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Evaluation of Abnormal Uterine Bleeding In Peri-Menopausal Women – Particular Emphasis on Role of Endocrinopathies in The Causation.

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Abstract

Introduction: Abnormal uterine bleeding occurs in 9 to 14 percent of women between menarche and menopause. This abnormal uterine bleeding generally can be divided into anovulatory and ovulatory patterns. Chronic anovulation can lead to irregular bleeding, prolonged unopposed estrogen stimulation of the endometrium, and increased risk of endometrial cancer. Hence in this study we evaluated Abnormal Uterine Bleeding In Peri-Menopausal Women – Particular emphasis On role of endocrinopathies in the causation.

Material and Methods: This study was conducted in the tertiary care teaching institute in the state of jammu and Kashmir, India where women ≥35yrs of age attending OPD for abnormal uterine bleeding were evaluated. After taking an informed consent, a proforma was filled that included information on subject history, examination and investigations. 200 such cases were taken.

Results: Out of 200 cases, **fibroid** accounted for 24.5% , **perimenopause** for 17.5%, **DUB** for 15%, **hypothyroid** for 13.5% **adenomyosis** for 12.5 % , **endometrial hyperplasia** for 12% , **diabetes mellitus** for 1.5% , and 3.5% cases had **multiple etiologies**.

Conclusion: Among the organic causes **fibroid, adenomyosis** and **endometrial hyperplasia**, where as among non organic causes **hypothyroidism** and **perimenopause itself** contributes the most common cause.

Keywords: Abnormal uterine bleeding, Perimenopause.

Introduction

Abnormal uterine bleeding generally can be divided into anovulatory and ovulatory patterns. Chronic anovulation can lead to irregular bleeding, prolonged unopposed estrogen stimulation of the endometrium, and increased risk of endometrial cancer. Causes include polycystic ovary syndrome, uncontrolled diabetes mellitus, thyroid dysfunction, hyperprolactinemia, and use of antipsychotics or antiepileptics. The ultimate causative factor for perimenopause and menopause is depletion of ovarian follicles. However, aging changes in non-ovarian

tissues, such as the hypothalamus, pituitary, uterus, and ovary, may also contribute to the perimenopause.

The International Federation of Gynaecology and Obstetrics has designed the PALM COEIN system to take into account the causes and entities that contribute to AUB. **Structural (PALM)** Polyp, Adenomyosis, Leiomyoma Submucosal, Malignancy and hyperplasia: **Non-structural (COEIN)** Coagulopathy, Ovulatory dysfunction, Endometriosis, Iatrogenic.

Aims and objectives

To study the etiology and the role of endocrinopathies in causing abnormal uterine bleeding in peri-menopausal women

Material and Methods

This prospective observational study was conducted in a tertiary care teaching institute in the state of Jammu and Kashmir, India. This study was conducted between September 2015 and march 2017. Patients were enrolled in the study after taken approval from hospital ethical committee and written informed consent from patients. All women ≥ 35 yrs having abnormal uterine bleeding were included. The patients excluded were Positive pregnancy test**,** uterus >12 weeks, previous abnormal endometrial biopsy, cervical pathology on speculum examination, abnormal cervical pap smear, hormone therapy within last 2 months, history of evidence suggestive of active pelvic infection, history of any chronic systemic disease like malignancy and chronic renal failure, bleeding disorders and acute illness cases like sepsis, trauma, etc. that may affect hormonal estimation. A proforma was filled that included information on subject's demographic profile, age, parity, history and examination. Those patients falling in the exclusion criteria were not included while rest of the patients continued to be the part of study. 200 such cases were taken over a period of 18 months. All baseline and other necessary investigation were carried out in such cases to know the exact etiology of their abnormal uterine bleeding and to detect endocrine causes also. USG TAS/TVS was used to detect structural pathologies. The subjects with TVS documented thick Endometrial thickness (ET ≥ 5mm) were subjected to diagnostic dilatation and curettage and endometrial curettings were sent for histopathologic examination . Patients with following complaints were taken.. **Amenorrhoea:** absence of menstruation for more than 3 cycles. **Oligomenorrhoea:** infrequent, irregularly timed episodes of bleeding usually occurring at intervals of more than 35 days. **Polymenorrhoea:** frequent episodes of menstruation, usually occurring at interval of 21 days or less. **Menorrhagia:** regularly timed episodes of bleeding excessive in amount (>80ml) and/ or duration of flow (>5days) **Menometrorrhagia:** excessive prolonged bleeding at irregularly timed and frequent intervals. **Hypomenorrhoea:** regularly timed but scanty episodes of bleeding. **Polymenorrhagia:** frequent episodes of excessive menstruation. **Diabetes mellitus** was diagnosed as per WHO guidelines. **Hypothyroidism And Hyperthyroidism:** Patients were diagnosed as hypothyroid when the TSH levels were > 6.5nIU/ml. Also wherever there was a positive history of thyroxine intake plus past documented history of hypothyroidism even if the TSH levels were in the normal range were labelled as hypothyroid. TSH levels < 0.5nIU/mL was used as a cut off value for labelling a patient as hyperthyroid. **Hyperprolactinemia:** Value of prolactin in adult females ≥27ng/ml was regarded as having hyperprolactinemia. **PCOS** Patient was diagnosed as the case of PCOS when she fulfilled the 2 out of 3 Rotterdam's criteria. In this study the patient were distributed according to the age and parity in various groups, then their menstrual disturbances were studied. After complete evaluation, patients where no abnormality was detected were put in the category of DUB and in rest of the patients, abnormalities both structural as well as hormonal were noted. Finally the

