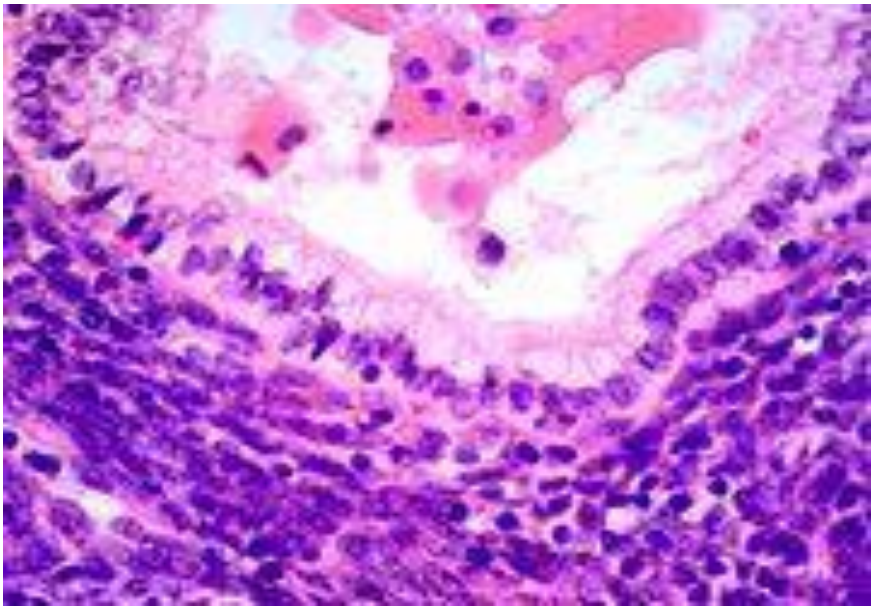


FIGURE 8: secretory endometrium

Menstruation

The corpus luteum degenerates if fertilization does not occur. There is sudden withdrawal of both estrogen and progesterone. Resulting in arrest of secretory changes in endometrium. The superficial endometrium loses its blood supply and necrosis occurs. Foci of necrosis appear in endometrium and they coalesce. Degeneration of vessel walls occur and menses is initiated. The duration of menses is usually about 3 – 5 days. Blood loss beyond 80ml is considered abnormal.

ENDOMTERIAL THICKNESS[10]

A very thin endometrial "stripe" (<5 mm), like a biopsy that yields minimal tissue, suggests an attenuated or denuded endometrium best treated first with estrogen rather than with a progestin or an estrogen-progestin combination.

In perimenopausal and postmenopausal women with abnormal bleeding, endometrial biopsy generally is considered unnecessary when the endometrial thickness is less than 4 or 5 mm because the risk of endometrial hyperplasia or cancer is remote.

In premenopausal women with abnormal bleeding, although there is no substantial direct evidence to support the extrapolation. Otherwise, the decision to biopsy or not should be based primarily on clinical suspicion and risk factors rather than on ultra-sonographic measurements of endometrial thickness.

A grossly increased endometrial thickness (>12 mm) increases the risk of disease and is an indication for sampling, even when clinical suspicion of pathology is otherwise low.

Biopsy is unnecessary when the endometrial thickness is less than 5 mm, that biopsy is indicated when the clinical history suggests long-term unopposed estrogen exposure even when the endometrial thickness is "normal" (5–12 mm), and that biopsy should be performed when endometrial thickness is greater than 12 mm even when clinical suspicion of disease is low.

CLINICAL TERMINOLOGY USED IN ABNORMAL UTERINE BLEEDING [3]

Normal

The normal menstrual bleeding is that having regular frequency which is normal in amount and duration with the cycles between 21 – 35 days.

Menorrhagia

Menorrhagia is prolonged or heavy cyclical bleeding which may excessive in amount or the number of days more than the normal flow. The cycle is not altered and the duration is more than 7 days or the blood loss is usually more than 80 ml.

Hypo menorrhea

Hypo menorrhea is defined as the normal regular cycles, but scanty in amount and duration. The causes includes endometrial problems like
Ashermans syndrome and Genital Tuberculosis.

Polymenorrhea

Polymenorrhea is defined as shortened cycles less than 21 days but the cycles are of normal frequency and the flow is normal in amount and duration. It is usually seen in inflammatory conditions of the ovaries like
Endometriosis and Pelvic Inflammatory Diseases.

Oligomenorrhea

Oligomenorrhea is defined as the reduction in the frequency of the menstrual cycles with the intervals between the cycles varying between 6 weeks to sometimes 6 months .Hormonal dysfunctions like PCOS , hyperprolatinomas and hypothyroidism are the important causes .These are usually anovulatory cycles .

Metrorrhagia

Metrorrhagia is defined as menstrual bleeding occurring in between normal cycles. Cervical polyp, endometrial polyp and the local lesions are the most common causes presenting with metrorrhagia.
Hormonal therapy can also be a cause.

Menometrorrhagia

Menometrorrhagia is having menstrual cycles irregularly with no common pattern but the flow is increased in amount and duration. In general, regular bleeding is likely to be due to organic problems and irregular bleeding is mainly due to ovulatory dysfunction and is usually due to dysfunctional uterine bleeding.

HISTOPATHOLOGY OF THE ENDOMETRIUM IN ABNORMAL UTERINE BLEEDING

Various histological patterns may be:-

1. Proliferative phase endometrium
2. Secretory phase endometrium
3. Endometrial hyperplasia
4. Irregular ripening of the endometrium
5. Irregular shedding of the endometrium
6. Atrophic endometrium
7. Disordered proliferative endometrium
8. Inactive endometrium
9. Carcinoma

Proliferative phase endometrium

The glands are small, uniform, widely spaced and lack tortuosity, they are tubular and lined by columnar epithelium with the nuclei placed at the base. By mid-proliferative phase (8-10days), glandular tortuosity begins and in late proliferative phase (11-14 days), the glands are markedly tortuous. There is appearance of pseduostratification due to heaping up of the columnar epithelium.[10]

Secretory phase endometrium

The glands increase in size. The lining epithelium becomes taller with clear cytoplasm and epithelial cells contain subnulcear vacuolation by day 16 of the cycle. The secretory activities subside by day 22. The glands progressively collapse and papillary tufts of epithelium project into the lumen giving the characteristic saw-tooth pattern. Stroma is edematous.[10]

Hyperplastic endometrium

Endometrial hyperplasia is defined as a proliferation of glands of irregular size and shape with an increase in the glands/stroma ratio.[26]

Classification of endometrial hyperplasia by International Society of Gynecological Pathologists

a) Simple hyperplasia without atypia: 1% progress to endometrial cancer
b) Complex hyperplasia without atypia: 3% progress to endometrial cancer
c) Simple hyperplasia with atypia: 8% progress to endometrial cancer
d) Complex hyperplasia with atypia: 27% progress to endometrial cancer

Simple hyperplasia is characterized by dilated or cystic glands which are round to slightly irregular shapes, with an increased glandular-to-stromal ratio without glandular crowding, and no cytologic atypia.

Complex hyperplasia has architecturally complex (budding and infolding), glandular crowdingds with less intervening stroma without atypia.

Atypical hyperplasia refers to cytological atypia and can be categorized as simple or complex, depending on the corresponding glandular architecture.

Criteria for cytologic atypia include large nuclei of variable size and shape that have lost polarity, increased nuclear-to-cytoplasmic ratios, prominent nucleoli, and irregularly clumped chromatin with parachromatin clearing.[27]

In 1994, the WHO classified endometrial hyperplasias into 4 categories:

1. simple hyperplasia without atypia
2. complex hyperplasia without atypia
3. simple atypical hyperplasia
4. complex atypical hyperplasia 1, 2.

In its latest classification 5 published in 2014, the WHO has clarified the matter: it now only differentiates between 2 categories of endometrial hyperplasia:

1. hyperplasia without atypia

2. atypical hyperplasia/endometrioid intraepithelial neoplasia.

This reduction to 2 categories was not only due to the need to do away with the confusing multitude of terms currently in use. Rather, it reflects a new understanding of molecular genetic changes.

Irregular ripening of the endometrium

The endometrium shows lag in development of more than 2 days from the expected day of the cycle. There is variation in the development of glands and stroma along with dissociation of development between glands and surrounding stroma. Adjacent to fairly normal secretory glands, which roughly correspond with the day of the cycle, there may be other glands that are poorly developed with basal vacuoles and small rounded nuclei in functionally inactive epithelial cells

Irregular shedding of the endometrium

Combination of secretory and proliferative changes are seen in curettings. Endometrial biopsy on 4th and 5th day of the cycle reveals evidence of late secretory activity as well as proliferative activity. Early proliferative glands appear admixed with irregular star-shaped secretory glands. The glandular cell have clear cytoplasm with shrunken nuclei, dense chromatin. The pre-decidual cells are shrunken and have a scanty cytoplasm with condensed nuclei rich in chromatin.

Atrophic endometrium

The endometrium is thin with few small glands scattered in atrophic stroma. The glands are lined by flattened epithelium without mitotic activity and Usually undergo pronounced cystic dilatation as the necks of the glands are occluded by the fibrotic stroma. The stroma is fibrous with decreased cellularity.

Disordered proliferative endometrium

Disordered proliferative pattern lies at one end of the spectrum of proliferative lesions of the endometrium with carcinoma at the other end with intervening stages of hyperplasias. It is an exaggeration of the normal proliferative phase without significant increase in the overall glands to stroma ratio. It denotes an endometrial appearance that is hyperplastic but without an increase in endometrial volume. It also refers to a proliferative phase endometrium that does not seem appropriate for any one time in the menstrual cycle, but is not abnormal enough to be considered hyperplastic. Disordered proliferative pattern resembles a simple hyperplasia, but the process is focal rather than diffuse.[28]

Inactive endometrium

It is the histologic pattern seen in endometrial biopsies from women who receive hormonal pills show combination of inactive glands, abortive secretion, decidual reaction, and a thin blood vessel is characteristic.[29]

PIPELLE ENDOMETRIAL BIOPSY

Office-based endometrial sampling with devices such as the Pipelle's Endometrial Aspirator is a safer, more convenient, less expensive and reliable alternative to dilation and curettage.

Patient Position

• Dorsal lithotomy

Landmarks

• Cervix and cervical os

Equipment

• Speculum
• Atraumatic vulsellum forceps
• Uterine sound
• 1- to-4 mm cervical dilators
• Betadine solution or swabs
• Formalin solution for pathology
• Endometrial biopsy device
• Pipelle's de Cornier Endometrial Aspirator: A disposable and flexible polypropylene endometrial suction curette that is 3 mm in diameter with a distal side port to collect tissue. Withdrawal of the piston from the sheath creates suction.

Advantages:

Easy to use and generally well tolerated by patients.

