UDC: 618.3+616.441-006.5]-036.8

The course of pregnancy and its result in women who have diffuse non-toxic goiter

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Key words: goiter, pregnancy, parturition, obstetric labor complications.

Pathologia 2018; 15 (1), 34–37

DOI: 10.14739/2310-1237.2018.1.129187

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Aim – to study the peculiarities of the pregnancy course and its result with women who have diffuse non-toxic goiter.

Materials and methods. The course of pregnancy and its result in 75 women with diffuse non-toxic goiter and in 75 women without thyroid pathology has been studied. The amount of thyroid-stimulating hormone (TSH), free triiodothyronine (FT_3) and free thyroxin (FT_4) was defined in blood serum, the concentration of iodine – in urine.

Results. The pregnancy in women who have diffuse non-toxic goiter goes with mild iodine deficiency (median 66.0 μg/l), an increase in TSH, a decrease in thyroid hormones and an integral thyroid index, compared with pregnant women without pathology of the thyroid gland. In 78.7 % (95 % CI 68.1–86.4 %) of women with diffuse non-toxic goiter, the thyroid gland enlargement is first detected during pregnancy. In 32.0 % (95 % CI 22.5–43.2 %) of women with diffuse nontoxic goiter in the second half of pregnancy subclinical hypothyroidism is developed. The presence of diffuse non-toxic goiter in the pregnant in comparison with the women without thyroid pathology increases the possibility of spontaneous abortion (OR 4.2; 95 % CI 2.0–8.9), iron-deficiency anemia (OR 2.3; 95 % CI 1.1–4.8), preeclampsia (OR 2.7; 95 % CI 1.2–6.2), placental dysfunction (OR 6.3; 95 % CI 3.1–12.8), fetal growth retardation (OR 5.6; 95% CI 1.2–26.6), premature labor (OR 5.6; 95 % CI 1.2–26.6), untimely outpouring of amniotic fluid (OR 2.2; 95 % CI 1.1–4.4), labor abnormalities (OR 2.8; 95 % CI 1.2–7.0).

Conclusions. In women with diffuse non-toxic goiter the likelihood of complications increases during pregnancy and childbirth, which points to the need to develop therapeutic and preventive measures aimed at their reduction.

Ключові слова: зоб, вагітність, пологи, акушерські ускладнення.

Патологія. – 2018. – Т. 15, № 1(42). – С. 34–37

Перебіг вагітності та її завершення в жінок із дифузним нетоксичним зобом

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Мета роботи – вивчити особливості перебігу вагітності та її завершення в жінок із дифузним нетоксичним зобом.

Матеріали та методи. Оцінили перебіг вагітності та її завершення в 75 жінок із дифузним нетоксичним зобом і в 75 жінок без патології щитоподібної залози. У сироватці крові визначили вміст тиреотропного гормона (ТТГ), вільного трийодтироніну ($вТ_3$) і вільного тироксину ($вТ_4$), в сечі – концентрації йоду.

Результати. Вагітність у жінок із дифузним нетоксичним зобом перебігає на тлі йодної недостатності легкого ступеня (медіана 66,0 мкг/л), збільшення ТТГ, зниження тиреоїдних гормонів та інтегрального тиреоїдного індексу порівняно з вагітними без патології щитоподібної залози. Збільшення щитоподібної залози під час вагітності виявляють у 78,7 % (95 % ДІ 68,1–86,4 %) жінок. У 32,0 % (95 % ДІ 22,5–43,2 %) жінок із дифузним нетоксичним зобом у другій половині вагітності розвивається субклінічний гіпотиреоз. Наявність у вагітних дифузного нетоксичного зоба, порівняно з жінками без патології щитоподібної залози, збільшує ймовірність загрози мимовільного аборту (ВШ 4,2; 95 % ДІ 2,0–8,9), залізодефіцитної анемії (ВШ 2,3; 95% ДІ 1,1–4,8), прееклампсії (ВШ 2,7; 95 % ДІ 1,2–6,2), плацентарної дисфункції (ВШ 6,3; 95 % ДІ 3,1–12,8), затримки росту плода (ВШ 5,6; 95 % ДІ 1,2–26,6), завершення вагітності передчасними пологами (ВШ 5,6; 95 % ДІ 1,2–26,6), несвоєчасного відходження навколоплідних вод (ВШ 2,2; 95 % ДІ 1,1–4,4), аномалій пологової діяльності (ВШ 2,8; 95 % ДІ 1,2–7,0).

