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Patterns of Thyroid Dysfunction among Women with Menstrual Disorder

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Abstract

Background and objectives: Thyroid dysfunction can lead to menstrual irregularities and infertility. Thus, this study aimed to assess the frequency and patterns of thyroid dysfunction in patients with menstrual disorders.

Methods: This prospective cross-sectional study was conducted at Shar Teaching Hospital, from June 01, 2023, to June 01, 2024, on 200 women with menstrual abnormality. Their thyroid hormone levels were estimated and the correlations between patients' age, type of thyroid dysfunction, and menstrual abnormality were determined.

Results: The mean age of women was 32.14 ± 7.6 years, and most of them were aged 31– 40 years (41.5%) with irregular menses (n=76). Women aged 31- 40 years had the highest incidence of menstrual abnormality (n=83), of which most cases were irregular menses (42.1%). Most patients had thyroid disorder (n=128), of which subclinical hypothyroidism reported the highest level (n=67). The highest mean level of thyroid stimulating hormone was found in patients with amenorrhea (20.81 ± 33.6 µIU/mL), free tri-iodo tyrosin in oligomenorrhea (3.35 ± 1.0 pg/dL) (p=0.02 and p=0.002, respectively) and free tetra-iodo tyrosin in both oligomenorrhea and irregular menses (1.20 ± 0.5 ng/dL). The vast majority of patients had positive anti-thyroid peroxidase antibody (51.5%) and negative thyroid stimulating hormone receptor binding antibody (91%) (p>0.05).

Conclusions: Subclinical hypothyroidism is common among patients with menstrual abnormalities, especially young adults. Thyroid-stimulating hormone and free tri-iodo tyrosin were directly associated with menstrual abnormalities, while both anti-thyroid peroxidase antibody and thyroid-stimulating hormone receptor binding antibody were not.

Keywords: Cross-sectional study, Menstrual disorder, Thyroid dysfunction, Endocrine disorder

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Introduction

The thyroid gland is a butterfly-shaped organ in the front of the neck that produces hormones that play a vital role in regulating blood pressure, body temperature, heart rate, metabolism, mood status/attention, energy level, and bone health. Thyroid dysfunction develops when the gland produces less amount of thyroid hormone (hypothyroidism) or a higher than average amount (hyperthyroidism).[1] Generally, thyroid disorders are among the most common endocrine diseases, and their onset increases with age. It is estimated that 26% of premenopausal and menopausal women are diagnosed with thyroid disease.[2] Thyroid disorders are more common in women than in men and older adults than in younger age groups. Postmenopausal and older women are particularly at risk of developing comorbidities and mortality related to thyroid dysfunction.[3] Thyroid dysfunction categorized into subclinical hypothyroidism, subclinical hyperthyroidism, overt hypothyroidism, and overt hyperthyroidism. Among these, subclinical hypothyroidism is most common among population (3.0 - 15%) that most often caused by autoimmune (Hashimoto) thyroiditis. Other causes include post-surgical or post-ablative hypothyroidism, central hypothyroidism, and medication-induced hypothyroidism (lithium, amiodarone, checkpoint inhibitors, and tyrosine kinase inhibitors).[4,5] Subclinical hypothyroidism may be associated with an increased risk of heart failure, coronary artery disease, stroke, and mortality. In addition, middle-aged patients with subclinical hypothyroidism may have cognitive impairment and nonspecific symptoms such as fatigue, and altered mood.[6,7] Thyroid function and the gonadal axes are related throughout the woman's fertile period. The relationship between the two glands is mutual. In particular, thyroid hormones affect the reproductive function both directly and indirectly through several actions.[2] In females, thyroid dysfunction can affect hormone balance and cause problems in puberty, menstruation, fertility, pregnancy and the postpartum period.[8,9] Menstrual disorders due to thyroid dysfunction are more common in older age groups, especially in developing countries, including abnormal uterine bleeding, amenorrhea, dysmenorrhea, menorrhagia, irregular menses, hypo/polymenorrhea and oligomenorrhea.[10-13] Internationally, there are several studies to relate the occurrence of thyroid dysfunction in adult females with menstrual disorders; however, there are very few studies in this locality on this concept. So, this study aimed to study the prevalence of thyroid dysfunction and thyroid autoimmunity in patients with menstrual disorders and to study their correlations.

