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PREVALANCE OF THYROID ABNORMALITY IN PERIMENOPAUSAL WOMEN WITH ABNORMAL UTERINE BLEEDING AND ITS ENDOMETRIAL PATTERN

Obstetrics & Gynaecology

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ABSTRACT

Background And Purpose Abnormal uterine bleeding is a common gynaecological problem in women which significantly affects the quality of life. The prevalence increases with age peaking just prior to menopause. In perimenopausal age, variation in normal cyclical pattern may be due to physiological hormonal changes or pathological. Most ovulatory dysfunction can be traced to endocrinopathies mainly thyroid disorders. It can present as spectrum of menstrual abnormalities ranging from amenorrhoea, infrequent bleeding to episodes of extreme heavy menstrual bleeding. Thyroid disorders are one of the preventable causes and if properly diagnosed, unnecessary surgical interventions can be avoided. **Methods:** This is a cross sectional study, conducted in the SAT hospital, Thiruvananthapuram, where women in age group of 45-55 with abnormal uterine bleeding attending gynaecology OP or as IP, for a period of one year after excluding cervical or genital infections, pregnancy and related causes of bleeding per vagina (PV) and postmenopausal bleeding were selected. Thorough history taking clinical examination and investigations including imaging, TSH, FT3, FT4 were done using questionnaire. Endometrial samples among those with thyroid abnormality were obtained. Data was analysed and statistical test of significance calculated by chi square test. **Results** In our study, 31.7% women with AUB was hypothyroid and 9.5% women were hyperthyroid. The most common pattern of perimenopausal AUB was frequent cycles, which was prolonged, irregular and associated with heavy flow. Irregular cycles were noted in both hyperthyroidism and hypothyroidism which was significant. 73 percent of women with a thyroid dysfunction had a palpable thyroid. 47.4% women had normal findings in USG which signify non-structural causes in perimenopausal women which was significant (p value <0.001). Out of those already diagnosed with thyroid disorder and on regular treatment, 76.7% had symptomatic relief while on treatment. **Conclusion** Thyroid disorders are prevalent among premenopausal women with AUB. Thyroid disorders should be considered as an important associated factor for menstrual abnormalities even in perimenopausal women. It is important to screen look for thyroid disorders in women coming with abnormal uterine bleeding. These are preventable causes of AUB. Prompt treatment of thyroid disorders enhances the quality of life of women and prevents unnecessary hormonal treatment and surgery.

KEYWORDS

abnormal uterine bleeding, perimenopausal, thyroid abnormality, Hypothyroidism, Hyperthyroidism

INTRODUCTION

Abnormal uterine bleeding is bleeding from the uterine corpus that is abnormal in frequency, regularity, volume, or duration and occurs in the absence of pregnancy. A frequency of 24-38 days, regularity of variation less than 20 days duration in 12 months, duration of 4.5 to 8 days and volume of 5-80 ml is considered normal. In perimenopausal age, variation in normal cyclical pattern may be due to physiological hormonal changes or pathological. The menstrual pattern is influenced by thyroid hormones either directly or indirectly. Thyroid hormones have direct impact on the ovaries and indirect impact on sex hormone binding globulin, prolactin and GnRH secretion and coagulation factors. Severe hypothyroidism is associated with ovulatory dysfunction due to numerous interactions of thyroid hormones with the reproductive system. Hyperprolactinaemia, due to increased TRH production, and altered GnRH pulsatile secretion, leads to a delay in LH response and inadequate maturation of corpus luteum. Thyroid hormones also act along with the FSH mediated LH/HCG receptor to exert direct stimulatory effects on granulosa cell function[1] and also effects on differentiation of the trophoblast have been found in many of the in vitro studies[2]. Hypothyroidism may also impact the fertility by altering the peripheral metabolism of oestrogen and by decreasing SHBG production. Both these pathways can result in abnormal feedback at the pituitary level. Independent of the hormonal changes, hypothyroidism can also lead to menorrhagia by altered production of coagulation factors (decreased levels of factors VII, VIII, IX and XI)[3]. Recently occult menorrhagia has been found to be an early manifestation of sub clinical hypothyroidism with disease becoming symptomatic only later on.

SHBG production is found to be increased in hyperthyroid women, the metabolism of oestrogen is altered and increased conversion of androgens to oestrogens. Hyperthyroxinemia increases the response of gonadotrophin to GnRH and thus an elevation of baseline gonadotrophin concentrations.