Disadvantage:

Smaller sample size compared to D& C

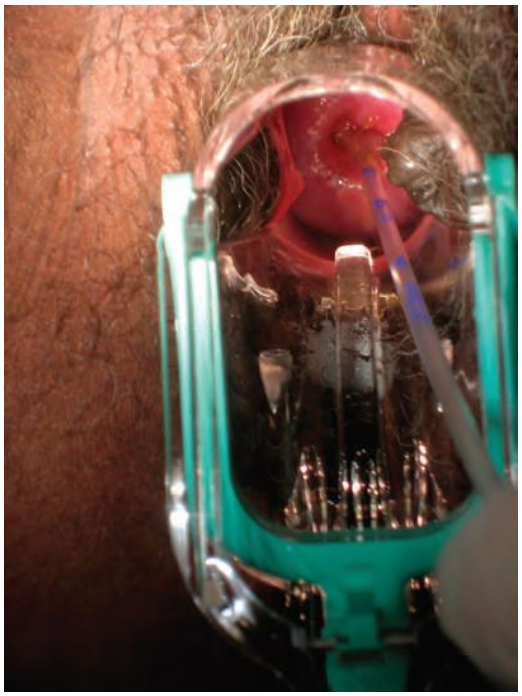


FIGURE: 9 endometrial sampling by pipelle's aspirator

Side Effects and Complications

•Transient cramping: Manage with NSAIDs pre- and post-procedure. Pain should resolve in 12 hours.

• Vasovagal reaction: Reposition the patient to a more comfortable supine position and allow her to rest until she does not feel light headed. Check vital signs.

• Bleeding: Apply pressure, silver nitrate sticks, or Monsel's solution. Advise the patient that she may expect some bleeding or spotting after the procedure.

• Rarely: Uterine perforation, severe bleeding, pelvic infection, bacteremia.

After care

• Recommend NSAIDs for cramping pain.

• Patient should notify MD with any persistent pain for over 48 hours not relieved with medication, heavy vaginal bleeding, foul-smelling vaginal discharge, fevers, or chills.

• No restrictions on activities or intercourse

Materials and methods

MATERIAL AND METHODS

Materials:

- An analysis of perimenopausal women aged 40-50yrs with abnormal uterine bleeding from the Department of Obstetrics and Gynaecology at R.L.Jalappa Hospital and Research Centre, Tamaka, Kolar.

- **STUDY DESIGN- Observational study.**
- **STUDY DURATION: JUNE 2017 to JULY 2018**
- **SAMPLE SIZE:** 80

INCLUSION CRITERIA:

- All patients of perimenopausal age group (40-50years) with abnormal uterine bleeding come to obstetrics and gynecology OPD, R.L.JALAPPA Hospital and research Centre, Tamaka, kolar.

EXCLUSION CRITERIA:

- Women on hormonal replacement treatment.
- Patients with obvious cause of bleeding from cervix and vagina. Eg: carcinoma of cervix.
- All patients who do not consent to be a part of study.

METHODOLOGY

- On Siemens Acuson X300 USG machine TVS assessment of various factors were done which included uterine size, endometrial thickness (ET), polyp and adnexal mass.
- Endometrial thickness was measured as maximal double layer thickness in mid-sagittal section at the thickest area of the endometrium near the fundus, including the outermost border of both sides of the endometrium.
- Patients with cyclical bleeding, endometrial sampling was done in the second half of the cycle.
- Endometrium was considered hyperplastic if thickness is =/>10mm in perimenopausal women and was taken up for endometrial sampling.

- Endometrial biopsy by pipelle's curette was done as an outpatient procedure; the pipelle's is introduced into uterine cavity without performing cervical dilatation and then withdrawn outside by rotatory movements to get a sample.
- Biopsy sample was collected in a bottle containing formalin and was sent for histopathological examination.
- In Histopathology report endometrium was designated as proliferative, secretory, atrophic, polyp, hyperplasia without atypia, hyperplasia with atypia and carcinoma.
- The Investigations such as Complete blood count, Blood grouping and Rh typing, routine urine analysis, RBS, BT, CT, thyroid function test will be done to rule out any other causes of abnormal uterine bleeding.

STATISTICAL ANALYSIS:

Data will be entered in MS excel and analyzed using SPSS 22 version software. Qualitative data will be presented in the form of Proportions and pie diagrams, bar charts will be used to represent graphically. Quantitative data will be presented as mean, standard deviation. Student's t test will be the test of significance for quantitative data and chi-square test will be the test of significance for qualitative data. p value <0.05 will be considered as statistically significant.

Sample Size:

Was estimated based on the expected difference in proportion of cause as 19.23% for abnormal uterine bleeding between USG and HPE from the study by **Archana Bhosle et al.,**. By using the formula

$$\text{Sample size} = \frac{Z_{1-\alpha/2}{}^2 \, p(1-p)}{d^2}$$

Here

$Z_{1-\alpha/2}$ = Is standard normal variate (at 5% type 1 error ($P<0.05$) it is 1.96 and at 1% type 1 error ($P<0.01$) it is 2.58). As in majority of studies P values are considered significant below 0.05 hence 1.96 is used in formula.

p = Expected proportion in population based on previous studies or pilot studies.

d = Absolute error or precision – Has to be decided by researcher.

P = 19.23 or 0.192

q = 80.77 or 0.81

d = 10% or 0.1

Using the above values at 95% Confidence level a sample size of 62 subjects with abnormal uterine bleeding will be included.

Considering 10% Nonresponse a sample size of 62 + 6.2 ≈ 68 subjects will be included in the study.

Results

RESULTS

A total of 80 women with abnormal uterine bleeding in perimenopausal age who fulfilled the inclusive criteria were examined during study period of 2 years. Maximum number of patients with abnormal uterine bleeding presented in age group 40-44 years. All the study subjects were undergoing Trans vaginal ultrasound, endometrial biopsy and submitted for histopathological examination. There were no cases in nulliparous women.

TABLE:1 DISTRIBUTION BASED ON AGE OF THE PATIENTS (IN YEARS)

AGE	Frequency	Percent
40-44years	43	53.8
45-50years	37	46.3
Total	80	100.0

CHART:1 DISTRIBUTION BASED ON AGE OF THE PATIENTS (IN YEARS)

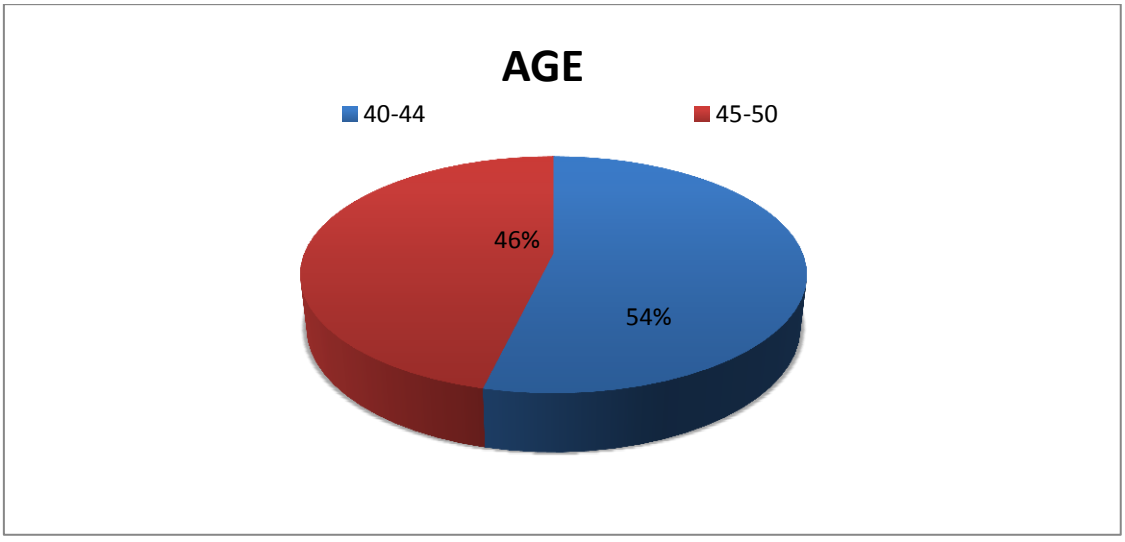


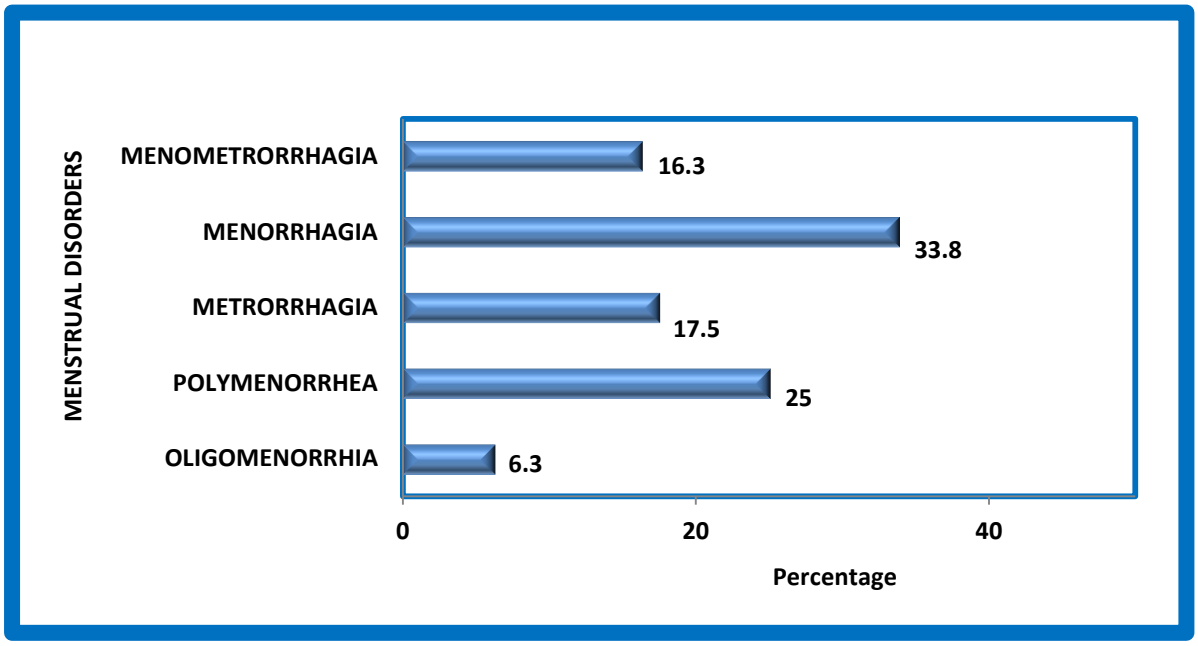
TABLE:2 DISTRIBUTION OF CASES BASED ON PARITY

	Frequency	Percent
Nulliparous	0	0
P1	5	6.3
P2	47	58.8
P3	22	27.5
≥ P4	6	7.5
TOTAL	80	100.0

TABLE 3: PRESENTATION OF SYPMTOMS IN PERIMENOPAUSAL AGE

MENSTRUAL DISORDERS	Frequency	Percent
OLIGOMENORRHIA	5	6.3
POLYMENORRHEA	20	25.0
METRORRHAGIA	14	17.5
MENORRHAGIA	27	33.8
MENOMETRORRHAGIA	13	16.3

