Thyroid diseases occupy the first place among all endocrine pathologies today and remain one of the most difficult problems. According to the Ministry of Health of Ukraine, over the past 5 years the number of thyroid diseases has increased by 5 times, and this indicator significantly differs in different regions of the country depending on a combination of environmental factors (remote stochastic effect of the Chernobyl accident, iodine deficiency, lifestyle, stress, malnutrition, micronutrient deficiencies, comorbidities, etc.). There is a close functional relationship between the thyroid and reproductive systems, which leads to a high probability of the development of combined disorders in one of these links of homeostasis. The problem of reproductive health disorders is of particular concern around the world and is relevant to the study of the nature of the effects of thyroid diseases on pregnancy. The prevalence and incidence of the thyroid disease vary in different regions of the country depending on the influence of environmental factors and their combination, one of which is iodine deficiency. The increasing number of stillborn infants, premature termination of pregnancy, infertility, deafness and strabismus of newborns, delayed physical, sexual and intellectual development of children, increasing cardiovascular diseases — this is not a complete list of negative effects of iodine deficiency on humans. The most common consequence of the iodine deficiency in pregnant women is subclinical hypothyroidism. Subclinical hypothyroidism is associated with many adverse events during pregnancy and with neonatal outcomes. The study of the peculiarities of the course of subclinical hypothyroidism in pregnant women in the iodine deficiency region today remains an urgent problem. This article presents an analysis of the publications of PubMed and Medline databases for the last decades.

**Keywords:** subclinical hypothyroidism; iodine deficiency; treatment
The effect of the thyroid gland on the reproductive system is realized both through the peripheral endocrine glands (gonads and adrenal glands) and through the central structures (neurotransmitter and hypothalamic-pituitary system). Increased or decreased content of thyroid hormones alters the processes of steroidogenesis, affecting the gonads directly, as well as through the hypothalamic-pituitary system, thereby violating the mechanism of their relationship, especially the principle of negative feedback. The influence of the thyroid pathology on menstrual and reproductive function is explained by metabolic disorders (especially by a decreased metabolic activity in hypothyroidism), which change the sensitivity of receptor systems to hormonal influences at different levels of regulation [6].

The thyroid function is closely related to the hypothalamic-pituitary-ovarian system, primarily due to the presence of common central regulatory mechanisms. The thyroid gland is one of the most important parts of the neuroendocrine system and has a significant impact on the reproductive function. Disorders of the thyroid gland can cause premature or late puberty, menstrual disorders, anovulation, infertility, miscarriage, fetal pathology. In its turn, the state of the reproductive system has a pronounced effect on the thyroid function. It is confirmed by changes in the thyroid function during pregnancy and lactation, in benign tumors and hyperplastic processes of the female genital organs, in patients with dysfunctional uterine bleeding [7].

Equilibrium in the pituitary-thyroid system is due to the interaction of tropic hormones of the pituitary gland and effector endocrine glands. The enlargement of the thyroid gland, even is not accompanied by the absence of clinical signs, is an early sign of internal disorders, and often — at least minimal deficiency of thyroid hormones [8].

Thyroid hormones provide the realization of genetically inherited information into a specific human image (in the absence of the thyroid gland without the replacement therapy, the mental retardation develops). That is, no matter how ingenious the hereditary information from the ancestors of the child might be, in the absence of thyroid hormones, this will not be realized [9].

Luteinizing hormone (LH), follicle-stimulating hormone (FSH), human chorionic gonadotropin and thyroid stimulating hormone (TSH) are complex glycoproteins consisting of α- and β-subunits. The structure of the α-subunit of LH, FSH, chorionic gonadotropin and TSH is identical, and the β-subunit is specific for each hormone and determines its luteinizing, follicle-stimulating and thyroid-stimulating activity. Estrogens stimulate the thyroid function by intensifying the synthesis of thyroxine-binding globulin in the liver. Experimental studies have shown the presence of receptors for TSH and T3 in the ovary, which determines the possibility of a direct effect of thyroid dysfunction on steroidogenesis, ovulation, corpus luteum function [10].

Estrogens and thyroid hormones can alter the excretion of TSH and prolactin, affecting different levels of regulation of TRH formation and secretion and specific hormonal responses of the anterior pituitary gland. The imbalance of thyroid hormones can change the concentration of active steroids inside the target cells of the hypothalamus and pituitary gland, thus disrupting the mechanism of positive and negative feedback [10].

In diseases of the thyroid gland with an impaired thyroid function of the pituitary gland changes the production and synchrony of the release of TRH — one of the regulators of pulsating gonadotropin release.