The decrease in menstrual flow is also related to effects on haemostatic factors, including the synthesis of factor VIII[4]. Ovulation is usually maintained hyperthyroid women, despite these metabolic changes, according to endometrial biopsies. Women with thyroid disorders usually have menstrual irregularities, infertility and increased morbidity during pregnancy[5].

With the introduction of serum thyroxine and serum thyroid stimulating hormone (TSH) radioimmunoassay the sensitivity and specificity of thyroid function testing has increased drastically[6]. A TSH value of 0.5-4.0 mU/L is highly suggestive of normal thyroid function[7]. A high TSH value (>5.0 mU/L) is always an indication for further testing, like free T_4 (FT_4) or a free thyroxin index (FTI). When there is a high likelihood of thyroid disease, i.e in the presence of risk factors or clinical signs and symptoms, initial testing should include a serum TSH and FT_4 or an FTI[8]. If the TSH in the grey shadow range (4.1–5.0 mU/L) then the chance of developing hypothyroidism is very likely and should be regularly screened. Treatment for subclinical hypothyroidism in asymptomatic persons with TSH value of <10 mU/L is still controversial[9]. The two major antibodies which affect the thyroid function are anti thyroid peroxidase (anti-TPO) and antithyroglobulin[7]. Both of them can be easily detected in the serum. The presence of anti-TPO and/or anti thyroglobulin antibodies in a patient with clinical hypothyroidism indicates Hashimoto's thyroiditis[7] and in a patient with clinical hyperthyroidism, we should think of chances of autoimmune thyroid disease Thyroid disorders are one of the preventable causes and if properly diagnosed, unnecessary surgical interventions can be avoided.

METHODS:

OBJECTIVE:

Primary Objective-

To estimate the proportion of thyroid abnormality in perimenopausal women with abnormal uterine bleeding.

Secondary Objective -

To assess the endometrial pattern in perimenopausal women with abnormal uterine bleeding having thyroid dysfunction

Study Design And Sample Size

The present study is cross sectional study conducted in the gynaecology department of SAT, Hospital Thiruvananthapuram for a period of one year from January 2019 to January 2020. Based on the study conducted by Byna et al (Thyroid abnormality in perimenopausal women with abnormal uterine bleeding by Byna P et al[10] published in International Journal of Research in Medical Sciences) sample size was determined to be 189.

Inclusion And Exclusion Criteria

Institutional ethics committee clearance was obtained for the study. All the patients who are in the age group of 45 to 55 who are able to give consent, and has abnormal uterine bleeding were included in the study.

Exclusion Criteria included

1. Women who have not given consent
2. Cervical or genital infections
3. Pregnancy and related causes of bleeding
4. Post-menopausal bleeding

All the women satisfying the eligibility criteria was selected and was assessed for the parameters including age, socioeconomic status, occupation, body mass index, menstrual history, frequency, regularity, duration and volume, marital status, parity, history of infertility, contraception history, clinical symptoms, thyroid function tests, ultrasound pelvis, histopathology report.

After taking informed consent, data collection was done thorough history taking regarding age, bleeding pattern, onset, duration, quantity of bleeding and complaints related to thyroid abnormality were noted. Clinical examination including general, neck, systemic and gynaecological examination were done. Investigations like blood routine, urine routine, ultrasound pelvis, TSH, FT3, FT4 were done. Endometrial samples obtained from biopsy, dilatation and curettage were utilized for this study. T3 and T4 were assayed by competitive Chemiluminescent immunoassay. TSH was also estimated. Then these data were entered into excel sheet. Categorical variables were expressed as proportions. Statistical test of significance by chi square test for categorical variables with a significance of 95% and pvalue <0.05 and student t tests for quantitative variables. Analysis of data was done by SPSS.

RESULTS:

A total of 189 cases of patients with AUB within age group 45-55 years attending the OP and IP department of Gynaecology were analysed. As per our study while evaluating patients with AUB 58.7% of patients were in the 45 to 50 age group. More than 50 % of the patients with AUB had a parity of two and above while only 5.8% of the AUB patients were nulliparous.

AUB and thyroid abnormality:

It was found that out of the 189 patients who were studied, 31.7% patients had high TSH indicating hypothyroidism whereas 9.5% patients had low TSH indicating hyperthyroidism. 58.7% patients had normal TSH levels.