major abnormality responsible for causing AUB was considered as its etiology.

Observation and Results

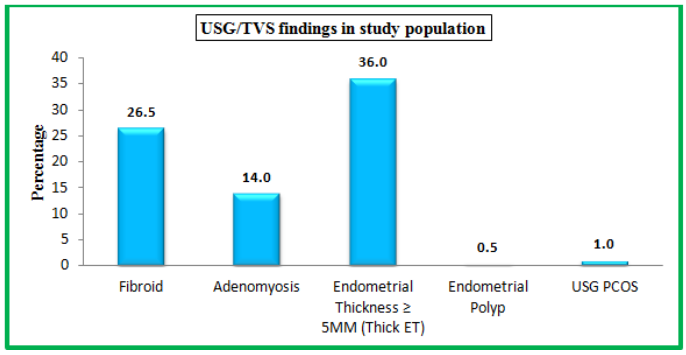

Figure 1

Table 1: Showing endocrinology of study patients.

Endocrinology	Frequency	Percentage
Hypothyroidism	81	40.5
Perimenopause (FSH Level ≥10µiu/L)	59	29.5
Diabetes Mellites	4	2
Hyperprolactinemia	1	0.5

Table 2: HPE findings of patients with thick Endometrium (72 cases)

HPE Findings		Frequency	Percentage
Hyperplastic Endometrium (31 cases)43.1%	Simple typical hyperplasia	21	29.2
	Simple atypical hyperplasia	2	2.8
	Complex typical hyperplasia	7	9.7
	Complex atypical hyperplasia	1	1.4
Proliferative phase		32	44.4
Secretory phase		9	12.5

Table 3 : Showing various abnormalities detected in study population

Abnormality	Total (n=170)		As a single abnormality (n=95)		In associationwith other abnormalities (n=75)	
	N	%	N	%	N	%
Adenomyosis	28	16.5	15	15.8	13	17.3
Endometrial hyperplasia	31	18.2	9	9.5	22	29.3
Perimenopause	59	34.7	24	25.3	35	46.6
Fibroid	53	31.1	19	20	34	45.3
Hypothyroidism	81	47.6	23	24.2	58	77.3
Diabetes Mellitus	4	2.3	3	3.1	1	1.3
Endometrial polyp	1	0.6	0	0	1	1.3
Hyperprolactinemia	1	0.6	0	0	1	1.3
PCOS	1	0.6	0	0	1	1.3

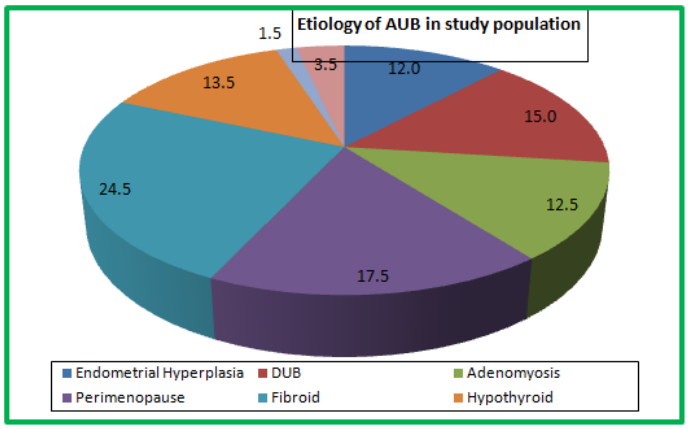

Figure 2

Discussion

In present study Menorrhagia was the commonest menstrual disorder encountered in 141cases(70.5%), The second most commonest menstrual disturbance was Menometrorrhagia in 92 cases (46%) followed by Polymenorrhagia in 69 cases(34.5%), Oligomenorrhoea in 42 cases (21%), Amenorrhoea in 36 cases (18%), Hypomenorrhoea in 33 cases(16.5%). Minimum number of patients presented with Polymenorrhoea i.e. in 23 cases (11.5%) which is comparable with the study by **Gupta et al (2013)**[1] where 72% cases had menorrhagia and least number of cases i.e 7% had Polymenorrhoea. **Muzaffar et al** found menorrhagia in 51.9% cases and polymenorrhoea in 9.2% cases.[2] **Jaiswar et al** evaluated women with abnormal uterine bleeding and found metrorrhagia in 18% cases and polymenorrhoea in 8% cases.[3] In a study by **Babbar K et al** it was seen that the most common