Thus, the multilateral mechanism of the influence of the thyroid pathology on menstrual and reproductive functions of the woman is accurately defined. Alongside with it, there are differences in disorders of the reproductive system depending on the form of the thyroid pathology [4].

As it has already been mentioned, the prevalence and incidence of the thyroid disease vary in different regions of the country depending on the influence of environmental factors and their combination, one of which is iodine deficiency.

Iodine deficiency is an important medical and social problem in many countries around the world. According to the World Health Organization (WHO), pathological conditions associated with iodine deficiency rank third in the list of 38 most common non-communicable human diseases. According to WHO experts, one-third of the world’s population belongs to the so-called “risk group” and is a potential target for the development of iodine deficiency diseases (IDD). The increasing number of stillborn babies, premature termination of pregnancy, infertility, deafness and strabismus of newborns, delayed physical, sexual and intellectual development of children, increasing cardiovascular disease — not a complete list of negative effects of “hidden hunger” on humans [11].

The iodine deficiency is a common natural phenomenon associated with iodine deficiency. It is calculated that in order to fully ensure the synthesis of TG and restore intra thyroid reserves, iodine should enter the human body in a stable amount, which depends on the age and functional state of the body [11].

The most common consequences of the iodine deficiency in pregnant women are subclinical hypothyroidism. Determination of TSH is a diagnostic marker of hyper- or hypothyroidism. Occasionally, the persistent hypothyroidism is caused by autoimmune thyroiditis (AIT) with elevated levels of antibodies to thyroid peroxidase (ATPO) or thyroglobulin, the consequences of surgical treatment, or radiation to the thyroid gland. Normal functioning of the thyroid gland is important for successful conception and pregnancy [12].

In a large prospective study of > 16,000 pregnant women with subclinical hypothyroidism, the risk of placental abruption and preterm birth was higher than in euthyroid women. In addition, their offspring were more likely to be admitted to the neonatal intensive care unit and had respiratory distress syndrome [13].

Other large studies comparing women with subclinical hypothyroidism and women with normal thyroid function during pregnancy have also demonstrated a link between subclinical hypothyroidism and miscarriage [14, 15], preterm birth [16, 17], and gestational diabetes [18], gestational hypertension [19, 20], eclampsia [19], premature placental abruption [21], intrauterine growth restriction and low birth weight [22].
The presence of TPO Ab appears to play a synergistic role with elevated TSH concentrations in increasing the risk of pregnancy complications. A recent large prospective study in China [23] found that pregnant women with higher TSH levels were 3.4 times more likely to have miscarriages than euthyroid women, and this risk tripled when these women also had positive TPO Ab levels.

Alternatively, two large prospective studies in the United States [24] and Finland [25] found no effect of subclinical hypothyroidism on pregnancy outcomes.

A meta-analysis [26] of 18 cohort studies examining 3,995 pregnant women with subclinical hypothyroidism found that pregnant women with subclinical hypothyroidism were twice as likely to lose pregnancy and were 2.6 times more likely to have stillbirths than women with normal thyroid function. They also had a higher risk of placental abruption and premature rupture of membranes. It was noted that the included studies had a low and moderate risk of accident, mainly due to limited representativeness of the studied samples, the lack of a significant difference in the evaluation of results.

Thyroid hormones are necessary for early brain development [27]. The mother's thyroid hormones are needed by the fetus until its own thyroid gland begins to function at ~14–18 weeks of gestation [28].

A retrospective study [29] reported that the IQ of children born to untreated, mostly mothers with overt hypothyroidism, was significantly lower than in children in the control group. However, the mean IQs did not differ significantly from those born to mothers who were treated (P = 0.20 and P = 0.90, respectively), although the treatment groups were small. Since then, several studies have reported that higher levels of maternal TSH during pregnancy may be associated with adverse effects on the neurocognitive functions of offspring [30, 31], while the others have not confirmed this [32, 33].

A recent meta-analysis [34], which included 11 observational studies, showed that compared to normal thyroid function, subclinical maternal hypothyroidism is associated with indicators of intellectual disability in offspring (odds ratio 2.14; 95% confidence interval, 1.20–3.83; P = 0.01).

In general, the conflicting results between the effects of subclinical hypothyroidism on the adverse effects of pregnancy may be partly explained by the different TSH cut-off values used in studies to determine subclinical hypothyroidism, taking into account TPO Ab+ and TPO Ab-. In addition, the thyroid function may change during pregnancy, and as a result, a woman diagnosed with subclinical hypothyroidism in early pregnancy may eventually develop overt hypothyroidism or spontaneously return to normal thyroid function [35].

