International Journal of Endocrinology

Оригінальні дослідження
Original Researches

UDC 618.03-06:616.441-002-073.7:612.882.3 DOI: https://doi.org/10.22141/2224-0721.20.2.2024.1372

O.S. Paienok[1], A.V. Paienok[1], B.V. Zadorozhna[1], B.R. Hrytsyshyn[2], S.V. Ihnatovych[2]
[1] Danylo Halytsky Lviv National Medical University, Lviv, Ukraine
[2] Lviv Regional Clinical Hospital, Lviv, Ukraine

The influence of thyroid disorders on the state of brain's bioelectrical activity in pregnant women

For citation: Mìžnarodnij endokrinologìčnij žurnal. 2024;20(2):115-119. doi: 10.22141/2224-0721.20.2.2024.1372

Abstract. ***Background.*** *Thyroid disease is the second most common endocrine disorder after diabetes in pregnancy. Thyroid hormones are crucial for the growth and maturation of many target tissues, especially the brain and skeleton. During critical periods in the first trimester of pregnancy, maternal thyroxine is essential for fetal development as it supplies thyroid hormone-dependent tissues. The purpose of the study was to research the features of the bioelectrical activity of the brain in pregnant women with thyroid pathology and determine the frequency of such changes.* ***Materials and methods.*** *The state of bioelectrical activity of the brain was evaluated by electroencephalography in 160 pregnant women with thyroid pathology. The biopotentials of the brain in the subjects were studied with software and hardware complex DX-NT32 (DX Complexes software, Kharkiv, Ukraine) and computer processing of electroencephalography data. Electrodes in the amount of 16 pieces were applied according to the international scheme 10/20 in the bipolar interpretation.* ***Results.*** *Specific changes in electroencephalograms characteristic of each type of thyroid pathology and dependent on its severity were revealed in pregnant women. Acquired disorders adversely affect the course of pregnancy and childbirth in women with thyroid pathology. Increased anxiety with depressive tendencies, reduced general activity, a feeling of depression, anxiety, and low mood were detected in women with thyroid disorders. The identified criteria make it possible to attribute these changes to the manifestations of a pathological neurotic state in conditions of maladaptation, which was confirmed by electroencephalography data.* ***Conclusions.*** *The detected disorders of spontaneous and evoked brain activity indicate the existence of a cerebral basis of psychological stress, which has a qualitative effect on electroencephalography. Acquired disorders negatively affect the course of pregnancy, childbirth, perinatal outcomes, and future development of the child.*

Keywords: *pregnant women; thyroid gland; diffuse non-toxic goiter; diffuse toxic goiter; electroencephalography*

Introduction

Thyroid disease is the second most common endocrine disorder after diabetes in pregnancy. Thyroid hormones are crucial for the growth and maturation of many target tissues, especially the brain and skeleton. During critical periods in the first trimester of pregnancy, maternal thyroxine is essential for fetal development as it supplies thyroid hormone-dependent tissues. The ontogeny of mature thyroid function involves organogenesis, and maturation of the hypothalamus, pituitary, and the thyroid gland; it is almost complete by the 12th-14th gestational week. In case of maternal hypothyroidism, substitution with levothyroxine must be started in early pregnancy. After the 14th gestational week, fetal brain development may already be irreversibly affected by lack of thyroid hormones [1].

Thyroid disorders represent one of the most frequent complications of pregnancy associated with adverse obstetric, fetal, and neonatal outcomes, especially in case of delayed diagnosis and suboptimal management [2]. Adequate thyroid hormone availability is important for an uncomplicated pregnancy and optimal fetal growth and development. Overt thyroid disease is associated with a wide range of adverse obstetric and child development outcomes. An increasing number of studies now indicate that milder forms of thyroid

