

## Hypothyroidism and Pregnancy

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### ABSTRACT

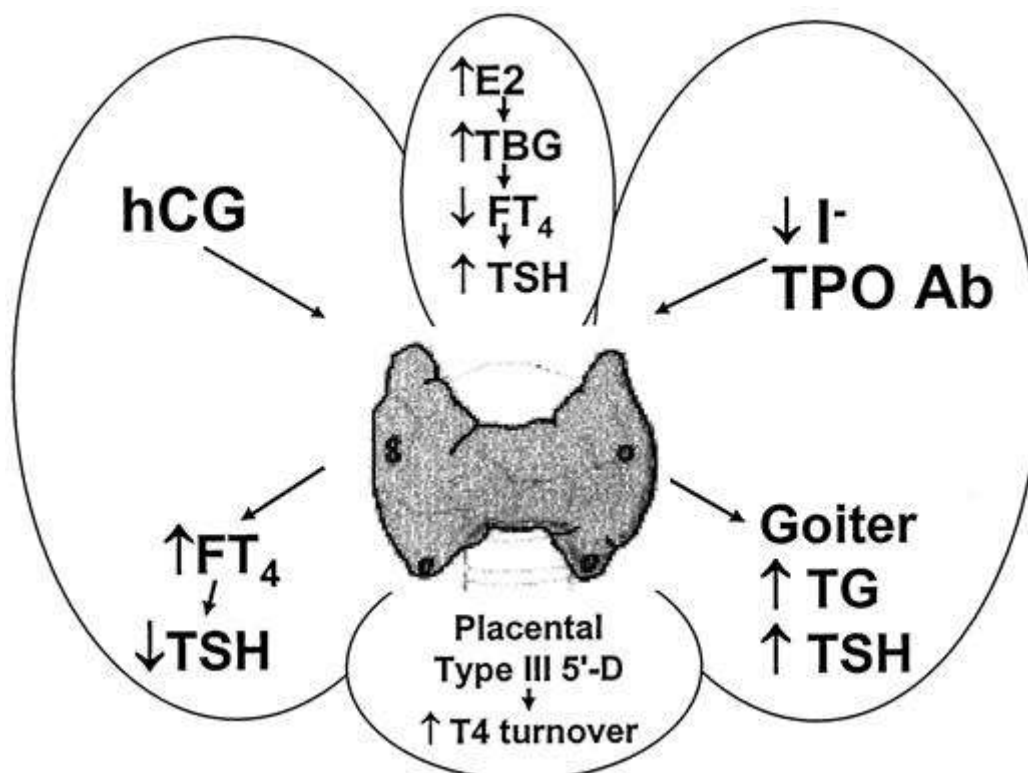
The functional state of the thyroid gland (TG) in pregnant women was studied. with hypothyroidism. The appointment of individual treatment using laser rapes on the thyroid gland contributes to a decrease in antibody titer to TPO and the level TTG.

**BACKGROUND:** Clinical thyroid dysfunction has been associated with pregnancy complications such as hypertension, preterm birth, low birth weight, placental abruption, and fetal death. The relationship between subclinical hypothyroidism and pregnancy outcomes has not been well studied. We undertook this prospective thyroid screening study to evaluate pregnancy outcomes in women with elevated thyrotropin (thyroid-stimulating hormone, TSH) and normal free thyroxine levels.

## Introduction

Pregnancy influences thyroid function in multiple ways. Not only does the maternal hypothalamic-pituitary-thyroid (HPT) axis undergo a series of adjustments, the fetus develops its own HPT axis and the placenta plays an active role in iodide and T4 transport and metabolism. Thus, an integrated three-compartment thyroid model exists during gestation <sup>[i]</sup>.

Early in pregnancy estrogen promotes production of a more highly sialylated T4-binding globulin isoform that is less rapidly degraded, resulting in increased serum T4-binding globulin and T4 concentrations (1–3). Although a transient decrease in serum free T4, followed by a rise in TSH to a new equilibrium, may occur <sup>[ii]</sup>, this is usually not appreciated with routine thyroid testing. A high circulating CG level in the first trimester leads to CG cross-reactivity with the TSH receptor, prompting a temporary increase in free T4 and partial suppression of TSH. The final physiologic change results from placental deiodination of maternal T4, which increases T4 turnover. In normal pregnant women, the thyroid gland maintains euthyroidism with only minor fluctuations in serum T4 and TSH. However, in women with limited thyroid reserve, due to thyroid autoimmunity or iodine deficiency, hypothyroidism can develop (Fig. 1).



Physiologic and nutritional influences on maternal thyroid function <sup>[iii]</sup> <sup>[iv]</sup> The sizes of the circles do not imply relative importance of each biochemical or physiologic pathway.

