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Study of menstrual disorders in thyroid dysfunction

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Abstract
Background: Abnormal uterine bleeding is the most common problem seen in patients attending the gynecology OPD. Incidence of AUB is 9 to 14%. Thyroid dysfunction causes broad spectrum of reproductive disorders and is one of the causes noted for abnormal uterine bleeding. Thyroid disorders are 10 times more common in women. Therefore, this study is to assess the menstrual and endometrial patterns in women with thyroid disorders.
Aims and objectives
1. To assess the menstrual patterns in women with thyroid disorders.
2. To assess the endometrial patterns in women with thyroid disorders.

Methodology: This is a descriptive study conducted in department of OBG, ESIC-PGIMSR Bengaluru. 100 patients with signs and symptoms of thyroid dysfunction will be taken. Patients will be grouped into 3 categories- hyperthyroid, hypothyroid and Subclinical hypothyroidism. Menstrual pattern in these patients are studied. Selected patients in peri-menopausal age group with thyroid dysfunction will be subjected to endometrial biopsy.
Results: Most common thyroid dysfunction is hypothyroidism seen in 60% of the patients. Most common menstrual irregularity is menorrhagia seen in 51% of the patients. In hypothyroidism patients menorrhagia is seen in 48.3%, in hyperthyroidism, menorrhagia is seen in 35.3% and in subclinical hypothyroidism it is seen in 69.6%of patients. Most common endometrial pattern is simple hyperplasia without atypia seen in 50% of the patients.
Conclusion: The present study concludes that there is a strong association between thyroid dysfunction and menstrual irregularities. Thyroid profile should be used in the screening of all the women with abnormal uterine bleeding. If thyroid dysfunction is timely detected and corrected, then menstrual irregularities will settle and unnecessary interventions like endometrial curettage and surgery could be avoided.

Keywords: hypothyroidism, hyperthyroidism, subclinical hypothyroidism, menstrual pattern, endometrial pattern, screening, simple hyperplasia without atypia

Introduction
According to FIGO, abnormal uterine bleeding is defined as bleeding from the uterine corpus that is abnormal in volume, regularity, frequency or duration and occurs in the absence of pregnancy. Abnormal uterine bleeding is a common complaint seen in gynaecology OPD and it occurs in 9 to 14% of women from menarche to menopause affecting the quality of life [1].
Thyroid disorders are 10 times more common in women and there is increasing prevalence of thyroid disorders in women which is possibly due to autoimmune nature [2]. Thyroid dysfunction causes a wide range of reproductive disorders like menstrual irregularities, abnormal sexual development, infertility [3].
Abnormal uterine bleeding is the most debilitating symptom which has resulted in unnecessary, incorrect and expensive treatment and especially surgery with increased risk of morbidity and mortality [4]
The categories of AUB are arranged according to the acronym PALM-COEIN: polyp, adenomyosis, leiomyoma, malignancy and hyperplasia, coagulopathy, ovulatory disorders, endometrial causes, iatrogenic, not classified [5]. Among all the etiologies listed above, ovulatory disorders are one of the most common cause which usually occur secondary to thyroid dysfunction. Many studies like Danese MD *et al.*, and Douglas L Wilansky *et al.*, have stated that any menstrual irregularity in non-pregnant women justifies screening for thyroid disorders [6, 7]. Timely detection of thyroid dysfunction in patients presenting with AUB and their proper management can prevent unnecessary surgical interventions. Hence this study is to assess the menstrual and endometrial patterns in women with thyroid disorders.

Materials and Methods
Source of Data and Materials
The present study is carried out among patients of thyroid dysfunction attending the Department of obstetrics and gynaecology, ESIC-PGIMSR Bengaluru between JAN 2018 to JUNE 2019

Inclusion Criteria
1. Patients who are willing to give written informed consent.
2. Patients attending gynaecology OPD with thyroid dysfunction in the age group of 18 to 45 years with abnormal uterine bleeding.