Для кореспонденції: Паєнок Олександр Станіславович, доктор медичних наук, професор, доцент кафедри акушерства і гінекології, медичний факультет № 1, Львівський національний медичний університет імені Данила Галицького, вул. Пекарська, 69, м. Львів, 79010, Україна; e-mail: alex.payenok@gmail.com
For correspondence: Oleksandr Paienok, MD, DSc, PhD, Professor, Associate Professor at the Department of Obstetrics and Gynecology, Medical Faculty 1, Danylo Halytsky Lviv National Medical University, Pekarska st., 69, Lviv, 79010, Ukraine; e-mail: alex.payenok@gmail.com
Full list of authors' information is available at the end of the article.

dysfunction are also associated with these adverse pregnancy outcomes. The definitions of both overt and subclinical thyroid dysfunction have changed considerably over the past few years, as new data indicate that the commonly used fixed upper limits of 2.5 or 3.0 mU/l for thyroid-stimulating hormone (TSH) are too low to define an abnormal thyroid function [3].

Research shows that during pregnancy, the size of the thyroid gland increases by 10 % in countries with adequate iodine stores and by approximately 20 to 40 % in countries with iodine deficiency. During pregnancy, thyroid hormone production increases by around 50 % along with a similar increase in total daily iodine requirements. Thyroid dysfunction in pregnant women including hypothyroidism and hyperthyroidism requires close monitoring and treatment as warranted. Occasionally, pregnancy may be complicated by thyroid nodules and thyroid cancer requiring further intervention [4].

It should be noted that metabolic and vascular disorders caused by a deficiency of thyroid hormones in the body of a pregnant woman contribute to brain damage, affect subcortical and mesodiencephalic structures, which play a significant role in brain electrogenesis [5, 6]. Electroencephalography (EEG) remains the main method for assessing the functional state of the brain. It makes it possible to determine the localization, degree and nature of disorders in the brain in various pathologies by the severity and nature of changes in bioelectrical activity [7].

The aim of our study was to research the features of the bioelectrical activity of the brain in pregnant women with thyroid pathology and determine the frequency of such changes.

Materials and methods

The state of bioelectrical activity of the brain according to the EEG data was studied in 160 pregnant women with different thyroid disorders (Table 1).

The diagnosis of thyroid pathology was established based on clinical data, the results of hormonal studies (serum levels of TSH and free thyroxine).

The biopotentials of the brain in the subjects were studied with software and hardware complex DX-NT32 (DX Complexes software, Kharkiv, Ukraine) and computer processing of EEG. Electrodes in the amount of 16 pieces were applied according to the international scheme 10/20 in the bipolar interpretation [8]. The examination was carried out in a semi-reclining position of the patient in a darkened room. The examination protocol consisted of 7 functional tests of 32 seconds each with closed and open eyes; 3 sequential stages of hyperventilation, combined photo-audio stimulation in 2 and 20 Hz mode. Recording artifacts were extracted by means of digital filtering both during the recording process and the analysis of the archived electroencephalographic curve (with filters FTS-35 Hz; FAC-0.35 Hz) [9].

The use of computer EEG analysis made it possible to reduce subjectivity in the interpretation of bioelectrical activity; and the use of the homographic EEG method in the system allowed for assessing the spatial localization of the focus of pathological activity.

Results

An important point for determining the specificity of EEG changes depending on the type and severity of thyropathies was, in our opinion, the uniformity of age and timing of gestational parameters among the groups. Therefore, the results of the distribution of the examined pregnant women are presented in Table 1.

As it is shown in Table 1, the age criterion and gestational period of the subjects were homogeneous, with no significant differences ($p > 0.05$).

During the electroencephalographic examination of pregnant women with stage 1 diffuse non-toxic goiter, regular alpha and beta rhythms were recorded. The percentage of theta and delta activity did not exceed the permissible limits of normal EEG (up to 15 %). We have not registered irritative, diffuse or paroxysmal changes in this group of pregnant women.

Changes in the bioelectrical activity of the brain detected on the EEG with stage 2 diffuse non-toxic goiter were mainly bore signs of diffuse disorganization of a polymorphic nature of various variants of paroxysmal manifestations, as well as a decrease reactivity on functional tests. Attention was drawn to a decrease in alpha and beta rhythms, in their amplitude and frequency (Fig. 1). The percentage of theta and delta waves of activity increased to 30 %. These changes increased depending on the progression of the severity of diffuse non-toxic goiter.