If subclinical hypothyroidism is diagnosed during pregnancy, then despite well-developed clinical guidelines for the treatment of pregnant women with overt hypothyroidism [36], there has long been no consensus on whether to treat women with subclinical hypothyroidism. The American Congress of Obstetricians and Gynecologists in 2007 found insufficient evidence to recommend treatment for subclinical hypothyroidism during pregnancy [37].

At that time, American Thyroid Association (ATA) in 2011 issued recommendations for the treatment of pregnant women with SCH, but only when they have positive levels of TPO Ab [38]. One year later, the Endocrine Society published its recommendation for the general treatment of all pregnant women with subclinical hypothyroidism, recognizing that this recommendation was based on low evidence [39]. A recent evaluation of all clinical practice guidelines for the treatment of hypothyroidism during pregnancy [40] found that they differed and that the ATA (2017) guidelines ranked the highest overall, mainly due to the achievement of the goal and the highest performance in science, are strict and retain editorial independence. As a result, it was concluded that these guidelines need to be significantly improved.

The results of a prospective study [40] clearly informed in the guidelines published in 2011–2012. In this study, ~4,500 women were randomized to 11 weeks of gestation and underwent general screening for thyroid dysfunction based on the presence of risk factors for thyroid disease. All pregnant women were screened for thyroid dysfunction and initiated if confirmed. Of the dysfunction group, only high-risk women were screened, whereas the low-risk group was screened at the end of pregnancy; therefore, these women did not receive therapy. LT4 therapy was initiated in hypothyroidism, which was detected at TSH > 2.5 mIU/l and a positive TPO Ab titer, so by definition, women with overt hypothyroidism were included, which was one of the limitations of the study. There was no significant difference between the total number of adverse events in the universal screening and the case detection group. Given only low-risk cohorts of women, complications were less likely to occur among women in the “universal screening” group than among women in the “case detection” group (OR 0.43; 95% CI 0.26–0.70) due to events that occurred. With unidentified and untreated patients with hypothyroidism (adverse effects were less likely with universal low-risk versus case detection, but no high-risk difference). However, the untreated group was significantly smaller (n = 34), so the study was not informative enough.

In a prospective study in China, LT4 treatment was recommended for pregnant women with subclinical hypothyroidism [14]. Comparing 28 women who received treatment and 168 women who did not receive treatment, there was no difference in the rates of pregnancy loss (relative risk 0.46; CI 0.12–1.84), preterm birth (RR 0.31; CI 0.02–5.13), gestational hypertension (RR 3.00; CI 0.28–31.99), low weight at birth (RR 0.65; CI 0.04–11.71), or obtained a low score on the Apgar scale (RR 0.65; CI 0.04–11.71). This study was limited due to the small sample size, which led to inaccurate results.

In 2012, the results of the study of controlled antenatal thyroid screening were published [41]. This was a multicentre, randomized study where 21,846 women were randomized at ~12 weeks of gestation to the thyroid dysfunction group or to the control group. Treatment at a dose of 150 mcg LT4 was started after 13 weeks of gestation, when women in the screening group were found to have TSH levels > 97.5 percentile, fT4 < 2.5 percentile. The study did not reveal a difference in the IQ of children aged 3 years (in
the treated average IQ 99, in the control group IQ 100). The subgroup analysis, which included only women who met the criteria for subclinical hypothyroidism, had similar results. The study was criticised for the late start of LT₄ therapy (perhaps too late in pregnancy to affect brain development) and the relatively high, fixed dosage of LT₄. Moreover, the question was raised as to whether we could accurately estimate the IQ of a 3-year-old child.

A retrospective single-centre study [42] showed that LT₄ therapy in pregnant women with subclinical hypothyroidism was associated with a lower risk of low birth weight and a low Apgar score, but there was no statistically significant difference in other adverse effects of pregnancy and neonates. Although there is evidence of a number of potentially unclear factors, including socioeconomic and concomitant obstetric conditions, which allowed for an adjusted analysis, this study was limited by its retrospective nature and biased selection. In another study [43] lower chances of miscarriage and macrosomia were reported in pregnant women with subclinical hypothyroidism treated with LT₄ (RR 0.34; C1 0.21–0.56 and RR 0.46; C1 0.28–0.74 respectively). This study was also limited by its biased selection.