Patients and methods

This prospective cross-sectional study was conducted at Shar Teaching Hospital, Sulaimaniyah City, Iraq, from June 01, 2023, to June 01, 2024, on 200 women with thyroid dysfunction and menstrual abnormalities. Patients having major complaints of menstrual disturbances such as menorrhagia, polymenorrhoea, polymenorrhagia, metrorrhagia, and oligo/hypomenorrhea were included. Whereas, patients on medication, who had overt clinical symptoms of thyroid dysfunction, pregnant, history of bleeding disorder, and goiter was excluded. The type of menstrual abnormality was indicated based on the patient's case history through face-to-face interviews. Then, menstrual abnormalities were categorized into amenorrhea, oligomenorrhea, menorrhagia, and irregular menses. At the same time, 5.0 mL blood samples were collected from each patient; serum was obtained to estimate thyroid hormone levels, including thyroid stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4), as well as thyroid auto-antibodies,

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including anti-thyroid peroxidase (anti-TPO) and TSH receptor binding antibody (TRAB). Patients were then grouped into euthyroid (normal), subclinical hypothyroid, subclinical hyperthyroid, overt hypothyroid, and overt hyperthyroid. Patients were considered euthyroid when the TSH, FT3, and FT4 levels were within the normal range (0.39 - 4.20 µIU/mL, 1.4 - 4.2 pg/mL, and 0.8 -2.0 ng/mL, respectively). When TSH was high with normal FT3 and FT4, they were labelled as subclinical hypothyroidism. In contrast, overt hypothyroidism was marked with high TSH and low FT3/FT4, subclinical hyperthyroidism when the TSH was low and normal FT3/FT4, and overt hyperthyroidism when TSH was low, and FT3/FT4 were high.[14] Finally, the correlations between different variables were determined using statistical analysis. Ethical approval was obtained from the Ethical and Scientific Committees of the Kurdistan Higher Council of Medical Specialties (KHCMS), Iraq, with reference number 892 on April 26, 2023. Permission was also obtained from the hospital's ethical committee. Participants verbal informed consent was obtained and they were informed about the nature and purpose of the study. The Statistical Package for Social Science (SPSS, IBM, Chicago, USA, version 27) was used for the data analysis. In addition, the Chi-Square test was used to find the association between independent and dependent variables. A $p \leq 0.05$ was considered statistically significant.

Results

The mean age of patients was 32.14 ± 7.6 years, ranging from 17- 46 years with a median of 32 years, and most of them were aged 31 – 40 years (n=83, 41.5%), while least of them were aged ≤20 years (n=15, 7.5%). Regarding the type of menstrual abnormalities, most patients had irregular menses (38%), followed by oligomenorrhea (34%), then menorrhagia (20.5%), and amenorrhea (7.5%). Additionally, 72 patients had euthyroid (36%), while 128 patients had thyroid dysfunction (64%), of which subclinical hypothyroidism reported the highest prevalence (n=67, 33.5%), followed by overt hypothyroid (n=34, 17%), then subclinical hyperthyroidism (n=18, 9.0%), and overt hyperthyroid (n=9.0, 4.5%), as shown in Table (1).

Table (1): Age distribution among studied patients with their clinical characteristics.

Variable	Frequency (Number)	Percentage of cases
Age (Years)		
≤ 20	15	7.5
21 – 30	70	35.0
31 – 40	83	41.5
> 40	32	16.0
Type of menstrual abnormality		
Amenorrhea	15	7.5
Oligomenorrhea	68	34.0
Menorrhagia	41	20.5
Irregular menses	76	38.0
Thyroid pattern		
Subclinical hypothyroidism	67	33.5
Subclinical hyperthyroidism	18	9.0
Euthyroid (Normal)	72	36%
Overt hyperthyroid	9.0	4.5
Overt hypothyroid	34	17
Total	200	100

Regarding the correlations between age and types of menstrual abnormalities among patients, oligomenorrhea and irregular menses are frequently observed among patients aged 21 - 30 years old (n=24 each). Whereas irregular menses were most commonly found among patients aged 31 - 40 years (n=32, 42.1%), >40 years (n=13, 17.1%), and ≤20 years (n=7.0, 9.2%). Collectively, women aged 31-40 years had the highest incidence of menstrual abnormalities (n=83, 41.5%). However, there was no significant correlation between age distribution and type of menstrual abnormality among patients (p=0.22), as shown in Table (2).