Exclusion Criteria
1. Diagnosed case of ovarian cyst, uterine fibroid, polyps, endometriosis, PCOD, malignant endometrial and cervical tumours
2. Patients with pelvic infections including endometritis

and PID.
3. Patients with a history of bleeding disorders
4. Pregnancy

Method of Collection of Data
Patients with signs and symptoms of thyroid dysfunction will be taken. A detailed history will be obtained with relevance to age, bleeding pattern, onset, duration, amount of bleeding, complaints related to thyroid dysfunction will be noted. Thorough clinical examination including a general examination, a gynaecological examination will be done. All these patients will be subjected to routine investigations –
HB%, CT, BT, and thyroid function tests: free T3, free T4 and TSH. Free T3 and free T4 will be assayed by chemiluminescent immunoassay.
Reference values according to our laboratory are
Free T4–0.58: 1.64 ng/ml
Free T3–2.45: 4.25 pg/ml
Serum TSH: 0.34–5.60 µiu/ml
Patients will be grouped into 3 categories
- Hyperthyroid (overactivity of thyroid gland)
- Hypothyroid (abnormally low activity of thyroid gland)
- Subclinical hypothyroidism (In this, an asymptomatic patient has a low normal FT4I (free thyroxine index) but a slightly elevated serum TSH level)

Abnormal menstrual patterns are like menorrhagia, oligomenorrhea, polymenorrhea, and amenorrhea.
Selected patients in the peri-menopausal age group with thyroid dysfunction will be subjected to endometrial biopsy for histopathological examination.

Duration of the Study: Eighteen months (JAN 2018 to JUNE 2019)

Type of Study: This is a descriptive study conducted in the department of OBG, ESIC-PGIMSR Bengaluru between JAN 2018 to JUNE 2019. The sample size being 100. All the women in the age group of 15 to 45 with thyroid dysfunction will be evaluated.

Sample Size
The sample size for the present study has been calculated by considering the 24% occurrence of menstrual disorders among the thyroid dysfunction patients from the published literature[7]. The minimum sample size has been calculated to be 100 diagnosed thyroid cases with .08 as an absolute marginal error at a 5% level of significance assuming a two-tailed hypothesis. Following formula has been used to calculate the sample size:

$$n = \frac{3.84xPQ}{D^2}$$

Where, P=.24, Q=1-P, and D=.08

Statistical analysis
Data were entered into Microsoft Excel datasheet and was analysed using SPSS 21 version software. Categorical data was represented in the form of Frequencies and proportions. A chi-square test was used as test of significance for qualitative data. Continuous data were represented as mean and standard deviation. ANNOVA test is used to measure p-value for continuous variable between two and more groups

Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram, Pie diagram and Scatter plots. P-value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Results and Observations

Table 1: Distribution of study subjects based on age group

		Frequency	%
Age Group	Less than 25 Years	9	9.0%
	Between 26 to 30 Years	19	19.0%
	Between 31 to 35 Years	23	23.0%
	Between 36 to 40 Years	24	24.0%
	More than 40 Years	25	25.0%

Most common age group in our study is more than 40 years which accounts for 25%

Table 2: Distribution of study subjects based on Marital Status

		Frequency	%
Marital Status	Married	95	95.0%
	Unmarried	5	5.0%

In our study married women constitute 95%.

Table 3: Distribution of study subjects based on Parity

		Frequency	%
Parity	0	6	6.0%
	1	19	19.0%
	2	52	52.0%
	3	20	20.0%
	4	2	2.0%
	5	1	1.0%

Most of the patients in our study with thyroid dysfunction are multiparous with parity of 2, and they constitute 52%.

Table 4: Distribution of study subjects based on Thyroid Disorders

		Frequency	%
Thyroid Disorder	Hyperthyroidism	17	17.0%
	Hypothyroid	60	60.0%
	Subclinical hypothyroid	23	23.0%

Most common thyroid dysfunction in our study is hypothyroidism which constitute 60%, followed by subclinical hypothyroidism (23%), and hyperthyroidism (17%)

Table 5: Distribution of study subjects based on menstrual irregularity.