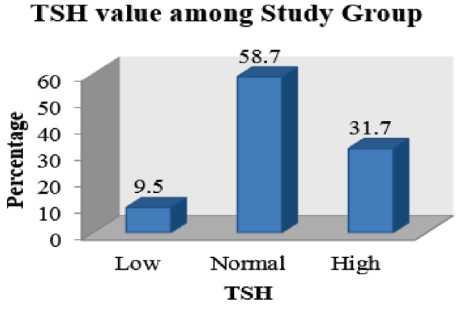

Figure 1

On assessment of the menstrual patterns in patients with hyperthyroidism, out of 18, 11 patients had infrequent cycles, 14 patients (77.8%) had irregular cycles, 50% patients had light menstrual flow and 27.7% (5 patients) had inter menstrual bleeding.

Table 1: Menstrual pattern of Hyperthyroidism

Menstrual pattern	Frequency	Percentage
Infrequent cycles	11	61.1
Irregular Cycles	14	77.8
Light menstrual flow	9	50
Inter menstrual bleed	5	27.7

And as shown in Table 2, among the 60 patients with hypothyroidism, 40 patients (66.6%) had heavy flow during menstruation, 86.7% (52) patients had irregular cycles, 27 patients (45%) had prolonged cycles, 28.3% (17 patients) had intermenstrual bleeding.

Table 2: Menstrual pattern of Hypothyroidism

Menstrual Pattern	Frequency	Percentage
Heavy Menstrual Bleeding	40	66.6
Irregular Cycles	52	86.7
Prolonged Cycles	27	45
Intermenstrual Bleed	17	28.3

Imaging with ultrasound in all the 189 patients shows that, 21.1% patients had fibroids, 8.4% patients had adenomyosis, 5.8 % patients had ovarian cyst, 5.8% patients had polyp, 6.9% patients had features of hyperplasia, whereas 52% patients had no positive findings in imaging which suggests majority of the patients had other functional causes of AUB

Thyroid abnormality and endometrial biopsy : Among the 65 patients with thyroid abnormality alone with no structural causes, 47.6% (31 patients) had proliferative endometrium, 27.6% (18 patients) had secretory endometrium, 15.3%(10 patients) had normal endometrial biopsy result, 1 patient (1.6%) had disordered proliferative endometrium, 3 patients (4.8%) had hyperplasia without atypia, 1 patient (1.6%) had hyperplasia with atypia, 1 patient (1.6%) had carcinoma, 50% (25 patients) with hypothyroidism had proliferative endometrium and 40% patients of patients with hyperthyroidism had proliferative endometrium. 15 patients (25%) with hypothyroidism had secretory endometrium and 3 patients (205) patients with hyperthyroidism had secretory endometrium. 12% patients with hypothyroidism and 26.8% patients with hyperthyroidism had normal endometrial biopsy

Table 3: - Thyroid disorders and endometrial biopsies

Endometrial Biopsy	Group			
	Hyperthyroid		Hypothyroid	
	n	%	n	%
Normal	4	26.8	6	12
Proliferative	6	40	25	50
Secretory	3	20	15	25
Disordered Proliferative	1	6.6	0	0
Hyperplasia without atypia	0	0	3	6
Hyperplasia with atypia	1	6.6	0	0
Carcinoma	0	0	1	2

DISCUSSION:

Thyroid disorders are seen more common in women with menstrual irregularities as compared to general population. They vary in regularity, frequency, volume and duration. A total of 189 patients with AUB attending the OP and IP were taken into the study. 58.7% patients belonged to 45-50 years whereas 41.3% patients belonged to 51-55 years which can be comparable to the study conducted by Indrani etal[11] which showed maximum patients belonged to the age group 45-49 years as compared to the age group 50-55 years.

94 patients (49.7%) patients had primary schooling and 68 patients (36%) in the study group were illiterate. 39.6% patients belonged to lower middle socioeconomic class, 39.1% patients belonged to upper lower socioeconomic class and 4.4% patients belonged to lower socioeconomic class.45% patients in the study group were overweight, 22.2% patients were obese and 32.8% patients had normal body weight. In the study group of women with AUB para 1 were of 21.1% which is slightly higher than study by Mangala Gowri et al[12]. (17.6%). 54.54% women of para 2 which is comparable to the study by Byna et al[10] (54.5%). Para 2 women were seen more in our study because most of the women were undergoing sterilization after two children.