Висновки. У жінок із дифузним нетоксичним зобом підвищується ймовірність ускладнень під час вагітності та в пологах, що вказує на необхідність розробки лікувально-профілактичних заходів, спрямованих на їхнє зниження.

Ключевые слова: зоб, беременность, роды, акушерские осложнения.

Патология. – 2018. – Т. 15, № 1(42). – С. 34–37

Течение беременности и ее исход у женщин с диффузным нетоксическим зобом

Л. П. Шелестова, Н. Н. Радченко

Цель работы – изучить особенности течения беременности и ее исход у женщин с диффузным нетоксическим зобом.

Материалы и методы. Оценено течение беременности и ее исход у 75 женщин с диффузным нетоксическим зобом и у 75 женщин без патологии щитовидной железы.

Результаты. Беременность у женщин с диффузным нетоксическим зобом протекает на фоне йодной недостаточности легкой степени (медиана 66,0 мкг/л), увеличения ТТГ, снижения тиреоидных гормонов и интегрального тиреоидного индекса по сравнению с беременными без патологии щитовидной железы. Увеличение щитовидной железы во время беременности отмечено у 78,7 % (95 % ДИ 68,1–86,4 %) женщин. У 32,0 % (95 % ДИ 22,5–43,2 %) женщин с диффузным нетоксическим зобом во второй половине беременности развивается субклинический гипотиреоз. Наличие у беременных диффузного нетоксического зоба, в сравнении с женщинами без патологии щитовидной железы, увеличивает вероятность угрозы самопроизвольного аборта (ОШ 4,2; 95 % ДИ 2,0–8,9), железодефицитной анемии (ОШ 2,3; 95 % ДИ 1,1–4,8), преэклампсии (ОШ 2,7; 95 % ДИ 1,2–6,2), плацентарной дисфункции (ОШ 6,3; 95 % ДИ 3,1–12,8), задержки

роста плода (ОШ 5,6; 95 % ДИ 1,2–26,6), преждевременных родов (ОШ 5,6; 95 % ДИ 1,2–26,6), несвоевременного излития околоплодных вод (ОШ 2,2; 95 % ДИ 1,1–4,4), аномалий родовой деятельности (ОШ 2,8; 95 % ДИ 1,2–7,0).

Выводы. У женщин с диффузным нетоксическим зобом увеличивается вероятность осложнений во время беременности и в родах, что указывает на необходимость разработки лечебно-профилактических мероприятий, направленных на их снижение.

The most common form of thyroid pathology among women is diffuse non-toxic goiter, the diagnosing of which happens more often during pregnancy and lactation [1–3]. Its frequency depends on the content of iodine in the environment and fluctuates from 5–10 % to 80–90 % [1]. Nowadays it is generally admitted that iodine deficiency goiter is latent hypothyreosis: hyperplastic thyroid tissue can support euthyroid state only for a certain time. Long-time influence of factors that damage the reserved compensatory abilities of goiter-changed thyroid runs out and its further enlargement can't stop thyroid deficiency [1, 2]. As a result of increased demand of body in thyroid hormones, especially during pregnancy, after-labour period and during lactation it is possible that at first signs of subclinical and then manifesting hypothyreosis can appear [4,5], that may negatively affect the pregnancy and its results.

