

Thyroid Profile in Patients with Dysfunctional Uterine Bleeding in a Tertiary Care Hospital

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Abstract

Introduction: In the outpatient clinic, Dysfunctional uterine bleeding (DUB) is a common diagnosis with considerable social and economic impact, making up to 20-30% cases. Complaints of heavy menstrual bleeding significantly affect the quality of life resulting in time off work, and also leading to surgical intervention including hysterectomy and ultimately posing a significant impact on the health care system. In India, thyroid disorders are among the most common endocrine diseases. Thyroid dysfunction is usually associated with reproductive disorders. Thyroid status is assessed in the present study which can help in timely and appropriate management and will prevent most of these problems. **Methods:** This prospective study consisted of 100 women who presented with menorrhagia and DUB to the out-patient department of OBG at Government General Hospital, Nalgonda Telangana, which is a tertiary level hospital, over a period of 6 months from January 2021 to June 2021. These patients were categorized as euthyroid, subclinical hypothyroid, hypothyroid or hyperthyroid based on thyroid profile. Thyroid hormones, viz., thyroid stimulating hormone TSH, total triiodothyronine T3 and tetraiodothyronine T4, were estimated by CLIA. Statistical analysis of the data was performed by using Microsoft Excel software. **Results:** In this study, menorrhagia was the predominant abnormality (69.2%) in cases with hypothyroidism, followed by metrorrhagia (60%). most common bleeding patterns were menorrhagia (52%) followed by Polymenorrhagia (14%) and Polymenorrhea (14%). Hypothyroidism was more prevalent among cases (80%) as compared with controls (20%). In patients with menorrhagia, 69.2 % of patients had hypothyroidism. **Discussion:** The study reveals that in patients with DUB, hypothyroidism and menorrhagia predominate as presenting symptoms. It can be concluded that DUB is closely associated with thyroid dysfunctions, which can be relieved by normalization of thyroid status. **Conclusion:** So, thyroid assessment should be routinely performed in all patients with menstrual irregularities as it is seen that menstrual irregularity precedes the occurrence of other clinical symptoms of thyroid dysfunction. This will help in early detection of the cause and prompt treatment of DUB patients.

Keywords: polymenorrhagia, TSH, CLIA, Hypothyroidism, Dysfunctional Uterine Bleeding.

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Introduction

Menstrual abnormalities in absence of any organic pelvic pathology forms a group of disorders known as Dysfunctional Uterine Bleeding (DUB) where there is a dysfunction at any level of the Hypothalamo-Pituitary-Ovarian axis resulting in disturbance in the rhythmical production of hormones by the ovary.

Dysfunctional Uterine Bleeding (DUB) is a common but complicated clinical presentation, accounting for at least 20% of new outpatient visits significantly affecting the quality of life.

It is defined as any variation from the normal menstrual cycle and includes changes in regularity, frequency, duration of flow, or amount of blood loss[1].

“FIGO PALM COEIN” classification for causes of Dysfunctional uterine bleeding includes both structural and non-structural causes. Structural causes are polyp, adenomyosis, fibroids, malignancies, and hyperplasia and non-structural causes include coagulopathy, endometrial causes, iatrogenic, and non-classified causes[2].

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Bleeding in any of the following situations is abnormal:

- Bleeding between periods.
- Irregular spotting in the menstrual cycle.
- Heavy bleeding during cycles, i.e., >80 mL
- Cycle length >35 or <21 days.
- Bleeding after intercourse.

The normal menstrual functions depend upon the complex interaction between the hypothalamic-pituitary-ovarian axis and endogenous hormones[3,4].

Any disruption in the normal physiology or anatomic changes in the endometrium, as well as alterations in the hormones of hypothalamic-pituitary-ovarian origin, affect menstrual cycles such as cycle length, regularity, and bleeding patterns.

Thyroid hormones play a key role in the menstrual and reproductive function of women. Thyroid dysfunction (both hypothyroidism and hyperthyroidism) is associated with menstrual abnormalities in females of all age groups.

The clinical objective of this study is to detect and treat thyroid disease before the symptoms and signs are significant and intense.

Menstrual abnormalities in the absence of any organic pelvic pathology form a group of disorders known as dysfunctional uterine bleeding (DUB) or nowadays more commonly referred to as abnormal uterine bleeding, where there is a dysfunction at any level

of the hypothalamo-pituitary-ovarian axis resulting in disturbance in the rhythmical production of hormones by the ovary.

