



Peculiarities of the Development of Hypothyroidism in Women of the Climacteric Period

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Abstract: This article presents the results of a study in which 100 menopausal women were examined. The pituitary-thyroid and pituitary-ovarian status was assessed in groups of women who differed in the functional state of the thyroid gland and in the course of the perimenopausal period. The conducted radioimmunoassay studies made it possible to establish that in the perimenopause there is an aggravation of the functional inferiority of the thyroid gland, especially pronounced in menopausal syndrome (CS), there is a significant mismatch in the activity of the hypothalamic-pituitary structures in CS against the background of hypothyroidism, which, in our opinion, is a predisposing factor to the predominance of severe forms. CS in women with hypothyroidism.

Key words: climacteric syndrome, hypothyroidism, amenorrhea.

Climacteric syndrome (CS) is a pathological symptom complex that often complicates the physiological course of the perimenopausal period. Various severity manifestations of CS occur in 40-60% of women at the turn of pre- and postmenopause. [1, 7,]. In the Republic of Uzbekistan, CS is diagnosed in 45.6% of women of transitional age [5]. This is a pathology with a variety of vegetative-vascular, psycho-emotional and metabolic-endocrine disorders that cause a significant decrease in the working capacity of women, affect the psycho-emotional status, and worsen the quality of life. To date, the problem of the occurrence of CS has not been fully studied, although many clinical and experimental works have been devoted to the study of its various aspects [2, 3]. However, the features of the course of the climacteric period in areas with an ecologically unfavorable situation, which include Dagestan, have been little studied.

It is known that many environmental factors in ecologically unfavorable regions contribute to an increase in the size and deterioration of the functional activity of the thyroid gland (TG). Consequently, the deterioration of the environmental situation enhances the effect of iodine deficiency and, thus, creates conditions for the growth of the tension of goiter endemia. [6, 7].

The Republic of Dagestan is one of the regions of Russia endemic for goiter. The prevalence of endemic goiter in the Republic of Dagestan ranges from 30 to 70%, which can be regarded as a severe degree of endemia and confirms the unfavorable state of the ecosystem in the region. [5].

In areas of pronounced endemia, the most typical manifestation of endemic goiter is hypothyroidism [4, 6]. As the observations of F. M. Egart [3] showed, hypothyroidism can also be attributed to the pathology of women in perimenopause. At the same time, the author emphasizes the need to differentiate the concept of age-related involution of the thyroid gland from the disease - hypothyroidism. Menopause, like any transitional period, requires the mobilization of all adaptive mechanisms of the body. In the zone of an unfavorable ecosystem, the adaptive capabilities of the organism are significantly reduced, therefore, in order to develop a system of recreational activities, it seems appropriate to find out how the menopause proceeds in women suffering from endemic goiter with hypothyroidism.

The aim of our study was to study the hormonal profile of the pituitary-thyroid and pituitary-ovarian systems and clinical features in perimenopausal women with endemic goiter and hypothyroidism.

Materials and methods. We examined 100 women, 60 of whom were diagnosed with endemic goiter with hypothyroidism. Of these, the main group consisted of 40 patients who developed CS against the background of a pathologically altered thyroid gland. The comparison group with the main group consisted of 20 women without CS, who also had endemic goiter with manifestations of hypothyroidism. .

The control group consisted of 40 healthy perimenopausal women without thyroid pathology. 20 of them had a pathological course of menopause (2nd control group) and 20 had a physiological course of the transition period (1st control group).

To identify the incidence of CS, its dependence on the parity and pathology of the thyroid gland, we developed a unified information card, which was used to study the nature of the menstrual function: the time of menarche, intensity, frequency, age of menopause, the time of onset of symptoms of CS.

When studying the generative function, the number of pregnancies, the intervals between them, outcomes, complications of pregnancy and childbirth, the types of birth control used, including abortions, were ascertained. The severity of CS was assessed by the Kupperman menopausal index modified by E. V. Uvarova (1982). Thorough clinical and laboratory studies were also provided.

