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A study on associated conditions among perimenopausal women presenting with abnormal uterine bleeding

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Abstract
In normal cycles, endometrial proliferation occurs under estrogenic stimulation after menstrual shedding of endometrium. During this phase, the endometrial glands grow and become tortuous. The secretory phase in the second half of the menstrual cycle is characterized by endothelial proliferation, thickening of the wall and coiling, forming the spiral arterioles on the ninth postovulatory day. Written informed consent taken from all patients enrolled in the study. They were evaluated by history, clinical examination and relevant investigations. Transvaginal ultrasound and endometrial biopsy done for all subjects. The endometrial biopsy specimen report obtained and compared and correlated with endometrial thickness by TVS. Anaemia was the most common condition associated with perimenopausal women with bleeding in this study group (35 patients) (23%).

Keywords: Perimenopausal Women, Endometrial Thickness, Anaemia

Introduction
The purpose of changes in the endometrium is to prepare the endometrium for implantation and growth of the fertilized ovum, if fertilization occurs. If fertilization does not occur, the endometrium is shed as menstruation. Indeed this cyclical bleeding is called as the "weeping of the disappointed uterus". The endometrial morphological changes connected with menstrual cycle are the consequence of endocrine events taking place in the ovary [1, 2].
In normal cycles, endometrial proliferation occurs under estrogenic stimulation after menstrual shedding of endometrium. During this phase, the endometrial glands grow and become tortuous. The secretory phase in the second half of the menstrual cycle is characterized by endothelial proliferation, thickening of the wall and coiling, forming the spiral arterioles on the ninth postovulatory day [3].
The menstrual cycle is divided into two cycles:
1. The ovarian cycle
2. Uterine cycle
The ovarian cycle is further divided into follicular and luteal phases. The uterine cycle is divided into corresponding proliferative and secretory phases.

Proliferative phase
It corresponds to the follicular phase of ovarian cycle. It starts from the menstrual phase and ends at ovulation. During this phase, estrogen is secreted from the growing follicle is responsible for the regeneration of the endometrium from the stratum basale. Raise in estrogen and associated hypoxia leads to secretion of vascular endothelial growth factor, which is a highly potent endothelial mitogen produced by the endometrium. This phenomenon plays a major role in angiogenesis and endometrial repair. Short, narrow and straight endometrial glands become longer and tortuous under the estrogen influence and the stroma becomes dense and compact. At the time of ovulation endometrium is 8-10 mm thick. This phase is of variable length depending on the event of ovulation [4].

Secretory phase
This phase begins after ovulation and is a progesterone phase. It corresponds to luteal phase of ovarian cycle. It extends from ovulation till the onset of next menstrual phase. This phase is responsible for secretory changes in the estrogen primed endometrium, is mainly by the effect of progesterone secreted from the corpus luteum.

The main aim of this phase is to produce appropriate environment for implantation and provide nutrition to the fertilized ovum. The progesterone leads to accumulation of protein rich eosinophilic material in the glands causes increased tortuosity and also bringing about pseudostratified appearance in the glandular epithelium. The stroma becomes more oedematous and vascular. This change is described as pseudo-decidualization.
At the peak of secretory phase, about one week after ovulation the endometrium is 10-12 mm thick. If the ovum is not fertilized, the corpus luteum degenerates and menstruation starts around 14th day after ovulation [5].

Menstrual phase
Shedding of endometrium occurs during this phase and it lasts in the range of two to seven days.

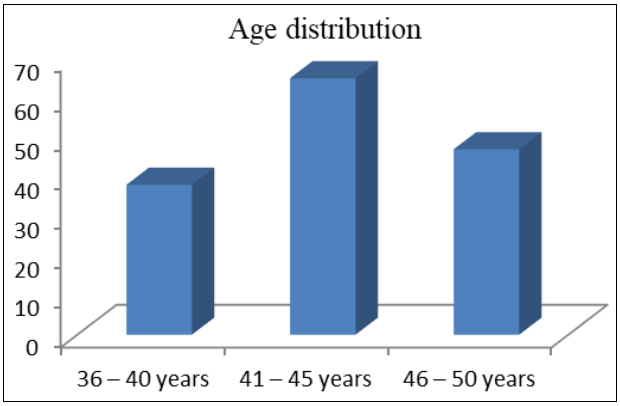
Methodology
Inclusion criteria
All cases of abnormal uterine bleeding in the perimenopausal age group (39-51years)

Exclusion criteria
1. Age less than 39 or more than 51 years of age.
2. Women who have attained menopause.
3. Women on hormonal treatment at the time of first presentation.
4. Women with intrauterine device in situ.
5. Women with endocrine disorders.
6. Women with bleeding disorders.
7. Women with adnexal pathology.
8. Women with Medical Disorders.

Study design: Hospital Based, Time Bound, prospective study.