DUB is classified by the character of menstrual cycle as ovulatory or an ovulatory. Out of all the aetiologies, age variations and clinical presentations like thyroid dysfunction (sub clinical or clinically evident) are becoming significantly important factors associated with DUB. The thyroid gland is known to play an important role in maintaining a healthy menstrual cycle[2,3].

It may be bleeding without a causative uterine lesion, such as tumor infection or complications of pregnancy, although frequently there may be associated cysts of the ovary. It comprises a major portion of abnormal menstruation cases, being the principal diagnosis in at least 10% of all new outpatient department patients. Dysfunctional uterine bleeding is classified by the character of menstrual cycle as ovulatory or an ovulatory. Out of all the etiologies, age variations and clinical presentations like thyroid dysfunction (subclinical or clinically evident) are becoming significantly important factors associated with DUB.

The thyroid gland is known to play an important role in maintaining a healthy menstrual cycle. The impact of thyroid hormones has been reported to be both direct, through the presence of thyroid hormone receptors on the ovaries, and indirect, through the impact on the secretion of sex hormone-binding globulin (SHBG), Prolactin, and gonadotropin releasing hormone (GnRH). Both hypothyroidism and hyperthyroidism are associated with a variety of changes in reproductive function including delayed onset of puberty, anovulatory cycles, and abnormally high fetal wastage[2,3,4].

Clinical experiences show increased menstrual flow to be the most common reproductive system manifestation of hypothyroidism. It is seen that women with hypothyroidism had abnormal menstrual pattern, with menorrhagia or heavy menstrual bleeding being the commonest. On the contrary, hyperthyroidism, is most commonly associated with oligomenorrhea and hypomenorrhea.

But it is also seen that manifestations of DUB can range in between both ends of the spectrum in case of hypothyroidism. Abnormal menstruation, particularly heavy and prolonged menses are frequent debilitating conditions resulting in the need for repeated curettage and hysterectomy with its attendant morbidity and mortality. Hysterectomy, being a major surgery with its associated significant surgical and psychological complications, is quite unacceptable to many women today. To avoid such complications and a major surgery at all, it is better to aim at finding out an etiological factor for these abnormal bleeding patterns and treat it conservatively. The introduction of serum triiodothyronine (T3) and tetraiodothyronine (T4 or thyroxine) and serum thyroid-stimulating hormone (TSH) radioimmunoassays has increased the sensitivity and specificity of thyroid function testing. The serum TSH assay has been shown to be a sensitive indicator of diminished thyroid functional reserve, since TSH levels become elevated before circulating serum thyroxine levels fall below the normal range[2-5].

So, we have undertaken this study to evaluate the thyroid status in apparently euthyroid patients with DUB presenting at a tertiary care hospital in Nalgonda, Telangana

Singh et al[6] found 63% of hypothyroid patients had anovulatory cycles. Recently "occult menorrhagia" has been found to be an early manifestation of subclinical hypothyroidism with disease becoming symptomatic later.

Various studies done earlier show that menorrhagia being the chief symptom in hypothyroidism. Prevalence of subclinical hypothyroidism is as high as 9.5% in women. Majority of subclinical hypothyroidism cases pass unrecognized because patients are usually asymptomatic. Prevalence of subclinical hypothyroidism is so high that it should be given enough consideration justifying the screening of women with menstrual irregularities even if no sign or symptom seen. The introduction of serum thyroxine (T3) and serum thyroid stimulating hormone (TSH) by CLIA has increased the sensitivity and specificity of thyroid function testing. Serum TSH assay has

been shown to be a sensitive indicator of diminished thyroid functional reserve, since TSH levels become elevated before circulating serum thyroxine levels fall below the normal range. This study is to evaluate thyroid function in patients having abnormal menstrual bleeding from puberty to premenopausal age groups to know prevalence of hypothyroidism in patients provisionally diagnosed as DUB for further management[5-7].

Inclusion Criteria

1. Patients presented with the chief complaint of abnormal uterine bleeding.
2. Patients between the age group of 18-45 years.
3. Patients who have provided the informed consent

Exclusion Criteria

1. Patients with previously known thyroid disorder.
2. Patients diagnosed with thyroid disease, hyperprolactinemia and coagulopathy.
3. Patients on anticoagulant drugs.
4. Patients who have not signed the informed consent.