Table 1. Age and gestational age of pregnant women with thyroid pathology

Group	n	Age	Weeks of pregnancy
Pregnant women with stage 1 diffuse non-toxic goiter	60	26.17 ± 0.68	20.83 ± 0.11
Pregnant women with stage 2 diffuse non-toxic goiter	40	27.53 ± 0.87 $p_1 > 0.05$	20.73 ± 0.18 $p_1 > 0.05$
Pregnant women with stage 1 diffuse toxic goiter	20	24.85 ± 1.16 $p_1 > 0.05$; $p_2 > 0.05$	20.50 ± 0.25 $p_1 > 0.05$; $p_2 > 0.05$
Pregnant women with stage 2 diffuse toxic goiter	20	26.30 ± 1.17 $p_1 > 0.05$; $p_2 > 0.05$; $p_3 > 0.05$	20.55 ± 0.22 $p_1 > 0.05$; $p_2 > 0.05$; $p_3 > 0.05$
Pregnant women after thyroidectomy	20	28.40 ± 1.07 $p_1 > 0.05$; $p_2 > 0.05$; $p_3 > 0.05$; $p_4 > 0.05$	20.80 ± 0.19 $p_1 > 0.05$; $p_2 > 0.05$; $p_3 > 0.05$; $p_4 > 0.05$

Notes: significance of differences in the corresponding indicators of pregnant women: p_1 — with stage 1 diffuse non-toxic goiter; p_2 — with stage 2 diffuse non-toxic goiter; p_3 — with stage 1 diffuse toxic goiter; p_4 — with stage 2 diffuse toxic goiter.

During the examination of pregnant women with diffuse toxic goiter, the bioelectrical activity of the brain was represented by slow-wave and acute-wave activity with signs of irritation of medio-basal structures in the form of flashes of sharp alpha-wave waves (Fig. 1).

At the same time, clinical manifestations of anxiety, irritability, nervousness, vegetative-vascular paroxysms were noted. A decrease in the content of TSH against the background of replacement therapy led to the occurrence of hypersynchronous alpha rhythm, paroxysmal activity of the affect sphere, which modified neurological symptoms in a drug-compensated hypothyroid state. Thyroid pathology affects not only the dysregulatory restructuring of the brain, but also the stability of cortical-subcortical-stem structures. When compensating for hypothyroidism, there is a potential reversibility of the above changes.

Weak correlation in pregnant women with a long history of thyroid disorders indicates the development of persistent cerebral disorders, which are associated not only with impaired thyroid function, but also with other pathological processes triggered in the body under hypothyroid conditions (lipid peroxidation, dysliloproteinemia, cerebral hemodynamic disorders).

In all pregnant women with diffuse toxic goiter and thyrotoxicosis, interhemispheric asymmetry was pronounced due to the formation of a focus of slow-wave activity in the frontal-pole areas, the frontal intermittent rhythmic delta activity. These waves were detected only in the group of pregnant women with thyrotoxicosis (Fig. 2).

A characteristic EEG feature in pregnant women with hypothyroidism was the presence of sleep spindles and K-complexes corresponding to the second stage of sleep in healthy people. Sleep spindles presented in the form of flashes of diffuse activity with a frequency of 11–15 Hz, which were most pronounced in the central leads with an amplitude of 50 mV. The duration of the spindles was 0.5 to 3 seconds with bilaterally synchronous placement, suggesting a connection with the central median subcortical centers (thalamic specific and nonspecific nuclei). K-complexes arose spontaneously or in response to photostimulation, as flashes of activity of two-phase high-amplitude waves with an initial negative phase, lasting approximately 0.5 seconds.

