



**ORIGINAL RESEARCH PAPER**

**Gynaecology**

**A STUDY ON ENDOMETRIAL THICKNESS BY ENDOVAGINAL SONOGRAHY WITH HISTOPATHOLOGY IN PERIMENOPAUSAL WOMEN IN A TERTIARY CARE CENTRE.**

**KEY WORDS:** Abnormal uterine bleeding, transvaginal USG, Endometrial sampling, perimenopausal bleeding.

<b>Dr.P.S.Jikki kalaiselvi</b>	Associate Professor of Obstetrics & Gynaecology, ACS Medical college, Chennai.
<b>Dr.G.Thenmozhi</b>	Assistant Professor of Obstetrics & Gynaecology, ACS Medical college, Chennai.
<b>Dr.Shanthi Dhinakaran</b>	Professor, Department of Obstetrics & Gynaecology ACS Medical college, Chennai.
<b>Dr.R.Dhivya</b>	Junior Resident Department of Obstetrics & Gynaecology, ACS Medical college, Chennai.
<b>Dr Christina Mary P Paul</b>	Professor, Department of Community Medicine
<b>Dr.G.Manju</b>	Senior Resident, Department of Obstetrics & Gynaecology, ACS Medical college, Chennai.

**ABSTRACT**  
**AIM:** To establish the relation of endometrial thickness by endovaginal sonography with histopathology in perimenopausal.  
**METHODS:** 100 women with perimenopausal abnormal uterine bleeding were selected & subjected transvaginal ultrasonography & endometrial sampling.  
**RESULTS:** Among 100 perimenopausal abnormal uterine bleeding patients 57 had endometrial thickness >0.8, 33 patients had 0.4 to 0.7 cm. 10 patients had <0.4mm. 60 patients HPE reports shows endometrial hyperplasia. This shows endometrial hyperplasia is common in perimenopausal age.

**INTRODUCTION**

Menstruation is a cyclical bleeding from uterine endometrium in response to ovarian hormones which are under the control of hypothalamo – pituitary-ovarian axis.

Abnormal uterine bleeding is a common gynaecological condition which is defined as a pathological bleeding from the uterus , unexplained on basis of neoplasia, infection or pregnancy (Telinde 1962 and 1985).

As it is a clinical entity which covers all forms of abnormal uterine bleeding in the absence of demonstrable pelvic pathology, the diagnosis is by exclusion of organic disease of genital tract which depends on the extent of investigations performed.

**DEFINITION OF PERIMENOPAUSAL PERIOD:**

Perimenopause is the period 2-8 years preceding menopause and 1 year after the final menses .

However a better practical definition is the phase preceding the onset of menopause, generally occurring around 40-50 years of age (beginning at age 47.5 lasting for 4 years) during which regular cycles of a woman transitions to a pattern of irregular cycles.

Menorrhagia is a cyclical bleeding at regular interval which is excessive in amount (>80ml)<sup>3</sup> or duration. Menorrhagia is thought to be associated with uterine fibroid, DUB, Adenomyosis , Pelvic infections, Endometrial polyp, Clotting defects. Polymenorrhagia, Intermenstrual bleeding and Metrorrhagia are other common disorders at perimenopause.

Adequate history, clinical examination which includes general examination, abdominal and pelvic examinations, haematological investigations, endocrinal assessment, transvaginal ultrasonography which is superior in excluding adnexal pathology, hysteroscopy and endometrial histopathology help in diagnosis.

In spite of vast advances, the exact cause of abnormal uterine bleeding could not be determined.

(Benson and Miller, 1956) Thought the cause of abnormal uterine bleeding to be due to dysfunction and attributed to derangement in hypothalamic – pituitary – ovarian – endometrial axis. (Speroff and Fritz, 1982). The role of ovary in controlling its own steroidogenic function and the ultimate endometrial response via the oestrogen feed back mechanism was stressed.

Kratochwil (1968) and Fleisher (1986) used Vagino sonography in detecting the pelvic lesions and reported the sonographic depiction of endometrium in normal menstrual cycle and in abnormal endometrium

Vaginal sonography helps in direct measurement of endometrial thickness. The relationship of endometrial thickness to menstrual blood loss was demonstrated by Dodson (1994). He concluded that thin endometrium and low oestradiol levels were observed in few cases of menorrhagia and that the thickened endometrium needs early curettage.