Materials and Methods

This is a Prospective study that was carried out by the Department of Biochemistry at Government Medical College, Nalgonda from January 2021 to June 2021. Ethical clearance was received from the Institutional Review Committee of Government Medical College, Nalgonda. All patients of abnormal uterine bleeding attending the gynecology department during this period from puberty to those who have not attended menopause were included.

Patients under hormonal treatment, using contraceptives, having bleeding disorders and pregnant patients were excluded from the study.

A complete history was taken from all patients with regards to age, parity, menstrual history, onset and duration of complaints, amount of blood flow and any other specific complaints.

Following which a thorough examination was carried out which includes a general physical examination, systemic examination, gynecological, and pelvic examination in married women. All the findings were noted down in a predesigned questionnaire. Basic routine investigations like hemoglobin, platelet, blood test, and ultrasound of abdomen and pelvis were performed.

Then the serum triiodothyronine (T3), thyroxine (T4), and thyroid-stimulating hormone (TSH) level were measured in all patients. Patients with thyroid-stimulating hormone <0.5 mIU/ml were considered as hyperthyroid and thyroid-stimulating hormone >5 mIU/ml were considered as hypothyroid.

The normal ranges of serum thyroid-stimulating hormone, triiodothyronine, and thyroxine in the hospital laboratory were 0.35 to 5.5 mIU/ml, 2.3 to 4.2 pg/ml, and 0.89 to 1.76 ng/dl. Statistical analysis of the data was performed by using Microsoft Excel software. A p value of less than or equal to 0.05 was considered significant. 0.35 µIU/mL to 4.94 µIU/mL (TSH). 0.58 ng/mL to 1.59ng/mL(T3)4.87 µg/dL to 11.72 µg/dL (t4)

Results

In this study, thyroid hormones of 50 cases and equal number of controls were analyzed. The mean age of study population was 32.9 ±10.12 years, with a range from 15 to 45 years. Maximum number of cases and controls, i.e., 17 (34%) were seen in the age group of 31 to 40 years, followed by 12 cases and controls in the 21 to 30 years age group (Table 1). It was found that maximum number of both the cases and controls (≈78%) were married and parous. Fig. 2 shows 50 cases that came with the complaint of different bleeding patterns, commonest being menorrhagia in 24 (48%) cases. After, analyses of serum TSH, T3, and T4 in both cases and controls, hypothyroid, euthyroid as well as hyperthyroid women were detected when both groups were taken together, i.e., a total of 100 study subjects.

From Table 3 it is evident that the thyroid function was significantly associated with DUB. Hypothyroidism was more prevalent among cases, i.e., 16 (32%) as compared with 2 controls (8%), which are statistically significant. Fig. 4 shows the relationship of hypothyroidism, euthyroidism, and hyperthyroidism to the different bleeding patterns of clinically diagnosed cases of DUB. In patients with menorrhagia, 69.2% of patients had hypothyroidism and 26.9%

of patients were euthyroid. Table 4 shows the relation of serum TSH levels to different types of bleeding patterns where the most common bleeding patterns were menorrhagia (52%) followed by polymenorrhagia (14%) and Polymenorrhea (14%). Likewise, it was seen that incidence of menorrhagia was higher (52%) than other bleeding patterns where serum T3 and T4 concentrations were low.

Table 1: Age-wise distribution of cases and controls

	Cases		Controls	
	Number	% of Total	Number	% of Total
≤20	10	20%	10	20%
21–30	12	24%	12	24%
31–40	17	34%	17	34%
≥41	11	22%	11	22%
Total	50	100%	50	100%

Distribution of cases and controls according to thyroid function
 $\chi^2=8.29$; Degrees of freedom=1 and $p<0.01$.