		Frequency	%
Menstrual Irregularities	Menorrhagia	51	51.0%
	Amenorrhea	18	18.0%
	Polymenorrhagia	21	21.0%
	Oligomenorrhea	9	9.0%
	Intermenstrual Spotting	1	1.0%

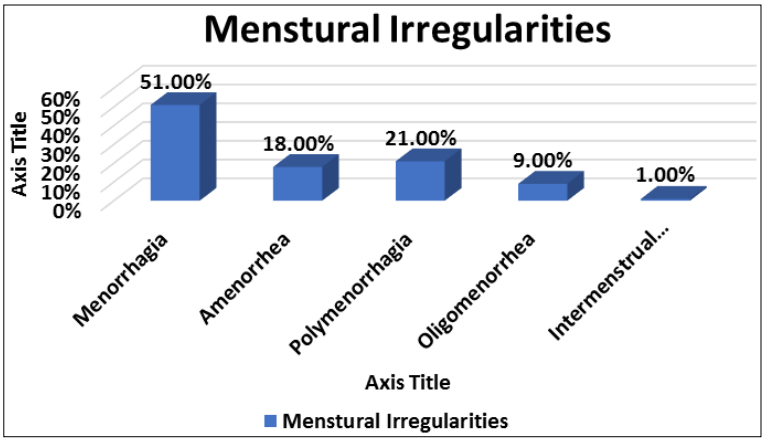

Fig 1: Graph wise distribution of study subjects based on Menstrual Irregularities

Most common menstrual pattern in our study, in patients with thyroid dysfunction is menorrhagia which accounts for 51%, followed by polymenorrhagia which constitutes 21%, and amenorrhea (18%)

Table 6: Distribution of Study Subjects Based on Endometrial Biopsy findings

	Count	Column N%
Simple Hyperplasia Without Atypia	16	50.0%
Proliferative Phase	5	15.6%
Secretary Endometrium	6	18.7%
Complex Hyperplasia Without Atypia	5	15.6%

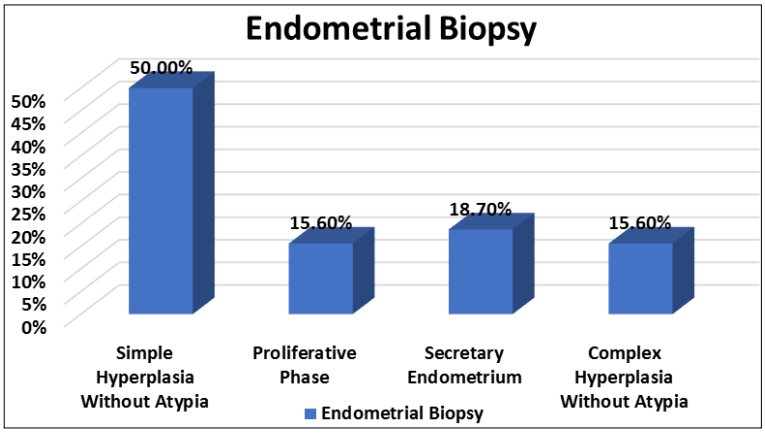

Fig 2: Graph wise distribution of study subjects based on Endometrial Biopsy.

Most common endometrial biopsy finding in our study is simple hyperplasia without atypia which constitutes 50% followed by secretory endometrium (18.70%), proliferative endometrium (15.6%) and complex hyperplasia without atypia (15.6%)

Table 7: Distribution of Thyroid Disorders based on the age of the Study subjects

		Thyroid Disorders					
		Hyperthyroidism		Hypothyroid		Subclinical Hypothyroidism	
		N	%	N	%	n	%
Age Group	Less than 25 Years	2	11.8%	6	10.0%	1	4.3%
	Between 26 to 30 Years	4	23.5%	10	16.7%	5	21.7%
	Between 31 to 35 Years	2	11.8%	15	25.0%	6	26.1%
	Between 36 to 40 Years	5	29.4%	13	21.7%	6	26.1%
	More than 40 Years	4	23.5%	16	26.7%	5	21.7%

Chi-square = 2.908 p=0.940

In our study, in hyperthyroidism, most of the patients belong to the age group of 36 to 40 years. In hypothyroidism most of the patients belong to the age group of more than 40 years which constitute 26.7%. And in subclinical hypothyroidism most of the patients belong to the age group of 31 to 35 years and 36 to 40 years which constitute 26.1% each.