CHART :2 PRESENTATION OF SYPMTOMS IN PERIMENOPAUSAL AGE

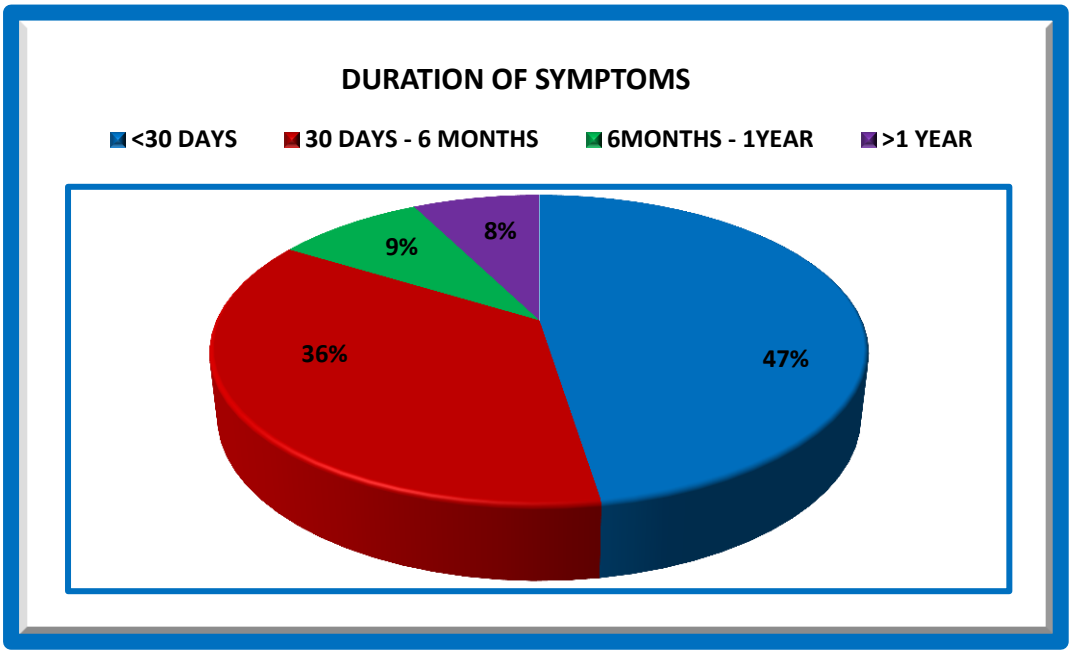


Of the women with abnormal uterine bleeding the varying range of symptoms were as follows: oligo menorrhea (6.3%), polymenorrhea (25%), metrorrhagia (17.5%), menorrhagia (33.8%) and menorrhagia (16.3).

TABLE 4: DURATION OF SYMPTOMS

DURATION OF SYMPTOMS	Frequency	Percent
1	38	47.5
2	29	36.3
3	7	8.8
4	6	7.5
Total	80	100.0

CHART: 3 DURATION OF SYMPTOMS



The complaints presented with varying duration: <30days (47.5%), 30days- 6months (36.3%), 6months – 1 year (8.8) and more than 1 year (7.5%).

TABLE: 5 DISTRIBUTION BASED ON UTERINE SIZE

Uterus size	Frequency	Percent
6weeks	21	26.3
8-10weeks	36	45.0
12-14weeks	15	18.8
>14weeks	8	10.0
Total	80	100.0

About 45% of the total women had 8 – 10 weeks of uterine size, confirmed by clinical examination. Others had uterine size upto 6 weeks (26.3%), 12- 14 weeks (18.8) and >14 weeks (10%).

TABLE: 6 MEDICAL DISORDERS IN PERINEMOPAUSAL WOMEN

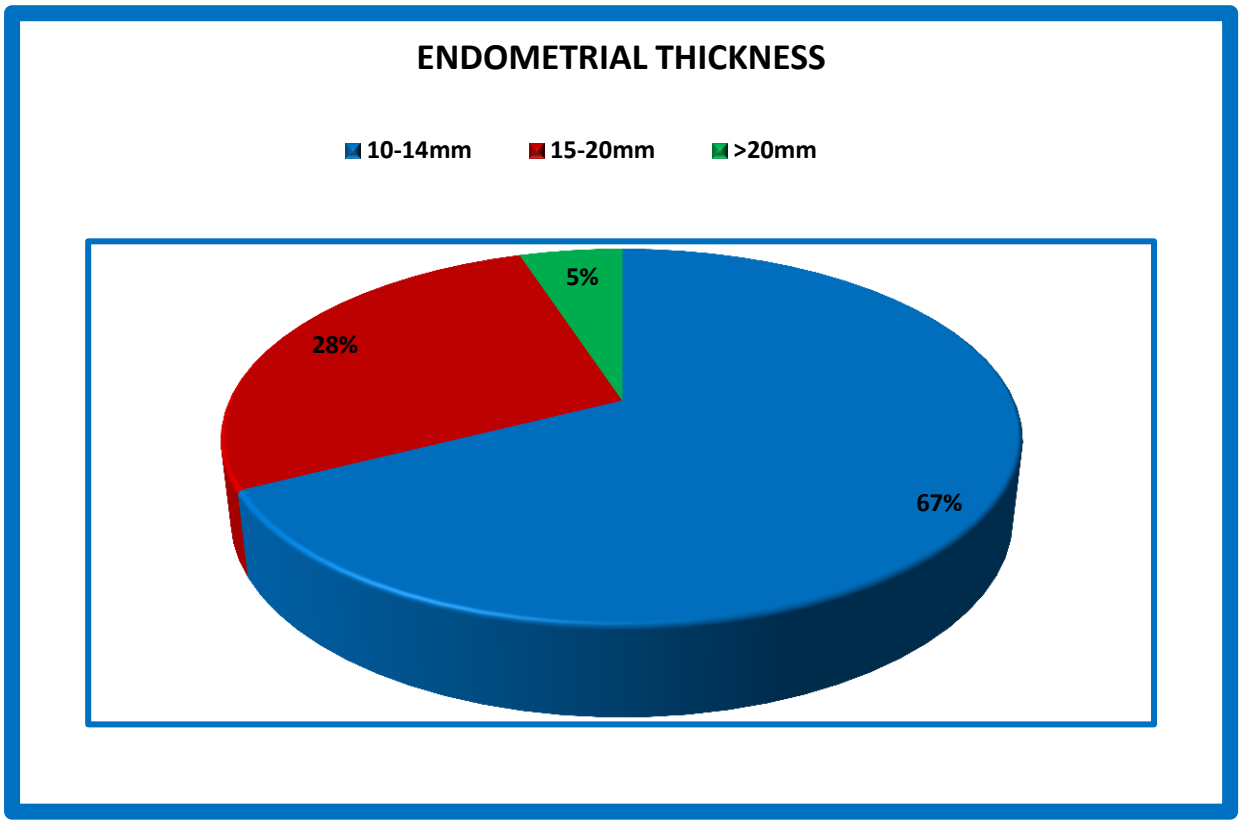
MEDICAL DISORDERS	Frequency	Percent
HYPERTENSION	4	5.0
DM	6	7.5
ASTHMA	2	2.5
NIL	68	85.0

Most patients didn't have any medical disorders. Others had hypertension (5%), diabetes mellitus (7.5%) and bronchial asthma (2.5%).

TABLE: 7 DISTRIBUTION BASED ON ENDOMETRIAL THICKNESS

ENDOMETRIAL THICKNESS	Frequency	Percent
1	54	67.5
2	22	27.5
3	4	5.0
Total	80	100.0

CHART:4 DISTRIBUTION BASED ON ENDOMETRIAL THICKNESS

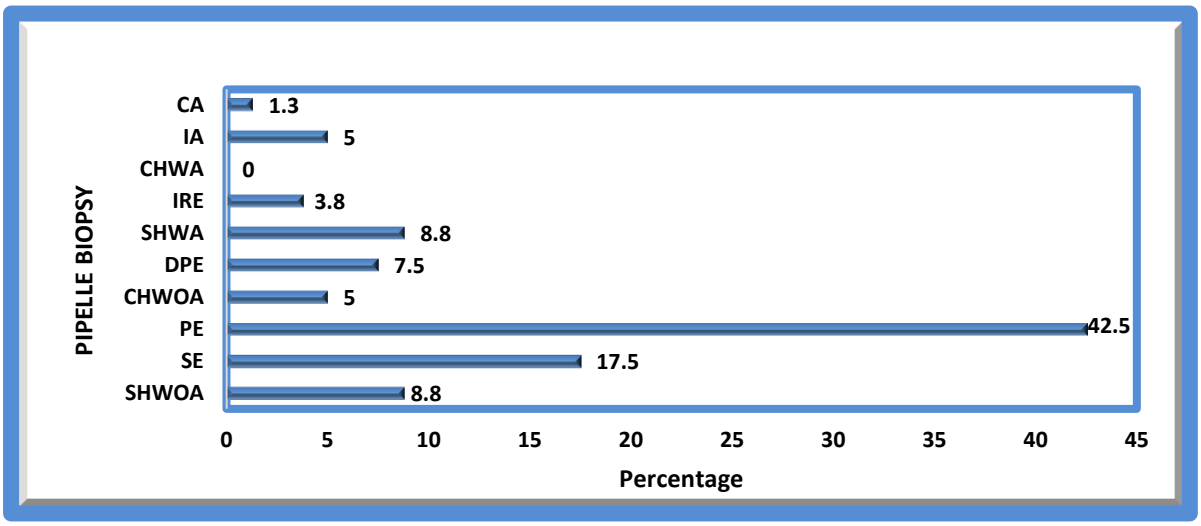


Based on findings of transvaginal scan, endometrial thickness was measured as follows: 67.5% cases showed 10-14mm, 27.5% cases showed 15-20mm and >20mm were 5%.

TABLE: 8 DISTRIBUTION OF HISTOPATHOLOGY REPORT BY PIPELLE'S BIOPSY

PIPELLE BIOPSY	Frequency	Percent
SHWOA	7	8.8
SE	14	17.5
PE	34	42.5
CHWOA	4	5.0
DPE	6	7.5
SHWA	7	8.8
IRE	3	3.8
CHWA	0	0
IA	4	5.0
CA	1	1.3

CHART: 5 DISTRIBUTION OF HISTOPATHOLOGY REPORT BY PIPELLE'S BIOPSY

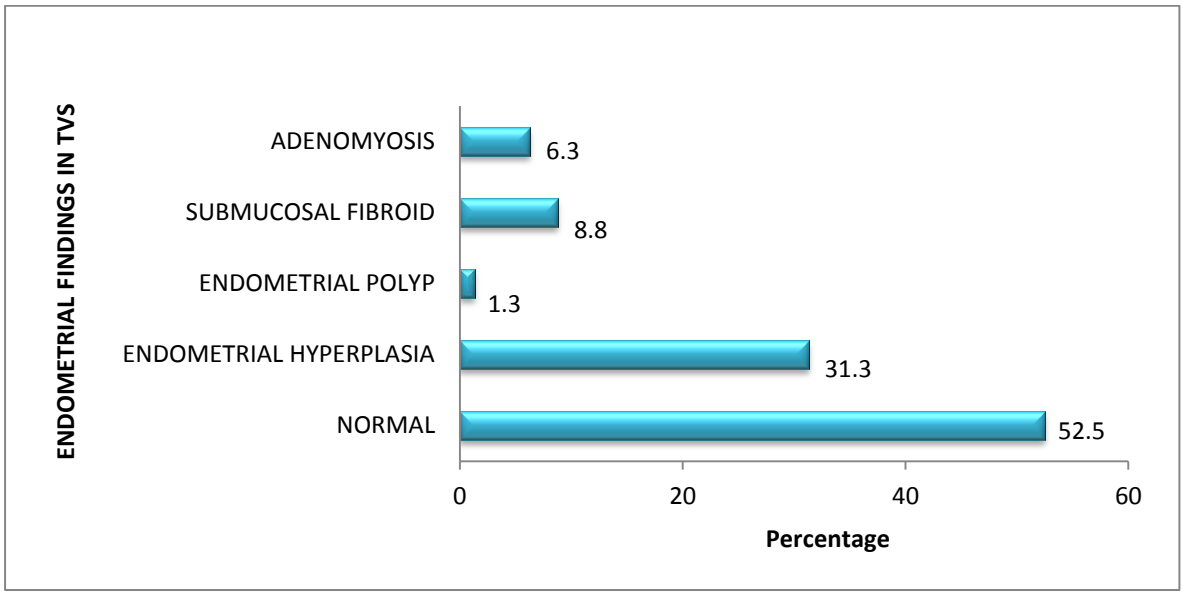


Of the cases who underwent endometrial sampling, 34 cases showed proliferative endometrium, 14 showed secretory endometrium, simple hyperplasia without atypia were 7, 7 showed simple hyperplasia with atypia, 6 cases showed disordered proliferative endometrium, 4 cases with complex hyperplasia without atypia, 3 cases had irregular endometrium. One case was diagnosed as endometrial carcinoma. 4 samples came as inadequate.