The results of the first national study in the United States have also been recently published [44]. Using a large database, 843 pregnant women with subclinical hypothyroidism treated with thyroid hormones were compared with 4562 women who did not take therapy. Treated women had a 38% lower risk of losing pregnancy than untreated women. However, treatment with thyroid hormones has been associated with an increased risk of preterm birth, diabetes mellitus and preeclampsia. A stratified analysis by TSH groups showed that women treated with higher TSH levels had fewer pregnancy losses than those with lower TSH levels. This lack of benefit, together with the stated risk of side effects, has raised concerns about possible over-treatment of women with TSH between 2.5 and 4.0 mIU/l. This study was limited by its retrospective follow-up structure, lack of clinical details (eg, gestational age at the beginning of LT₄ therapy, TPO Ab status).

Another recent randomized study [45] showed that despite the lack of a beneficial effect of LT₄ therapy, to reduce preterm birth in women with subclinical hypothyroidism TPO Ab- and TSH from 2.5 to 10.0 mIU/l, it was found that LT₄ can reduce this complication (RR 0.38; 95% CI 0.15–0.98; P = 0.04).

Similarly, the Tehran Thyroid Study showed a 70 and 83% reduction in preterm birth and neonatal hospitalization in pregnant women treated with LT₄ and TPO Ab+, respectively [46]. The effect of positive LT₄ treatment was observed mainly among TPO Ab+ women with TSH ≥ 4.0 mIU/l.

ATA recommends treatment of maternal hypothyroidism to establish maternal TSH concentrations < 2.5 mIU/l [47]. ATA also suggests repeating thyroid function tests at least every 4 weeks during the first half of pregnancy and again at least once about 30 weeks of pregnancy [47]. Alternatively, the European Endocrine Society proposes to repeat thyroid function tests every 4–6 weeks during pregnancy [39] and, like ATA, recommends adjusting the dose of LT₄ to maintain TSH levels within the target trimester ranges: I trimester — 0.1–2.5 mIU/ml, II trimester — 0.2–3.0 mIU/ml, III trimester — 0.3–3.0 mIU/ml.

After delivery, LT₄ should be reduced to the patient’s previous dose. Additional testing of the thyroid function should be performed ~ 6 weeks after delivery [47]. For women who received LT₄ during pregnancy, LT₄ could potentially be discontinued, especially when the LT₄ dose is < 50 mcg. The decision to discontinue LT₄ should, if desired, be made by the patient and physician. If LT₄ is discontinued, serum TSH levels should be assessed after 66 weeks [47].

A retrospective single-centre study [42] showed that 54% of pregnant women with subclinical hypothyroidism who started taking LT₄ discontinued treatment after delivery/miscarriage.

The first challenge for making recommendations for subclinical hypothyroidism is to determine the normal TSH ranges and to determine the level associated with adverse effects. Currently, most patients receive treatment using fixed threshold levels of TSH, which are determined by laboratories.

It is essential to conduct studies that can help clinicians prescribe therapy using appropriate control ranges. Although randomized clinical trials that evaluate the effect of LT₄ therapy on the clinical outcomes of patients with subclinical hypothyroidism are available, the identification of patients in need of treatment remains a challenge, largely due to the limited nature of these studies.

One of the important limitations of these studies is the initiation of LT₄ therapy in the second trimester of pregnancy. It is believed that if LT₄ affects early adverse pregnancy outcomes (eg., miscarriage), this therapy should be started as close as possible to conception. In addition, these studies included predominantly healthy patients; it is possible that those who are at greater risk of complications will benefit more from treatment [42].

To date, important predictors of adverse effects in patients with subclinical hypothyroidism have been identified, such as an autoimmune status of the thyroid gland and the degree of elevated TSH levels.

To improve the quality of evidence for the treatment of subclinical hypothyroidism during pregnancy, large multi-centre randomized clinical trials are needed in which LT₄ treatment is started early, with pre-scheduled subgroup analysis based on the risk of complications to determine not only whether LT₄ therapy has a positive effect, but what patients are more likely to benefit from it. Although there is sufficient clinical data, little is known about the physiological mechanism by which mild thyroid dysfunction can lead to adverse pregnancy outcomes, or how LT₄ therapy will lead to better outcomes.

Subclinical hypothyroidism is associated with many adverse events during pregnancy and neonatal consequences. LT₄ treatment has been associated with better reproductive outcomes, reduced risk of pregnancy and preterm birth, in women using assisted reproductive technologies. However, well-conducted large randomized trials using LT₄ in early pregnancy and in the planning stage of pregnancy are still needed in this area [48, 49].

Analyzing the above-provided information, it can be argued that most studies do not reflect the gestational age at which hypothyroidism was diagnosed, there is no clear
data on which indicators and in which trimester titrated LT4 replacement therapy. Also, the studies do not provide any data on whether pregnant women lived in iodine-deficient regions or not.