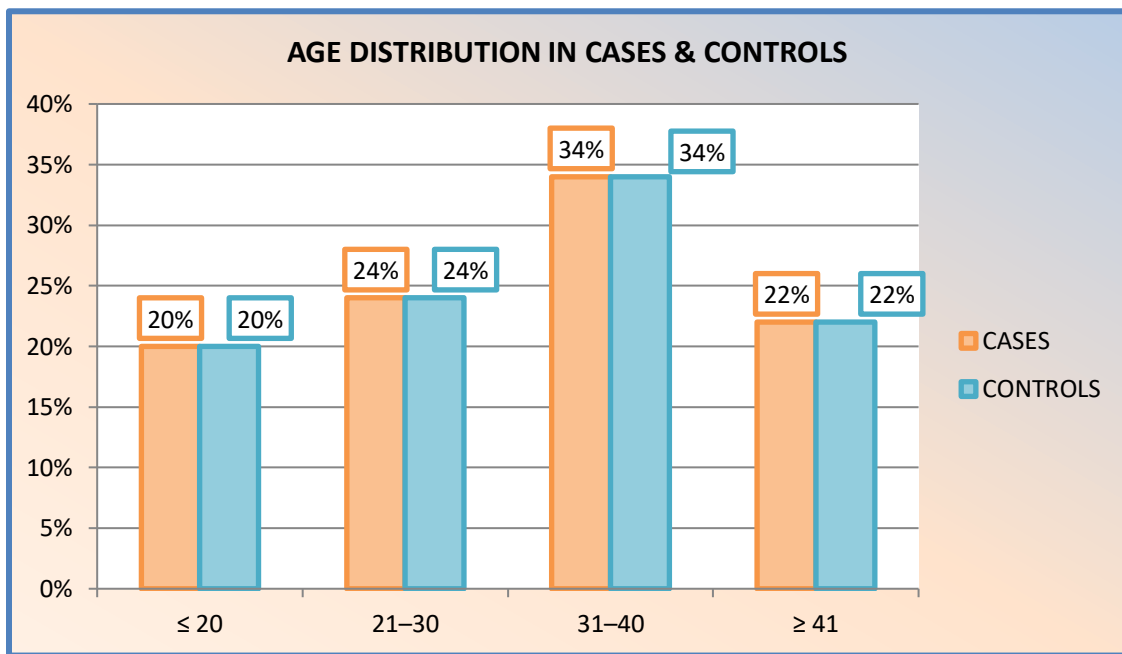


Fig. 1: Age wise distribution among cases and controls

Table 2: Bleeding pattern of DUB in cases

Bleeding Pattern	No. of cases	%
Metrorrhagia	5	10.0%
Hypomenorrhea	2	4.0%
Menorrhagia	26	52.0%
Oligomenorrhea	3	6.0%
Polymenorrhagia	7	14.0%
Polymenorrhea	7	14.0%
Total	50	100.0%

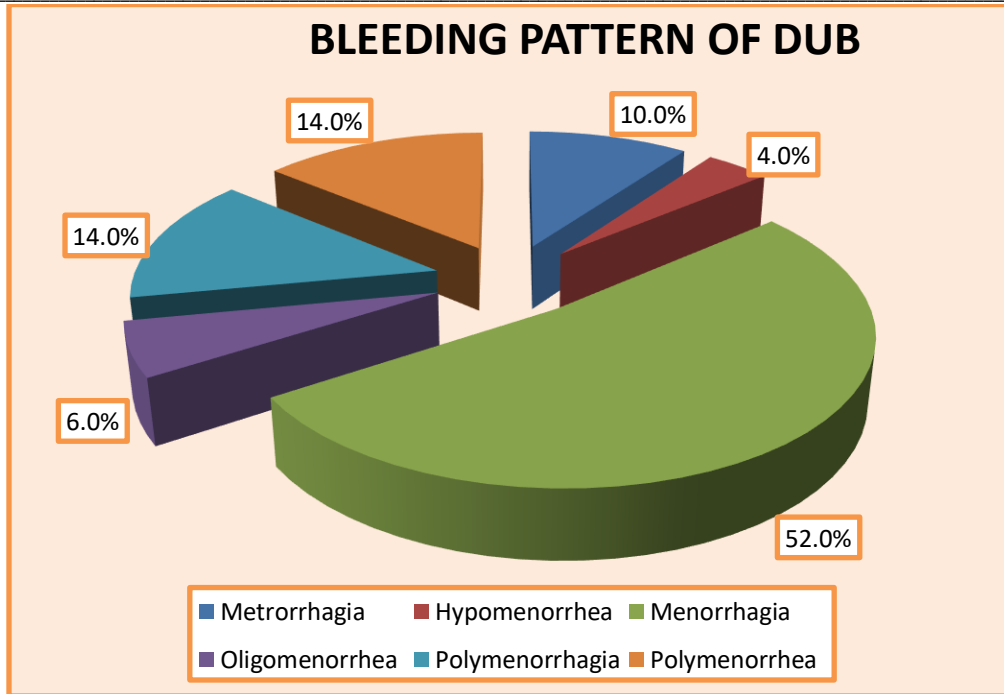


Fig. 2: Bleeding pattern of DUB in cases

Table 3: Distribution of Thyroid functional status in cases and controls

Thyroid Function	Cases		Controls		Total
	Number	% of Total	Number	% of Total	
Hypothyroid	16	32%	4	8%	20
Euthyroid	34	68%	44	88%	78
Hyperthyroid	0	0%	2	4%	2
Total	50	100%	50	100%	100