The hormone-forming function of the pituitary-thyroid and pituitary-ovarian systems was studied by determining the levels of thyroid-stimulating hormone (TSH), triiodothyronine (T3), thyroxine (T4), follicle-stimulating hormone (FSH), luteinizing hormone (LH) on a radioisotope analyzer from the company "Gamma-800" in 40 women with endemic goiter (hypothyroidism) and CS, 20 women in the comparison group and 40 women in the 1st and 2nd control groups.

The dimensions of the thyroid gland and its structure were assessed using ultrasound on the apparatus. Venous blood was taken on the 6-7th day of the menstrual cycle in the presence of menstruation, and in postmenopausal women - in the morning before meals.

Results. Our studies made it possible to find out that women with hypothyroidism were more likely to experience late puberty compared to women with unchanged thyroid status. Late puberty in the pathology of the thyroid gland in women with CS was found in 41.37% of cases, and with its unchanged condition - in 32.3%. The mean age of menarche was 15 ± 1.2 and 12 ± 1.3 years, respectively ($p < 0.05$). Thus, it can be assumed that in a region with a reduced content of iodine in water and other food products, with late puberty and changes in thyroid status, the likelihood of developing CS is increased.

An analysis of the reproductive history showed that with an increase in the frequency of childbirth, the number of women with endemic goiter with hypothyroidism increases. So, out of 60 women with thyroid pathology, 29 had multiple births (4 births or more), and only 14 out of 40 women in the control groups. Based on this, it can be assumed that frequent childbirth can contribute to the occurrence of thyroid pathology, which affects the further function of the reproductive system and the timing of its extinction. The mean age of menopause was 46.15 ± 0.35 and 48.55 ± 0.72 years, respectively.

In women of the main group, chronic inflammatory diseases of the genitals were revealed. The most frequent among them were inflammatory processes of the uterine appendages and erosion of the cervix. A retrospective analysis of outpatient records revealed that 40 women had certain manifestations of CS, including 18 women with severe, 14 with mild form. In the 1st and 2nd control groups there were women of the transitional period without hypothyroidism. CS was detected only in 20 of them, with a severe form in 4 women, and a mild form in 10 women. Based on this, it can be assumed that hypothyroidism contributes to a more severe course of CS. Symptoms of vegetovascular dysfunction (sweating, increased blood pressure, headaches, pain in the heart area, hot flashes, dizziness, numbness) were detected in 18 women with hypothyroidism, with increased blood pressure and sweating being the most common. 16 women had psycho-emotional manifestations: depression, irritability, insomnia, sexual dysfunction. Metabolic and endocrine disorders (obesity, diabetes mellitus, itching of the vulva) were detected in 6 patients.

Most researchers believe that in the process of aging a woman, changes in the functional state of the thyroid gland occur: the biosynthesis of thyroid hormones and their secretion decrease [1]. However, there is another opinion. So, D. Bartuska did not reveal changes in the content of T4, TSH with age, however, he observed a decrease in the level of T3. V. E. Balansh showed in her studies that the concentration of TSH in the blood during physiological menopause is reduced by 1.5 times, which is regarded by the author as one of the adaptive mechanisms in the aging process. In the work of T. Kh.-M. Khashaeva and S.-M. A. Omarova [4] showed that during CS in women with preserved thyroid function, an increase in TSH levels by 2–2.3 times was noted, which is probably due to a change in the activity of the hypothalamic centers against the background of an age-related decrease in ovarian function.

We studied the state of the pituitary-thyroid system depending on both the function of the thyroid gland and the course of the perimenopausal period. The research data are given in table 1.

Comparison of hormone levels in the 2nd control and main groups showed a significant increase in the content of TSH and a trend towards a decrease in the level of T3. T4 levels were identical.