Therefore, the study of the peculiarities of the course of subclinical hypothyroidism in pregnant women in the iodine deficiency region today remains an urgent problem and requires further research.

Conflicts of interests. Authors declare the absence of any conflicts of interests and their own financial interest that might be construed to influence the results or interpretation of their manuscript.

References

1. Tkachenko VI, Maksumets YaA, Vyduborets NV, Kovalenko OF. Analysis of the prevalence and morbidity of thyroid pathology among the population of Kyiv region and Ukraine for 2007–2017. Mïžnarodnîj endokrinologìčnîj zurnal. 2018;14(3):279-284. doi: 10.22144/2224-0721.14.3.2018.136426. (in Ukrainian).

2. Tronko M, Brenner AV, Bogdanova T, et al. Thyroid neoplasia risk is increased nearly 30 years after the Chernobyl accident. Int J Cancer. 2017 Oct 15;141(8):1585-1588. doi: 10.1002/ijc.30857.

3. Thomas GA, Tronko MD, Tsyb AF, Tuttle RM. What have we learnt from Chernobyl? What have we still to learn? Clin Oncol (R Coll Radiol). 2011 May;23(4):229-33. doi: 10.1016/j.clon.2011.02.001.

4. Cho MK. Thyroid dysfunction and subfertility. Clin Exp Reprod Med. 2015 Dec;42(4):131-5. doi: 10.5653/cerm.2015.42.4.131.

5. Krassas GE, Poppe K, Glinnor D. Thyroid function and human reproductive health. Endocr Rev. 2010 Oct;31(5):702-55. doi: 10.1210/er.2009-0041.

6. de Escobar GM, Obregon MJ, del Rey FE. Maternal thyroid hormones early in pregnancy and fetal brain development. Best Pract Res Clin Endocrinol Metab. 2004 Jun;18(2):225-48. doi: 10.1016/j.beem.2004.03.012.

7. Brent GA. The debate over thyroid-function screening in pregnancy. N Engl J Med. 2012 Feb 9;366(6):562-3. doi: 10.1056/NEJMra1112591.

8. Verma I, Sood R, Jungea S, Kaur S. Prevalence of hypothyroidism in infertile women and evaluation of response of treatment for hypothyroidism on infertility. Int J Appl Basic Med Res. 2012 Jan;2(1):17-9. doi: 10.4103/2229-516X.96795.

9. Davis LB, Lathi RB, Dahan MH. The effect of infertility medication on thyroid function in hypothyroid women who conceive. Thyroid. 2007 Aug;17(8):773-7. doi: 10.1089/thy.2007.0065.

10. Pankiv V, Pankiv I. Association of vitamin D status with body mass index in adolescents in Ukraine. Romanian Journal of Diabetes, Nutrition and Metabolic Diseases. 2018;25(4):377-381.

11. Julving LR, Larsen MD, Fedder J, Friedman S, Nørgård BM. The chance of a live birth after assisted reproduction in women with thyroid disorders. Clin Epidemiol. 2019 Aug 9;11:683-694. doi: 10.2147/CLEP.S208574.

12. Cui YJ, Liu N, Zhong LP, Duan HJ, Dong YH, Wu Z, Su H. Serum and follicular fluid thyroid hormone levels and assisted reproductive technology outcomes. Reprod Biol Endocrinol. 2019 Nov 7;17(1):90. doi: 10.1186/s12958-019-0529-0.

13. Casey BM, Dashe JS, Wells CE, McIntire DD, Byrd W, Leveno KJ, Cunningham FG. Subclinical hypothyroidism and pregnancy outcomes. Obstet Gynecol. 2005 Feb;105(2):239-45. doi: 10.1097/01.AOG.0000152345.99421.22.

14. Wang S, Teng WP, Li JX, Wang WW, Shan ZY. Effects of maternal subclinical hypothyroidism on obstetrical outcomes during early pregnancy. J Endocrinol Invest. 2012 Mar;35(3):322-5. doi: 10.3275/7772.

15. Schneuer FJ, Nassar N, Tasevski V, Morris JM, Roberts CL. Association and predictive accuracy of high TSH serum levels in first trimester and adverse pregnancy outcomes. J Clin Endocrinol Metab. 2012 Sep;97(9):3115-22. doi: 10.1210/jc.2012-1193.

16. Feldhusen AD, Pedersen PL, Larsen J, Toft Kristensen T, Ellervik C, Kvetny J. Impaired Fertility Associated with Subclinical Hypothyroidism and Thyroid Autoimmunity: The Danish General Suburban Population Study. J Pregnancy. 2015;2015:132718. doi: 10.1155/2015/132718.