TABLE: 9 DISTRIBUTION BASED ON TVS FINDINGS

ENDOMETRIAL FINDINGS IN TVS	Frequency	Percent
NORMAL	42	52.5
ENDOMETRIAL HYPERPLASIA	25	31.3
ENDOMETRIAL POLYP	1	1.3
SUBMUCOSAL FIBROID	7	8.8
ADENOMYOSIS	5	6.3

CHART: 6 DISTRIBUTION BASED ON TVS FINDINGS

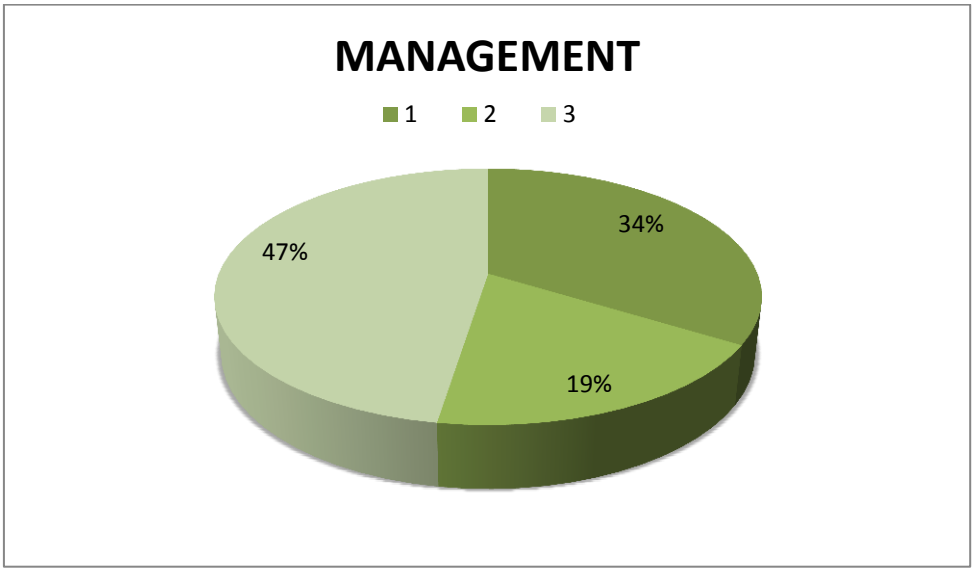


As per the TVS findings, 42 of the subjects had normal endometrial findings. Other 38 cases had showed endometrial findings as follows: endometrial hyperplasia (31.3%), endometrial polyp (1.3%), submucosal fibroid (8.8%) and adenomyosis (6.3%).

TABLE: 10 DISTRIBUTION BASED ON MANAGEMENT

MANAGEMENT	Frequency	Percent
1	27	33.8
2	15	18.8
3	38	47.5
Total	80	100.0

CHART: 7 DISTRIBUTION BASED ON MANAGEMENT



After the final diagnosis for the causes of abnormal uterine bleeding following transvaginal scan and histopathological reports. Out of all the 80 study subjects, 15 cases were surgically managed, medical management was given for 27 cases, and the remaining 38 cases underwent surgical management following failed medical management.

TABLE: 11 COMPARISON OF PRESENTING SYMPTOMS AND HISTHOPATHOLOGY

Hp	Symptoms				
	OLIGOMENORRHIA	POLYMENORRHEA	METRORRHAGIA	MENORRHAGIA	MENOMETRORRHAGIA
SHWOA	1	3	0	1	2
SE	0	6	4	1	2
PE	2	6	5	16	5
CHWOA	1	1	1	1	0
DPE	0	1	1	2	2
SHWA	0	2	2	3	0
IRE	0	1	1	0	1
IA	0	0	0	3	1
CA	1	0	0	0	0
P=0.11					

In my study, comparison of presenting symptoms and histopathological reports is not significant statistically.

TABLE: 12 COMPARISON OF PRESENTING SYMPTOMS AND HISTHOPATHOLOGY

Hp	TVS				
	NORMAL	ENDOMETRIAL HYPERPLASIA	ENDOMETRIAL POLYP	SUBMUCOSAL FIBROID	ADENOMYOSIS
SHWOA	4	3	0	0	0
SE	9	1	0	2	2
PE	26	5	0	1	2
CHWOA	0	4	0	0	0
DPE	0	2	0	2	1
SHWA	1	6	0	0	0
IRE	1	2	0	0	0
IA	1	1	1	2	0
CA	0	1	0	0	0
P<0.001					

This study shows that comparison of transvaginal scan findings and histopathology is statistically significant.

TABLE: 13 COMPARISON OF PRESENTING SYMPTOMS AND TVS FINDINGS

TVS	Symptoms				
	OLIGOMENORRHIA	POLYMENORRHEA	METRORRHAGIA	MENORRHAGIA	MENOMETRORRHAGIA
NORMAL	2	12	5	15	7
ENDOMETRIAL HYPERPLASIA	3	4	7	8	3
ENDOMETRIAL POLYP	0	0	0	1	0
SUBMUCOSAL FIBROID	0	1	2	4	0
ADENOMYOSIS	0	2	1	1	1
P=0.81					

According to TVS scan patients presenting with oligomenorrhea, 2 cases had normal findings and 3 cases had endometrial hyperplasia.

According to TVS scan patients presenting with polymenorrhea, 12 cases had normal findings, 4 cases had endometrial hyperplasia, 1 case had submucosal fibroid and 2 cases had adenomyosis.

According to TVS scan patients presenting with metrorrhagia, 5 cases had normal findings, 7 cases had endometrial hyperplasia, 2 cases had submucosal fibroid and 1 case had adenomyosis.

According to TVS scan patients presenting with menorrhagia, 15 cases had normal findings, 8 cases had endometrial hyperplasia, 1 case had endometrial polyp, 4 cases had submucosal fibroid and 1 case had adenomyosis.

According to TVS scan patients presenting with menometrorrhagia, 7 cases had normal findings, 3 cases had endometrial hyperplasia and 1 case had adenomyosis.

TABLE: 14 COMPARISON OF PRESENTING SYMPTOMS AND ENDOMETRIAL THICKNESS

Symptoms	ENDOMETRIAL THICKNESS		
	10-14mm	15-20mm	>20mm
OLIGOMENORRHIA	1	2	2
POLYMENORRHEA	14	5	1
METRORRHAGIA	12	2	0
MENORRHAGIA	17	10	1
MENOMETRORRHAGIA	9	4	0

Out of 80 subjects, 53 subjects had endometrial thickness of 10-14mm, 23 subjects had endometrial thickness of 15-20mm and 4 have endometrial thickness >20mm.

Out of 53 cases with endometrial thickness of 10-14mm, 1 presented with oligomenorrhea, 14 presented with polymenorrhea, 12 presented with metrorrhagia, 17 presented with menorrhagia and 9 with menometrorrhagia.

TABLE: 15 COMPARISON OF HISTOPATHOLOGY AND ENDOMETRIAL THICKNESS

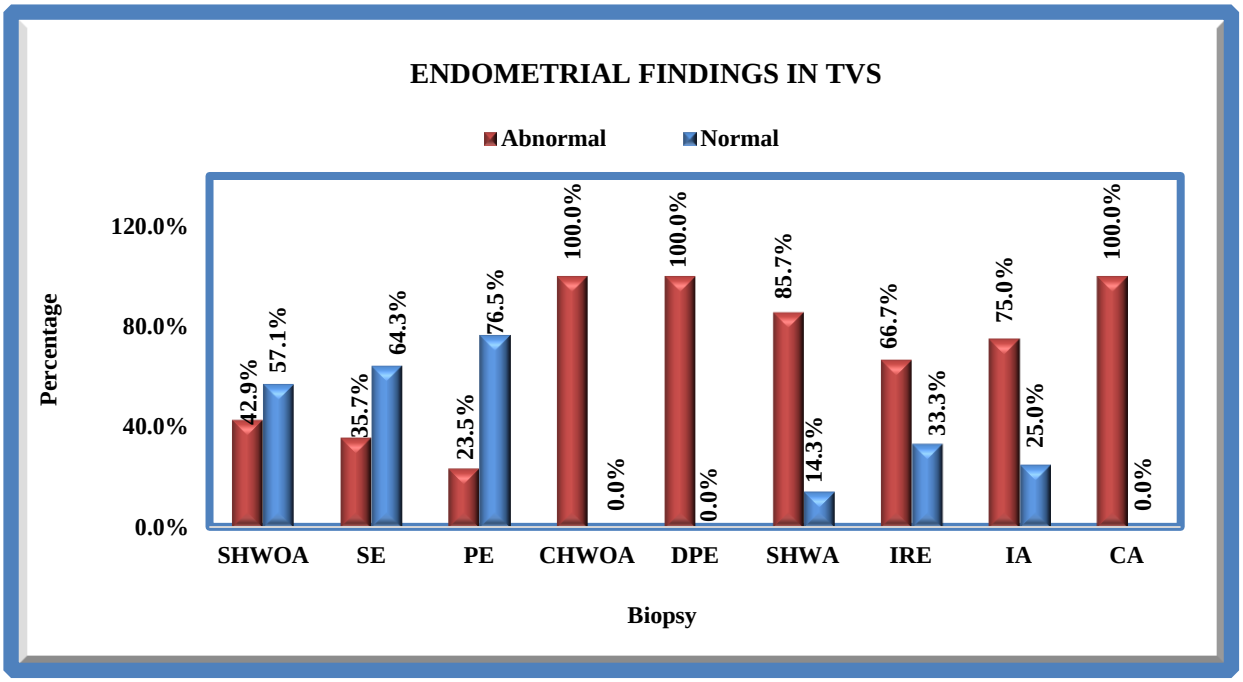
Hp	ENDOMETRIAL THICKNESS		
	10-14mm	15-20mm	>20mm
SHWOA	4	1	2
SE	7	7	0
PE	24	10	0
CHWOA	2	1	1
DPE	5	1	0
SHWA	6	1	0
IRE	3	0	0
IA	3	1	0
CA	0	0	1
P=0.001			

This study showed that comparison of endometrial thickness found in transvaginal scan and histopathology reports was statistically significant.