Table I. Levels of T3, T4, TSH in physiological and pathological menopause (M ± t)

Group of patients	T3, nmol/l	T4, nmol/l	TSH, mIU/l
1. Comparison group (n = 20)	1.21 ± 0.1	112,3 ± 3,5	2,72 ± 0,21
2. Main group (n = 40)	1,65 ± 0,17	119,4 ± 3,7	4,81 ± 0,11
3. 1st control group па (n = 20)	1,48 ± 0,11	118,9 ± 5,9	2,21 ± 0,15
4. 2nd control group (n = 20)	1,88 ± 0,12	120,0 ± 5,2	4,40 ± 0,13
P1-2	< 0,05	> 0,05	< 0,001
P3-4	< 0,05	> 0,05	< 0,001

When comparing the hormonal parameters of patients with CS and healthy women in perimenopause, the following picture was revealed. The levels of T3 and TSH increase significantly both in the main group and in the 2nd control group, regardless of thyroid status, but it should be noted that the content of TSH in endemic goiter with hypothyroidism increases significantly compared not only with the comparison group, but also with 2- th control group. Thus, the level of TSH in hypothyroidism and CS was 4.81 ± 0.11 mIU/l, i.e., it was 1.8 times higher than in the comparison group (2.27 ± 0.22 mIU/l). It also became significantly higher than in the 2nd control group.

The level of TSH in the 2nd control group was 4.40 ± 0.13 mIU/l, which is 2 times higher than the level of the 1st control group (2.21 ± 0.15 mIU/l). The levels of T3 in the main and 2nd control group were 1.65 ± 0.17 and 1.88 ± 0.12 nmol / l, respectively, which is significantly higher than the values of the comparison group and the 1st control group: $1.21 \pm 0, 1$ and 1.48 ± 0.11 nmol/l, respectively. This condition is not a sign of hyperthyroidism, since along with an increase in the level of T3, the content of TSH also increases, the level of which increases inconsistently with the level of T3. Thus, during CS, TSH and T3 are activated, and in hypothyroidism this is more pronounced, which is manifested by a significantly higher level of TSH and a tendency to increase the content of T3. The obtained results suggest that the presence of CS is one of the reasons for the increase in the concentration of TSH in the blood serum. Along with this, the moment stimulating the production of TSH is the insufficient inhibition of the functional activity of the hypothalamic and pituitary structures, associated with a decrease in thyroid function during hypothyroidism. Thus, a mutually aggravating effect of CS and hypothyroidism on the functional activity of the thyroid gland and the thyrotropic function of the pituitary gland was noted. We have established the dependence of the severity of the CS on the level of TSH, which increased according to the severity of the disease, and in hypothyroidism it was significantly higher and compared with the indicators for a full thyroid gland (Table 2). The levels of peripheral hormones did not show dependence on the severity of CS.

Table 2. Levels T3, T4, TSH depending on the severity of the CS (M ± t)

Severity of CS	Normal thyroid function (n=20)			Hypothyroidism (n = 40)		
	T ₃ , nmol/l	T ₄ , nmol/l	TTG, mIU/l	T ₃ , nmol/l	T ₄ , nmol/l	TTG. mIU/l
1.Light degree	$1,48 \pm 0,13$	$119,7 \pm 4,96$	$3,17 \pm 0,10$	$1,36 \pm 0,13$	$118,3 \pm 5,7$	$3,86 \pm 0,33$
2.Average degree	$1,80 \pm 0,10$	$117,6 \pm 3,92$	$3,97 \pm 0,21$	$1,65 \pm 0,21$	$119,2 \pm 4,2$	$4,73 \pm 0,17$
3.Severe degree	$2,10 \pm 0,11$	$121,7 \pm 7,32$	$4,93 \pm 0,12$	$1,90 \pm 0,12$	$115,2 \pm 6,52$	$6,64 \pm 0,27$
P1—2	> 0.05	> 0.05	< 0,01	> 0,05	> 0,05	< 0,05
P2—3	> 0,05	> 0,05	< 0,001	> 0,05	> 0,05	< 0,001

Thus, the study of the level of thyrotropin depending on the state of the thyroid gland revealed its significant increase in the combination of hypothyroidism and moderate and severe CS. This is confirmed by our clinical data on a more severe course of CS in endemic goiter with hypothyroidism. When studying the hormonal profile of the pituitary-ovarian system in the group of women with hypothyroidism in physiological menopause, there was a tendency to increase the level of FSH and decrease the level of LH compared with women with preserved thyroid function.

