Journal of
Endocrinology and Thyroid Research
ISSN: 2573-2188

Juniper Publishers
key to the Researchers

Mini Review
Volume 7 Issue 3 - August 2023
DOI: 10.19080/JETR.2023.07.555715

J Endocrinol Thyroid Res


# Dysmenorrhea In Hypothyroidism

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**Submission:** August 17, 2023**; Published:** August 24, 2023

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**Abstract**

Thyroid disorders influence the overall organism growth and function. It disturbs menarche cycle and might lead to infertility in females. In this work, we evaluated the effect of hypothyroidism on levels of T4, TSH, FSH and LH, and menstrual cycle length and signs of dysmenorrhea. We found that T4, TSH and FSH were significantly augmented in hypothyroidism- treated women than in euthyroid. Furthermore, hypothyroidism prolongs the menstrual cycle and results in severe pain and discomfort in women. The patho-physiological process of these reproductive disorders involves the hypothalamus- pituitary axis direct effects of thyroid hormones on ovaries and uteri. Such issues should be considered during hypothyroidism treatment to preserve women's fertility.

**Key words:** Dysmenorrhea; infertility; hypothalamus- pituitary axis; hypothyroidism; pre-eclampsia

**Abbreviations:** TSH: Thyroid Stimulating Hormone; HPA: Hypothalamus- Pituitary Axis; LH: Luteinizing Hormone; FSH: Follicle Stimulating Hormone

## Introduction

Thyroiditis is a public health disorder of grown incidence and accounts for about 40 %. of the overall diagnosed endocrine disorders. Aging, iodine deficiency, intoxications, and congenital malformations are the main risk factors causing the disease [1] Particularly, hypothyroidism spontaneously affects 0.5 to 2 % of women, worldwide. [2] Thyroid hormones regulate the organism growth and overall metabolism through the activation of mitochondrial turnover, in young people. Besides, alterations in their levels might result in several physio pathological disorders such as thermoregulation, growth, development, and response to other endocrine and neural regulatory processes [3]. Accordingly, clinical findings showed an association between thyroiditis and female's reproductive dysfunction and infertility. [4]. Stuckey et al (2010) reported a tight correlation between thyroid stimulating hormone (TSH) and estrogen in women with hypothyroidism undergoing super-ovulation for in vitro fecundation. Such results prove the dual cross-talking between thyroids and ovaries through the hypothalamus- pituitary axis HPA [5]. Further studies approved the association of several reproductive health problems to thyroiditis in females, including cardiovascular disorders, miscarriage, pre-eclampsia, stillbirth, and menstrual dysregulation [6-8] In this work, we investigated the relationship of hypothyroidism in procreation age with females' changes of their menstrual cycle, as indicator of reproductive disorder.

## Patients and Methods

A total of 53 women (20 to 45 years old), consulting a local hospital for diagnosis and follow-up of thyroiditis were recruited. All of them gave a written informed- consent for participation. Our study design was in conformity with the declaration of Helsinki ethical Principles for medical research involving human subjects. Participants' sociodemographic parameters and history of menstrual cycle (total cycle duration, length of menstruation, severe pain / discomfort sensation and absenteeism from work, for the last three months) were recorded via a direct interview questionnaire. The mean values of the last three months were considered for the statistical study. Among participants, 12 patients suffered from hypothyroidism and received levothyroxine hormonal replacement as treatment. Other women presented normal thyroid function. Blood circulating levels of thyroxine 4 (T4), thyroid stimulating hormone (TSH) luteinizing hormone (LH) and follicle stimulating hormone (FSH) were determined

by enzyme linked fluorescent assay, in accordance with the manufacturer's instructions (VIDAS, Biomérieux, France). Chi-square and non-parametric Mann-Whitney test were used to compare results between the two states of thyroids. Statistics were carried out using the SPSS program for Windows. 17 (IBM corporation), with a confidence interval of 0.95.

## Results and discussion

Thyroiditis was usually associated to several pathological disorders such as impairment of heart and lung function, and osteoporosis [9] It was also reported to disturb reproductive function at different levels [5-8] Accordingly, we observed that females having hypothyroidism manifest deep hormonal disturbances. Although they received a levothyroxine hormonal replacement, women having hypothyroidism presented significantly higher levels of thyroxine 4 and thyroid stimulating hormone (2.07±0.76 ng/L and 2.00±0.90 UI/L, respectively for T4 and TSH) in comparison to those presenting euthyroidism (EuT) (0.98±0.09 ng/L and 1.41±0.67 UI/L, respectively for T4 and TSH) (Figure 1).