TABLE: 16 COMPARISON OF HISTOPATHOLOGY AND ENDOMETRIAL FINDINGS BOTH NORMAL AND ABNORMAL

Biopsy	ENDOMETRIAL FINDINGS IN TVS			
	Abnormal		Normal	
	Count	%	Count	%
SHWOA	3	42.9%	4	57.1%
SE	5	35.7%	9	64.3%
PE	8	23.5%	26	76.5%
CHWOA	4	100.0%	0	0%
DPE	6	100.0%	0	0%
SHWA	6	85.7%	1	14.3%
IRE	2	66.7%	1	33.3%
IA	3	75.0%	1	25.0%
CA	1	100.0%	0	0%

CHART: 8 COMPARISON OF HISTOPATHOLOGY AND ENDOMETRIAL FINDINGS BOTH NORMAL AND ABNORMAL



Cases whose histopathology report showed simple hyperplasia without atypia, on transvaginal scan showed that 3 had abnormal findings and 4 had normal findings.

Cases whose histopathology report showed secretory endometrium, on transvaginal scan showed that 5 had abnormal findings and 9 had normal findings.

Cases whose histopathology report showed proliferative endometrium, on transvaginal scan showed that 8 had abnormal findings and 26 had normal findings.

Cases whose histopathology report showed complex hyperplasia without atypia, on transvaginal scan showed that 4 had abnormal findings.

Cases whose histopathology report showed disordered proliferative endometrium, on transvaginal scan showed that 6 had abnormal findings.

Cases whose histopathology report simple hyperplasia with atypia, on transvaginal scan showed that 6 had abnormal findings and 1 had normal findings.

Cases whose histopathology report showed irregular endometrium, on transvaginal scan showed that 2 had abnormal findings and 1 had normal findings.

Cases whose histopathology report showed endometrial carcinoma, on transvaginal scan showed that 1 had abnormal findings.

Discussion

DISCUSSION

As AUB is the problem responsible for most of the gynaecologic consultations in the perimenopausal age group, thorough evaluation is a must especially in this age group to rule out endometrial cancer or its precursor lesion - endometrial hyperplasia.

This study includes 80 perimenopausal women with abnormal uterine bleeding who were evaluated.

Sonographic and histological assessment of the endometrium is the corner stone of diagnosis in the current practice.

TABLE: 17: DISCUSSION BASED ON AGE

AGE	PRESENT STUDY	JAIN ET AL[30]
40-44years	53.8	48
45-50 years	46.3	52

In this study, out of 80 study subjects about 54% belonged to the age group of range 40-44 years.

According to age distribution in study by Jain et al, maximum no of cases between age group of 40 to 44 with 48%, and 38% of cases between age group of 45-49 yr. This suggests abnormal uterine bleeding is common in perimenopausal women.[30]

Varadarajan R in their study they reported maximum number of cases (56.0 %) belonged to the age group 40 – 43 yrs.[31]

Verma U also observed 41% of cases belong to age group in 44 to 47 years.[32]

TABBLE: 18:DISCUSSION BASED ON PARITY

PARITY	PRESENT STUDY	GUPTA ET AL[33]
NULLIPAROUS	0	0
P1	5	4
P2	47	32
P3	22	47
>P4	6	17

And most of the effected women were biparous (58.8%) next followed by triparous (27.5%). In this study none of the cases were nulliparous.

TABLE: 19:DISCUSSION ON PRESENTING SYMPTOMS

MENSTRUAL DISORDERS	PRESENT STUDY	PILLAI ET AL[36]	KUMARI M ET AL[34]
OLIGOMENORRHIA	6.3	0	5.8
POLYMENORRHEA	25.0	21.6	38.6
METRORRHAGIA	17.5	46.6	24.3
MENORRHAGIA	33.8	17	1.4
MENOMETRORRHAGIA	16.3	11.4	14.3

Our study and two other studies done by Patil et al and the other by Bhosale et al found menorrhagia to be the most common pattern of abnormal uterine bleeding.[34,35]

In Pillai SS study menorrhagia was the most common clinical presentation seen in 46.5% of cases followed by menometrorrhagia at 21.5% which is very similar to the study by Jetley et al.[36]

BASED ON DURATION OF SYMPTOMS

The complaints presented with varying duration: <30days (47.5%), 30days- 6months (36.3%), 6months – 1 year (8.8) and more than 1 year (7.5%).

BASED ON UTERINE SIZE

About 45% of the total women had 8 – 10 weeks of uterine size, confirmed by clinical examination. Others had uterine size up to 6 weeks (26.3%), 12- 14 weeks (18.8) and >14 weeks (10%).

BASED ON ENDOMETRIAL THICKNESS

Based on findings of transvaginal scan, endometrial thickness was measured as follows: 67.5% cases showed 10-14mm, 27.5% cases showed 15-20mm and >20mm were 5%.

The study by Chatapavit et al. concluded that endometrial thickness of 8 mm or less is less likely to be associated with malignant pathology in perimenopausal women with abnormal uterine bleeding.

In study by Jain et al, TVS at endometrial thickness 5 to 8 mm, no endometrial pathology was found this was compared with other studies.[30]

Veena BT revealed normal endometrium in 45% (majority of these patients had endometrial thickness less than 9mm).[37]

BASED ON MEDICAL DISORDERS

Most patients didn't have any medical disorders. Others had hypertension (5%), diabetes mellitus (7.5%) and bronchial asthma (2.5%).

COMPARISON OF PRESENTING SYMPTOMS AND HISTOPATHOLOGY REPORTS

In this study, Out of 7 study subjects with simple hyperplasia without atypia, 1 presented with oligo menorrhea, 3 presented with polymenorrhea, 1 with menorrhagia and 2 presented with metro menorrhagia.

In this study, Out of 14 study subjects with secretory endometrium, 6 presented with polymenorrhea, 4 with menorrhagia, 1 presented with me and 2 presented with metro menorrhagia.

In this study, Out of 34 study subjects with proliferative endometrium, 2 presented with oligomenorrhea, 6 presented with polymenorrhea, 5 presented with metrorrhagia, 16 with menorrhagia and 5 presented with metro menorrhagia.

In this study, Out of 4 study subjects with complex hyperplasia without atypia, 1 presented with oligo menorrhea, 1 presented with polymenorrhea, 1 presented with metrorrhagia and 1 with menorrhagia.

In this study, Out of 6 study subjects with disordered proliferative endometrium, 1 presented with polymenorrhea, 1 presented with metrorrhagia, 2 with menorrhagia and 2 presented with metro menorrhagia.

In this study, Out of 7 study subjects with simple hyperplasia with atypia, 2 presented with polymenorrhea, 2 presented with metrorrhagia and 3 with menorrhagia.

In this study, Out of 3 study subjects with irregular endometrium, 1 presented with polymenorrhea, 1 presented with metrorrhagia and 1 presented with metromenorrhagia.

In this study, One case was diagnosed as endometrial carcinoma who presented as oligomenorrhea.

In my study, comparison of presenting symptoms and histopathological reports is not significant statistically.

TABLE: 20: BASED ON HISTOPATHOLOGY REPORT

PIPELLE BIOPSY	PRESENT CASES	PILLAI ET AL[36]
SHWOA	8.8	10.2
SE	17.5	18.2
PE	42.5	27.2
CHWOA	5.0	3.4
DPE	7.5	22.7
SHWA	8.8	0
IRE	3.8	0
CHWA	0	5.7
IA	5.0	3.4
CA	1.3	4.6

Proliferative endometrium was the most common finding on histopathological examination in study carried out by Pillai SS, which was similar to this study.

Jetley et al. Study showed, secretory endometrium was the most common finding at 32.4% followed by proliferative endometrium.[38]

In our study the most common endometrial histopathology pattern that was found related to AUB was secretory endometrium. It was found in 57% of our cases whereas in Patil et al study endometrial hyperplasia was most commonly (40%) associated with AUB.

Study done by Bhosle they showed simple hyperplasia in 17.8% of cases.

TABLE: 21:BASED ON TVS FINDINGS

ENDOMETRIAL FINDINGS IN TVS	PRESENT STUDY	PILLAI ET AL[36]
NORMAL	52.5	50
ENDOMETRIAL HYPERPLASIA	31.3	24
ENDOMETRIAL POLYP	1.3	14
SUBMUCOSAL FIBROID	8.8	8
ADENOMYOSIS	6.3	4

In women with perimenopausal bleeding the percentage of Endometrial carcinoma was 4%, the percentage of endometrial Hyperplasia was 26%, the percentage of women with adenomyosis was 14% myoma uterus 8% and 2% of women had endometrial polyps of 2% had endometritis.

BASED ON MANAGEMENT:

After the final diagnosis for the causes of abnormal uterine bleeding following transvaginal scan and histopathological reports. Out of all the 80 study subjects, 15 cases were surgically managed, medical management was given for 27 cases, and the remaining 38 cases underwent surgical management following failed medical management.

COMPARISON OF TVS FINDINGS AND HISTOPATHOLOGY REPORTS

In study by El-khayat et al. those with endometrial thickness of 20 mm or greater, only 20% had hyperplasia. Whereas in 40% the etiology was endometrial polyp the remaining 40% the etiology was both endometrial polyp and hyperplasia.

This is in concurrence with Deckardt et al. which studied histological diagnosis and related endometrial thickness obtained by endovaginal scanning in a similar study comparing TVS, hysteroscopy, and D&C for the diagnoses of
intrauterine pathology in 1286 women complaining of perimenopausal bleeding

COMPARISON OF PRESENTING SYMTOMS AND TVS FINDINGS

Inthis study, Out of 7 study subjects with simple hyperplasia without atypia, 1 presented with oligomenorrhea, 3 presented with polymenorrhea, 1 with menorrhagia and 2 presented with metromenorrhagia.

Out of 14 study subjects with secretory endometrium, 6 presented with polymenorrhea, 4 with menorrhagia, 1 presented with me and 2 presented with metromenorrhagia.

Out of 34 study subjects with proliferative endometrium, 2 presented with oligomenorrhea, 6 presented with polymenorrhea, 5 presented with metrorrhagia, 16 with menorrhagia and 5 presented with metromenorrhagia.

Out of 4 study subjects with complex hyperplasia without atypia, 1 presented with oligomenorrhea, 1 presented with polymenorrhea, 1 presented with metrorrhagia and 1 with menorrhagia.

Out of 6 study subjects with disordered proliferative endometrium, 1 presented with polymenorrhea, 1 presented with metrorrhagia, 2 with menorrhagia and 2 presented with metromenorrhagia.

Out of 7 study subjects with simple hyperplasia with atypia, 2 presented with polymenorrhea, 2 presented with metrorrhagia and 3 with menorrhagia.

