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Evaluation and management of Perimenaopausal bleeding.

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I. Introduction

World Health Organisation defines perimenopause or menopausal transition as the period 2-8 years preceding menopause and 1 year after the final menses. It is the interval from the begining of declining ovarian function to the final ovarian failure. The age of onset & duration of this perimenopausal period can vary greatly. It usually starts in a woman's 40s, but can start in the late 30s as well. It lasts up until menopause and also includes the first year after menopause.

However, the idea that any type of irregular bleeding during the perimenopausal period probably is due to menopause is a common misconception. Hence any woman complaining of abnormal bleeding must not be left alone.

Abnormal uterine bleeding(AUB) before the menopause accounts for 20% of visits to the gynaecology clinic and almost 25% of gynaecological operations.

Menorrhagia, polymenorrhagia, intermenstrual bleeding and metrorrhagia are common menstrual disorders at perimenopause. Additionally, decreased mental clarity, diminished concentration, vaginal dryness, decreased libido, hot flushes, and night sweats are classic hallmarks of perimenopause.

Abnormal bleeding in the perimenopausal age group may be an expression of a changed hormonal milieu or it could be the result of benign or malignant lesions of female genital tract.

During perimenopause, the ovarian cycles become anovulatory. The end result is unopposed oestrogenic stimulation of endometrium, which predisposes to endometrial hyperplasia, a premalignant pathology and endometrial carcinoma eventually. Dysfunctional uterine bleeding (DUB), fibroid uterus and adenomyosis are the common hyperoestrogenic conditions. Hence, it is essential to carry out thorough clinical examination and investigations to find out the etiological factor in a perimenopausal patient presenting with abnormal uterine bleeding.

So, all perimenopausal women with irregular bleeding warrant further investigation[1]. Though evaluation of AUB in perimenopausal women is challenging[2].

Here, the patient who presents with abnormal bleeding poses two distinct but important challenges for the clinician. The first is the exclusion of cancer or hyperplasia; the second is dealing with the annoyance as well as the fear that the bleeding engenders in the patient.

The most important step in the management of abnormal uterine bleeding is an accurate diagnosis[3].

Diagnosis is done by a detailed history, physical exam, a PAP Smear, relevant blood investigations, an ultrasound, and a Hysteroscopy coupled with endometrial biopsy.

Depending upon the clinical diagnosis, patient is offered therapy. Medical treatment is the primary mode of treatment for perimenopausal bleeding when malignancy is ruled out.

Medical treatment consists of non-steroidal anti-inflammatory drugs (NSAIDs), oral contraceptives (OCs), oral progesterone, a progesterone-releasing intrauterine device (IUD), or antifibrinolytics. If these first-line treatments fail, more invasive surgical options have to be considered[4].

In this study, an attempt has been made to analyze the different causes of perimenopausal bleeding and compare the different modalities of treatment to the extent possible.

Objectives of the study :

- To study the etiopathology of perimenopausal bleeding.
- To determine the incidence of benign and malignant causes of perimenopausal bleeding.
- To evaluate various modalities of treatment of perimenopausal bleeding.

II. Materials & Methods

Study area

Our study was an prospective study, which was done in urban area of Pune. Our hospital has an outreach center, so there are patients even from rural areas taking treatment in our hospital. Thus, we could include patients from each stratum of society.

Study population

The study population included perimenopausal women attending our gynaecological outpatient department fulfilling the inclusion criteria of the study. Our study population included patients from both the urban & rural areas.

Sample size & sample technique

101 women attending our gynaecological outpatient department, in the age group 40-55, presenting with abnormal per vaginal bleeding were included in the study.

Data collection technique and tools

- A detailed history was taken.
- All patients were examined thoroughly.
- Relevant blood investigations were carried out.
- Ultrasonographic evaluation of the women was performed preferably post-menstrually to look for endometrial thickness and anatomical lesions.
- Hysteroscopy with endometrial sampling was carried out, preferably in the second half of the cycle and specimen was sent for histopathological exam (HPE).
- The HPE reports were analyzed and these women were further managed either conservatively or surgically depending upon the report.
- Medical treatment- was recommended if no organic pelvic pathology identified. This was offered in the form of antifibrinolytics, progesterone, OC pills, LNG-IUD on case to case basis.
- Surgical treatment- was recommended for patients who have an organic pelvic pathology which requires intervention or in cases of failure of medical therapy.These women were counseled for Balloon thermal ablation or Hysterectomy.