Aim

To study the peculiarities of the course of pregnancy and its result in women who have diffuse non-toxic goiter.

Materials and methods

The course of pregnancy and its result in 75 women with diffuse non-toxic goiter has been studied. Criteria for inclusion of patients into the group with diffuse non-toxic goiter: the thyroid gland volume is more than 18 cm^3 according to the echography; absence of autoimmune process; registration in the women's consultation in the first trimester of gestation; absence of concomitant severe extragenital pathology. A group of patients without pathology of the thyroid gland and iodine deficiency comprised 75 women in the same gestation period. During registration for pregnancy all the women were consulted by the endocrinologist.

According to visual-palpatory evaluation of patients' thyroid the preliminary information about form, size, consistence and mobility of thyroid were obtained.

The diagnosis of diffuse enlargement of thyroid was based on the results of the ultrasonography made on the apparatus ALOKA-SSD-550-7,5 mHz (Japan). Thyroid volume was calculated by the formula of J. Brunn et al. (1981) [6].

The study of the thyroid status of pregnant women was carried out by determining serum levels of thyroid-stimulating hormone (TSH) and free thyroid hormones (free triiodothyronine (FT_3) and free thyroxin (FT_4)) levels in the blood serum and by immunoenzymatic method with the help of set of the company "Chema-Medica" (Moscow) and "Thyroid IFA-TTG" (Saint-Petersburg). Using the obtained data the integral thyroid index was calculated – this is the rate of thyroid hormones to their hypophyseal regulator according to the formula:

$$\text{Integral thyroid index} = \frac{FT_3 + FT_4}{TSH}.$$

In norm the integral thyroid index equals to 7.04–27.21, the decrease of this index reflects even the initial stages of hypothyreosis [7].

For evaluation of the severity of autoimmune reactions the antibodies to the thyroid tissue – thyroglobulin were defined with the help of set "Thyroid IFA-TTG" (Saint-Petersburg) and microsomal fraction – "EIAgen Anti – TMAb" (Italy). The concentration of iodine in the urine was determined by the cerium-arsenic method.

The processing of statistical information data was held with the usage of software SPSS Statistics17.0. As the majority of variables didn't correspond to normal distribution, they were represented by median (Me) and interquartile latitude – 25 and 75 percentile (25; 75 %). The comparison of indexes between groups was held with the help of non-parametric Mann–Whitney U-test. For frequency 95 % confidence interval (95 % CI) was defined by Wilson method. The comparisons of qualitative features were held by applying of Pearson Chi-square criterion with Yates's correction. Odds ratio (OR) and 95 % CI to this number was calculated.

Results and discussion

When assessing ioduria, it was noted that the median in pregnant women with diffuse non-toxic goiter corresponded to mild iodine deficiency (66.0 (50.2; 78.4) μg/l). According to the study, 77.3 % (58 of 75) of this group had mild iodine deficiency, and 22.7 % (17 of 75) had an average degree. Iodine preparations were prescribed for women of this group, according to the order of the Ministry of Health of Ukraine No. 415 of 15.07.2011. In pregnant women without a pathology of the thyroid gland, the excretion of iodine in the urine was 206 (160.2; 228.0) μg/l and corresponded to the normal iodine content.

In the pregnant with diffuse non-toxic goiter in comparison with the pregnant without thyroid pathology the statistically significant enlargement of TSH concentration was observed (2.9 (2.7; 3.2) against 2.3 (1.9; 2.6) μIU/ml; U = 613, Z = -8.3, P < 0.001) and decrease of thyroid hormones (FT_3 – (6.2 (5.9; 6.6) against 6.5 (6.1; 6.9) pmol/l; U = 2246, Z = -2.1, P = 0.033 and FT_4 – (15.1 (13.7; 16.4) against 15.8 (15.2; 17.0) pmol/l; U = 2129, Z = -2.6, P = 0.010). It is necessary to point out that in the pregnant who had diffuse non-toxic goiter the rate of integral thyroid index testified the initial state of hypothyreosis (7.4 (6.7; 8.3)) and were statistically significantly lower than in the pregnant without thyroid pathology – (9.4 (8.3; 12.1); U = 0, Z = -10.6, P < 0.001). In 28 (37.3 %, 95 % CI 27.3–48.6 %) of pregnant women, the index was below 7.04, indicating the initial stages of subclinical hypothyroidism (*Fig. 1*).