Table 8: Distribution of Thyroid Disorders based on the Marital Status of Study subjects

		Thyroid Disorders					
		Hyperthyroidism		Hypothyroid		Subclinical Hypothyroidism	
		n	%	n	%	n	%
Marital Status	Married	16	94.1%	57	95.0%	22	95.7%
	Unmarried	1	5.9%	3	5.0%	1	4.3%

Chi square = 0.048 p= 0.976

Table 9: Distribution of Thyroid Disorders based on the Menstrual Irregularities of Study subjects

		Thyroid Disorders					
		Hyperthyroidism		Hypothyroid		Subclinical Hypothyroidism	
		N	%	N	N	%	n
Menstrual Irregularities	Menorrhagia	6	35.3%	29	48.3%	16	69.6%
	Amenorrhea	4	23.5%	11	18.3%	3	13.0%
	Polymenorrhagia	3	17.6%	15	25.0%	3	13.0%
	Oligomenorrhea	4	23.5%	4	6.7%	1	4.3%
	Intermenstrual Spotting	0	0.0%	1	1.7%	0	0.0%

Chi square = 9.878 p=0.274

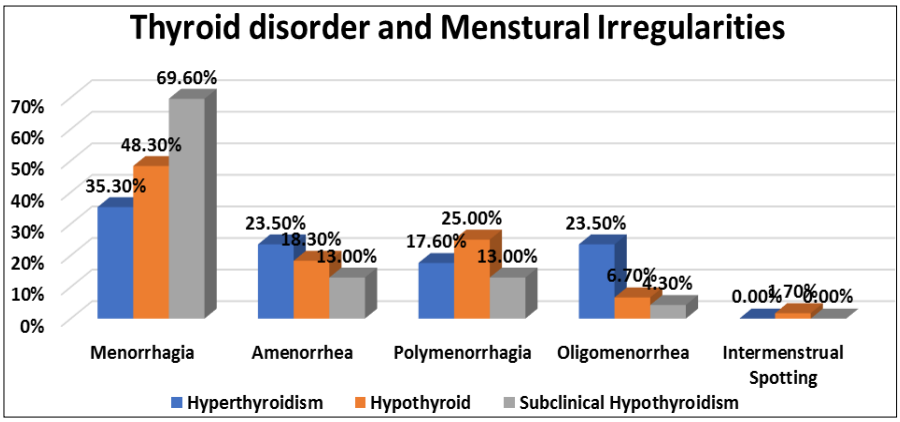

Fig 3: Graph wise distribution of menstrual irregularities among thyroid disorders

In our study, in hypothyroidism patient's menorrhagia is seen in 48.3%, in hyperthyroidism it is seen in 35.3% and in subclinical hypothyroidism, it is found to be 69.6%. The next most common menstrual abnormality in hypothyroidism patients is polymenorrhagia (25%) followed by amenorrhea (18.3%). In the case of hyperthyroidism next most common menstrual abnormality are amenorrhea (23.5%) and oligomenorrhea (23.5%).

Table 10: Comparison of menorrhagia with other menstrual irregularities in patients with hypothyroidism (including subclinical hypothyroidism) and hyperthyroidism.

Menstrual irregularities	Hyperthyroidism		Hypothyroidism	
Menorhagia+polymenorrhagia	9	52.9%	63	75.9%
Other menstrual irregularities	8	47%	20	24.1%

Chi square=3.69 p=0.05

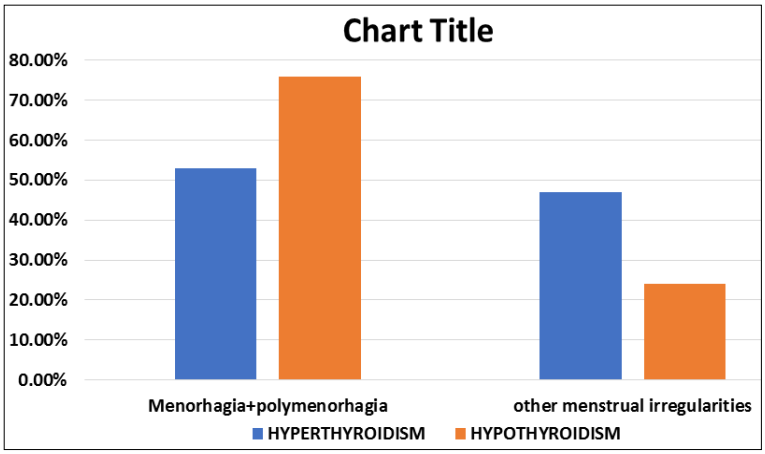

Fig 4: Graph wise Comparison of menorrhagia with other menstrual irregularities in patients with hypothyroidism (including subclinical hypothyroidism) and hyperthyroidism.