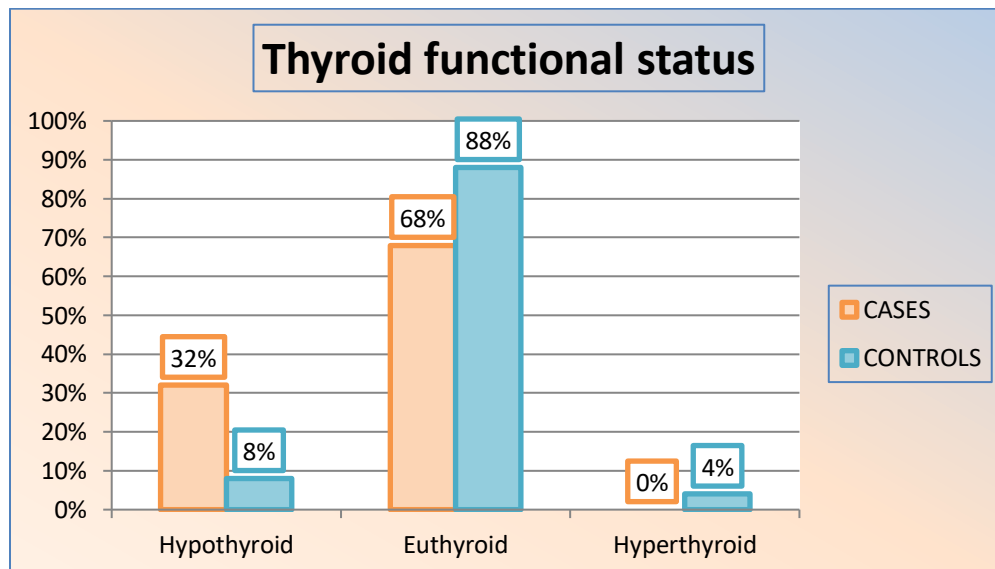


Fig. 3: Thyroid functional status among cases and controls

Table 4: Thyroid-stimulating hormone levels and different bleeding patterns of the cases

TSH (µIU/mL)	No. of Cases	Metrorrhagia		Hypomenorrhea		Menorrhagia		Oligomenorrhea		Polymenorrhagia		Polymenorrhagia	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
< 0.5	6	1	20%	0	0%	4	15.4%	1	33.3%	0		0	
0.5- 4.5	32	2	40%	2	100%	14	53.8%	2	66.7%	6	85.7%	6	85.7%
4.51 – 7.0	10	2	40%	0		7	26.9%	0		1	14.3%	0	
≥ 7.0	2	0	0%	0		1	3.8%	0		0		1	14.3%
TOTAL	50	5	1	2		26	-	3		7		7	