It should be noted that in 24 (32.0 %, 95 % CI 22.5–43.2 %) of women in the second half of pregnancy subclinical hypothyroidism developed. Diagnosis of sub-

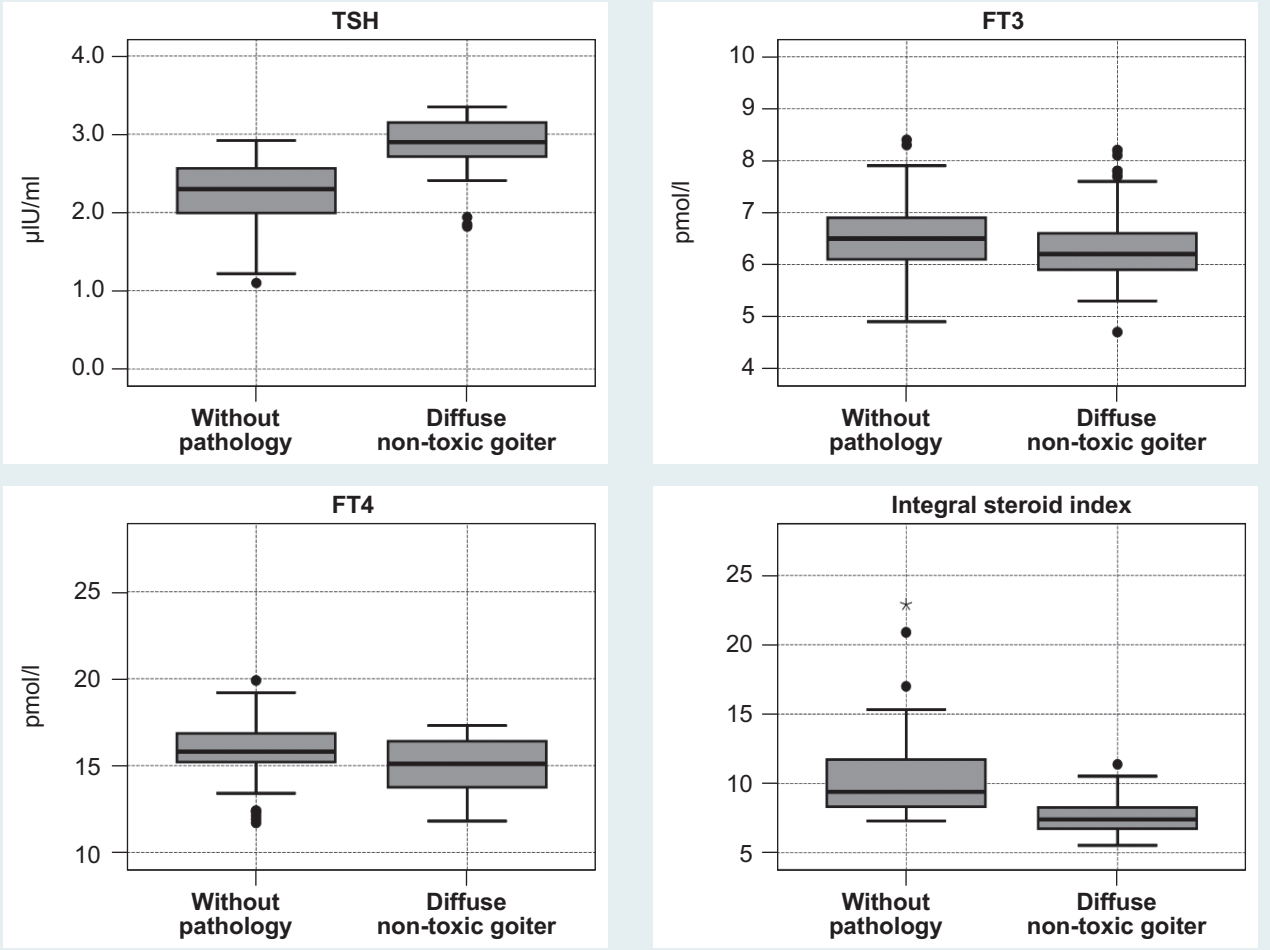

Fig. 1. The peculiarities of the main indicators of thyroid system in women who have diffuse non-toxic goiter.

clinical hypothyroidism was set on the basis of an increase in the TSH content of more than 3.0 μIU/ml for pregnant women in the second-third trimesters of pregnancy, the content of FT3 and FT4 was normal [8]. For pregnant women with subclinical hypothyroidism hormone replacement therapy with L-thyroxine preparations followed by TSH level control every 4 weeks during pregnancy was prescribed. The dose of L-thyroxine was selected individually so that the TSH level was less than 2.5 μU/l and was calculated on the basis of 1.2 μg/kg per day.

The increase of antibody titer to thyroglobulin and to microsomal fraction of thyroid gland was revealed with none of the pregnant.

Due to the research held it was registered that in the majority of women with diffuse non-toxic goiter, that is with 59 out of 75, that equaled to 78.7 % (95 % CI 68.1–86.4 %), the enlargement of thyroid was revealed namely during pregnancy, perhaps this is connected with the fact that during pregnancy the woman's thyroid experiences additional stress, the functional activity of thyroid increases and pregnancy can often provoke pathology of thyroid gland [1,4,5].