Data analysis

The data was analyzed from all the observations made during the course of the study.

Statistical analysis was done using SPSS 19.0 and Minitab 15.0 statistical softwares.

- ✓ The clinical and HPE findings were correlated.
- ✓ Ultrasonographic and HPE findings of endometrial hyperplasia, fibroid, polyps, adenomyosis were correlated.
- ✓ Hysteroscopic and HPE findings of hyperplasia were correlated.
- ✓ Ultrasonographic and hysteroscopic findings of polyp were correlated.
- ✓ Histopathological reports of endometrial pattern and that of the hysterectomy specimens were correlated.

- Sensitivity and specificity was calculated for comparison of the 2 diagnostic methods.
- We have also calculated KAPPA co-efficient to find out diagnostic accuracy of respective methods (agreement between the different investigations).

III. Observation

1. Age-wise (years) distribution of patients.

Age group (years)	Number of patients	Percentage (%)
40-44	57	56.44
45-49	32	31.68
50-54	12	11.88
Total	101	100.00

Out of 101 patients presenting with abnormal bleeding, maximum patients (i.e.56.44 %), belonged to the age group 40-44 years.

2. Distribution of patients with respect to parity.

Parity	Number of patients	Percentage (%)
Nulliparous	2	2.0
Parous	99	98.0
Total	101	100.0

Abnormal bleeding was noted more often in multiparous women.

3. Distribution of patients with respect to associated medical disorders.

Personal history	Number of patients	Percentage (%)
Hypertension	18	17.82
Diabetes Mellitus	5	4.95
Hypothyroidism	4	3.96

Hypertension was encountered in 17.82% patients, while 4.95% were diabetic and 3.9% were hypothyroid.

4. Distribution of patients with respect to bleeding patterns.

Bleeding type	Number of patients	Percentage (%)
Menorrhagia	86	85.15
Polymenorrhoea	12	11.88
Intermenstrual bleeding	15	14.85
Oligomenorrhoea	4	3.96
Amenorrhoea followed by menorrhagia (metropathica haemorrhagica)	3	2.97
Post-coital bleeding	1	0.99
Menorrhagia + intermenstrual bleeding (menometrorrhagia)	3	2.97

Menorrhagia was the commonest presentation which was noted in 85.15% women while 14.85% women presented with intermenstrual bleeding.

5. PAP smear findings

PAP smear findings	Number of patients	Percentage (%)
Normal	96	95.0
AGUS	4	3.96
ASCUS	1	0.99

PAP Smear was normal in 96 patients and abnormal in 5 patients. However, all the 5 patients with abnormal PAP Smear had normal colposcopy findings.

6. Ultrasonography (USG) findings

USG findings	Number of patients	Percentage (%)
Bulky uterus	42	41.58
Thickened endometrium	62	61.39
Fibroid uterus	32	31.68
Adenomyosis	8	7.92
Endometrial polyp	9	8.91
Ovarian cyst	1	0.99

- Thickened endometrium was the commonest finding on USG in perimenopausal women presenting with abnormal uterine bleeding.
- Fibroid uterus was detected in 31.68% women in this study.

7. Hysteroscopy findings

Hysteroscopy findings	Number of patients (n=96)	Percentage (%)
Normal	30	31.25
Profuse endometrium	51	53.13
Scanty endometrium	5	5.21
Cervical polyp	7	7.29
Endometrial polyp	16	16.67

Hysteroscopy was performed in 96 women.

- Profuse endometrium was the commonest hysteroscopic finding seen in 53.13% women.
- Endometrial polyps were detected in 17% while cervical polyps in 7% women on hysteroscopy.

8. Histopatholgical examination (HPE) of endometrium

a.

HPE findings	Number of patients	Percentage (%)
Proliferative endometrium	37	38.54
Secretory endometrium	26	27.08
Benign endometrial, cervical polyp	18	18.75
Tissue insufficient	1	1.04
Endometrial hyperplasia	27	28.13
Carcinoma endometrium	1	1.04

- Endometrium was proliferative in 38.5% patients and secretory in 27% patients.
- Twenty-eight percent women were found to have endometrial hyperplasia whereas carcinoma endometrium was detected in 1% in our study group.

b. Endometrial hyperplasia on HPE

Types of Hyperplasia	Number of patients
Simple typical	26
Complex typical	0
Simple atypical	0
Complex atypical	1

- Simple typical hyperplasia was found in 26 patients.
- None of the patients had either complex typical or simple atypical hyperplasia.
- Complex atypical hyperplasia was observed in 1 patient.