Thus, it can be argued that for thyrotoxicosis, the characteristic EEG sign is the frontal intermittent rhythmic delta activity. With hypothyroidism in pregnant women, an EEG study reveals an epileptiform background.

Discussion

Thyroid dysfunctions such as hypothyroidism, thyrotoxicosis and thyroid nodules may develop during pregnancy leading to abortion, placental abruptions, preeclampsia, preterm delivery and reduced intellectual function in the offspring [11]. Epidemiological data have shown the significant role of maternal thyroid hormone in fetal neurologic development and maternal health [12].

It has been suggested that the deleterious effects of thyroid dysfunction can also extend beyond pregnancy and delivery to affect neuro-intellectual development in the early life of the child [13]. Pregnancy poses an important challenge to the maternal thyroid gland as hormone requirements are increased during gestation as a result of an increase in thyroid-binding globulin, the stimulatory effect of human chorionic gonadotropin on TSH receptors and increased peripheral thyroid hormone requirements [14].

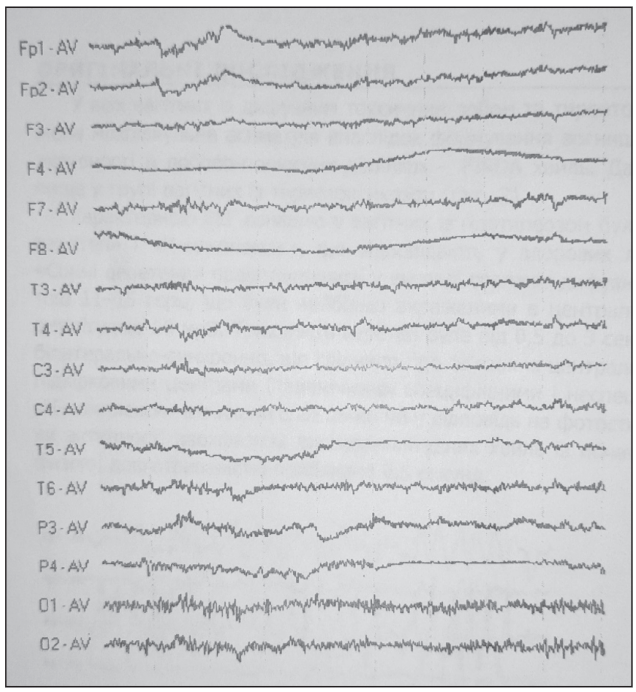

Figure 1. EEG of pregnant woman M., 26 years old (second trimester), with stage 2 diffuse non-toxic goiter

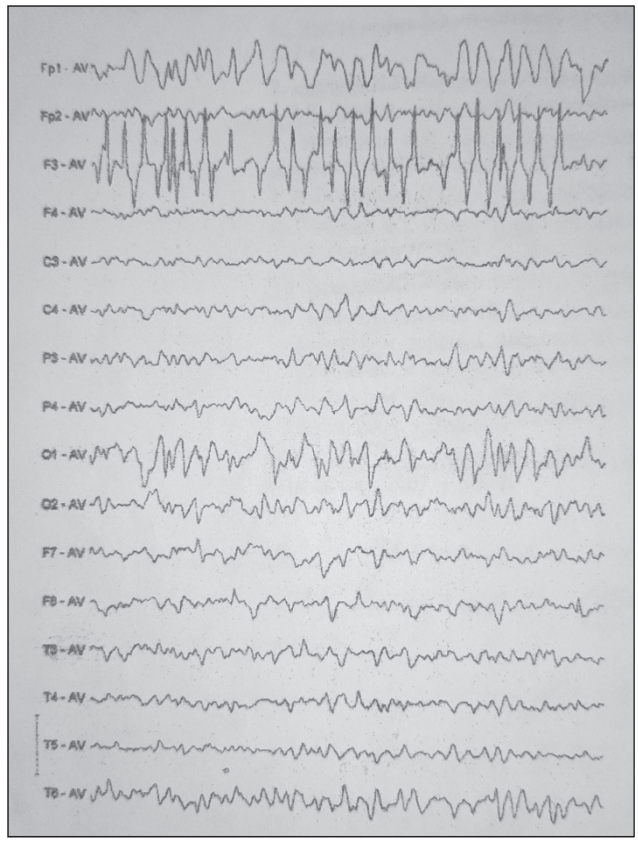

Figure 2. EEG of pregnant woman M., 28 years old (second trimester), with stage 2 diffuse non-toxic goiter and thyrotoxicosis