Analyzing the complaints of the pregnant it was noted that 21 (28.0 %; 95 % CI 19.1–39.0 %) patients with diffuse non-toxic goiter had clinical symptoms that are typical to hypofunction of thyroid: dry skin, weakness, drowsiness, light pasty of eyelids and face, brittle or hair loss, headache, constipation. But, according to our point of view the given percent can be reduced due to the fact that women could connect these symptoms with pregnancy and not pay the proper attention to them.

The study of obstetrician anamnesis showed that 9 (31.0 %) out of 29 re-pregnant women with diffuse non-toxic goiter had spontaneous abortion in anamnesis while there were only 3 (7.5 %) out of 40 re-pregnant women without thyroid pathology, the difference is statistically significant ($\chi^2_{(1)} = 4.947$, P = 0.026).

Thus, the existence of diffuse non-toxic goiter increases the possibility of spontaneous abortion more than by five times (OR 5.6 %; 95 % CI 1.3–22.9) that corresponds to the literature data [2,5,9] about the fact that dysfunction of thyroid holds the first place among the causes of pregnancy miscarriage.

The course of the present pregnancy in women who have diffuse non-toxic goiter statistically significantly more often than in women without such pathology was complicated with the danger of spontaneous abortion (correspondingly 37 (49.3 %) cases against 14 (18.7 %); $\chi^2_{(1)} = 14.379$, P < 0.001; OR 4.2; 95 % CI 2.0–8.9), iron-deficiency anemia (29 (38.7 %) against 16 (21.3 %); $\chi^2_{(1)} = 4.571$, P = 0.033; OR 2.3; 95 % CI 1.1–4.8), pre-eclampsia (22 (29.3 %) against 10 (13.3 %); $\chi^2_{(1)} = 4.807$,

P = 0.028; OR 2.7; 95 % CI 1.2–6.2), placental dysfunction (51 (68.0 %) against 19 (25.3 %); $\chi^2_{(1)}$ = 25.741, P < 0.001; OR 6.3; 95 % CI 3.1–12.8), fetal growth retardation – (10 (13.3 %) against 2 (2.7 %); $\chi^2_{(1)}$ = 4.438, P = 0.035; OR 5.6; 95 % CI 1.2–26.6).