Comparative study of endometrial thickness by transvaginal sonography with endometrial histopathology was undertaken at kilpauk medical college and hospital in Chennai from July 2013 in 100 perimenopausal women (over 40yrs age) with Abnormal uterine bleeding.

**DEFINITION OF ABNORMAL UTERINE BLEEDING:**

Abnormal uterine bleeding was defined as bleeding in the absence of clinically detectable pathology of reproductive organs.

**Hormones :-** Intracellular concentration of steroids and steroid receptors are essential factors that control the extent of hormone action in target cells (1979) Tseng. Hirschmann and Adler (1907) showed that the endometrium is a cyclical tissue undergoing biphasic changes and abnormal uterine bleeding is attributed to endometrial hyperplasia. Schroder (1914-15) studied endocrinal and histopathological aspects of metropathia haemorrhagica.

(1924) Shaw classified dysfunctional uterine bleeding according to the nature of bleeding.

1. Metropathia haemorrhagica.

2. Functional epimenorrhoea.

- 1) Ovular** a) Functional epimenorrhoea  
 b) Functional menorrhagia  
 i) irregular ripening  
 ii) irregular shedding

- 2) Anovular** a) Threshold bleeding  
 b) Metropathia haemorrhagica  
 There are several classifications of AUB Or DUB

1. **Primary AUB** : Abnormal bleeding from uterus where there is no disease of genital tract, no Intra uterine contraceptive device insertion (IUCD), no sex hormone usage.  
 2. **Secondary AUB** : It is secondary to the usage of IUCD, administration of sex hormones and also secondary to the organic disease outside the genital tract.

**Ovular AUB** : Irregular ripening of endometrium, irregular shedding, following IUCD insertion, following sterilization operation.

**Anovulatory AUB** : Threshold bleeding of puberty menorrhagia, metropathia haemorrhagica and perimenopausal AUB.

**Mechanism Of Bleeding In Normal And Abnormal Menstruation**

The suggested mechanism of initiation of bleeding are

- i) Dehydration of stroma due to tighter coiling of spiral arteries and ischemia of blood vessel wall with extravasation of blood. (Markee, 1946)ref 6
- ii) Release of autonomic mediators from nerves supplying spiral arteries distal to the arterio-venous anastomosis in the endometrium causing shunting of blood through the anastomosis with ischemia of vessel wall beyond the anastomosis and extravasation of blood (Okkels, 1950).
- iii) Tissue metabolites may be released either as a result of ischemia or as a result of release of proteolytic enzymes. Arrest of bleeding is the result of the combined effects of prolonged vaso-constriction, plugging of spiral arteries and resumption of oestrogen secretion by growing follicle.

**Abnormal Uterine Bleeding In Perimenopausal Women ( above 40yrs of age) :**

**Causes :**

Endometrium regulates the steroid concentration by,

- i) Enzyme induction to control the rate of metabolism and intracellular concentration of oestrogen.
- ii) Synthesis of oestrogen and progesterone receptors in the endometrium which regulates the circulating oestrogen, progesterone by binding.

Oestrogen increases both oestrogen and progesterone receptors, where as progesterone decreases the post ovulatory content of oestrogen receptors, impairs the transfer of oestrogen to nuclear receptors and increases the metabolism there by decreasing the intracellular concentration of oestrogen.

**It is proved by the above that :**

- i) Inadequate oestrogen interferes the luteal phase of menstrual cycles by inhibiting progesterone receptors.
- ii) Inadequate progesterone fails to inhibit the oestrogen receptors and thereby decreases the metabolism of oestrogen and increases its intracellular concentration.

Most of the perimenopausal women have anovulatory menstrual cycles due to depletion of ovarian capital as a result of repeated ovulation during reproductive period and atresia of the follicles.

Endometrial hyperplasia results from lack of progesterone and with constant stimulation of endometrium by oestrogen. Few atypical endometrial hyperplasia progress to endometrial carcinoma.

The role of fibrin, platelets, other coagulative factors like capillary

fragility was studied by Christians et al (1960).

**Prostaglandins** :- Arachidonic acid is released from phospholipids in cell membranes by phospholipase A2. Arachidonic acid is metabolized by cyclo-oxygenase into PGF2 alpha (vasoconstrictor and a weakly platelet aggregator), PGE2 (Vasodilator and platelet aggregation inhibitor), PGI2 (potent vasodilator and platelet aggregation inhibitor) and TXA2 (potent vaso constrictor and platelet aggregator), PGD2 (platelet aggregation inhibitor).