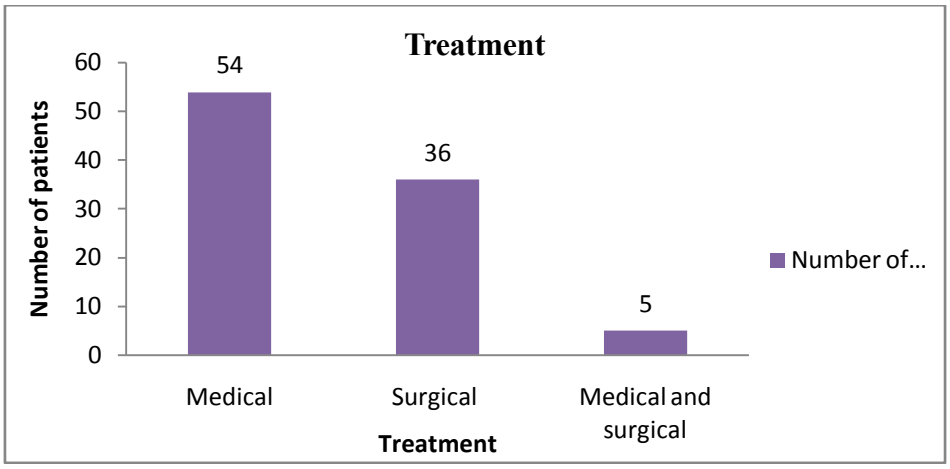
9. Distribution of patients with respect to diagnosis.

Diagnosis	Number of patients	Percentage (%)
Anovulatory DUB	32	31.68
Ovulatory DUB	17	16.83
Adenomyosis	3	2.97
Fibroid uterus	15	14.85
Simple hyperplasia	23	22.77
Endometrial polyp	10	9.90
Endocervical polyp	7	6.93
Cervical polyp	2	1.98
Atypical complex hyperplasia	1	0.99
Carcinoma	1	0.99

- Anovulatory DUB was the commonest cause of abnormal bleeding in the perimenopause accounting for 31.68% patients.
- Simple hyperplasia was responsible for 22.77% of the cases of abnormal bleeding.

10. Distribution of treatment

Treatment	Number of patients	Percentage (%)
Medical	54	53.47
Surgical	36	35.64
Medical and surgical	5	4.95



Medical treatment was offered to 53.5% patients, surgical treatment to 35.6% patients whereas 4.95% patients required combined medical and surgical treatment.

a. Medical treatment

Medical treatment	Number of patients	Percentage (%)
Antifibrinolytics	7	12.96
Progesterone	41	75.93
Esterogen+Progesterone	3	5.56
LNG-IUS	3	5.56

Out of the patients offered medical treatment, 75.93% were treated with progesterone while 12.96% were given antifibrinolytics.
5.56% patients opted for LNG-IUS.

b. Surgical treatment

Surgical treatment		Number of patients	Percentage (%)
Polypectomy		18	50.00
Hysterectomy	TAH	8	22.22
	Radical	1	2.78
	Vaginal	3	8.33
	LAVH	2	5.56
Balloon thermal ablation		1	2.78

In our study, 14 patients underwent hysterectomy.
One patient opted for balloon thermal ablation as an alternative to hysterectomy.

11. Distribution of patients with respect to bleeding pattern and HPE.

Endometrium on HPE / Bleeding pattern	Proliferative	Secretory	Benign endometrial, cervical polyp	Endometrial hyperplasia	Carcinoma endometrium
Menorrhagia (n=86)	31	23	11	21	1
Polymenorrhoea	5	5	2	0	0
Intermenstrual bleeding (n=15)	5	2	8	4	0
Oligomenorrhoea	0	1	1	2	0
Amenorrhoea	2	0	0	1	0

followed by menorrhagia					
Post-coital bleeding (n=1)	0	0	1	1	0

- Menorrhagia was the commonest menstrual disorder, seen in 86 patients. Simple endometrial hyperplasia was encountered in 20 patients presenting with menorrhagia whereas 1 patient had atypical complex hyperplasia of endometrium. Endometrial carcinoma was diagnosed in 1 patient who presented with menorrhagia.
- Benign endometrial or cervical polyps were responsible for 8 out of 15 cases of intermenstrual bleeding.
- Only 1 patient presented with post-coital bleeding and was eventually found to have both benign endocervical polyp and simple endometrial hyperplasia.