31.7% (60 patients) had high TSH indicating hypothyroidism, and 9.5% (18 patients) had hyperthyroidism. Most of the women with peri menopausal abnormal uterine bleeding had frequent menstrual cycle (52.4%), irregular (85.7%) cycles, prolonged (59.3%) bleeding, heavy (56.6%) menstrual flow.

This is comparable to study by Indrani et al where heavy menstrual bleeding with increased frequency (53%) was the most common pattern. Hypothyroidism is associated with prolonged (45%) cycles as compared to study by Singh et al[13] and heavy flow (50%) as compared to study by Padmaleela et al[14] (HMB in 50%), irregular (86.7%), inter menstrual bleeding (28.3%). Hyperthyroidism is associated with infrequent (61.1%), irregular (77.8%) and light (50%) menstrual flow, inter menstrual bleeding (27.7%).

86.7% women with high TSH had hypothyroid symptoms and all women with hyperthyroidism had hyperthyroid symptoms which has a p value <0.001 which is statistically significant. 73.1% women with thyroid abnormality had palpable thyroid and 26.9% women with thyroid abnormality had no palpable thyroid, p value <0.001, hence it is statistically significant.

Considering the aetiology of AUB based on imaging, 21.1% women with AUB had fibroid, 8.4% had adenomyosis which is comparable to study by Bhavani et al[15] (2015) (8.3%), 5.8% had polyp, 5.8% had ovarian cyst which is comparable to study by Byna et al (5.4% had ovarian cyst), 6.9% had findings of hyperplasia, 52% had normal imaging. This is comparable to study by Bhavani et al[15] where 45.5% of them had non-structural causes of abnormal uterine bleeding. Thus, non-structural causes are an important cause of perimenopausal AUB. None of the patients with thyroid abnormality had history of coagulopathy and iatrogenic factors contributing to AUB. In our study, 25.9% of women with AUB had hypothyroidism as their only cause of AUB excluding other causes whereas 8.4% had hyperthyroidism as their only cause of AUB. This is slightly more than the study by Byna et al[10] (21.8% were with hypothyroidism, 12.72 % with hyperthyroidism). Out of the women with hypothyroidism, 16 patients had normal FT4, indicating subclinical hypothyroidism. This is comparable to the study by Sharma P et al[16] where 17 patients had subclinical hypothyroidism. T3, T4 workup should be done in patients with AUB, or else subclinical hypothyroidism may be missed. 39(50%) women were diagnosed earlier with thyroid abnormality but on irregular treatment, only 20(25.6%) women were diagnosed and on regular treatment and 19(24.4%) women were newly diagnosed. Patients on regular treatment for thyroid disorders had less chances of abnormal uterine bleeding as compared to those not on regular treatment.

Out of the patients with thyroid disorders, 64.6% patients belonged to 45-50 years, 35.4% patients belonged to 51-55 years which was not significant. 49.2% patients belonged to lower middle socio-economic status and 35.3% patients belonged to upper lower socioeconomic status, indicating that thyroid abnormality in AUB was more common in lower and middle socioeconomic class which is comparable to study by Nayana Kolli et al[17] where majority of the patients belonged to lower socio-economic class. There was no significant association between thyroid abnormality and age, socioeconomic status, parity, BMI, history of abortions or infertility.

The most common endometrial pattern of AUB in thyroid disorder was proliferative (47.6%) followed by secretory (27.6%), normal in 15.3%. The most common of endometrial pattern in hypothyroidism was proliferative (50%) and in hyperthyroidism was also proliferative (40%) comparable to study by Neelu Sharma et al where proliferative endometrium was found in hypothyroidism and hyperthyroidism. Thus, the finding of proliferative endometrium was comparatively lower in hyperthyroid than hypothyroid cases which shows that depression of HPO axis is not that severe to cause anovulation in all cases of hyperthyroidism.

CONCLUSION:

From the study we came to a conclusion that the thyroid disorders, more commonly hypothyroidism is an important cause of abnormal uterine bleeding even in perimenopause. Identification of non-structural causes of AUB and treating them can prevent unnecessary hormonal treatment and surgical intervention. Hypothyroidism is associated with heavy and irregular cycles whereas hypothyroidism is associated with light and irregular cycles. Palpation of thyroid swelling, asking for symptoms associated with them are found to be significant and useful. Full panel of thyroid testing including Free T4 and T3 along with TSH is must in these patients to identify the entity of subclinical thyroid disorders. Patients who are already diagnosed with thyroid abnormality and on regular medication have a reduced occurrence of AUB.

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