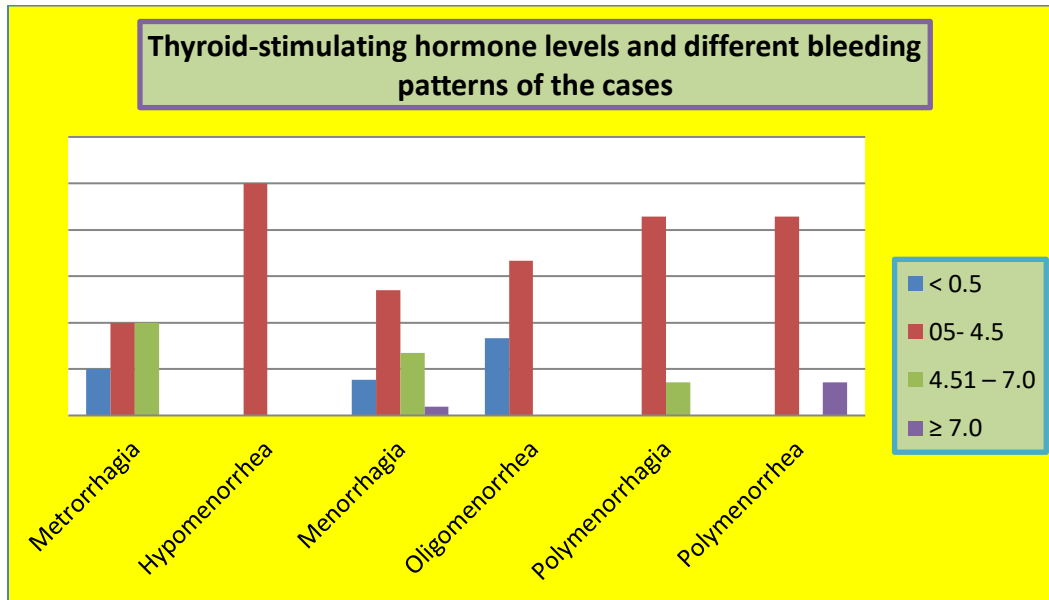


Fig. 4: Thyroid-stimulating hormone levels and different bleeding patterns of the cases

Discussion

Abnormal uterine bleeding is a frequently encountered condition in the present scenario in the gynaecology outpatient department and is an important cause of menstrual pattern abnormality. Thyroid disorders in general and hypothyroidism, in particular, are extremely common in women of reproductive age group. Menarche, pubertal growth and development, menstrual cycles, fertility and fetal development, post-partum period, reproductive years, and menopausal years are all profoundly influenced by the thyroid status of the woman.

Thyroid disorders have been seen to affect the menstrual pattern in females and present with a varied spectrum of bleeding patterns. Menstrual disturbances may accompany and even may precede thyroid dysfunction and may accompany clinical alterations. The present study revealed that thyroid hormone levels were altered in DUB patients. From Table 1 the highest incidence was found in the 31 to 40 years age group (34%) followed by 24% in the 21 to 30 years group.

Doifode and Fernandes[8] also reported maximum number of patients belonged to age group of 31 to 40 years. This is also in accordance with Patel et al who stated that abnormal menstruation is more common in the third and fifth decades. He reported a similar incidence of 46% in the 21 to 30 years age group and observed that dysfunctional menstruation was more common among parous women than in nulliparous women. This was because of alterations in spiral arterioles of endometrium with age and parity, which constitutes an important local factor in hemorrhage. Dass and Chugh[9] reported the highest incidence in the 41 to 50 years age group, which is 32.5% followed by 28.2% incidence in the 31 to 40 years age group.

Narula gave the highest incidence among the age group between 31 and 40 years (32.8%) followed by the next common age group of 41 to 50 years (29.1%). In the present study, 76% of the cases were parous and the commonest type of menstrual abnormality encountered was menorrhagia (52%)[10].

In the present study, 32 % cases (16 cases out of 50 patients) with menstrual abnormality had an abnormal thyroid function test. All of them were hypothyroid. It was seen that hypothyroidism was more prevalent among cases (16 out of 20 hypothyroid (80%)) as compared with 4 controls out of a total of 16 (20 %).

Sharma and Parmar[11] and Chakrabarti et al[12] have found similar incidences in their respective studies. On the contrary, Lahiri et al[13] reported very high incidence of menstrual abnormality in 53% cases of hypothyroidism. Gowri et al[14] found hypothyroidism in 17.6% cases but reported oligomenorrhea as the commonest abnormality. In the present study, there were no cases of hyperthyroidism with menstrual abnormality. This low incidence of cases with hyperthyroidism may be because in this part of the country, hyperthyroidism is not as common as hypothyroidism. Also, patients with hyperthyroidism present more with other symptoms of hyperthyroidism to a physician than to a gynecologist.

In this study, menorrhagia was the predominant abnormality (69.2%) in cases with hypothyroidism, followed by metrorrhagia (60%). Scott and Mussey[15] also reported menorrhagia and metrorrhagia combined as the most common irregularity in 75% cases with hypothyroidism.