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Table (2): The correlations between age and types of menstrual abnormalities.

Age (Years)	Menstrual Type				Total	p-value
	Amenorrhea (n=15)	Oligo menorrhea (n=68)	Menorrhagia (n=41)	Irregular menses (n=76)		
	Number (%)					
≤ 20	1.0 (6.7)	6.0 (8.8)	1.0 (2.4)	7.0 (9.2)	15 (7.5)	0.22
21 - 30	10 (66.7)	24 (35.3)	12 (29.3)	24 (31.6)	70 (35.0)	
31 - 40	2.0 (13.3)	30 (44.1)	19 (46.3)	32 (42.1)	83 (41.5)	
> 40	2.0 (13.3)	8.0 (11.8)	9.0 (22.0)	13 (17.1)	32 (16)	
Mean ±SD	28.73 ± 6.3	32.03 ± 7.6	33.51 ± 7.5	32.16 ± 7.7	32.14 ±7.6	

Concerning the correlations between thyroid patterns and types of menstrual abnormalities, 72 patients with menstrual abnormalities had normal thyroid patterns (n=72, 36%). At the same time, the remaining patients (n=138) had thyroid dysfunction together with menstrual abnormality. Among them, irregular menses were more common (n=67), especially in patients with subclinical hypothyroidism (n=17), overt hypothyroid (n=14), subclinical hyperthyroidism (n=7.0), and overt hyperthyroid (n=3.0). Simultaneously, oligomenorrhea (n=28), menorrhagia (n=17), and amenorrhea (n=5.0) were most commonly found in patients with subclinical hypothyroidism. There was no significant correlation between patterns of thyroid dysfunction and type of menstrual abnormalities (p>0.05), as shown in Table (3).

Table (3): The correlations between thyroid pattern and types of menstrual abnormalities.

Thyroid Pattern	Menstrual Type				Total	p-value
	Amenorrhea (n=15)	Oligo menorrhea (n=68)	Menorrhagia (n=41)	Irregular menses (n=76)		
	Number (%)					
Subclinical hypothyroidism	5.0 (33.3)	28 (41.2)	17(41.5)	17 (22.4)	67 (33.5)	0.07
Subclinical hyperthyroidism	2.0 (13.3)	5.0 (7.4)	4.0 (9.8)	7.0 (9.2)	18 (9.0)	0.90
Euthyroid (Normal)	4.0 (26.7)	23 (33.8)	10(24.4)	35 (46.1)	72 (36)	0.09
Overt hyperthyroid	0.0 (0.0)	4.0 (5.9)	2.0 (4.9)	3.0 (3.9)	9.0 (4.5)	0.78
Overt hypothyroid	4.0 (26.7)	8.0 (11.8)	8.0(19.5)	14 (18.4)	34 (17)	0.46

Concerning correlations between thyroid pattern and age of the patients, most patients aged 21- 30 and 31 - 40 years had subclinical hypothyroidism (n=21 and n=29, respectively), followed by overt hypothyroid (n=9.0, n=14, respectively). Collectively, 72 (36%) patients in all age groups had euthyroid, while thyroid dysfunction was more common among the age group 31 - 40 years (n=52), followed by 21 - 30 years (n=42), then >40 years (n=22), while age group ≤20 years reported the less value (n=12). There is no significant correlation between patterns of thyroid dysfunction and various age groups of the patients (p>0.05), as shown in Table (4).

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Table (4): The correlations between thyroid pattern and age of the patients.

Thyroid Pattern	Age (Years)				Total	p-value
	≤ 20 (n=15)	21 - 30 (n=70)	31 – 40 (n=83)	> 40 (n=32)		
	Number (%)					
Subclinical hypothyroidism	5.0 (33.3)	21 (30)	29 (34.9)	12 (37.5)	67 (33.5)	0.88
Subclinical hyperthyroidism	3.0 (20)	7.0 (10)	8.0 (9.6)	0.0 (0.0)	18 (9.0)	0.14
Euthyroid (Normal)	3.0 (20)	28 (40)	31 (37.3)	10 (31.3)	72 (36)	0.47
Overt hyperthyroid	2.0 (13.3)	5.0 (7.1)	1.0 (1.2)	1.0 (3.1)	9.0 (4.5)	0.11
Overt hypothyroid	2.0 (13.3)	9.0 (12.9)	14 (16.9)	9.0(28.1)	34 (17)	0.28