12. Diagnosis vs. Bleeding pattern

Bleeding pattern / Diagnosis	Meno-rrhagia	Polymeno-rrhoea	Inter-menstrual bleeding	Oligo menorrhoea	Ameno-rrhoea f/b meno-rrhagia	Post-coital bleeding
Anovulatory DUB	27	5	4	0	2	0
Ovulatory DUB	15	3	1	1	0	0
Adeno-myosis	3	1	0	0	0	0
Fibroid uterus	15	1	0	0	0	0
Simple hyperplasia	20	0	4	1	1	1
Endometrial polyp	6	1	4	1	0	0
Endocervical polyp	5	1	3	0	0	1
Cervical polyp	1	0	1	0	0	0
Atypical complex hyperplasia	1	0	0	1	0	0
Carcinoma	1	0	0	0	0	0

- Majority of patients diagnosed as DUB had presented with menorrhagia.
- Of the 26 cases of Simple endometrial hyperplasia, 20 patients had presented with menorrhagia whereas intermenstrual bleeding occurred in 4 patients.
- Menorrhagia was the presenting complaint in all the 15 cases of fibroid uterus.
- All patients with endometrial or endocervical polyps had presented with either menorrhagia or intermenstrual bleeding.

13. Pre-operative diagnosis vs. Histopathology report of hysterectomy specimens.

Diagnosis	Histopathology report of hysterectomy specimens				
	Simple hyperplasia	Benign leiomyoma (Fibroid)	Atypical complex hyper-plasia	Adenomyosis	Carcinoma
DUB (n=4)	1	1	0	0	0
Adenomyosis (n=1)	0	1	0	0	0
Fibroid uterus (n=6)	3	6	0	0	0
Simple hyperplasia (n=4)	1	2	0	0	0
Atypical complex hyperplasia (n=1)	0	0	1	1	0
Carcinoma (n=1)	0	0	0	0	1

15. Distribution of patients with respect to USG findings and HPE findings
a. Adenomyosis

USG	HPE		Total
	Present	Absent	
Present	0	1	1
Absent	1	7	8
Total	1	8	9

USG for adenomyosis:

Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
0.00%	87.50%	0.00%	87.50%

b. Hyperplasia

USG	HPE		Total
	Present	Absent	
Present	19	42	61
Absent	6	29	35
Total	25	71	96

TVS showed thickened endometrium in 61 patients, of which hyperplasia was detected in only 19 patients (31%).

c. Fibroids

USG	HPE		Total
	Present	Absent	
Present	6	0	6
Absent	1	2	3
Total	7	2	9

Out of 7 patients with fibroid uterus on HPE, USG diagnosed 6 patients.

d. Polyp

USG	HPE		Total
	Present	Absent	
Present	7	2	9
Absent	11	77	88
Total	18	79	97

Out of 18 patients with polyp on HPE, USG diagnosed only 7 patients.

16. Distribution of patients with respect to Hysteroscopy findings and HPE findings for hyperplasia.

Hysteroscopy	HPE		Total
	Present	Absent	
Present	19	32	51
Absent	6	39	45
Total	25	71	96

Hysteroscopy for endometrial hyperplasia:

Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
76.00%	54.93%	37.25%	86.67%

- Hysteroscopy diagnosed 19 out of 25 patients of endometrial hyperplasia (confirmed by HPE).
- On the other hand, 32 patients with hysteroscopic appearance of endometrial hyperplasia were negative for hyperplasia on HPE.

17. Distribution of patients with respect to USG findings and hysteroscopy findings for polyp.

USG	Hysteroscopy		Total
	Present	Absent	
Present	5	4	9
Absent	12	76	88
Total	17	80	97

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USG for polyp:

Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
29.41%	95.00%	55.56%	86.36%

- USG diagnosed only 5 out of 17 patients who had polyps on hysteroscopy
- On the other hand, 4 patients diagnosed as having polyp on USG, had no polyp on hysteroscopy.

Salient findings

- The incidence of perimenopausal bleeding was 22.6% of all the women attending our gynaecological OPD.
- Maximum patients (56.44%) belonged to the age group 40-44 years.
- Ninety-eight percent women with abnormal bleeding were multiparous and 2% were nulliparous.

