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Effect of thyroid gland dysfunction on menstrual pattern among reproductive age group women

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Abstract---Background: Thyroid hormones play an important role in the body. As a result, any imbalance in these hormones can affect all physiological and metabolic functions of the body, including the health of the reproductive system. Objectives: Assessing the menstrual pattern and investigating the differences in effect of thyroid gland dysfunction on menstrual pattern between case and control. Methodology: A descriptive (case-control) study implemented for 100 women in 15-45 years of reproductive age group, from two hospitals in Salah Al-Din Governorate/Iraq. The study conducted from the period (31th of October 2021 to 2th of August 2022) included obtaining a blood sample for TSH, fT3 and fT4 tests on 50 women with thyroid disorders and 50 women in control group. Results: The finding shows the highest percentage, in the case group (74%) had an abnormal cycle, and most types of menstrual abnormalities were menorrhagia (32%), oligomenorrhea (18%), and polymenorrhea (10%), compared with control group (82%) were having a normal cycle. Conclusions: The highest percentage was abnormality pattern and menorrhagia was their commonest menstrual disorders in case group compared with control group.

Keywords---Thyroid gland dysfunction, Hyperthyroidism, Hypothyroidism, Menstrual pattern, Reproductive age group.

Introduction

The thyroid gland is an endocrine organ, shaped like a butterfly, and it is one of the largest endocrine glands. It is located on the front side of the neck in front of

the trachea. The function of this gland is the production and stores of two major hormones T4(thyroxine or tetraiodothyronine) and T3 (triiodothyronine) which helps in the regulation of heart rate, blood pressure and body temperature and also helps in the regulation of rate of chemical reactions (metabolism) and growth and development in the body [1].The hypothalamic pituitary axis regulates production of thyroid hormones through the thyroid-releasing hormone which secreted from the hypothalamus which stimulates the thyroid-stimulating hormone from anterior pituitary gland. The prevalence of thyroid disorders are one of a very common medical condition. The function of the thyroid gland can be secondarily affected from higher centers signal in the brain (hypothalamic pituitary axis) or primarily influenced from the gland itself (more common) ([2]8). Thyroid disorders are among the most common endocrine disorders in the world. It is effecting ten times the women than men [3]. About 200 million people worldwide were estimated with iodine diet deficiency, and in the United States in each year there was 1.8 percent of them take thyroid replacement medication to treat hypothyroidism, in addition 360.000 new cases of hyperthyroidism was detected [4]. The serum thyroid-stimulating hormone is the best primary test of thyroid function. Based on blood samples taken to estimate TSH, T4 and T3. Four groups can be found: Hyperthyroidism, Subclinical hyperthyroidism, Hypothyroidism and Subclinical hypothyroidism [5]. It is defined as a high serum thyroid-stimulating hormone (TSH) level, with triiodothyronine and thyroxine levels below the normal reference range [6]. The prevalence of hypothyroidism in the developed countries are about 4-5 percent [7]. Since the 1950s, the effect of hypothyroidism on the pattern of the menstrual cycle has been identified and leads to changes in blood flow and cycle length [8]. The menstrual irregularity in Iraqi women diagnosed with hypothyroidism was 24 percent. In addition, studies showed that the incidence of hypothyroidism with menorrhagia was about 33.3percent while with oligomenorrhea was about 44.4percent [9]. Subclinical hypothyroidism (SCH) is defined as an elevated serum TSH level with a normal free T4 and T3 levels, which is usually asymptomatic or associated with mild symptoms and signs like weakness, menstrual irregularities, lethargy and skin changes [1]. The prevalence of menstrual disorders were observed in 52percent of subclinical hypothyroidism [10,11,12] . Hyperthyroidism is a condition that occurs when thyroid-stimulating hormone level is low with free T3 and T4 levels are high [13] . The association of hyperthyroidism with amenorrhea has been described as early as 1840 by Von Bosedow [14]. Subclinical hyperthyroidism is defined by a low serum thyroid-stimulating hormone concentration, with normal free T3 and T4 concentrations [15,16]. Thyroid disorders are responsible for many menstrual disorders in the absence of genital organic causes like polycystic ovaries, and elevated prolactin hormone including: Menorrhagia is a condition of heavy and prolonged bleeding lasting more than 7 days or blood flow of more than 80 ml. Metrorrhagia: irregular bleeding intervals that occur between expected menstrual periods and considered a type of abnormal uterine bleeding [17] . Polymenorrhea is a condition in which the menstrual cycle is abnormal, of short duration, in addition to frequent intervals less than 21 days [18] . Oligomenorrhea is defined as an infrequent and irregularly menstrual bleeding at intervals of more than 35 or 40 days and less than 3 months, affecting about 80percent of women in the period of 20-40 years [19] . Hypomenorrhea is defined as a scant flow of menstrual bleeding but regular in time which lasts for less than two days [20] . There was a relationship between thyroid disorders and the pattern of the menstrual cycle,