Moreover, the highest mean level of TSH was found in patients with amenorrhea (20.81±33.6 µIU/L), while the highest mean level of FT3 hormone was found in patients with oligomenorrhea (3.35±1.0 pg/dL). The highest mean level of FT4 hormone was found in patients with both oligomenorrhea and irregular menses (1.20±0.5 ng/dL). Thus, significant differences were seen for mean TSH (p=0.02) and FT3 (p=0.002) levels among patients with menstrual abnormalities, as shown in Table (5).

Table (5): The correlations between thyroid hormones and type of menstrual abnormalities.

Variable	Menstrual abnormality (Mean ± SD)				Total (n=200)	p-value
	Amenorrhea (n= 15)	Oligomenorrhea (n= 68)	Menorrhagia (n= 41)	Irregular menses (n = 76)		
TSH (µIU/L)	20.81 ± 33.6	9.03 ± 16.7	7.52 ± 6.3	7.23 ± 10.7	8.92 ± 15.4	0.02*
FT3 (pg/dL)	2.57 ± 0.36	3.35 ± 1.0	3.03 ± 0.5	3.18 ± 0.6	3.16 ± 0.76	0.002*
FT4 (ng/dL)	0.93 ± 0.38	1.20 ± 0.5	1.09 ± 0.4	1.20 ± 0.5	1.16 ± 0.5	0.16

TSH: Thyroid stimulating hormone, FT3: Free triiodothyronine, FT4: Free thyroxin, *: Significant difference using ANOVA test

Furthermore, most patients had a positive anti-TOP antibody (n=103, 51.5%), especially those with irregular menses (n=37). However, most patients had a negative TRAB level (n=182, 91%), especially those with irregular menses (n=70). Both anti-TPO and TRAB antibodies are not significantly associated with menstrual abnormalities among patients (p=0.39 and p=0.8, respectively), as shown in Table (6).

Table (6): The correlations between thyroid hormones and type of menstrual abnormalities.

Variable		Menstrual abnormality				Total (n=200)	p-value
		Amenorrhea (n=15)	Oligo menorrhea (n=68)	Menorrhagia (n=41)	Irregular menses (n=76)		
Anti-TPO (IU/mL)	Yes	8.0	32	26	37	103(51.5)	0.39#
	No	7.0	36	15	38	97 (48.5)	
TRAB	Yes	1.0	8.0	3.0	6.0	18 (9.0)	0.8$
	No	14	60	38	70	182 (91)	

TPO: Thyroid peroxidase, TRAB: Thyroid stimulating hormone receptor binding antibody
#: Performed by Chi-square test; $: Performed by Fisher exact test