In our study, menorrhagia with polymenorrhagia is seen in 52.9% of the patients with hyperthyroidism. In patients with hypothyroidism (including subclinical hypothyroidism) it is seen in 75.9%. The p value is 0.05 which is statistically significant.

Table 11: Distribution of Thyroid Disorders based on the Endometrial Biopsy Findings of Study subjects

		Thyroid Disorders					
		Hyperthyroidism		Hypothyroid		Subclinical Hypothyroidism	
		N	%	n	%	N	%
Endometrial Biopsy	Simple Hyperplasia Without Atypia	2	50.0%	10	45.5%	4	66.7%
	Proliferative Phase	0	0.0%	4	18.2%	1	16.7%
	Secretary Endometrium	2	50.0%	3	13.6%	1	16.7%
	Complex Hyperplasia Without Atypia	0	0.0%	5	22.7%	0	0.0%

Pooled chi square = 0.848 p=0.654

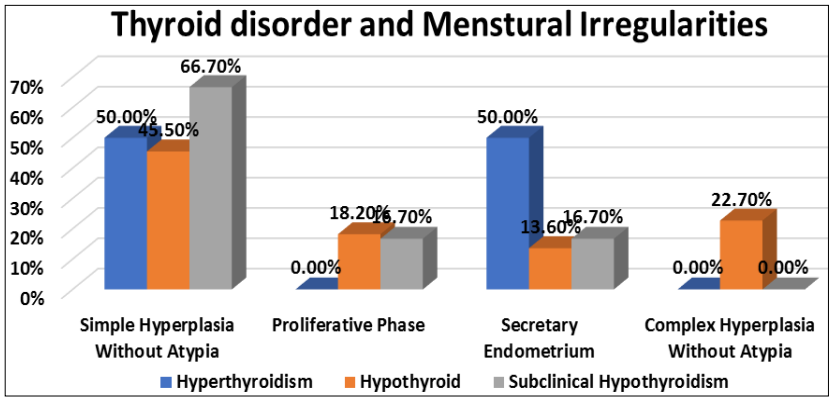

Fig 5: Graph wise distribution of Endometrial Biopsy among thyroid disorders

In our study, the most common endometrial biopsy finding in hypothyroidism is simple hyperplasia without atypia (45.5%), followed by complex hyperplasia without atypia (22.7%). In hyperthyroidism patients, the endometrial pattern is found to be simple hyperplasia without atypia and secretory phase which constitute 50% each. In subclinical hypothyroidism, the most common pattern is again simple hyperplasia without atypia (66.7%).

Discussion

Thyroid hormones play an important role in normal reproductive physiology by interacting with sex hormone-binding globulin and by direct binding of the hormones to the ovary and endometrium. Thyroid disorders result in a spectrum of menstrual irregularities ranging from menorrhagia to amenorrhea. It may affect the quality of life. This study is done on 100 patients with thyroid dysfunction and their menstrual irregularities are studied, in the department of obstetrics and gynecology, ESIC PGIMSR, Bengaluru.

The most common age group in our study is more than 40 years which accounts for 25%. Between 36 to 40 years it is 24%. In Anju Verma [8] *et al*. study, 54.5% of women with thyroid dysfunction with menstrual irregularities belonged to the age group of 35 to 45 years. In Ramya MR [9] *et al*. study maximum number of patients was found to be in the age group of 21 to 30 years. In Prasad Yeshwant Deshmukh [10]. *et al* study majority of the patients belonged to the age group of 41 to 45 years which is comparable to our study. The prevalence of thyroid disorders increases with increasing age.

In our study thyroid dysfunction is mainly noted in the multiparous women which accounts for 79%. The majority are with parity 2. In Anju Verma[8] *et al* study, 88% of women with thyroid dysfunction were multiparous. In Ramya[41] *et al* study the maximum number of patients are multiparous with parity of 2.

In our study hypothyroidism is found to be present in 60%, subclinical hypothyroidism in 23% patients and hyperthyroidism in 17% of patients. Maximum menstrual disturbances are found in patients with hypothyroidism. In Anju Verma [8] *et al*. study, out of 50 cases of thyroid dysfunction, 45 cases were hypothyroid and 5 cases were hyperthyroid. In Ramya [9] *et al*. study, 64 patients were hypothyroid and 2 had subclinical hypothyroidism, and no cases of hyperthyroidism were present. In Prasad Yeshwant Deshmukh [10] *et al*. study 9% of the patients were hypothyroid, 18% had subclinical hypothyroidism, and 3% were hyperthyroid.