Out of 3 study subjects with irregular endometrium, 1 presented with polymenorrhea, 1 presented with metrorrhagia and 1 presented with metromenorrhagia.

One case was diagnosed as endometrial carcinoma who presented as oligomenorrhea.

In my study, comparison of presenting symptoms and histopathological reports is not significant statistically.

COMPARISON OF ET AND PRESENTING SYMPTOMS

In this study, In cases with TVS findings as normal, their histopathology reports showed that 4 cases had simple hyperplasia without atypia, 9 cases had secretory endometrium, 26 cases showed proliferative endometrium, 1 case had simple hyperplasia with atypia, 1 case had irregular endometrium and 1 biopsy report came as inadequate.

In cases with TVS findings showing endometrial hyperplasia, their histopathology reports showed that 3 cases had simple hyperplasia without atypia, 1 case had secretory endometrium, 5 cases showed proliferative endometrium, 4 cases had complex hyperplasia without atypia, 2 cases has disordered proliferative endometrium, 6 cases had simple hyperplasia with atypia, 2 cases had irregular endometrium, 1 biopsy report came as inadequate and 1 case was diagnosed as endometrial carcinoma.
In cases with TVS findings showing endometrial polyp, their histopathology reports showed that the sample was inadequate.

In cases with TVS findings showing submucosal fibroid, their histopathology reports showed that 2 cases had secretory endometrium, 1 case showed proliferative endometrium, 2 cases has disordered proliferative endometrium and 2 biopsy report came as inadequate.

In cases with TVS findings showing adenomyosis, their histopathology reports showed that 2 cases had secretory endometrium, 2 cases showed proliferative endometrium and 1 case has disordered proliferative endometrium.

This study shows that comparison of transvaginal scan findings and histopathology is statistically significant.

COMPARSION OF ET AND HISTOPATHOLOGY

In this study, Out of 53 cases with endometrial thickness of 10-14mm, 1 presented with oligomenorrhea, 14 presented with polymenorrhea, 12 presented with metrorrhagia, 17 presented with menorrhagia and 9 with menometrorrhagia.

Out of 23 cases with endometrial thickness of 15-20mm, 2 presented with oligomenorrhea, 5 presented with polymenorrhea, 2 presented with metrorrhagia, 10 presented with menorrhagia and 4 with menometrorrhagia.

Out of 4 cases with endometrial thickness of >20mm, 2 presented with oligomenorrhea, 1 presented with polymenorrhea and 1 presented with menorrhagia.

COMPARISON OF NORMAL AND ABNORMAL TVS FINDINGS WITH HISTOPATHOLOGY REPORTS

In the present study,

-cases whose histopathology report showed simple hyperplasia without atypia, on transvaginal scan showed that 3 had abnormal findings and 4 had normal findings.

-Cases whose histopathology report showed secretory endometrium, on transvaginal scan showed that 5 had abnormal findings and 9 had normal findings.

-Cases whose histopathology report showed proliferative endometrium, on transvaginal scan showed that 8 had abnormal findings and 26 had normal findings.

-Cases whose histopathology report showed complex hyperplasia without atypia, on transvaginal scan showed that 4 had abnormal findings.

Cases whose histopathology report showed disordered proliferative endometrium, on transvaginal scan showed that 6 had abnormal findings.

Cases whose histopathology report simple hyperplasia with atypia, on transvaginal scan showed that 6 had abnormal findings and 1 had normal findings.

Cases whose histopathology report showed irregular endometrium, on transvaginal scan showed that 2 had abnormal findings and 1 had normal findings.

Cases whose histopathology report showed endometrial carcinoma, on transvaginal scan showed that 1 had abnormal findings.

Summary

SUMMARY

1. The present study included 80 women of perimenopausal age group with abnormal uterine bleeding.
2. Among these 54% belonged the age group of 40-44 years.
3. Most perimenopausal women with abnormal uterine bleeding were biparous (58.7%).
4. Maximum number of patients (68%) had endometrial thickness of 10-14mm on TVS.
5. The most common presenting symptom among perimenopausal women with abnormal uterine bleeding is menorrhagia (35%), followed by polymenorrhea (25%).
6. Most of the patients presented with symptoms with duration of <30days (47.5%).
7. Most of the perimenopausal women with abnormal uterine bleeding (45.3%) have no associated comorbidity.
8. Most common histopathological finding was proliferative endometrium (42.5%), followed by secretory endometrium (17.5%).
9. The TVS among perimenopausal women presenting with abnormal uterine bleeding is mostly normal (52.5%).
10. TVS showed good correlation with histopathology findings for submucosal fibroied, endometrial hyperplasia and endometrial polyp.
11. One case was diagnosed with endometrial carcinoma who presented with oligomenorrhea, the TVS showed endometrial hyperplasia and the ET was >20mm.
12. TVS can be taken as a diagnostic tool in settings where hysteroscopy is not available.
13. Out of all the 80 histopathology reports 3 samples came as in adequate.
14. Pipelle's is a office based procedure which is patient friendly, no necessity for anesthesia and no need for dilatation.

Conclusion

CONCLUSION:

Incidence of intracavitary uterine pathology in patients presenting with abnormal uterine bleeding is high.

This is true when considering the 40 -50 yrs. age group who most of the times present with heavy regular bleeding, clinically enlarged uterus and significant anemia.

When this is combined with endometrial sampling by pipelle's aspiration it can supplement The shortcomings of dilatation and curettage.

Dilatation and curettage being a blind procedure requires hospitalization and general anesthesia which can be safely replaced by an alternate valid, safe and non. Invasive technique for evaluating the endometrial pathology in women with perimenopausal bleeding.

Pipelle's aspiration is office based procedure, it can be done in out patients without the need for anaesthesia.

Transvaginal sonogram is a simple, non-invasive convenient way to indirectly visualise the endometrial cavity.

If trans vaginal scan is incorporated into gynecology office setting and along with bimanual pelvic examination can enhance our anatomic diagnosis.

This study proves that transvaginal findings correlate well with the histopathology findings.

LIMITATIONS:

The pipelle's endometrial aspiration is not accurate as the sample is not taken from focal lesion.

The study included small number of study subjects.

Bibliography

BIBLIOGRAPHY:

1. Soules MR, Sherman S, Parott E. Stages of reproductive aging workshop (STRAW). J. Womens Health, Gender Based Med. 2001 ; 10 : 843-8
2. Awwad JT, Toth TL, Schiff I .Abnormal uterine bleeding in the perimenopause .Int J Fertil .and Menopausal Stud . 1993;38(5);261-9
3. JEFFCOAT
4. Schorge , John O , Williams , J . whitridge , Williams gynecology , pg 175 , The Mc graw Hill companies , china ,press , 2008
5. Epstein E, Ramirez A, Skoog L, Valentin L. Transvaginal sonography , saline contrast sonohysterography and hysteroscopy for the investigation of women with postmenopausal bleeding and endometrium > 5 mm . Ultrasound Obstet Gynecol. 2001 ; 18 : 157 – 62
6. FIGO classification system (PALM – COEIN) for the causes of abnormal uterine bleeding in non gravid women of reproductive age. *International Journal of Gynecology and Obstetrics* 2011 ; 113 : 3 – 13
7. Dastur A. History of endosonography,chapter -1,USG in obstetrics and gynaecology, 1st edition.,Edt .G.Malhotra,2-19pp.
8. Schwner SR.,Labaovac J. Transvaginal pelvic ultrasonography. J.Ultrasound,Med.1984;3:381-83.
9. Ferenczy A, Pathophysiology of endometrial bleeding, Maturitas 45:1, 2003
10. Clinical gynecologic endocrinology and infertility ninth edition Leon Speroff and Marc A fritz chapter 15 : 600.
11. Munro MG, CritchleyHOD ,BorderMS,Fraser IS.FIGO classification system(PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age.Int J GynaecolObstet(Internet).elsevier B.V;2011 Apr(cited 2014 Oct 26);113(1):3-13.Avaliable from :http://www.ncbi.nim.nih.gov/pubmed.
12. LevensEd, DechrneyAH. Diagnosis of abnormal uterine bleeding in reproductive aged women.AmcollobstetGynecolPract Bull.2012:120(1):197- 206.
13. Benacerraf BR, Shipp TD, Bromley B. which patients benefit from a 3D reconstructed coronal view of the uterus added to standard routine 2D pelvic sonography? AJR 2008; 190(3):626-629.

14. Curry Thomas S , Dowdey James E , Murry Robert C. Christensen's physics of diagnostic radiology , 4th ed. Lippincott Williams & Wilkins ,1990 :323-372.
15. Rumack CM. Diagnostic ultrasound.Srd ed. St Louis, Missouri, Mosby,Elsevier, 2009:527-587
16. Kufahl J, Pedersen 1, Eriksen PS, et al. Transvaginal ultrasound, endometrial cytology sampled by Gynoscann and histology obtained by Uterine Explora Curette compared to the histology of the uterine specimen. Acta Obstet Gynecol Scand 1997; 76:790-796.
17. Tsuda H, Kawabata M, Yamamoto K, et al. Prospective study to compare endometrial cytology and transvaginal ultrasonography for identification of endometrial malignancies. Gynecol Oncol 1997; 65:383-386.
18. GJusa-Chiferi MG, Gon9alves WJ, Baracat EC, et al. Transvaginal ultrasound, uterine biopsy and hysteroscopy for postmenopausal bleeding. Int J Gynecol Obstet 1996; 55:39-44.
19. Yong EL, Baird DT, Hillier SG, Mediation of gonadotropinstimulated growth and differentiation of human granulosa cells by adenosine-3', 5'-monophosphate: one molecule, two messages, Clin Endocrinol 37:51, 1992.
20. Eppig JJ, Chesnel F, Hirao Y, O‟‟Brien MJ, Pendola FL, Watanabe S, Wigglesworth K, Oocyte control of granulosa cell development: how and why, Hum Reprod 12(Suppl):127, 1997.
21. Liu JH, Yen SSC, Induction of midcycle gonadotropin surge by ovarian steroids in women: a critical evaluation, J Clin Endocrinol Metab 57:797, 1983.
22. Girsh E, Milvae RA, Wang W, Meidan R, Effect of endothelin-1 on bovine luteal cell function: role in prostaglandin F2a-induced antisteroidogenic action, Endocrinology 137:1306, 1996.
23. Berek JS , Adashi EY , Hillard PA (eds) Novak‟‟s gynecology 15 th edition , chapter 7 reproductive physiology g 149 Ferenczy A , Bertrand G , Gelfand MM .proliferation kinetics of human endometrium during normal menstrual cycle *Am J Obstet gynecol 1979 ; 133 : 859 – 86*
24. . Ferenczy A , Bertrand G , Gelfand MM .proliferation kinetics of human endometrium during normal menstrual cycle *Am J Obstet gynecol 1979 ; 133 : 859 - 867*