presentation during perimenopause was menorrhagia(62.1%).[4] USG (especially transvaginal) showed thick Endometrium i.e ≥5mm in 72 cases, fibroid (submucosal and of significant size) in 53 cases , adenomyosis in 28 cases, endometrial polyp in 1 case, Polycystic ovaries in 2 cases but patients with thick ET(72 cases) were further subjected to diagnostic dilatation and curettage among which maximum patients showed proliferative endometrium in 32 cases (44.4%), followed by endometrial hyperplasia in 31 cases (43.1%), and secretory phase in 9 cases (12.5%).Among endometrial hyperplasia simple typical hyperplasia constituted maximum number of cases 21 cases (29.2%), followed by complex typical hyperplasia in 7 cases (9.7%), simple atypical hyperplasia in 2 cases (2.8%), complex atypical hyperplasia in only 1 case (1.4%) which is comparable with study done by

Mukhopadhay Indrani et al(2017) [5]

In our study population, endocrinology revealed hypothyroid in 81 cases , perimenopause in 59 cases, hyperglycemia in 4 cases , hyperprolactinemia in 1 cases. No case of hyperthyroid, hyperandrogenism was detected in our study.

Out of 200 cases, in 30 cases no abnormality was detected so they were categorized as DUB and in rest 170 cases various abnormalities were studied as a single entity (N=95) and in association with other abnormalities (N=75). Out of total 170 cases, 81 cases (47.6%) showed hypothyroidism followed by perimenopause in 59 cases (34.7%), fibroid in 53 cases (31.1%), endomerial hyperplasia in 31 cases (18.2%) and adenomyosis in 28 cases (16.5%). Small percentage was also contributed by diabetes mellitus, endometrial polyp , hyperprolactinemia and PCOS. So of all these 170 cases, hypothyroidisim contributes the maximum i.e. 47.6%. In cases where only single abnormality was detected (N=95) perimenopause was seen in 25.3%, hypothyroidism in 24.2% , fibroid in 20% cases, adenomyosis in 15.8% cases endometrial hyperplasia in 9.5% cases and diabetes in 3.1% cases. Among the cases having various associated abnormalities (N=75) maximum cases showed hypothyroidism in 77.3% followed by perimenopause in 46.6% and fibroid in 45.3% These results showed that hypothyroidism has an overall significant impact on causing the menstrual irregulaties in the study population i.e in in 47.6% both as a single cause (24.2%) as well as in association with other causes (77.3%) but still it was not the major etiological factor because in majority of patients TSH levels were just borderline and patients were already on treatment for it, thus had controlled hypothyroidism. The other major contributing factor is the perimenopause itself which is diagnosed in our study by high FSH levels seen in 34.7% of total 170 cases . Among organic causes fibroid was mostly seen both as a single cause (20%) and in association with other causes.(45.3%). **Byna et al (2015)[6]** found hypothyroidism in 21.8% and fibroid in 5.4% only.

After comparing all the contributing abnormalities , final diagnosis was given to all patients individually on the basis of main contributing etiology. In that way **fibroid** accounted for 24.5% cases, **perimenopause** for 17.5%, **DUB** for 15% cases , **hypothyroid** for 13.5% cases **adenomyosis** for 12.5 % cases, **endometrial hyperplasia** for 12% cases, , **diabetes mellitus** for 1.5% cases, and 3.5% cases had **multiple etiologies** including fibroid, adenomyosis and endometrial hyperplasia. So these three structural etiologies contribute even more than described above, suggesting that structural causes outweigh the hormonal causes in causing AUB. Also among all organic cause, fibroid accounted for the majority of the cause i.e.53 of 105 cases (50.4%) which is comparable with a study of **LTMMC hospital Mumbai[7] & DHQ hospital Multan[8]** in which abnormal uterine bleeding evaluation revealed fibroid in 54% & 54.8% cases. Among the

organic causes **fibroid, adenomyosis** and **endometrial hyperplasia** contributes the most common cause which also gives a clue of high estrogen activity in this age group, where as among non organic causes **hypothyroidism** and **high level of FSH predicting perimenopause** has a good correlation with AUB than any other cause in the study age group.

Conclusion: Among the organic causes **fibroid, adenomyosis** and **endometrial hyperplasia**, where as among non organic causes **hypothyroidism** and **perimenopause itself** contributes the most common cause

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