In our study, the most common abnormal uterine bleeding presentation overall is menorrhagia which is seen in 51% of the patients followed by polymenorrhagia (21%) and amenorrhea (18%). P value for menorrhagia is 0.05, which is statistically significant.

In our study, in hypothyroidism patients menorrhagia is seen in 48.3%, in hyperthyroidism it is seen in 35.3% and in subclinical hypothyroidism it is found to be 69.6%. The next most common menstrual abnormality in hypothyroidism patients is polymenorrhagia (25%) followed by amenorrhea (18.3%). In the case of hyperthyroidism next most common menstrual abnormality are amenorrhea (23.5%) and oligomenorrhea (23.5%). In hypothyroidism due to altered GnRH pulsatality, there is anovulation and increased oestrogen levels which leads to menorrhagia.

Comparison of menstrual irregularity in the present study versus the other studies

The incidence of menorrhagia in hypothyroid patients in the Prentice [11] *et al*. study it is 36% and in Pushpa Bikha Rom [12]. *et al* study it is 40%. In the Kaur [13] *et al*. study 64.3%

had menorrhagia, 21.4% had oligomenorrhea, and 14.28% had metrorrhagia. In Pahwa [14]. *et al*. study 94% had menorrhagia and 10.5% had polymenorrhea. In the Padmaleela[15] *et al* study, the commonest menstrual complaint was menorrhagia (53.3%) followed by polymenorrhea (13.3%), and 20% had oligomenorrhea. In the Kaur[13] *et al* study, the patients with hyperthyroidism were found to have oligomenorrhea. In the Pahwa [14]. *et al*. study, of the two hyperthyroid patients, both had menorrhagia. In the Padmaleela [15] *et al*. study, among the hyperthyroid patients, 42.8% had menorrhagia, 28.6% had polymenorrhea, and 14.3% had oligomenorrhea. In Prasad Yeshwant Deshmukh[10] *et al* study 62.5% of patients with hypothyroidism had menorrhagia, and 50% of the patients with subclinical hypothyroidism had polymenorrhea, and 13.3% of patients with hyperthyroidism had oligomenorrhea.

In our study, endometrial biopsy is done in patients mainly in the perimenopausal age group. The most common endometrial pattern in hypothyroidism is simple hyperplasia without atypia (45.5%), followed by complex hyperplasia without atypia (22.7%). In hyperthyroidism patients, the endometrial pattern is found to be simple hyperplasia without atypia and secretory phase which constitute 50% each. In subclinical hypothyroidism, the most common pattern is again simple hyperplasia without atypia (66.7%). In hypothyroidism decreased GnRH pulsatality is noted which can cause anovulation. Anovulation and unopposed oestrogen activity cause proliferative endometrium which leads to endometrial hyperplasia. In hyperthyroidism, increased levels of thyroid hormones are at risk of developing proliferative endometrium and eventually endometrial hyperplasia by the direct binding of the hormones to the receptors.

Comparison of endometrial biopsy report in thyroid disorders in our study versus the rest in hypothyroidism

In the Kaur [13] *et al*. study, 64.3% of hypothyroid patients had proliferative endometrium, 21.4% had endometrial hyperplasia, and the rest 14.3% had secretory endometrium. In Neelu Sharma[16] *et al* study 36.36% had proliferative, 36.36% had secretory and 27.27% had atrophic endometrium in hypothyroid patients. In hyperthyroid patients, they found that 42.84% had proliferative, 28.56% had secretory, and 14.28% had hyperplastic endometrium. In the Padmaleela [15] *et al*. study, the most common finding on endometrial biopsy is the proliferative endometrium (59.1%) both in hypothyroid (60%) and hyperthyroid cases (57.1%). Cystic Glandular Hyperplasia was found only in 13.3% and secretory endometrium in 26.7% of the hypothyroid patients.

Conclusion

It may be concluded from the present study that there is a strong association between thyroid dysfunction and menstrual irregularities, mainly menorrhagia. Thyroid profile should be used in the screening of all the women with abnormal uterine bleeding. If thyroid dysfunction is timely detected and corrected, then menstrual irregularities will settle and unnecessary interventions like curettage and surgery could be avoided. As the cost to benefit ratio is low, it emphasizes the need for the screening.

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