17. Korevaar Tj, Schalekamp-Timmermans S, de Rijke YB, et al. Hypothyroxinemia and TPO-antibody positivity are risk factors for premature delivery: the generation R study. J Clin Endocrinol Metab. 2013 Nov;98(11):4382-90. doi: 10.1210/jc.2013-2855.

18. Tudela CM, Casey BM, McIntire DD, Cunningham FG. Relationship of subclinical thyroid disease to the incidence of gestational diabetes. Obstet Gynecol. 2012 May;119(5):983-8. doi: 10.1097/AOG.0b013e318250aeeb.

19. Wilson KL, Casey BM, McIntire DD, Halvorson LM, Cunningham FG. Subclinical thyroid disease and the incidence of hypertension in pregnancy. Obstet Gynecol. 2012 Feb;119(2 Pt 1):315-20. doi: 10.1097/AOG.0b013e318240de6a.

20. Chen LM, Du WJ, Dai J, et al. Effects of subclinical hypothyroidism on maternal and perinatal outcomes during pregnancy: a single-center cohort study of a Chinese population. PLoS One. 2014 Oct 29;9(10):e109364. doi: 10.1371/journal.pone.0109364.

21. Wang S, Teng WP, Li JX, Wang WW, Shan ZY. Effects of maternal subclinical hypothyroidism on obstetrical outcomes during early pregnancy. J Endocrinol Invest. 2012 Mar;35(3):322-5. doi: 10.3275/7772.

22. Feldhusen AD, Larsen J, Pedersen PL, Toft Kristensen T, Kvetny J. Pregnancy-induced alterations in mitochondrial function in euthyroid pregnant women and pregnant women with subclinical hypothyroidism; relation to adverse outcome. J Clin Transl Endocrinol. 2013 Dec 24;1(1):e13-e17. doi: 10.1016/j.jcete.2013.12.003.

23. Liu H, Shan Z, Li C, et al. Maternal subclinical hypothyroidism, thyroid autoimmunity, and the risk of miscarriage: a prospective cohort study. Thyroid. 2014 Nov;24(11):1642-9. doi: 10.1089/thy.2014.0029.

24. Cleary-Goldman J, Malone FD, Lambert-Messerlian G, Sullivan L, Canick J, Porter TF, Luthy D, Gross S, Bianchi DW, D’Alton ME. Maternal thyroid dysfunction and pregnancy outcome. Obstet Gynecol. 2008 Jul;112(1):85-92. doi: 10.1097/AOG.0b013e31819888d7.

25. Männistö T, Väänäsmäki M, Poata A, et al. Thyroid dysfunction and autoantibodies during pregnancy as predictive factors of pregnancy complications and maternal morbidity in later life. J Clin Endocrinol Metab. 2010 Mar;95(3):1084-94. doi: 10.1210/jc.2009-1904.

26. Maraka S, Ospina NM, O’Keefe DT, et al. Subclinical Hypothyroidism in Pregnancy: A Systematic Review and Meta-Analy-
Огляд літератури

Thyroid. 2016 Apr;26(4):580-90. doi: 10.1089/thy.2015.0418.

27. Bernal J, Nunez J. Thyroid hormones and brain development. Eur J Endocrinol. 1995 Oct;133(4):390-8. doi: 10.1530/eje.0.1330390.

28. Zimmermann MB. Iodine deficiency. Endocr Rev. 2009 Jun;30(4):376-408. doi: 10.1210/er.2009-0011.

29. Haddow JE, Palomaki GE, Allan WC, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. N Engl J Med. 1999 Aug 19;341(8):549-55. doi: 10.1056/NEJM199908193410801.

30. Päkkilä T, Männistö T, Hartikainen AL, et al. Maternal and Child’s Thyroid Function and Child’s Intellect and Scholastic Performance. Thyroid. 2015 Dec;25(12):1363-74. doi: 10.1089/thy.2015.0197.

31. Williams F, Watson J, Ogston S, Hume R, Willatts P, Visser T. Scottish Preterm Thyroid Group. Mild maternal thyroid dysfunc

32. Henrichs J, Bongers-Schokking JJ, Schenk JJ, et al. Maternals thyroid function during early pregnancy and cognitive functioning in early childhood: the generation R study. J Clin Endocrinol Metab. 2010 Sep;95(9):4227-34. doi: 10.1210/jc.2010-0415.

33. Chen LM, Chen QS, Jin GX, et al. Effect of gestational subclinical hypothyroidism on early neurodevelopment of offspring. J Perinatol. 2015 Sep;35(9):678-82. doi: 10.1038/jp.2015.66.