Also gestational course both in women who have diffuse non-toxic goiter and in women without thyroid pathology was complicated with edema of the pregnant (correspondingly 23 (30.7 %) and 17 (22.7 %); $\chi^2_{(1)}$ = 0.852, P = 0.356; OR 1.5; 95 % CI 0.7–3.1), hypotension (17 (22.7 %) and 9 (12.0 %); $\chi^2_{(1)}$ = 2.280, P = 0.131; OR 2.1; 95 % CI 0.9–5.2), gestational pyelonephritis (8 (10.7 %) and 5 (6.7 %); $\chi^2_{(1)}$ = 0.337, P = 0.562; OR 1.7; 95 % CI 0.5–5.4).

It should be noted that during electrocardiographic examination the deviations were revealed characterized by decrease in voltage, violation of all types of conductivity and rhythm (26 (34.7 %) against 13 (17.3 %); $\chi^2_{(1)}$ = 4.990, P = 0.026; OR 2.5; 95 % CI 1.2–5.4) in every third woman with diffuse non-toxic goiter.

Initial unfavourable background and complicated course of pregnancy in women who have diffuse non-toxic goiter reflected both in the course of pregnancy and labor results. In women who have diffuse non-toxic goiter premature labor happened more often than with women without pathology in thyroid gland (10 (13.3 %) against 2 (2.7 %); $\chi^2_{(1)}$ = 4.438, P = 0.035; OR 5.6; 95 % CI 1.2–26.6), untimely outpouring of amniotic fluid (29 (38.7 %) against 17 (22.7 %); $\chi^2_{(1)}$ = 3.794, P = 0.051; OR 2.2; 95 % CI 1.1–4.4), labor abnormalities (19 (25.3 %) against 8 (10.7 %); $\chi^2_{(1)}$ = 4.517, P = 0.034; OR 2.8; 95 % CI 1.2–7.0). Also the tendency to the increase of frequency of Caesarian section (15 (20.0 %) against 7 (9.3 %); $\chi^2_{(1)}$ = 2.610, P = 0.106; OR 2.4; 95 % CI 0.9–6.4) was registered in women who have diffuse non-toxic goiter.

Conclusions

1. In pregnant women with diffuse non-toxic goiter, the median corresponds to a mild degree of iodine deficiency (66.0 μg/l), a statistically significant increase in TSH, a decrease in thyroid hormones and an integral thyroid index, compared with pregnant women without pathology of the thyroid gland.

2. In 78.7 % (95 % CI 68.1–86.4 %) of women with diffuse non-toxic goiter, the thyroid gland enlargement is first detected during pregnancy. In 32.0 % (95 % CI 22.5–43.2 %) of women with diffuse nontoxic goiter in the second half of pregnancy subclinical hypothyroidism is developed.

3. In women with diffuse non-toxic goiter the likelihood of complications during pregnancy and childbirth increases, which points to the need to develop therapeutic and preventive measures aimed at their reduction.

Prospects for future scientific research. There is currently no national guidance orders, which clearly highlights the issues of diagnosis and treatment of changes in the thyroid gland in pregnant women. It is advisable to develop them, taking into account the existing recommendations of the American and European associations, which in recent years have been referenced by leading Ukrainian endocrinologists. The revealed complications during pregnancy and labor in women who have diffuse non-toxic goiter point to the necessity of working out the treatment and preventive measures aiming to reduction of obstetric complications.

Conflicts of Interest: authors have no conflict of interest to declare.
Конфлікт інтересів: відсутній.

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Надійшла до редакції / Received: 05.09.2017
Після доопрацювання / Revised: 20.12.2017
Прийнято до друку / Accepted: 09.01.2018

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