Thus, the findings are in accordance with these studies and menorrhagia is more common in hypothyroidism. Similar findings were reported in studies where they demonstrated that menstrual irregularities were significantly more frequent in hypo- or

hyperthyroidism as compared with control cases. They found that polymenorrhea is common in hypothyroidism and hypomenorrhea is common in hyperthyroidism. The menstrual irregularities and bleeding problems in hypothyroidism are attributed to multiple factors like high TSH levels or altered GnRH pulses from hypothalamus causing decrease in pituitary gonadotropin secretion or defect in luteinizing hormone secretion with persistent follicle-stimulating hormone secretion. This results in chronic an ovulation in hypothyroidism or luteal phase defects in less severe cases. An ovulation resulting from either Grave's disease or myxedema disturbs the menstrual cycle. Hypothyroidism also alters the peripheral metabolism of estrogen and decreases SHBG production, causing rise in serum estrogen level. This, in turn, causes abnormal feedback at the pituitary level. Hypothyroidism can also lead to menorrhagia by altered production of coagulation factors (decreased levels of factors VII to IX and XI)[16].

Deshmukh et al[17] conducted a study to investigate thyroid functions in patients with AUB as initial diagnosis and then sent the patients with abnormal results, to physician for further workup and optimization. Thyroid dysfunction was detected in 30% of the study population. Out of those subclinical hypothyroidism was found in 18% of patients, overt hypothyroidism in 9% of patients and hyperthyroidism in only 3 % of the patients. Polymenorrhagia and menorrhagia were found to be common in subclinical hypothyroid patients. On the other hand, oligomenorrhea was common in hyperthyroid patients. Subclinical and overt hypothyroidism were most prevalent type of thyroid dysfunctions associated with menorrhagia most of the time. Therefore, the researchers suggested obligatory evaluation of thyroid function for the women presenting with dysfunctional uterine bleeding.

A study carried out by Sudhir et al[18] was designed to evaluate thyroid function derangement in women presenting with abnormal uterine bleeding, detected cases were managed in collaboration with physician. Thyroid dysfunction was detected in 20 % of patients, out of those 20% patients, 16% were with hypothyroidism and just 4% were hyperthyroid. Majority of subclinical hypothyroid patients presented with polymenorrhagia and menorrhagia[19].

In the studies done by Parveen et al[20] and Bhavani et al[21] mean age of thyroid dysfunction was 31- 40 years and 41- 50 years. And Deshmukh et al[17] found mean age to be 41- 45 years followed by less than 20 years. And study by Subedi et al[22], Nepal, mean age was in 35-40 years range and prevalence of thyroid dysfunction being 11 %. Among the causes of DUB , structural causes accounted for 54.5 % cases . Leiomyoma being the commonest cause.

In the studies done by Parveen et al[20], Dhanpal et al[23] and Bhavani et al[21] found that menorrhagia was the most common bleeding disorder and also was associated with thyroid dysfunction. Joshi et al[25] showed 44% of women with menstrual abnormalities apparently were euthyroid. Kaur et al[26] in their study diagnosed 15% of cases with subclinical hypothyroidism. In our study 11% of cases constituted subclinical hypothyroidism. Hence TSH appears to be the most sensitive test to evaluate thyroid function as it was abnormal in 100% of cases detected to have the disorder.

Etiology of DUB would help in proper management of the patient, treating both the menstrual abnormality along with associated thyroid dysfunction and also would be cost effective. It must be ruled out as soon as possible because frequently, disorders of thyroid gland function are underestimated and in asymptomatic cases it is commonly neglected by practitioners. So, all these studies suggest that thyroid dysfunction in females with DUB is higher. Therefore, appropriate evaluation and early screening must be opted to reduce the related risk. Thyroid disorders can affect various physiological phenomena particularly menstruation.

Therefore, optimally treated thyroid dysfunction will not only have beneficial impact on menstrual disorder, but it will also help in improving fertility. The patients with thyroid dysfunction are

frequently found to have disturbed menstruation, fertility issues and complications during antenatal period and puerperium[24].

Conclusion

There is a close relationship of thyroid hormones and steroid hormone action and production regarding normal function of the ovary and conception.

The study reveals that in patients with DUB, hypothyroidism and menorrhagia predominate as presenting symptoms. It can be concluded that DUB is closely associated with thyroid dysfunctions, which can be relieved by normalization of thyroid status. So, thyroid assessment should be routinely performed in all patients with menstrual irregularities as it is seen that menstrual irregularity precedes the occurrence of other clinical symptoms of thyroid dysfunction. This will help in early detection of the cause and prompt treatment of DUB patients and definitely will have an impact on reduction in incidence of hysterectomy.

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