The average value of FSH in the pathology of the thyroid system was 65.8 ± 5.91 IU/l, with unchanged function of the gland - 52.6 ± 4.68 IU/l. The LH level in endemic goiter with hypothyroidism was 41.08 ± 3.79 IU/l, and in unchanged thyroid status it was 48.21 ± 2.8 IU/l. The

LH/FSH ratio index was 0.62 in thyroid pathology and 0.92 in its normal state. Consequently, in perimenopausal women with an altered thyroid status (in particular, with hypothyroidism), there is a significant mismatch in the activity of the hypothalamic structures in the regulation of the gonadotropic function of the pituitary gland, which may be one of the factors contributing to the occurrence of pathological symptoms of menopause. The level of gonadotropins in women with CS, which developed against the background of reduced thyroid function, was higher. With full thyroid function, the FSH level was 65.3 ± 4.96 IU/l, LH - 51.69 ± 3.55 IU/l, and with hypothyroidism - 68.17 ± 6.99 and $51.8 \pm 3, 57$ IU/l, respectively.

Table 3

FSH and LH levels depending on on the severity of the CS (M ± t)				
Severity of CS	Normal thyroid function (n = 20)		Hypothyroidism (n = 40)	
	FSG, IU/l	L G, IU/l	FSG, IU/l	L G, IU/l
1. Severe degree	$64,0 \pm 5,31$	$40,73 \pm 2,20$	$66,03 \pm 5,19$	$38,78 \pm 2,01$
2. Average degree	$66,83 \pm 6,05$	$51,94 \pm 3,23$	$70,73 \pm 7,71$	$48,9 \pm 3,16$
3. Light degree	$68,0 \pm 6,48$	$59,6 \pm 2,01$	$81,04 \pm 8,32$	$57,2 \pm 3,23$
P1-2	> 0,05	< 0,01	> 0,05	< 0,05
P2—3	> 0,05	< 0,05	> 0,05	< 0,05

Also, we made an attempt to find out whether there is a pattern of changes in the level of gonadotropins depending on the severity of the CS. The study of FSH and LH indicators according to the severity of the CS is shown in Table. 3.

Our studies have shown the absence of any dependence of the severity of CS on the level of FSH in patients with normal thyroid gland; As for the level of LH, it significantly decreased with increasing severity of CS. This picture was noted with unchanged thyroid status: the LH level was 40.73 ± 2.20 IU/l in severe CS, 51.94 ± 3.23 IU/l in moderate and 59.6 ± 2.01 IU/l with a mild degree. The difference between the indicators is significant ($P_1 < 0.01$; $p_2 < 0.05$). A similar picture was noted in hypothyroidism.

The LH/FSH index decreased with increasing severity of CS: from 0.88 to 0.64 with an unchanged state of the thyroid gland and from 0.70 to 0.57 with hypothyroidism. Similar data were obtained by Sh. Khodjaeva [15], who conducted studies in groups of women, taking into account the state of the thyroid gland.

The results obtained allow us to conclude that the functional state of the thyroid gland affects not only the thyrotropic, but also the gonadotropic activity of the pituitary gland. Clinical symptoms of pathological menopause in women with hypothyroidism, in our opinion, are associated with both the severity of thyroid insufficiency and the LH/FSH index.

Conclusion. Late puberty, high infectious index, inflammatory diseases of the genitals, frequent childbirth, hypothyroidism caused by endemic goiter are premorbid background for the complicated course of the perimenopausal period.

Thyroid pathology (endemic goiter with hypothyroidism) in combination with high parity should be attributed to unfavorable factors that significantly accelerate the onset of menopause and, consequently, the acceleration of aging. The mean age of menopause in women with endemic goiter with hypothyroidism is 46.15 ± 0.35 years.

The hypothyroid status contributes to the mismatch of the activity of the hypothalamic-pituitary structures, which is expressed in a significant increase in the concentration of FSH compared to LH. A

decrease in the LH / FSH index below 0.7 and a high TSH are predictive risk factors for the development of severe forms of CS.

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