Maternal thyroid dysfunction is associated with increased risk for early abortion, preterm delivery, neonatal morbidity, and other obstetric complications. Early diagnosis of thyroid dysfunction in pregnant women and treatment for thyroid dysfunction during pregnancy is important and cost-effective to avoid both fetal and maternal complications secondary to thyroid dysfunction [15].

Different studies have shown that thyroid dysfunction is common in pregnancy. The major causes for this dysfunction are hormonal and metabolic changes during pregnancy leading to profound alterations in the biochemical parameters of the thyroid function [16]. Understanding the normal physiological adaptation of the pituitary-thyroidal axis in pregnancy enables us to manage cases of thyroid dysfunction. Uncorrected thyroid function in pregnancy has adverse effects on fetal and maternal well-being [17].

Thyroid disease usually affects females of the reproductive age group and caring for these women during pregnancy requires close monitoring of both the mother and the fetus. Appropriate diagnosis, and management of thyroid dysfunction in the pre-pregnancy, pregnancy and post-pregnancy periods are important to minimize the risk of complications, long-term effects in the mother and fetus [18].

Clinical evaluation of the patient's symptoms as well as laboratory testing should be done carefully to assess thyroid function during pregnancy [19]. All pregnant mothers are advised to undergo thyroid function testing, and those with thyroid dysfunction should be given appropriate treatment and follow-up until thyroid function returns to normal. Developmental follow-up of the babies born to mothers with thyroid dysfunction is also recommended in order to identify cognitive and other deficiencies as early as possible and provide appropriate management [20].

Anxiety and depression symptoms in pregnancy typically affect between 10 and 25 % of women. Elevated symptoms of depression and anxiety are associated with increased risk of preterm birth, postpartum depression, and behavioral difficulties in children.

Conclusions

Increased anxiety with depressive tendencies reduced general activity; a feeling of depression, anxiety, and low mood were detected in women with thyroid disorders.

The identified criteria make it possible to attribute these changes to the manifestations of a pathological neurotic state in conditions of maladaptation, which was confirmed by electroencephalography data.

The detected disorders of spontaneous and evoked brain activity indicate the existence of a cerebral basis of psychological stress, which has a qualitative effect on electroencephalography. Acquired disorders adversely affect the course of pregnancy, childbirth, perinatal outcomes, and future development of the child.

References

1. Springer D, Jiskra J, Limanova Z, Zima T, Potlukova E. Thyroid in pregnancy: From physiology to screening. Crit Rev Clin Lab Sci. 2017 Mar;54(2):102-116. doi: 10.1080/10408363.2016.1269309.

2. Tsakiridis I, Giouleka S, Kourtis A, Mamopoulos A, Athanasiadis A, Dagklis T. Thyroid Disease in Pregnancy: A Descriptive Review of Guidelines. Obstet Gynecol Surv. 2022 Jan;77(1):45-62. doi: 10.1097/OGX.0000000000000960.

3. Korevaar TIM, Medici M, Visser TJ, Peeters RP. Thyroid disease in pregnancy: new insights in diagnosis and clinical management. Nat Rev Endocrinol. 2017 Oct;13(10):610-622. doi: 10.1038/nrendo.2017.93.

4. Yap YW, Onyekwelu E, Alam U. Thyroid disease in pregnancy. Clin Med (Lond). 2023 Mar;23(2):125-128. doi: 10.7861/clinmed.2023-0018.