Fetal thyroid ontogeny begins at 10–12 weeks gestation and is not complete until delivery; T4 is not secreted until 18–20 weeks (1, 3). T4 is critical for many aspects of brain development including neurogenesis, neuronal migration, axon and dendrite formation, myelination, synaptogenesis, and neurotransmitter regulation <sup>[v]</sup>. Although these requirements evolve over months <sup>[vi]</sup>, an especially critical time is the second trimester <sup>[vii]</sup>.

Contrary to past belief, thyroid hormone crosses the placenta. Animal studies have shown that maternal T4 reaches the fetus <sup>[viii]</sup>. T4 has been measured in human coelomic fluid as early as 4 weeks gestation <sup>[ix]</sup> and is detectable in cord blood of newborns with athyreosis or thyroid

dysgenesis [x].

### Causes of thyroid dysfunction

Abnormal thyroid gland function may be restricted to the fetus, the expectant mother, or both (Table 1). Fetal hypothyroidism can be permanent or transient. When transient, it results from transplacental passage of autoantibodies or drugs, or to immaturity of the HPT axis in premature infants. Combined maternal and fetal hypothyroidism is almost always due to iodine deficiency [xi] [xii], but thyroid-binding inhibitory immunoglobulin (TBII) has been implicated on occasion [xiii]. Severe maternal hypothyroidism is not common, but mild thyroid failure in which the serum TSH is elevated with a normal free T<sub>4</sub> level has been reported in 2.5% of pregnancies [xiv].

**Table 1.**  
**Causes of maternal and fetal hypothyroidism**

Fetal
<b>Congenital</b>
<b>TBII (transient)</b>
<b>Antithyroid drugs</b>
<b>Prematurity</b>
<b>Maternal and fetal</b>
<b>Iodine deficiency (severe, mild/moderate)</b>
<b>TBII</b>
<b>Maternal (overt, subclinical)</b>
<b>Autoimmunity</b>
<b>Postthyroidectomy</b>

The impact of severe iodine deficiency or congenital hypothyroidism on the fetus and newborn is profound, as are the effects of overt maternal hypothyroidism on pregnancy. The severity, timing of onset and duration, as well as postnatal management, all influence fetal and neonatal brain development. It is now believed that even mild maternal hypothyroidism (from mild iodine deficiency, thyroid autoimmunity, or thyroid under-replacement) may affect fetal brain development. The implications of this finding are yet to be clearly defined, but have raised many questions that need resolution.

### The Effect Of Hypothyroidism In Pregnancy

Thyroid disease in pregnant women affect the development of dysfunctions the thyroid gland in the fetus, as well as Nest during the gestational process. By- this among endocrinologists and gynecologists The problem of thyrorological Zora for pregnant. An important aspect of the control of thyroid function is assessment of the concentration of thyroid stimulating hormone on (TSH), free triiodothyronine (fT3) and free thyroxine (fT4). Many questions cause reference indicators concentration TSH, fT3 and fT4 in separate trimesters pregnancy [xv]. Analysis of the reproductive state women's health and the factors that shape it showed deterioration in pregnancy. especially due to thyroid pathology, the frequency of which has recently been significant has increased [xvi] [xvii]. Termination in the 70s years of the last century, the mass iodine phylactics, lack of purposeful consistent work on its restoration reduction of iodine intake containing products led to significant growth of thyroid diseases, especially most at risk of developing iodine deficiency disorders (children, pregnant nursing). Significantly increased number of women with euthyroid differential subclinical fusal and nodular goiter hypothyroidism and thyrotoxicosis [xviii]

A number of physiological processes occurring during pregnancy affects the exchange of thyroid hormones<sup>[xix][xx]</sup>. TO These include: - increase in protein concentration, hormone-binding thyroid PS (especially thyroxine and globulin, thyroxin), in response to estrogen levels are already early the duration of pregnancy; - growth of level of chorionic gon - Dotropin (CG), thyrotropin. CG dosing syncytiotrophoblasts, binds to the receptor for TSH and acquires retreats its own thyroid-active ness that only matters in case of high levels of CG. Wherein inhibition of TSH secretion occurs and increasing the concentration of TK and T4 in synovo It is higher than normal; - increased iodine excretion with urine due to an increase in glomerular filtration radios during pregnancy<sup>[xxi][xxii]</sup>.