through the effect of thyroid-stimulating hormone on the reproductive system where the similarity of TSH with gonadotropin - leutinizing hormone (LH) in addition to follicle stimulating hormone (FSH). And the presence of thyroid hormone receptors on the ovaries where this effect can occur directly on the ovaries or indirectly through hyperprolactinemia alters pulsatile GnRH secretion resulting in a delay in the LH response, which again leads to luteal phase defects and by interacting with sex hormone-binding globulin (SHBG) [21] .

Methodology

Research Design: A case-control study (observational study) was conducted to achieve the study objectives, for the evaluation of effect of thyroid gland dysfunction on menstrual pattern among reproductive age group women.

Sample size: The study was conducted on 100 women participants.

Population: 50 women with thyroid disorders and 50 women in control group.

Research setting: This study was conducted in Al-Shirqat General Hospital and Salah Al-Din General Hospital in Salah Al-Din Governorate, Iraq.

Sampling Criteria

Inclusion Criteria
1- Women who age between (15-45) years old.
2- Single and married.
3- Women who suffer from symptoms and signs of thyroid gland dysfunction or suspected with the symptoms favoring the thyroid disorders(newly discovered cases).

Exclusion Criteria
1- Women with age less than 15 and more than 45 years old.
2- Pregnant and menopausal women, and history of bleeding disorder.
3- Women who are on any hormonal preparation (e.g Oral Contraceptive Pills), and women who had Intrauterine Contraceptive Device (IUCD).
4- Women on thyroid replacement therapy, patients with goiter, but thyroid function test negative, and women with euthyroid.
5- Presence of fibroids or polyps, and a known case of Polycystic Ovarian Disease (PCOD).

Data Collection Method

Data were collected during a face-to-face interview by using of a questionnaire method which developed by the researcher's. The study conducted from 31th of October 2021 to 2th of August 2022, from all clients who came to Salah Al-Din General Hospital and Al-Shirqat General Hospital. A physical examination and neck examination were performed for all clients who showed symptoms and signs of thyroid gland dysfunction or suspected with the symptoms favoring thyroid disorders who attended for medical consultation clinic, surgical consultation clinic, and the obstetrics and gynecology consultation clinic. The time which was

the researcher's spent with each participate during data collection and blood sampling about 15-25 minute, during which blood pressure was measured in the sitting position by a mercury sphygmomanometer (Omron, Japan), on the right arm after at least 5min of rest, then a thyroid function test was done. The blood taken from the participants were placed in plan tubes with a simple cap at room temperature for 10-20 minutes for clotting. Then put into a centrifuge at 3500 rpm for 5 minutes, where the serum was taken. The serum is placed in the refrigerator and frozen at less than 20°C and then sent to the private laboratory in Mosul city. In the laboratory, specimens left to thaw at room temperature until assay. Specimens were mixed thoroughly after thawing, by gently inverting, and then used in the Finecare™ FIA Meter III Plus (Model No: FS-205(. Guangzhou Wondfo Biotech. No.8 Lizhishan, 510663, made in China using a ready for use kits. Tools included: Focus on the Socio-demographic data of the participants included in the sample, focus on the thyroid gland dysfunction, focus on the menstrual disorder, focus on the thyroid function test, and focus on the thyroid function test interpretation. Normal value TSH (o.3-4.2 mIU/L), free T3 (2.8-7.1 pmoI/L), and free T4 (12-22 pmoI/L).

Statistical Analysis

The data analysis was done by using IBM SPSS software version 25.0 and Microsoft office 2010. The descriptive statistics was used to calculate frequency, percentage and to compare the difference between quantitative variables, analyzed using an independent T-test at 0.05 level of significance[22,23,24,25] .