In women with ovulatory abnormal uterine bleeding the order of prostaglandin production is altered from normal order i.e., from PGF2/PGD2/PGE2 to PGE2/PGD2/PGF2.

In addition there is increased production of PGI2 in the myometrium. PGE2 and PGI2 causes vasodilatation and platelet inhibition leading to prolonged bleeding

**Role of leukotrienes** : Leukotrienes are eicosanoids produced by the action of lipo oxygenase on arachidonic acid . Leukotrienes cause intense dose dependent vasoconstriction followed by plasma leakage and extravasation of erythrocytes. Leukotrienes are produced by leucocytes. Leukotrienes could be responsible for vascular lesions and endothelial gaps in spiral arterioles and venules, which precede menstruation. Excessive infiltration of endometrium with leucocytes leads to excessive production of leukotrienes and results in excess menstrual blood loss.

**Haemostasis in Abnormal uterine bleeding** :Primary haemostasis in the spiral arterioles is achieved by formation of platelet plugs and fibrin. These platelet plugs may shed along with fragments of endometrium as they are lifted off with reopening the spiral arterioles. About in 24 hours most of the superficial layers of the endometrium have been found shed off and few plugs are seen. After 24 hours vaso-constriction of the spiral arterioles together with the swelling of the endothelial cells occludes the spiral arterioles. Reepithelialization from the basal glands starts from 2<sup>nd</sup> day and is completed by 3<sup>rd</sup> day. Reepithelialization depends on oestrogen levels. Any derangement in the above mechanism (i.e.) deficient formation of platelet plugs and delay in reepithelialization prolongs the bleeding.

**Fibrinolytic systems :-**

Fibrinolysis is an important mechanism for the liquid nature of the menstrual blood which ensures easy and rapid discharge of menstrual blood. Endometrium and cervix are the sites where the marked fibrinolytic activity is seen. Plasminogen activators are more during the first day of bleeding. Fibrinolytic activity is more in abnormal uterine bleeding (Rybo 1966).

**Excessive menstrual blood loss is due to :**

- i) increased formation of lysosomes leading to increased synthesis of phospholipase A2, arachidonic acid, prostaglandins, plasminogen activators and fibrinolytic activity.
- ii) Haematological factors
- iii) Hormonal environment in which the endometrium is shed . of all these the important factor is ovarian hormones.

Other factors that influence the menstrual blood loss.

- 1) Adrenal gland :**
- 2). Endocrinal :**
- 3) Anaemia** :- Taymor (1964) suggested that anaemia may be a cause as well as result of menorrhagia. Development of anaemia depends on blood loss as well as iron intake and efficiency of erythropoietic system. Iron deficiency may cause inadequacy of spiral arterioles. Haematological disorders such as thrombocytopenia and von willibrand diseases are associated with pubertal abnormal uterine bleeding.
- 4) OBESITY** :-Obesity has a disruptive effect on hormonal balance as oestrogen is distributed in the body fat. Oestrogen produced during follicular phase gets diluted in larger volume

of fat. The metabolic clearance also appears to be increased in obesity. Net result is low serum oestrogen which is insufficient to trigger LH surge leading to anovulation which often resolves by weight reduction.

**5) Psychobiological Factors :** Gonadotrophic releasing hormone secretion is regulated by balance of noradrenaline and dopamine. Emotional stress promotes dopaminergic hyperfunction which inhibits the LH surge causing anovulation. In response to stress, release of ACTH linked endorphin acts as a modulator at synapses in the hypothalamus. Other possible endogenous neuromodulators of stress are melanocyte stimulating hormone from pituitary and melatonin from pineal gland (Young & Reame 1983).

**Secondary AUB :-** Secondary to intrauterine contraceptive device and steroidal contraception.

Intrauterine contraceptive device menorrhagia is due to

- a) Superficial ulceration of endometrium and increased vascularity and interstitial red cell extravasation.
- b) High levels of plasminogen activator and fibrinolytic activity.
- c) Increased number of macrophages which produces PGE2, PGF2, plasminogen activator and fibrinolytic enzymes
- d) It causes delayed follicular formation and delayed reepithelialization.

Association of surgical sterilization and abnormal uterine bleeding:

- a) Interruption of vascular transport of the ovarian hormone or some unknown factor from the ovary to uterus.
- b) Deficient ovarian function with a fall in mid- luteal progesterone levels.