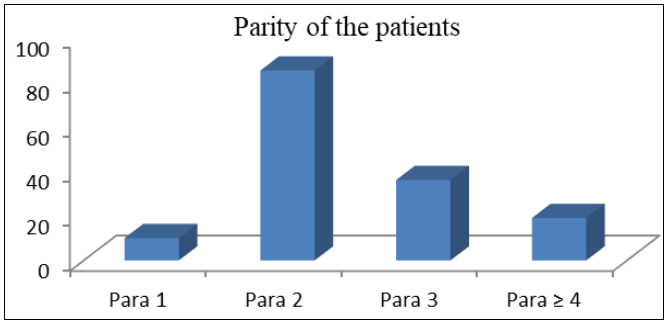
Sample size: 150. Cases of abnormal uterine bleeding outpatients and inpatients.
Written informed consent taken from all patients enrolled in the study. They were evaluated by history, clinical examination and relevant investigations. Transvaginal ultrasound and endometrial biopsy done for all subjects. The endometrial biopsy specimen report obtained and compared and correlated with endometrial thickness by TVS.

Results



Graph 1: Age distribution

Most of the patients in the study were between 41-45 years (43.33%). Mean age of patients was found to be 44.04 ±3.33 years. Mean of menarche was found to be 12.89 ± 1.30 years.



Graph 2: Parity of the patients

Majority of the women are multiparous (94.4%)

Table 1: Associated conditions

Associated Risks	No. of patients
Hypertension	7
Diabetes Mellitus	6
Hypothyroidism	3
Anemia	35

Anaemia was the most common condition associated with perimenopausal women with bleeding in this study group (35 patients) (23%).

Discussion
Any uterine bleeding outside the normal volume, duration, regularity or frequency is considered abnormal uterine bleeding.
Abnormal uterine bleeding (AUB) is also defined as bleeding pattern that differs in frequency, duration and amount from a pattern observed during a normal menstrual cycle or after menopause.
Abnormal uterine bleeding include both dysfunctional uterine bleeding and bleeding from structural causes like fibroids, polyps and endometrial carcinoma.
The bleeding can be a sign of a serious underlying condition necessitating aggressive treatment that could include a major procedure [6].
Excess menstrual bleeding affects more than 20% of perimenopausal women. The incidence of uterine organic disease is high in perimenopausal age group, it is because of menstrual cycles at this time are likely to be anovulatory, the risk of endometrial hyperplasia as a result of unopposed estrogen effect on the endometrium becomes more pronounced. The premalignant potential of the condition should not be underestimated. It was reported that 20% of women undergoing hysterectomy for endometrial hyperplasia were found to harbour coexisting endometrial carcinoma.
The word “climacteric” another term for perimenopause, is derived from the Greek Klimakter meaning “rung of the ladder” or “critical period of life”, defined as the transitory phase in the human female between ages of reproductive and non-reproductive ability. Perimenopause or menopausal transition is defined by World Health Organisation (WHO) as the period in the beginning 2-8 years prior to final menstrual period and lasting upto 12 months after the final menstrual period [7].
The endocrine changes at the climacteric has undergone extensive investigations and contributions of various workers and have been reviewed by Anderson (1979).
The first sign of perimenopause is a change in menstrual bleeding. Clinical studies show that approximately 90% of women experienced menstrual irregularity during this period and only 10 -12% of women will have sudden amennorrhoea.

The changes in the ovarian function which result in the menopause, in fact commence in utero. The number of oocytes in the fetal ovary is maximum at 20th week of intrauterine gestation, after which there is progressive decline during the second half of the intrauterine life, childhood, puberty and throught the reproductive period. From 35 years of age, follicular development tends to become more deficient progressively. In the last 5 -10 years of reproductive life, the proportion of anovulatory cycles increases and the menstrual cycles may become irregular with unduly long and short cycles.[8] Studies done by Sherman *et al.* (1986) have shown that perimenopausal women aged 40-55 years with regular menstrual cycles had lower levels of plasma estradiol, while their FSH levels are high. The rise in the LH in general occurs later and less marked failure in ovulation or inadequate corpus luteum formation or inadequate progesterone secretion results in unopposed estrogen secretion and may give rise to DUB, endometrial hyperplasia or endometrial carcinoma.

Irregularities of cycle during perimenopause indicates decreasing ovarian function. This may still be within normal range, causing endometrial glands to proliferate. A hyperplastic pattern noted in anovulatory cycles. The arrangement of glands, their spacing and growth pattern, height and maturity of the lining epithelium will vary markedly. Sometimes, the glands are lined by tall columnar epithelium and there is a proliferative hyperplasia. It may cause cysto-glandular hyperplasia. The sharp fall in estrogen and progesterone, after physiologic decline in ovarian function leads to atrophic endometrium after some years. When the last cycles are irregular and an ovulatory, the endometrium shows hyperplastic pattern whereas it is ovulatory and regular when the endometrium is in simple atrophic pattern [4, 9].

Conclusion

- 150 patients with abnormal uterine bleeding in the perimenopausal age group (39-51) underwent TVS followed by dilatation and curettage and endometrium was sent for histopathological examination.
- Most common age group is 41-45(43.3%) with a mean age of 44.04+_3.33yrs
- Anaemia was the most common medical condition associated with perimenopausal women with bleeding in this study group 23%(35 patients)

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