25. Noyes RW, Hertig AW, Rock J. Dating of the endometrial biopsy .Fertil Steril 1950 ; 1 : 3 – 25.
26. Montgomery BE, Daum GS, Dunton CJ. Endometrial hyperplasia: A review. Obstet & Gynecol Sur 2004;59(5):368-378.
27. 49. Lurain JR. Uterine cancer. In: Berek & Novak's gynecology, 14th edn: Lippincott Williams & Wilkins, Philadelphia 2007: 1343-1402.
28. 50. Dadhania B, Dhruva G , Agravat A, Pujara K..Histopathological study of endometrium in dysfunctional uterine bleeding. Int J Res Med. 2013; 2(1);20-24
29. 51. Baral R, Pudasaini S. Histological patterns of endometrial samples in abnormal uterine bleeding. J Path Nepal 2011;1:13-16.
30. Jain M, Chakraborty S. Evaluation of abnormal uterine bleeding with transvaginal sonography. Int J Reprod Contracept Obstet Gynecol 2017;6.
31. Varadarajan R, Sreekantha SM. Role of hysteroscopy in abnormal uterine bleeding in perimenopausal age group. J Evol Med Dent Sci. 2013;2(10):1504-9.
32. Verma U, Garg R, Singh S, Yadav P, Rani R. Diagnostic approach in perimenopausal women with abnormal uterine bleeding. J South Asian Federation Menopause Societies. 2014;2(1):12-4.
33. Gupta A, Rathore AM, Manaktala U, Rudingwa P. Evaluation and histopathological correlation of abnormal uterine bleeding in perimenopausal women. IJBAR. 2013;4(8):509-13.
34. Pillai SS. Sonographic and histopathological correlation and evaluation of endometrium in perimenopausal women with abnormal uterine bleeding. Int J Reprod Contracept Obstet Gynecol 2014;3:113-7.
35. Patil R, Patil RK, Andola SK, Laheru V, Bhandar M. Histopathological spectrum of endometrium in dysfuctional uterine bleeding. Int J Biol Med Res.2013;4(1):2798-801. Bhosle A, Fonseca M. Evaluation and Histopathological Correlation of Abnormal Uterine Bleeding in Perimenopausal Women. Bombay Hospital Journal. 2010;52(1):69-72.
36. Jetley S, Rana S, Jairajpuri ZS. Morphological spectrum of endometrial pathology in middle aged women with atypical uterine bleeding - a study of 219 cases. J Midlife Health. 2013;4:216-20.
37. Veena BT, Shivalingaiah N. Role of transvaginal sonography and diagnostic hysteroscopy in abnormal uterine bleeding. JCDR. 2014;8(12):OC06.

38. Jetley S, Rana S, Jairajpuri ZS. Morphological spectrum of endometrial pathology in middle aged women with atypical uterine bleeding - a study of 219 cases. J Midlife Health. 2013;4:216-20.
39. El-khayat W, Sleet ME, Mahdi EY. Comparative study of transvaginal sonography and hysteroscopy for the detection of pathological endometrial lesions in women with perimenopausal bleeding. Middle East Fertility Society Journal. 2011 Mar 1;16(1):77-82.
40. Deckardt R, Lueken RP, Gallinat A, Möller CP, Busche D, Nugent W, Salfelder A, Dohnke H, Hoffmeister U, Dewitt E, Hennefründ J. Comparison of transvaginal ultrasound, hysteroscopy, and dilatation and curettage in the diagnosis of abnormal vaginal bleeding and intrauterine pathology in perimenopausal and postmenopausal women. The Journal of the American Association of Gynecologic Laparoscopists. 2002 Aug 1;9(3):277-82

Annexures

ANNEXURES

PATIENT INFORMATION SHEET

Study title: **ENDOMETRIAL STUDY OF PERIMENOPAUSAL ABNORMAL UTERINE BLEEDING BY TRANSVAGINAL SONOGRAPHY AND ITS CORRELATION WITH HISTOPATHOLOGY**

Study location: R L Jallappa Hospital and Research Centre attached to Sri DevrajUrs Medical College. Tamaka, Kolar

Details:

In patients of age group 40-50 years with symptoms of Polymenorrhagia/ menorrhagia coming to R.L.Jallappa hospital .

Patients in this study will have to undergo complete general physical examination, obstetric examination, routine blood investigations such as Complete blood count, Blood grouping and Rh typing, HIV, HBsAg , VDRL, routine urine analysis, RBS, BT, CT, thyroid function test will be done.

Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in the study we will collect information (as per proforma) from you or a person responsible for you or both. Relevant history will be taken. This information collected will be used only for dissertation and publication.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

For further information contact

Dr. Velicheti Satya Sree

Post graduate

Department of obstetrics and gynecology, SDUMC , Kolar.

PROFORMA

Name : I.P.No:

Age: D.O.A:

Occupation: D.O.D:

Address:

Husband's Occupation:

Socio-economic Status:

History of presenting illness:

Menstrual history:

- Age of menarche:
- Past menstrual history:
- Age of menopause if attained:

Obstetric history:

ML: No. of children:

Last child birth: Sterilization:

Past history:

Family History:

Personal History:

Sleep: Appetite:

Diet: Bowel & Bladder:

G.P.E:

- Build: Nourishment:
- Pallor: Icterus: Cyanosis: Clubbing:
- Lymphadenopathy: Pedal edema:
- Pulse: B.P.: Temp:

- Breast: Thyroid:
- Systemic examination:
- CVS:
- RS:
- CNS:

- Abdominal Examination:
- Local Examination:
- External Genitalia:
- P/S: P/V:

- Investigations:
- Complete blood picture
- BT, CT
- Urine Examination
- Random Blood sugar
- Pap smear
- Thyroid function tests
- USG:
- Diagnosis:

ಮಾಹಿತಿಯುಕ್ತ ಸಮ್ಮತಿ ಪತ್ರ

ಶೀರ್ಷಿಕೆ: ಅಸಹಜ ಗರ್ಭಾಶಯದ ರಕ್ತಸ್ರಾವ ವಿಕಿರಣಶಾಸ್ತ್ರೀಯ ಮತ್ತು ಹಿಸ್ಟೊ ರೋಗ ಪರಸ್ಪರ ಪೆರಿ ಮುಟ್ಟು ನಿಲ್ಲುತ್ತಿರುವ ಮಹಿಳೆಯರು

ಪ್ರಮುಖ ಸಂಶೋಧಕರು: ಡಾ. ವಿ. ಸತ್ಯ ಶ್ರೀ

ಮಾರ್ಗದರ್ಶನದಲ್ಲಿ: ಡಾ. ಇ .ಗೋಮತಿ

ಹೆಸರು:

ವಯಸ್ಸು:

ವಿಳಾಸ:

೧. ನನ್ನ ಸ್ವಂತ ಭಾಷೆಯಲ್ಲಿ ಮತ್ತು ಸರಳ ರೀತಿಯಲ್ಲಿ ಈ ಅಧ್ಯಯನದ ಮಾಹಿತಿ ನೀಡಲಾಗಿದೆ. ಈ ಸಂದರ್ಭದಲ್ಲಿ ಬೇಕಾದ ತಪಾಸಣೆಗಳು ಮತ್ತು ಛಾಯಾಚಿತ್ರಗಳ ಅವಶ್ಯಕತೆಗಳಿಗೆ ನಾನು ಸಹಕರಿಸುತ್ತೇನೆ.

೨. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನಿರ್ಮಾಣವಾದ ವೈದ್ಯಕೀಯ ಮಾಹಿತಿ ಆಸ್ಪತ್ರೆಯ ಭಾಗವಾಗಿದ್ದು, ಗೌಪ್ಯವಾಗಿ ಇಡಲಾಗುವುದು.

೩. ನನ್ನ ಭಾಗವಹಿಸುವಿಕೆಯನ್ನು , ನಾನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ನನ್ನ ಸಹಮತಿಯನ್ನು ಹಿಂದೆಪಡೆಯಬಹುದು ಹಾಗು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ನನ್ನ ಭಾಗಸುವಿಕೆ ನಿಲ್ಲಿಸಬಹುದು.

೪. ಈ ಅಧ್ಯಯನದಿಂದ ಉದ್ಭವಿಸುವ ಯಾವುದೇ ಮಾಹಿತಿ ಅಥವಾ ಫಲಿತಾಂಶವನ್ನು ವೈಜ್ಞಾನಿಕ ಉದ್ದೇಶಗಳಿಗೆ ಉಪಯೋಗಿಸಲು ಒಪ್ಪುತ್ತೇನೆ.

೫. ನನಗೆ _____ (ಮುಖ್ಯ ಸಂಶೋಧಕ) ನನ್ನ ಭಾಷೆಯಲ್ಲಿಯೇ, ಸಂಶೋಧನೆ ಹಾಗು ಅಧ್ಯಯನದ ವಿಧಿ, ವಿಧಾನಗಳ ಬಗ್ಗೆ ಮತ್ತು ನಾನು ಅನುಭವಿಸಬಹುದಾದ ಸಂಭಾವ್ಯ ಅಪಾಯಗಳು ಮತ್ತು ಅನಾನುಕೂಲತೆಗಳ ಕುರಿತು ವಿವರಿಸಲಾಗಿದೆ. ನಾನು ಈ ಸಂಶೋಧನಾ ಯೋಜನೆಯ ವಿಷಯವಾಗಿ ಭಾಗವಹಿಸಲು ಸಹಕರಿಸುತ್ತೇನೆ.

ಭಾಗವಹಿಸುವವರ ಸಹಿ:

ಸಾಕ್ಷಿಯ ಸಹಿ: ದಿನಾಂಕ:

ನಾನು ---------- ಈ ಸಂಶೋಧನೆಯ ಉದ್ದೇಶ ಹಾಗು ಇದರಿಂದ ಉಂಟಾಗುವ ಅಪಾಯಗಳು ಮತ್ತು ಲಾಭಗಳನ್ನು ನನ್ನ ಸಾಮರ್ಥ್ಯಕ್ಕೆ ಸಾಧ್ಯವಾದ ರೀತಿಯಲ್ಲಿ ವಿವರಿಸಿದ್ದೇನೆ.

ಮುಖ್ಯ ಸಂಶೋಧಕ / ಗೈಡ್ ಸಹಿ: ದಿನಾಂಕ:

CONSENT FORM

Study title: ENDOMETRIAL STUDY OF PERIMENOPAUSAL ABNORMAL UTERINE BLEEDING BY TRANSVAGINAL SONOGRAPHY AND ITS CORRELATION WITH HISTOPATHOLOGY
Chief researcher/ PG guide's name: DR. VELICHETI SATYA SREE
Under the guidance of: DR. E. GOMATHY

Name of the subject:
Age :
Address :

a. I have been informed in my own vernacular language the purpose of the study, the necessity of relevant investigations to be carried out and photographs to be taken.
b. I understand that the medical information produced by this study will become part of institutional record and will be kept confidential by the said institute.
c. I understand that my participation is voluntary and may refuse to participate or may withdraw my consent and discontinue participation at any time without prejudice to my present or future care at this institution.
d. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).
e. I confirm that _____ (chief researcher/ name of PG guide) has explained to me the purpose of research and the study procedure that I will undergo and the possible risks and discomforts that I may experience, in my own language. I hereby agree to give valid consent to participate as a subject in this research project.

Participant's signature
Signature of the witness: Date:

I have explained to _____ (subject) the purpose of the research, the possible risk and benefits to the best of my ability.