In perimenopausal women over (90%) the menstrual cycles are anovulatory. In the absence of growth limiting progesterone, endometrium attains abnormal growth without concomitant structural support. The tissue increasingly display intensive vascularity, back to back glandularity without intervening structural support matrix. The bleeding involves random portion of endometrium at variable times and in asynchronous sequences. The excessive growth because of irregular stimulus causes prolonged excessive bleeding as more tissue is available and there is disorderly abrupt, random break down of tissues with consequent opening of multiple vascular channels There is no vasoconstriction rhythmicity, no tight coiling of spiral vessels, no orderly collapse to induce haemostasis. The anovulatory tissue depends on healing effects of endogenous oestrogen to stop local bleeding which is temporary.

**MATERIALS AND METHODS**

The present investigations on the Abnormal uterine bleeding in perimenopausal women by Vagino sonography were undertaken at Kilpauk medical college and hospital in Chennai from July 2013. For this purpose 100 women with perimenopausal abnormal uterine bleeding (after the age of 40 yrs) were selected at random for study. A thorough clinical examination which includes general, systemic and pelvic examination after a detailed history was done. These patients were subjected for transvaginal sonographic examinations prior to diagnostic endometrial sampling to measure endometrial thickness. The endometrial thickness was measured from anterior myometrio endometrial junction to the central cavity. The total antero- posterior thickness of endometrium was measured and half of it was taken as endometrial thickness where the central cavity was not visualized. The size of the uterus measured and ovarian volume. Diagnostic endometrial sampling was done premenstrually in women with regular menstrual cycles and on the day of menstruation in patients with irregular cycles

**RESULTS:**

**CLINICAL EVALUATION :**

The results of clinically evaluated perimenopausal abnormal

uterine bleeding in one hundred cases are as follows.

Out of 100 cases, 93 cases are parous and 7 cases are nulliparous.

Uterus size clinically was found > 6 weeks in 41 cases.(Bulky Uterus)

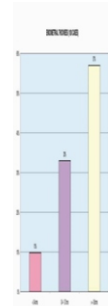
30 patients had hypertension and 13 patients had Type II Diabetes Mellitus.

62 patients had undergone sterilization

20 cases were observed to be obese. In addition 1 case of fibroadenosis and 1 case of polyp was also observed.

40 patients had haemoglobin levels < 10gms

ii) Endovaginal sonography :  
Endometrial thickness was measured with transvaginal sonography and the data are presented.

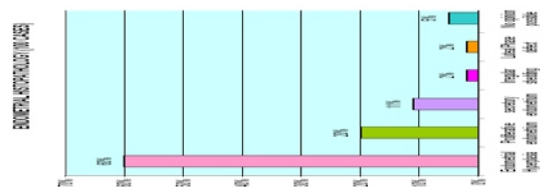


**Table 1 : Endometrial thickness in 100 cases of Perimenopausal woman (40-50yrs) with abnormal uterine bleeding by transvaginal sonography**

Thickness of endometrium	No of cases	Percentage
<b>0.8cm or more</b>	57	57
<b>0.4 – 0.7cm</b>	33	33
<b>&lt; 0.4cm</b>	10	10
<b>Total</b>	100	100

The commonly observed endometrial thickness was 0.8 cms or more in 57% of cases. In these patients sampling was done immediately. The next common endometrial thickness observed was ranging 0.4-0.7cms in 33% cases of perimenopausal women with abnormal uterine bleeding which is normal during reproductive period. Premenstrual endometrial sampling was done in these patients.

Endometrial thickness of < 0.4cms was observed in 10% of cases in whom endometrial sampling was done after controlling the bleeding with styptics.



**ENDOMETRIAL HISTOPATHOLOGY**

**Table-2: In 100 cases of women with perimenopausal (40-50yrs) abnormal uterine bleeding the common pattern of endometrial histopathology**

Endometrial Histopathology	No of cases	Percentage
<b>Endometrial hyperplasia</b>	60	60%
<b>Proliferative endometrium</b>	20	20%
<b>Secretory endometrium</b>	11	11%
<b>Irregular shedding</b>	2	2%
<b>Luteal phase defect</b>	2	2%

No opinion possible	5	5%
<b>Total</b>	100	100%

The common pattern of endometrium observed in 100 cases of perimenopausal abnormal uterine bleeding revealed that endometrial hyperplasia was in 60 cases. This shows that the endometrial hyperplasia is common in perimenopausal age (40-50yrs) group.