34. Thompson W, Russell G, Baragwanath G, Matthews J, Vaidya B, Thompson-Coon J. Maternal thyroid hormone insufficiency during pregnancy and risk of neurodevelopmental disor

35. Li C, Shan Z, Mao J, Wang W, Xie X, Zhou W, et al. Assessment of thyroid function during first-trimester pregnancy: what is the rational upper limit of serum TSH during the first trimester in Chinese pregnant women? J Clin Endocrinol Metab. 2014 Jan;99(1):73-9. doi: 10.1210/jc.2013-1674.

36. Alexander KE, Pearce EN, Brent GA, et al. 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. Thyroid. 2017 Mar;27(3):315-389. doi: 10.1089/thy.2016.0457.

37. Committee on Patient Safety and Quality Improvement; Committee on Professional Liability. ACOG Committee Opinion No. 381: Subclinical hypothyroidism in pregnancy. Obstet Gynecol. 2007 Oct;110(4):959-60. doi: 10.1097/01.AOG.0000263932.05311.d4.

38. Stagnaro-Green A, Abalovich M, Alexander E, et al. American Thyroid Association Taskforce on Thyroid Disease During Pregnancy and Postpartum. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid. 2011 Oct;21(10):1081-125. doi: 10.1089/thy.2011.0087.

39. Abalovich M, Amino N, Barbour LA, et al. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2007 Aug;92(8 Suppl):S1-47. doi: 10.1210/jc.2007-0141.

40. Negro R, Schwartz A, Gismondi R, Tinelli A, Mangieri T, Stagnaro-Green A. Universal screening versus case finding for detection and treatment of thyroid hormonal dysfunction during pregnancy. J Clin Endocrinol Metab. 2010 Apr;95(4):1699-707. doi: 10.1210/jc.2009-2009.

41. Bath SC, Rayman MP. Antenatal thyroid screening and childhood cognitive function. N Engl J Med. 2012 Apr 26;366(17):1640-1; author reply 1641. doi: 10.1056/NEJMct1202720.

42. Maraka S, Singh Osypina NM, O’Keefe DT, et al. Effects of Levothyroxine Therapy on Pregnancy Outcomes in Women with Subclinical Hypothyroidism. Thyroid. 2016 Jul;26(7):980-6. doi: 10.1089/thy.2016.0014.

43. Ma L, Qi H, Chai X, et al. The effects of screening and intervention of subclinical hypothyroidism on pregnancy outcomes: a prospective multicenter single-blind, randomized, controlled study of thyroid function screening test during pregnancy. J Matern Fetal Neonatal Med. 2016;29(9):1391-4. doi: 10.3109/14767058.2015.1049150.

44. Maraka S, Mwangi R, McCoy RG, et al. Thyroid hormone treatment among pregnant women with subclinical hypothyroidism: US national assessment. BMJ. 2017 Jan 25;356:i6865. doi: 10.1136/bmj.i6865.

45. Nazarpour S, Ramezani Tehrani F, et al. Effects of Levothyroxine on Pregnant Women With Subclinical Hypothyroidism, Negative for Thyroid Peroxidase Antibodies. J Clin Endocrinol Metab. 2018 Mar 1;103(3):926-935. doi: 10.1210/jc.2017-01850.

46. Nazarpour S, Ramezani Tehrani F, Simbar M, et al. Effects of levothyroxine treatment on pregnancy outcomes in pregnant women with autoimmune thyroid disease. Eur J Endocrinol. 2017 Feb;176(2):253-265. doi: 10.1536/eje.2016-0545.

47. Alexander KE, Pearce EN, Brent GA, et al. 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. Thyroid. 2017 Mar;27(3):315-389. doi: 10.1089/thy.2016.0457.

48. Rodriguez-Gutierrez R, Gionfriddo MR, et al. Shared decision making in endocrinology: present and future directions. Lancet Diabetes Endocrinol. 2016 Aug;4(8):706-716. doi: 10.1016/S2221-8357(15)00468-4.

49. Maraka S, Singh Osypina NM, Mastorakos G, O’Keefe DT. Subclinical Hypothyroidism in Women Planning Conception and During Pregnancy: Who Should Be Treated and How? J Endocr Soc. 2018 May 3;2(6):533-546. doi: 10.1210/js.2018-00090.