Table: Thyroid Function Test Interpretation.

Test	Normal Reference	Interpretation
TSH	0.3 – 4.2 mIU/L	> 4.2 mIU/L hypothyroidism/subclinical hypo, < 0.3 mIU/L hyperthyroidism/ subclinical hyperthyroidism
FreeT3	2.8-7.1 PmoI/L	< 2.8 PmoI/L hypo, > 7.1 PmoI/L hyper, normal (2.8-7.1) PmoI/L subclinical hypo/hyper
FreeT4	12-22PmoI/L	< 12 PmoI/L hypo, > 22 PmoI/L hyper, normal (12-22) PmoI/L subclinical hypo/hyper

Results

Table 1. Distribution of the Study Sample according to the Socio-demographic Data

Demographic Data	Groups	Case Group		Control Group	
		Freq.	%	Freq.	%
Parity	Nullipara	3	6.0	3	6.0
	Para 1	3	6.0	2	4.0
	Para 2	**18**	**36.0**	4	8.0
	Para 3	4	8.0	8	16.0
	More Than Para 3	12	24.0	**18**	**36.0**
	Single	10	20.0	15	30.0
	Total	50	100.0	50	100.0

This table shows the socio-demographic data of the study sample. As for the number of children, in case group (20%) were single and (6%) were nullipara, multiparous (74%) most of them had two children (36%), while in the control group (30%) were single and (6%) were nullipara, multiparous (64%) most of them had more than three children (36%) (Table 1).

Table 2. Menstrual Pattern Type Distribution

Demographic Data	Groups	Case Group		Control Group	
		Freq.	%	Freq.	%
Pattern of menstrual cycle	Normal	13	26.0	**41**	**82.0**
	Abnormal	**37**	**74.0**	9	18.0
	Total	50	100.0	50	100.0
Menorrhagia	No	34	68.0	49	98.0
	Yes	**16**	**32.0**	1	2.0
	Total	50	100.0	50	100.0
Oligomenorrhea	No	41	82.0	45	90.0
	Yes	**9**	**18.0**	**5**	**10.0**
	Total	50	100.0	50	100.0
Polymenorrhea	No	45	90.0	49	98.0
	Yes	**5**	**10.0**	1	2.0
	Total	50	100.0	50	100.0
Amenorrhea	No	47	94.0	49	98.0
	Yes	3	6.0	1	2.0
	Total	50	100.0	50	100.0
Metrorrhagia	No	49	98.0	50	100.0
	Yes	1	2.0	0	0.0
	Total	50	100.0	50	100.0
Hypomenorrhea	No	47	94.0	49	98.0
	Yes	3	6.0	1	2.0
	Total	50	100.0	50	100.0

This table shows that the highest percentage, in the case group (74%) had an abnormal cycle, and most types of menstrual abnormalities were menorrhagia (32%), oligomenorrhea (18%), and polymenorrhea (10%), while in the control group the highest percentage (82%) of having a normal cycle, and the highest percentage of menstrual abnormalities was oligomenorrhea (10%) (Table 2).

Table 3. Distribution of Thyroid Function

Thyroid function	Groups	Case Group		Control Group	
		Freq.	%	Freq.	%
Thyroid function test interpretation	Normal	0	0	**50**	**100.0**
	Hypothyroidism	**13**	**26.0**	0	0.0
	Subclinical Hypothyroidism	**21**	**42.0**	0	0.0
	Hyperthyroidism	9	18.0	0	0.0
	Subclinical	7	14.0	0	0.0

	Hyperthyroidism				
	Total	50	100.0	50	100.0

This table shows thyroid function, in case group the highest percentage (42%) were subclinical hypothyroidism, followed by (26%) were hypothyroidism, while in the control group, (100%) had a normal thyroid function (Table 3).

Table 4. Mean of Differences in Effect of Thyroid Gland Dysfunction on Menstrual Pattern between Case and Control Group

		N	Mean	Std. Deviation	Std. Error Mean	t	df	Sig. (2-tailed)
Pattern of menstrual cycle	With thyroid dysfunction	50	1.74	.443	.063	6.723	98	.000
	Normal thyroid function	50	1.18	.388	.055			

This table shows the average differences between patients with thyroid disorders and healthy people at the significance level of 0.05, and since the p-value = 0.05<000, that is, there were very highly statistically significant differences between patients and healthy subjects (Table 4).