5. Björnholm L, Orell O, Kerkelä M, et al. Maternal Thyroid Function During Pregnancy and Offspring White Matter Microstructure in Early Adulthood: A Prospective Birth Cohort Study. Thyroid. 2023 Oct;33(10):1245-1254. doi: 10.1089/thy.2022.0699.

6. Korevaar TI, Muetzel R, Medici M, et al. Association of maternal thyroid function during early pregnancy with offspring IQ and brain morphology in childhood: a population-based prospective cohort study. Lancet Diabetes Endocrinol. 2016 Jan;4(1):35-43. doi: 10.1016/S2213-8587(15)00327-7.

7. Cao J, Zhao Y, Shan X, et al. Brain functional and effective connectivity based on electroencephalography recordings: A review. Hum Brain Mapp. 2022 Feb 1;43(2):860-879. doi: 10.1002/hbm.25683.

8. Wang N, Zhang L, Liu G. EEG-based research on brain functional networks in cognition. Biomed Mater Eng. 2015;26 Suppl 1:S1107-14. doi: 10.3233/BME-151407.

9. Stevenson NJ, Lai MM, Starkman HE, Colditz PB, Wixey JA. Electroencephalographic studies in growth-restricted and small-for-gestational-age neonates. Pediatr Res. 2022 Dec;92(6):1527-1534. doi: 10.1038/s41390-022-01992-2.

10. Alexander EK, 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.

11. Alemu A, Terefe B, Abebe M, Biadgo B. Thyroid hormone dysfunction during pregnancy: A review. Int J Reprod Biomed. 2016 Nov;14(11):677-686.

12. Taylor PN, Zouras S, Min T, Nagarahaj K, Lazarus JH, Okosieme O. Thyroid Screening in Early Pregnancy: Pros and Cons. Front Endocrinol (Lausanne). 2018 Oct 25;9:626. doi: 10.3389/fendo.2018.00626.

13. Lee SY, Pearce EN. Testing, Monitoring, and Treatment of Thyroid Dysfunction in Pregnancy. J Clin Endocrinol Metab. 2021 Mar 8;106(3):883-892. doi: 10.1210/clinem/dgaa945.

14. Lee SY, Cabral HJ, Aschengrau A, Pearce EN. Associations Between Maternal Thyroid Function in Pregnancy and Obstetric and Perinatal Outcomes. J Clin Endocrinol Metab. 2020 May 1;105(5):e2015–23. doi: 10.1210/clinem/dgz275.

15. Ferreira JL, Gomes M, Príncipe RM. Controversial Screening for Thyroid Dysfunction in Preconception and Pregnancy: An Evidence-Based Review. J Family Reprod Health. 2020 Dec;14(4):209-220. doi: 10.18502/jfrh.v14i4.5204.

16. Cherenko MS, Cherenko SM. Management of thyroid disorders during and after pregnancy. Reproductive endocrinology. 2019;(45):14-18. doi: 10.18370/2309-4117.2019.45.14-18.

17. Buldyhina Y, Strafun L, Terekhova H, Shliakhtych S, Pankiv V. Diagnosis and treatment of thyrotoxicosis during pregnancy and in the postpartum period. A fragment of 2017 Guidelines of the American Thyroid Association for the diagnosis and management of

thyroid disease during pregnancy and the postpartum. Mìžnarodnij endokrinologìčnij žurnal. 2019;15(2):165-177. doi: 10.22141/2224-0721.15.2.2019.166111.

18. Romanenko T, Chayka O. Features of Thyroid Function in Pregnant Women Against Iodine Deficiency. Mìžnarodnij endokrinologìčnij žurnal. 2014;(60):89-94. doi: 10.22141/2224-0721.4.60.2014.76687.

19. Iwen KA, Lehnert H. Thyroid and pregnancy. Internist (Berl). 2018 Jul;59(7):654-660. German. doi: 10.1007/s00108-018-0435-0.

20. Bogović Crnčić T, Girotto N, Ilić Tomaš M, et al. Innate Immunity in Autoimmune Thyroid Disease during Pregnancy. Int J Mol Sci. 2023 Oct 22;24(20):15442. doi: 10.3390/ijms242015442.