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Discussion

Multiple studies worldwide proved and confirmed that thyroid dysfunction can cause a large number of menstrual aberrations.[15,16] Thus, we designed to study this issue in our locality to clarify the way to diagnose and treat these disorders properly. In this study, the mean age of the patients with thyroid dysfunction and menstrual abnormality was 32.14±7.6 years, and most were aged 31 - 40 years (41.5%). These outcomes are similar to that of Deshmukh et al. who found that most patients were aged 31 - 40 years (44%) and Kumari et al. reported 44.6% in the same age group with a mean patient age of 31.33±7.25 years.[15,17] Most patients had irregular menses (38%), followed by oligomenorrhea (34%), then menorrhagia (20.5%), and the least had amenorrhea (7.5%). Deshmukh et al.[15] found that menorrhagia was most common among patients (40%), followed by polymenorrhagia/amenorrhea (18% each), then oligomenorrhoea (15%), and hypomenorrhea (2.0%). Whereas Ajmani et al. found that 50% of patients had menorrhagia, 20% had hypo/oligomenorrhea, 16% had polymenorrhea, 12% had metrorrhagia, and only 2.0% had amenorrhea. [14] Kumar et al. found menorrhagia to be the more common (46.42%), followed by hypo/oligomenorrhea (17.86%), then metrorrhagia (16.08%), polymonorrhea (10.71%), and amenorrhea (8.93%).[17] These variations might be related to the environmental conditions, climate status, patient's age, sample size, and study duration. Additionally, we found that most patients had thyroid dysfunction (64%), and the least were euthyroid (36%), which is opposite to the outcomes of Ajmani et al. who found that 56% of patients were euthyroid and 44% had some forms of thyroid dysfunction. [14] Also, our findings are contrary to that of Deshmukh et al. who found that 70% of patients were euthyroid and the rest had thyroid dysfunction (30%).[15] These disparities among studies might be related to changes in hormone levels due to age, stress, certain health conditions, medications, and comorbidities. Furthermore, in this study, no significant correlation was detected between patterns of thyroid dysfunction and type of menstrual abnormalities ($p>0.05$) among women. Most patients (n=138) had thyroid dysfunction together with menstrual abnormality, of which irregular menses were more common (n=67), especially in patients with subclinical hypothyroidism, overt hypothyroid, subclinical hyperthyroidism, and overt hyperthyroid. Whereas oligomenorrhea, menorrhagia, and amenorrhea were most commonly found in patients with subclinical hypothyroidism. In contrast to this study, Deshmukh et al. found 30% of patients had thyroid dysfunction; among them, 18% had subclinical hypothyroidism, 9% of patients had hypothyroidism, and only 3.0% of patients had hyperthyroidism, polymenorrhagia, and menorrhagia, while most of the hyperthyroid cases were oligomenorrheic. [15] However, this study is aligned with the outcomes of Ajmani et al. who found hypothyroidism as the most common abnormality (34%), of which 20% had subclinical hypothyroidism, and 10% had hyperthyroid (2.0% were subclinical hyperthyroid, and 8.0% were overt hyperthyroid). [14] These variations might be related to patients' different lifestyles, degrees of stress, hormonal disturbance, and dietary habits. Moreover, we found no significant correlations ($p>0.05$) between patients' age group and their types of menstrual abnormalities. However, the highest incidence of menstrual abnormalities (n=83) was found among the 31- 40 years and irregular menses were most commonly found among patients (n=76), of which the majority were 21 - 30 years (n=24). Lakshmi and Kaur, found the most common age group with menstrual irregularities to be 41-50

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women (45.9%), followed by 31- 40 years (34.1%).[18] Also, they found menorrhagia to be more common (53.3%). Also, there were no correlations between thyroid patterns and different age groups (p>0.05). Most patients aged 21 - 30 and 31 - 40 years had subclinical hypothyroidism, followed by overt hypothyroidism. Thyroid dysfunction was more common among the age group 31 – 40 years, followed by 21 - 30 years, >40 years, and then the age group ≤20 years. In this respect, Deshmukh et al. indicated that patients in the age group 40 - 45 had the highest level of thyroid dysfunction (4.8%), followed by the age group ≥20 and 31 - ≤40 years (31.8% each), then 21- ≤30 years (22.2%).[15] Also, they mentioned that most patients in the age group 31 - ≤40 had thyroid dysfunction (n=14), of which 12 cases were subclinical hypothyroidism, similar to this study. These variations might be related to patients' parity, reproductivity, hormonal status, stress, and environmental factors. Moreover, the highest mean level of TSH was found among patients with amenorrhea. In contrast, a higher mean level of FT3 hormone was found in those with oligomenorrhea, and the highest mean level of FT4 hormone in patients with oligomenorrhea/irregular menses. Thus, significant differences were seen for TSH (p=0.02) and FT3 levels (p=0.002), but not FT4 levels. This study demonstrated that most patients had positive anti-TPO antibodies (n=103, 51.5%), especially those with irregular menses (n=37). Ajmani et al. found a high TSH level and positive anti-TPO in patients with menstrual abnormalities. [14] Also, we found that most patients had negative TRAB levels (n=182, 91%), especially those with irregular menses (n=70) (p>0.05). These results emphasize the significance of thyroid hormones and antibody estimation in patients with menstrual disorders.

Conclusions

Most patients with menstrual abnormalities had thyroid dysfunction, especially subclinical hypothyroidism. Thyroid dysfunction and menstrual abnormality, especially irregular menses, were more common among young adult women. This study's limitations are the small sample size, the lack of a control group, the single-center study, the study duration, and the lack of molecular study due to insufficient fatalities and specific funding.

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Conflict of interest

The authors reported no potential conflict of interest.

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