**Comparison of endometrial thickness to histopathology :**

**Table 3 : Histopathological Report of study subjects showing various Endometrial thickness in transvaginal sonography:**

Histopathology of endometrium	TVS showing Endometrial Thickness 0.8 cms or more in 57 cases	TVS Showing Endometrial Thickness 0.7 to 0.4 in 33 cases	TVS Showing Endometrial Thickness of less than 0.4
Endometrial hyperplasia	96.4%	12.12%	10%
Luteal phase effect	3.51%	-	
Proliferative Endometrium	-	48.49%	40%
Secretory Endometrium	-	33.3%	-
Irregular Shedding	-	-	20%
No Opinion Possible	-	6.06%	30%
<b>Total</b>	100%	100%	100%

Endometrial hyperplasia was the common histological feature observed in patients with endometrial thickness 0.8cms or more.

This shows that 96.49% of cases correlates with endometrial hyperplasia which may be due to anovulation.

**DISCUSSION**

The main aim and objective of the present investigation is to clinically evaluate perimenopausal abnormal uterine bleeding in women aged over 40 yrs by their endometrial thickness measured by transvaginal sonography with endometrial histopathology.

In the study undertaken, hundred cases of abnormal uterine bleeding in perimenopausal women (age 40-50 YRS)

The incidence of abnormal uterine bleeding among the outpatient attending the above period at KILPAUK MEDICAL COLLEGE during JULY 2013 to JULY 2014 was about 20%. The incidence of abnormal uterine bleeding in various parts of India ranged between 8-23.8%. Out of 100 cases of abnormal uterine bleeding studied, endometrial hyperplasia was as high as 60% (Table – 2). Comparison of endometrial hyperplasia from 1949 – 2003 revealed an increase in the incidence of endometrial hyperplasia by 60% and secretory endometrium only in 11% Endometrial hyperplasia may be due to anovulation leading to unopposed action of oestrogen in absence of corpus luteal progesterone in perimenopausal age group. Progesterone inhibits the oestrogen receptors and increases the oestrogen metabolism and there by reduces the intercellular concentration of oestrogen. In anovulatory cycles due to absence of progesterone, oestrogen promotes the abnormal growth of endometrial tissue leading to endometrial hyperplasia.

**SUMMARY AND CONCLUSIONS**

In the present study the aim is to show the clinicopathologic relation between transvaginal sonography and endometrial curettage in perimenopausal women with abnormal uterine bleeding. It is observed that the endometrial hyperplasia and thickened endometrium are the main features in women above 40yrs of age with abnormal uterine bleeding. Significant result was observed between the histological picture of endometrial

hyperplasia and transvaginal sonographic appearance of the thickened endometrium.

All the patients who showed a thickened endometrium sonographically subjected them for endometrial sampling. Other pelvic pathology was also excluded by transvaginal sonography.

When there is abnormally thickened endometrium, there is prolonged and heavy bleeding which leads to deterioration of the patients health. A thick proliferative endometrium reflects progesterone inadequacy. Anovulation was a major feature in perimenopausal women.

Sonographic and histologic study of the endometrium guide us in the diagnosis and treatment of perimenopausal abnormal uterine bleeding.

Sonographic is a non-invasive, affordable, easy method available today. Histopathologic study though invasive is a simple and accurate procedure to diagnose endometrial disease.

Though undoubtedly, sophisticated techniques like Hysteroscopy and Hystero-laparoscopy are the goldstandards as diagnostic and therapeutic aids in abnormal uterine bleeding, but access to these techniques in are country can be difficult due to financial constrains. By combining transvaginal sonography and endometrial sampling we have two simple and inexpensive ways to detect early endometrial disease and increase the life expectancy of women in perimenopausal age with abnormal uterine bleeding.

**BIBLIOGRAPHY**

1. Davey DA, Dewhurst's text book of obstetrics & Gynaecology 5th edn. 590-607.
2. Albers JR, Hull SK, Wesley MA. Abnormal uterine bleeding. Am Fam Phys 2004; 69: 1915.
3. Deanna Etelner, Difaf Jakubovicz. Approach to diagnosis and management of AUB.
4. Dodson M.G.J Rep.med. 39 (5) 362-372, 1994.
5. Pickles J Obstet Gynaec 1965:14
6. Markee J. Anat. Rec 94 : 481, 1946.