Received 27.12.2023
Revised 04.03.2024
Accepted 20.03.2024

Information about authors

Oleksandr Paienok, MD, DSc, PhD, Professor, Associate Professor at the Department of Obstetrics and Gynecology, Medical Faculty 1, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine; e-mail: alex.payenok@gmail.com; https://orcid.org/0000-0002-8517-7424

Anzhelika Paienok, MD, DSc, PhD, Professor, Head of the Department of Neuropathology and Neurosurgery of Postgraduate Education, Faculty of Postgraduate Education, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine; e-mail: a.payenok@gmail.com; https://orcid.org/0000-0003-0531-751X

Bozhena Zadorozhna, MD, DSc, PhD, Professor, Department of Neuropathology and Neurosurgery of Postgraduate Education, Faculty of Postgraduate Education, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine; e-mail: bozhenazadorozhna@gmail.com; https://orcid.org/0000-0001-6717-5233

Bohdan Hrytsyshyn, PhD, Obstetrician and Gynecologist, Lviv Regional Clinical Hospital, Lviv, Ukraine; e-mail: bohdanhrytsyshyn@gmail.com; https://orcid.org/0009-0007-9819-7866

Serhii Ihnatovych, Obstetrician and Gynecologist, Lviv Regional Clinical Hospital, Lviv, Ukraine; e-mail: sergiyignatovich@gmail.com

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

Паєнок О.С.[1], Паєнок А.В.[1], Задорожна Б.В.[1], Грицишин Б.Р.[2], Ігнатович С.В.[2]
[1] Львівський національний медичний університет імені Данила Галицького, м. Львів, Україна
[2] КНП ЛОР «Львівська обласна клінічна лікарня», м. Львів, Україна

Вплив патології щитоподібної залози на стан біоелектричної активності головного мозку у вагітних

Резюме. ***Актуальність.*** Захворювання щитоподібної залози під час вагітності є другими за поширеністю ендокринними розладами після гестаційного діабету. Гормони щитоподібної залози мають вирішальне значення для росту та дозрівання багатьох тканин, особливо головного мозку й скелета. У критичні періоди в першому триместрі вагітності материнський тироксин необхідний для розвитку плода, оскільки він забезпечує тканини, залежні від тиреоїдних гормонів. ***Мета дослідження:*** вивчити особливості біоелектричної активності головного мозку у вагітних із патологією щитоподібної залози та частоту таких змін. ***Матеріали та методи.*** У 160 вагітних із патологією щитоподібної залози визначали стан біоелектричної активності головного мозку методом електроенцефалографії. Біопотенціали досліджували за допомогою програмно-апаратного комплексу DX-NT32 з програмним забезпеченням DX Complexes (Харків, Україна) та комп'ютерної обробки електроенцефалограм. Електроди в кількості 16 штук застосовували за міжнародною схемою 10/20 в біполярній інтерпретації. ***Результати.*** Виявлено специфічні зміни на електроенцефалограмах, характерні для кожного виду тиреоїдної патології, що залежать від її тяжкості. Встановлені порушення негативно впливають на перебіг вагітності та пологів у жінок із патологією щитоподібної залози. У таких пацієнток виявлено підвищену тривожність із депресивними нахилами, зниження загальної активності, відчуття пригніченості, тривоги, зниження настрою. Виявлені критерії дають змогу віднести ці зміни до проявів патологічного невротичного стану в умовах дезадаптації, що підтверджено даними електроенцефалографії. ***Висновки.*** Порушення спонтанної та викликаної діяльності мозку свідчать про наявність церебральної основи психологічного стресу, що має якісний ефект на електроенцефалографічні дані. Набуті порушення негативно впливають на перебіг вагітності, пологи, перинатальні наслідки та подальший розвиток дитини.

Ключові слова: вагітність; щитоподібна залоза; дифузний нетоксичний зоб; дифузний токсичний зоб; електроенцефалографія