Chief Researcher/ Guide signature Date:

DATE	HOSPITAL NUMBER	AGE	PARITY	MENSTRUAL DISORDERS					DURATION OF SYMPTOMS	UTERINE SIZE	MEDICAL DISORDERS				ENDOMETRIAL THICKNESS	PIPELLE BIOPSY										ENDOMETRIAL FINDINGS IN TVS					MANAGEMENT
				OLIGOMENORRHIA	POLYMENORRHEA	METRORRHAGIA	MENORRHAGIA	MENOMETRORRHAGIA			HYPERTENSION	DM	ASTHMA	NIL		SHWOA	SE	PE	CHWOA	DPE	SHWA	IRE	CHWA	IA	CA	NORMAL	ENDOMETRIAL HYPERPLASIA	ENDOMETRIAL POLYP	SUBMUCOSAL FIBROID	ADENOMYOSIS	
03/01/2018	529996	1	1	0	0	0	0	1	1	2	0	0	0	1	2	0	1	0	0	0	0	0	0	0	0	1		0			2
05/01/2018	531633	0	2	1	0	0	0	0	2	1	0	0	0	1	1	0	0	0	1	0	0	0	0	0	0		1	0			1
05/01/2017	531723	1	2	0	1	0	0	0	4	3	0	1	0	0	3	1	0	0	0	0	0	0	0	0	0	1		0			3
02/01/2018	541615	1	3	0	0	0	1	0	1	1	0	0	0	1	2	0	0	0	0	0	0	0	0	1	0	1		1			2
12/02/2018	544929	0	4	0	1	0	0	0	1	4	0	0	0	1	1	0	1	0	0	0	0	0	0	0	0	1		0			1
13/02/2018	545059	1	2	0	0	0	1	0	3	2	0	0	0	1	2	0	0	1	0	0	0	0	0	0	0		1	0			1
21/02/2018	549603	1	3	0	1	0	0	0	1	2	0	1	0	0	1	1	0	0	0	0	0	0	0	0	0	1		0			3
03/09/2018	620582	0	2	0	0	0	1	0	2	1	0	0	0	1	2	0	0	0	0	0	1	0	0	0	0		1	0			3
14/03/2018	558084	1	2	0	0	1	0	0	4	3	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0		1	0	1		2
20/03/2018	558649	0	2	0	0	0	1	0	1	4	0	0	0	1	2	0	0	1	0	0	0	0	0	0	0	1	1	0			3
24/03/2018	557122	1	3	0	0	1	0	0	2	2	0	0	0	1	1	0	0	0	0	0	0	1	0	0	0		1	0			1
24/03/2018	561796	1	2	0	0	1	0	0	1	1	0	0	0	1	1	0	1	0	0	0	0	0	0	0	0	1		0			1
02/04/2018	562618	0	2	0	1	0	0	0	3	1	1	0	0	0	1	0	1	0	0	0	0	0	0	0	0	1		0			2
06/04/2018	564453	1	3	1	0	0	0	0	1	3	0	0	0	1	3	1	0	0	0	0	0	0	0	0	0	1		0			3
12/04/2018	568304	0	4	0	0	0	1	0	1	2	0	0	0	1	2	0	0	1	0	0	0	0	0	0	0		1	0			3
13/11/2017	539776	0	2	0	1	0	0	0	2	2	0	0	0	1	1	0	0	0	0	0	1	0	0	0	0		1	0			1
13/11/2018	569094	0	3	0	1	0	0	0	1	3	0	0	0	1	1	0	1	0	0	0	0	0	0	0	0	1		0			3
22/04/2018	571516	1	1	0	0	1	0	0	2	1	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0		1	0			1
22/04/2018	542072	0	2	1	0	0	0	0	2	3	0	0	0	1	3	0	0	0	0	0	0	0	0	0	1		1	0			1
30/04/2018	572063	0	2	0	0	0	1	0	3	2	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0			0	1		2
04/05/2018	575650	0	3	1	0	0	0	0	4	1	0	1	0	0	2	0	0	1	0	0	0	0	0	0	0		1	0			3
05/05/2018	575021	0	2	0	0	0	1	0	1	2	0	0	0	1	3	0	0	0	1	0	0	0	0	0	0		1	0			1
05/05/2018	573985	1	3	0	0	0	1	0	2	4	0	0	0	1	2	0	0	1	0	0	0	0	0	0	0	1		0			1
05/05/2018	569809	0	1	0	0	0	1	0	2	2	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0			0		1	2
05/05/2018	577298	1	2	0	0	1	0	0	1	1	0	0	0	1	1	0	0	0	0	0	1	0	0	0	0		1	0			3
19/05/2018	581684	1	4	0	0	0	0	1	1	2	0	0	0	1	2	0	0	1	0	0	0	0	0	0	0	1		0			3
11/06/2018	589479	1	2	1	0	0	0	0	4	3	0	0	0	1	2	0	0	1	0	0	0	0	0	0	0	1		0			1
11/06/2018	588029	1	2	0	0	0	0	0	1	4	0	0	0	1	2	0	1	0	0	0	0	0	0	0	0	1		0			1
12/06/2018	587206	1	2	0	0	0	1	0	2	2	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1		0			2
13/06/2018	590840	0	3	0	0	0	0	1	1	2	0	0	0	1	2	0	0	0	0	1	0	0	0	0	0		1	0			3
17/06/2018	587214	0	2	0	0	0	1	0	3	3	0	0	0	1	2	0	0	1	0	0	0	0	0	0	0	1		0			1
21/06/2018	592084	0	2	0	0	0	1	0	2	1	0	0	0	1	2	0	1	0	0	0	0	0	0	0	0	1		0			3
23/06/2018	522021	0	2	0	1	0	0	0	1	2	0	0	0	1	2	0	0	1	0	0	0	0	0	0	0	1		0			2
30/06/2018	599260	1	1	0	0	1	0	0	2	2	0	0	0	1	1	0	0	0	1	0	0	0	0	0	0		1	0			1
30/06/2018	597033	1	3	0	0	0	0	1	2	4	1	0	0	0	2	1	0	0	0	0	0	0	0	0	0	1		0			2
16/07/2018	604490	1	4	0	0	0	1	0	2	2	0	0	0	1	1	0	0	0	0	0	0	0	0	1	0			0	1		3
19/07/2018	606686	0	2	0	0	1	0	0	1	3	0	0	1	0	2	0	0	1	0	0	0	0	0	0	0	1		0			1
21/07/2018	605501	1	3	0	0	0	1	0	1	1	0	0	0	1	1	0	0	0	0	0	0	0	0	1	0		1	0	1		3
23/07/2018	606860	0	2	0	0	0	1	0	1	2	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1		0			1
07/08/2018	611773	1	3	0	0	0	1	0	2	3	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1		0			2
07/08/2018	612401	0	2	0	0	1	0	0	2	1	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1		0			3
04/06/2018	587206	1	2	0	0	0	1	0	1	2	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0			0	1		1
19/06/2018	282269	1	2	0	0	0	0	1	4	2	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1		0			1
30/06/2018	599261	1	4	0	1	0	0	0	2	2	0	1	0	0	1	0	0	0	0	0	1	0	0	0	0		1	0			1

02/07/2018	599859	0	3	0	1	0	0	0	2	2	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0			0		1	2
27/06/2018	598420	0	1	0	1	0	0	0	1	1	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1		0			3
13/07/2018	604491	0	2	0	1	0	0	0	3	3	0	0	0	1	2	0	1	0	0	0	0	0	0	0	0	1		0			1
01/08/2018	611465	0	2	0	0	0	1	0	1	4	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1		0			3
28/03/2018	562787	1	2	0	0	1	0	0	2	1	0	0	0	1	1	0	1	0	0	0	0	0	0	0	0	1		0			2
28/02/2018	247407	0	2	0	0	0	0	1	1	2	0	0	0	1	1	0	0	0	0	0	0	1	0	0	0	1	1	0			3
17/02/2018	547964	1	2	0	0	1	0	0	1	3	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1		0			3
17/02/2018	548196	1	3	0	1	0	0	0	2	1	1	0	0	0	1	1	0	0	0	0	0	0	0	0	0		1	0			1
13/05/2018	579819	0	2	0	0	1	0	0	2	2	0	0	0	1	1	0	1	0	0	0	0	0	0	0	0		1	0			1
08/05/2018	578274	1	3	0	1	0	0	0	2	2	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1		0			3
30/04/2018	575388	1	2	0	0	0	0	1	1	3	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0			0			2
30/04/2018	575163	0	2	0	1	0	0	0	2	2	0	0	0	1	2	0	0	0	1	0	0	0	0	0	0		1	0			3
04/05/2018	576574	0	2	0	1	0	0	0	3	2	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1		0			1
05/01/2018	532094	0	4	0	0	1	0	0	1	3	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0			0		1	3
06/01/2018	532210	0	3	0	0	1	0	0	2	1	0	0	0	1	1	0	0	0	0	0	1	0	0	0	0		1	0			3
05/01/2018	530448	1	2	0	0	0	0	1	2	2	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1		0			3
31/01/2018	541615	1	2	0	1	0	0	0	1	4	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1		0			3
22/01/2018	537091	1	2	0	0	0	0	1	1	2	0	0	0	1	1	0	0	0	0	0	0	0	0	1	0			0			1
28/01/2018	540292	1	2	0	0	1	0	0	1	2	0	1	0	0	2	0	1	0	0	0	0	0	0	0	0			0	1		3
20/09/2018	490651	0	3	0	1	0	0	0	2	2	0	0	1	0	2	0	1	0	0	0	0	0	0	0	0			0	1		3
09/08/2017	471718	0	3	0	1	0	0	0	1	1	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1		0			2
08/07/2018	455490	1	2	0	0	0	1	0	2	2	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0			0			3
17/07/2017	460474	0	2	0	0	0	1	0	4	2	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1		0			3
22/07/2017	462114	0	2	0	0	0	1	0	1	3	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1		0			1
26/07/2017	461944	0	3	0	0	0	1	0	1	1	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0		1	0			3
17/03/2018	559114	1	2	0	0	0	0	1	2	2	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1		0			3
07/02/2018	542464	0	2	0	0	0	0	1	3	1	0	0	0	1	1	0	1	0	0	0	0	0	0	0	0			0		1	3
07/10/2017	498478	1	3	0	0	0	1	0	1	2	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1		0			3
04/10/2017	470166	0	3	0	0	0	1	0	1	4	0	0	0	1	1	0	0	0	0	0	1	0	0	0	0		1	0			1
14/09/2017	488380	0	2	0	0	0	1	0	1	2	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1		0			3
25/07/2017	463402	0	2	0	1	0	0	0	2	1	0	0	0	1	2	0	1	0	0	0	0	0	0	0	0			0		1	3
25/07/2017	465238	0	2	0	0	0	0	1	2	2	1	0	0	0	1	0	0	0	0	1	0	0	0	0	0			0			2
20/01/2017	389873	1	3	0	1	0	0	0	1	3	0	0	0	1	1	0	0	0	0	0	0	1	0	0	0			0			3
15/09/2018	509708	0	3	0	0	0	1	0	1	1	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	1		0			3
	589321	0	2	0	0	0	0	1	1	1	0	1	0	0	1	1	0	0	0	0	0	0	0	0	0		1	0			3
	465231	0	2	0	0	0	1	0	1	2	0	0	0	1	1	0	0	0	0	0	1	0	0	0	0	1		0			1