There was also a significant increase in follicle stimulating hormone in hypothyroidism (13.93±4.87 UI/L and 6.89±4.56 UI/L, respectively for HypoT and EuT). In contrast, the level of the luteinizing hormone (LH) did not present significant variations between the two states of thyroid (9.4±2.42 UI/L and 8.94±4.32 UI/L, respectively for EuT and HypoT). Similar findings have been reported by several previous studies both in managed and non- managed thyroiditis [5,10,11]. In agreement with other clinical results [13,14], hypothyroidism was also accompanied by significant prolongation of the total length of the menstrual cycle (Figure 1) and elevated percent of women suffering from severe menses- related pain or discomfort (Table 1). The culminating knowledge suggests that women are at higher risk to get procreation's problems and to lose their fertility due to hypothyroidism. The development of such reproductive disorders might involve a distortion of the feedback- loop connecting thyroids to the reproductive tract through HPA. In effect, thyroxine hormone depletion causes the hypersecretion of TSH and GnRH by the hypothalamus and consequently disturbs the production of FSH, LH, prolactin (PRL) and sex hormones (estrogen and progesterone) that regulate ovaries and uterine cyclic activity [15-17] (Figure 2). Furthermore, ovaries and uterine endometrium were proven to be sensitive to thyroid hormones that share a pool of nuclear hormone receptor elements with steroid hormones through which their crosstalk and regulate reproductive functions, such as ovarian follicles' development, vascularization of uterine endometrium and endometrial cells' proliferation [18]. Although levothyroxine was shown to greatly improve patients with deficient thyroids' hormones, it might induce preterm birth and prenatal growth retardation [19], probably through a mechanism involving the elicitation of hypertension and pre-eclampsia during pregnancy [20-22].

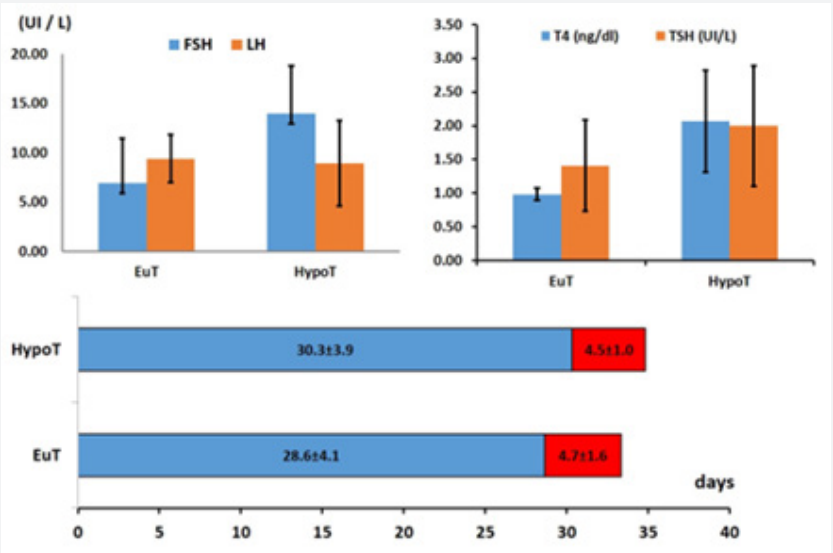


**Figure 1:** levels of T4, TSH, LH and FSH hormones and total length of the menstrual cycle in women presenting euthyroidism (EuT) or hypothyroidism (HypoT).

## Conclusion

Hypothyroidism is a common disorder in females. Although hormonal replacement remains the best efficacious treatment for the disease, it might lead to reproductive disorders including utero-ovarian cycle irregularities and thereby infertility. This suggests the need for a regular clinical follow-up for both thyroid and sexual hormones in women under thyroid hormonal replacement to ameliorate their status and preserve their procreative potential.


How to cite this article: Bedoui I, Jedli O, Bouzenna H, Hammadi I, Nassoubi O, et al. Dysmenorrhea In Hypothyroidism. J Endocrinol Thyroid Res. 2022; 7(3): 555715. DOI: 10.19080/JETR.2023.07.555715

**Table 1:** sociodemographic and dysmenhorrea-related description of participants

| | EuT | HypoT |
|---|---|---|
| Age (years) | 33.4±7.9 | 38.7±7.8 |
| BMI (Kg.m-2) | 26.0±5.1 | 27.4±2.1 |
| Married (%) | 0.36 | 0.08 ** |
| Dysmenhorrea related signs | | |
| absenteism (%) | 0.44 | 0.25 |
| severe pain (%) | 0.37 | 0.80** |
| Pain duration (days) | 1.62±1.41 | 1.50±0.80 |

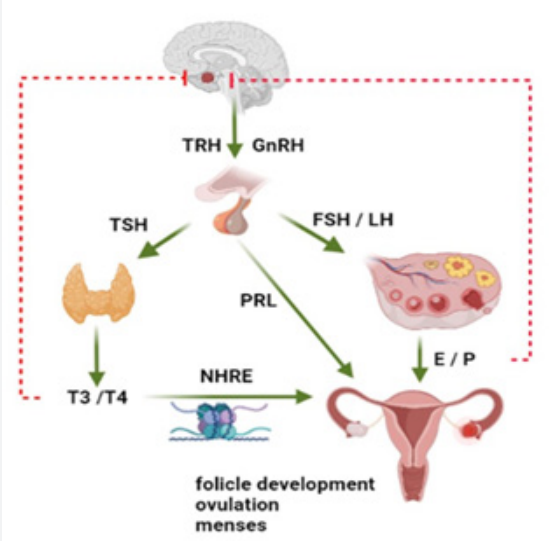


**Figure 2:** Relationship of thyroid hormones with female menstrual cycle regulation.

E: estrogen, FSH: follicle stimulating hormone, GnRH: gonadotropin releasing hormone, LH: luteinizing hormone, NHRE: nucleus hormone receptor element, P: progesterone, PRL: prolactin T3: thyroxin 3, T4: thyroxin 4, TRH: thyroid releasing hormone, and TSH: thyroid stimulating hormone, dotted line: negative feed-back, arrows: hormones' liberation or action.

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