- Menorrhagia was the commonest presentation which was noted in 85.15% women while 14.85% women presented with intermenstrual bleeding.
- Hypertension was encountered in 17.82% patients with abnormal bleeding, while 4.95% were diabetic and 3.9% were hypothyroid.
- PAP Smear was normal in 95% cases and abnormal in 5% cases. However, Colposcopy was normal in all patients with abnormal PAP Smear.
- DUB was the commonest cause of abnormal bleeding in the perimenopause accounting for 48.5% cases. The incidence of anovulatory DUB was 31.68%. Majority of patients diagnosed as DUB had presented with menorrhagia.
- Four patients with DUB underwent hysterectomy. Simple hyperplasia was encountered in 1 patient and uterine fibroid was found in 1 patient in post-hysterectomy specimen.
- Simple hyperplasia was responsible for 22.77% of the cases of abnormal bleeding.

Seventy-eight percent of patients with Simple hyperplasia had presented with menorrhagia, 14% had intermenstrual bleeding, 4% had amenorrhoea followed by menorrhagia and 4% had post-coital bleeding.

- Fibroid uterus accounted for AUB in 15% of women. Menorrhagia was the presenting complaint in all the patients of fibroid uterus.
- All patients with endometrial or endocervical polyps had presented with either menorrhagia or intermenstrual bleeding.
- Twenty-seven percent women with intermenstrual bleeding had simple hyperplasia of endometrium and none had atypia or malignancy, 26% had endometrial polyp, 20% had endocervical polyp and 7% cervical polyp.
- One case of carcinoma endometrium was encountered.
- Hyperplasia was detected in 31% patients having thick endometrium on TVS. Whereas, 30% patients with endometrial hyperplasia had normal endometrial thickness on TVS.
- Seventy percent patients having endometrial hyperplasia by diagnostic D&C had hysteroscopic impression of hyperplasia.
- Patients with intrauterine polyps and submucosal fibroids had excellent relief of symptoms following operative hysteroscopy.
- Out of 54 patients treated medically, 64% cases of responded to progesterone and 5.56% patients responded to O.C. pills.
- Out of 7 patients treated with antifibrinolytics, 5 patients had relief from their symptoms.
- LNG-IUS was found to be very effective in 2 patients with simple hyperplasia of endometrium who were offered this treatment.
- In our study, 14 patients underwent hysterectomy. One patient with DUB opted for balloon thermal ablation as an alternative to hysterectomy and showed good response.
- Of the patients who underwent hysterectomy, 28.6% were for DUB, 42.7% for fibroid uterus, 28.6% for simple hyperplasia of endometrium, 7% for atypical hyperplasia of endometrium, 7% for carcinoma endometrium and 7% for adenomyosis.

IV. Conclusion:

Abnormal uterine bleeding occurring at perimenopausal age needs thorough evaluation, as it could be the only clinical manifestation of endometrial cancer. DUB, Endometrial hyperplasia and Fibroid uterus were the principal causes of abnormal uterine bleeding in this study. Diagnosis was aided by a detailed history, physical exam, a PAP Smear, relevant blood investigations, an ultrasound, and a Hysteroscopy coupled with endometrial biopsy.

Medical management with the avoidance of possibly unnecessary surgery, is the best choice, unless uterine pathology is present. Hormone therapy or hysterectomies were the only modalities of treatment available in the past. However now women have a variety of options like LNG-IUS and thermal balloon endometrial ablation prior to resorting to definitive surgery like hysterectomy. The liberal use of hysterectomy to treat DUB reflects the failure to identify an organic cause for abnormal uterine bleeding which is present in most women.

V. Recommendations-

1. Counselling of patients with dysfunctional bleeding should incorporate medical approach, levonorgestrel releasing IUD, endometrial ablation and hysterectomy since all the treatment modalities have their advantages and disadvantages.
2. DUB is a diagnosis of exclusion. Only after ruling out a long list of conditions is it acceptable to diagnose DUB and treat as such. It is unacceptable to treat a woman with undiagnosed abnormal bleeding on the

assumption that it is DUB. Such treatment will often fail and, unfortunately, may lead to an unnecessary hysterectomy.

3. The levonorgestrel intrauterine system an excellent means to control abnormal uterine bleeding and should be considered in patients with abnormal uterine bleeding having a normal uterine cavity.
4. Thermal balloon endometrial ablation is a simple, safe and effective technique, useful in treating menorrhagia and dysfunctional bleeding in women with a normal uterine cavity who have negative workup results and should be used for the permanent treatment of DUB as an alternative to hysterectomy in well selected cases.
5. Hysterectomy as a treatment for DUB should be considered only as a last resort.

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