gestation is hypothetical reo According to literature data among different variants of thyroid dis- functions in women of reproductive Rasta leading place belongs to the hypo- thyroid and autoimmune thyroiditis (AIT), which is the most frequent cause primary hypothyroidism<sup>[xxiii]</sup>. Pathogenetic basis of clinical manifestations of hypothyroidism is violation energy exchange due to the lack of thyroid mountains which leads to a decrease in the exchange As a result, the metabolic violations occur functioning of various organs and systems, including the development of clinical manifestations of reproductive dysfunction tive system<sup>[xxiv]</sup>. Specific relationship reproductive system and hypo-system thalamus-pituitary-thyroid confirmed changes in functional activity Thyroid gland during puberty, personal phases of ovarian-menstrual cycle, during pregnancy, after abortion and menopause<sup>[xxv]</sup>. The most common cause Noah hypothyroidism is an autoimmune thyroiditis. Due to impaired function suppressor T-lymphocytes and immunological system over-supervision occurs ration of T-lymphocytes (T-helpers), which stimulate B-lymphocytes, subpopulations T-cell and B-cell, T-cytotoxic lymphocytes, NK cells. At the same time fecal cytokines and lymphocytes kina are also involved in the processes of dest thyroid surgery The number of NK cells with AIT increased. Mediator Nk- cytotoxicity - tumor necrosis factor Li (TNF) - is released from thyroid stimulating lymphocytes with AIT, what plays an important role in the development of Inferior stage of it - hypothyroidism. Tireo cytes, like lymphocytes, can produce IL-1 and IL-6, stimulator B- lymphocytes. Both cytokines, like IL-2, involved in the pathogenesis of autoimmune process. Resulting from interactions of T-lymphocytes and NK- cells y-info promotes expression genes I and II class HLA-systems on the surface of thyrocytes that have inhibitory effect on autoimmune process, perhaps through increasing the The number of T-suppressors and the subsequent decrease in T-helper activity<sup>[xxvi]</sup>. In our studies among a random sample of 208 pregnant hypothyroidism was detected in 28.4% of cases (59 pregnant women). The purpose of the study is to study the function the national condition of the thyroid gland in pregnant women with hypothyroidism and determine effective treatment with the use of laser therapy on the thyroid area.

### Materials and methods

Determined levels of TSH (normal from 0.4 to 4.0 mIU / l), and antibodies to thyroid peroxidase (AT-TPO) (norm <35 ME / ml) For comparison, quantitative data repeated observations within one groups used criterion Stu for dependent samples. Analysis was carried out with the help of programs STA- TISTICA 10 and Microsoft Excel 2010. The main group included 59 women at different stages of pregnancy in according to the following criteria: hypothyroidism, lack of data any thyroid pathology in history and severe concomitant pathology. Average age the subjects were  $28.47 \pm 5.65$  years.

### Results and its discussion

When assessing thyroid function in women with hypothyroidism (Table 2), which received whether treatment was obtained the following

**Table 2 Dynamics of the level of AT-TPO and TTG (n = 59)**

Indicator	Before treatment M ± SD	After treatment, M ± SD	p (student criterion for dependent samples)
TSH	7.67 ± 2.43	4.31 ± 2.16	p <0.0001
AT-TPO	25.61 ± 11.59	20.19 ± 13.96	p <0.0003

Statistical analysis with using student t-test for dependent samples showed that after treatment value of TSH levels (p <0.0001) and AT-TPO (p <0.003) in the group of patients with hypothyroidism is statistically significant less than before treatment. The presence of elevated antibody titer Thyroid gland is regarded as fairly common strange phenomenon in the general population. Its frequency ranges from 3 to 18% is a known risk factor. development of hypothyroidism. According to the Weggem annual risk of development hypothyroidism in women with elevated titer of antibodies to thyroid peroxidase (TPO) and euthyroidism (normal level TSH) is 2.1% [xxvii]. Pregnancy is a powerful fi- biological stimulator of the thyroid gland [xxviii]. By itself, an increased antibody titer to TPO is considered a risk factor for so-called gestational hypothyroxinemia and even associated with a certain risk deterioration of indicators, mental development of children [xxix]. Many researchers have proposed wide screening of impaired function early thyroid pregnancy and before planning it [xxx]. Prevalence increased titer of antibodies TPO among women repro a very significant age and is about 10% [xxxi]. Communication data is widely reported. between autoimmune diseases of the thyroid gland (clinical and subclinical) and non- gestation Known that 31% of women with miscarriage there are antithyroid antibodies, and often that of preterm labor in women with symptomatic immune thyroid impairment is 16% [xxxii]. According to various authors [xxxiii] AIT clearly correlates with a worsening fertilization of ova, non- has a positive effect on the development of embryos, their implantation in ART programs and, Yatno, can serve as a marker reduction the level of positive results of such programs. Moreover, known work [xxxiv], whose results testify that even when reaching a pregnant thyroid antibodies may significantly to degrade the process of sewing. According to some authors [xxxv], antibodies to the thyroid directly affect the development of the trophoblast, however others consider their action mediated due to increased activation T cells and T lymphocyte production toxic cytokines. Higher frequency of miscarriage in autoimmune thyroiditis is is a consequence of the activation of autoimmune and not impaired thyroid function. It is established that in pregnant women with AIT often reduced functional thyroid ny reserve subclinical hypothyroidism throughout 42% of women with autoimmune disorders [xxxvi].

### findings

The appointment of individual treatment using laser therapy on the area Thyroid gland helps to reduce the level of TSH (p <0.0001) and AT-TPO (p <0.003) in the group patients with hypothyroidism. Given the impact of the development of autoimno munichny diseases of a thyroid gland on development pregnancy and gestation, non- doubtful scientific and practical interest represents the study of the results of thyroid laser therapy women with hypothyroidism

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