Information about authors

Pasyechko N.V., MD, PhD, Professor, Head of the Department of internal medicine 1, l. Ya. Horbachevsky Ternopil National Medical University, Ternopil, Ukraine; e-mail: pasyechkonv@gmail.com; ORCID: https://orcid.org/0000-0002-8201-4269

Kulchinska J.M., PhD student, Department of internal medicine 1, l. Ya. Horbachevsky Ternopil National Medical University, Ternopil, Ukraine; e-mail: kulchinska@tdmu.edu.ua

Naumova L.V., MD, PhD, Associate Professor at the Department of internal medicine 1, l. Ya. Horbachevsky Ternopil National Medical University, Ternopil, Ukraine; e-mail: naumova@tdmu.edu.ua; ORCID: https://orcid.org/0000-0002-3115-3509
Субклінічний гіпотиреоз у вагітних в йододефіцитному регіоні: лікувати чи ні?

Резюме. Захворювання щитоподібної залози в структурі ендокринної патології останнім часом посідають перше місце. За даними Міністерства охорони здоров’я України, за останні 5 років кількість захворювань щитоподібної залози збільшилася у 5 разів, причому даний показник суттєво відрізняється в різних регіонах країни залежно від сукупності чинників зовнішнього середовища (віддалений стохастичний ефект аварії на Чернобильській АЕС, йодний дефіцит, спосіб життя, стрес, нерациональне харчування, недостатність мікролімітів, супутні захворювання тощо). При цьому відомий тісний функціональний взаємозв’язок тиреоїдної та репродуктивної систем, що зумовлює високу ймовірність розвитку поширеного порушень щитоподібної залози на вагітність. Показники захворюваності на патології щитоподібної залози та їх поширеності відрізняються в різних регіонах країни залежно від впливу чинників зовнішнього середовища та їх комбінацій, одним із таких є дефіцит йоду. Збільшення кількості мертвонароджених немовлят, передчасне переривання вагітності, тугоухість та косоокість новонароджених, затримка фізичного, статевого і інтелектуального розвитку дітей, ростом проявляється ассоціація субклінічного гіпотиреозу у вагітних із йодним дефіцитом. Найбільш частими наслідками йодного дефіциту у вагітних є субклінічний гіпотиреоз. Субклінічний гіпотиреоз асоціюється з багатьма небезпечними подіями під час вагітності та неонатальних наслідках. Вивчення особливостей перебігу субклінічного гіпотиреозу у вагітних в йододефіцитному регіоні на сьогодні залишається актуальною проблемою. У статті наведений аналіз публікацій баз даних PubMed, Medline за останні десятиліття.

Ключові слова: субклінічний гіпотиреоз; йодний дефіцит; лікування

Субклінічний гіпотиреоз у беременних в йододефицитном регионе: лечить или нет?

Резюме. Заболевания щитовидной железы в структуре эндокринной патологии в последние годы занимают первое место. По данным Министерства здравоохранения Украины, за последние 5 лет количество заболеваний щитовидной железы увеличилось в 5 раз, причем данный показатель существенно отличается в различных регионах страны в зависимости от совокупности факторов внешней среды (удаленный стохастический эффект аварии на Чернобыльской АЭС, йодный дефицит, образ жизни, стресс, нерациональное питание, недостаточность миореалейментов, сопутствующие заболевания и т.д.). При этом известна тесная функциональная взаимосвязь тиреоидной и репродуктивной систем, что приводит к высокой вероятности развития объединенных нарушений при расстройствах одной из этих звеньев гомеостаза. Проблема нарушений репродуктивного здоровья вызывает особенное серьезное беспокойство во всем мире и является актуальной по изучению влияния заболеваний щитовидной железы на беременность. Показатели заболеваемости патологиями щитовидной железы и их распространенности отличаются в разных регионах страны в зависимости от влияния факторов внешней среды и их комбинации, одним из таких является дефицит йода. Увеличение количества мертворожденных младенцев, преждевременное прерывание беременности, бесплодие, тугоухость и косоокий новорожденных, задержка физического, полового и интеллектуального развития детей, рост показателей сердечно-сосудистых заболеваний — далеко не полный перечень негативного влияния йодного дефицита на человека. Наиболее частыми последствиями йодного дефицита у беременных является субклінічний гіпотиреоз. Субклінічний гіпотиреоз ассоциируется со многими неблагоприятными событиями во время беременности и неонатальными последствиями. Изучение особенностей течения субклінічного гіпотиреозу у беременных в йододефицитном регионе на сегодня остается актуальной проблемой. В статье представлен анализ публикаций баз данных PubMed, Medline за последние десятилетия.

Ключевые слова: субклінічний гіпотиреоз; йодный дефицит; лечение

Vol. 16, No. 6, 2020
http://iej.zaslavsky.com.ua 477