Discussion

In the present study, it has been taken reproductive age group patients between 15-45 years (n-100). In the present study, it has been noticed a relationship between the number of births and thyroid disorders, where the maximum numbers of patients were para two 36%, compared with control group whose more than para three formed the highest rate of 36% as shown (Table 1). The present study agrees with the previous studies conducted by [26], where the highest percentage of para 2 was (32%, 89.09% respectively).

In the present study, the abnormal menstrual cycle pattern was found to be 37 (74%) higher percentage among women with thyroid disorder, and most types of menstrual abnormalities were menorrhagia (32%), oligomenorrhea (18%), and polymenorrhea 10% in case group, compared with control group 41 (82%) were the highest percentage among participants with a normal menstrual cycle and the highest percentage of menstrual abnormalities was oligomenorrhea (10%) as shown in the (Table 2). In the study by [27,28] , obtained similar results in their study i.e, maximum frequency of abnormal menstrual pattern (29, 23 respectively). In terms of the distribution of the highest frequency of abnormal menstruation types, the present study agrees with the previous studies by [29,30,31] , where they obtained similar results for menorrhagia, oligomenorrhea and polymenorrhea (52 (52%), 19 (19 %), 15 (15%), 28, 12, 8 respectively). The current study disagrees with a study conducted by [32] in Sudan, the majority of the total respondents were 53.9% have normal menstrual cycle pattern, 19% suffered from polymenorrhea, 12.4% reported oligomenorrhea, and 1.4% suffered from menorrhagia. The difference between the two studies is that the study conducted

by (Yassin et al., 2015) was on patients with thyroid disorders who underwent treatment, while the current study was conducted on newly discovered cases before taking treatment.

In the current study, through the results of the thyroid function test, it has been found the highest percentage of subclinical hypothyroidism 42%, followed by hypothyroidism 26%, compared with control group 100% normal thyroid function as shown in the (Table 3). From the researcher's point of view, thyroid disorders are common in women, especially subclinical hypothyroidism, as a result, of exposure to immune diseases and subclinical hypothyroidism after postpartum period. Present study agrees with the studies they conducted (Ajmani et al., 2017; Deshmukh et al., 2019; Sadbhawna et al., 2019), where they obtained the same results, the highest rate of subclinical hypothyroidism, followed by hypothyroidism ((20% , 14%), (18%, 9%), (8.54%, 6.40%) respectively).

Through the present study, it has been found very highly statistically significant differences at the significance level of 0.05, in the effect of thyroid disorders on the menstrual pattern among affected female patients compared with control group as shown in the (Table 4). From opinion of the researcher's, this difference occurred in the effect of thyroid gland dysfunction on the menstrual cycle pattern through direct and indirect association with reproductive hormones. Present study agrees with the study of Krassas et al, who found a prevalence of menstrual disorders 23% among 171 hypothyroidism patients while being only 8% in 214 controls ($p < 0.05$) [33] . Studies show that various cells in the ovary, including epithelium and granulosa cells, and oocytes express receptors of thyroid hormone. The proliferation of granulosa cells is enhanced by TSH which has a synergistic effect with follicle stimulating hormone (FSH). On the other hand, studies have shown that thyroid hormones prevent their apoptosis and regulate FSH stimulation in follicles. In the process of folliculogenesis, with increasing serum estrogen levels, thyroid hormones bound to thyroid-binding globulin (TBG) increases, and the result of these phenomena is an increase in TSH level and a decrease in free thyroxin. Thyroid hormone, which plays an important role in the process of follicle growth has been found in the follicular fluid and its irregularity may impede follicular development [34,35] . However, these results can confirm the study's findings.

Conclusions

The most common types of thyroid gland dysfunction among reproductive age group women at Salah Al-Din Governorate is the subclinical hypothyroidism followed by hypothyroidism compared with control group, most of the case group had two children compared to the control group who had more than three children. Patients with abnormality pattern and the most common type of abnormal cycle was menorrhagia compared with control group. A very highly significant cause of menstrual abnormality is thyroid gland dysfunction compared with control group at the significance level of 0.05.

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