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Endocrine and Metabolic Predictors of Adverse Pregnancy Outcomes in Women with Autoimmune Thyroiditis

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Abstract: Autoimmune thyroiditis (AIT) is one of the most common endocrine disorders in women of reproductive age and is associated with a high risk of metabolic disturbances and adverse pregnancy outcomes. The aim of the present study was to evaluate endocrine and metabolic predictors of unfavorable gestational and perinatal outcomes in pregnant women with autoimmune thyroiditis, hypothyroidism, and obesity. A prospective comparative clinical study was conducted involving 120 pregnant women divided into a main group consisting of women with autoimmune thyroiditis, hypothyroidism, and obesity, and a control group of healthy pregnant women. Comprehensive clinical, hormonal, biochemical, and ultrasound examinations were performed, including assessment of thyroid-stimulating hormone, free thyroxine, anti-thyroid peroxidase antibodies, selenium, vitamin D, calcium, lipid profile, and glucose metabolism parameters. The study demonstrated that women with autoimmune thyroiditis had significant endocrine and metabolic abnormalities characterized by elevated TSH levels, reduced free thyroxine concentrations, obesity, dyslipidemia, insulin resistance, and micronutrient deficiencies. These disturbances were associated with a significantly increased frequency of threatened miscarriage, preeclampsia, placental insufficiency, preterm birth, fetal growth restriction, and impaired neonatal adaptation. The findings confirm that autoimmune thyroiditis should be considered a multifactorial systemic disorder affecting both maternal metabolism and pregnancy outcomes. Early diagnosis of thyroid dysfunction and metabolic imbalance, together with personalized management and micronutrient correction, may improve obstetric and perinatal outcomes in women with autoimmune thyroid disease.

Keywords: Autoimmune thyroiditis, pregnancy, hypothyroidism, obesity, metabolic disorders, endocrine dysfunction, perinatal outcomes, thyroid hormones, micronutrient deficiency, insulin resistance.

Introduction: In recent years, thyroid disorders have become one of the leading endocrine pathologies among women of reproductive age. Autoimmune thyroiditis (AIT) is of particular clinical importance, as it represents the main cause of hypothyroidism during pregnancy and is associated with a high risk of obstetric and perinatal complications [1,5]. According to current studies, the prevalence of autoimmune thyroid diseases among women of reproductive age reaches 10–26%, while subclinical forms of thyroid dysfunction frequently remain undiagnosed before pregnancy [2].

Pregnancy is accompanied by profound hormonal, immunological, and metabolic changes that may trigger the manifestation or progression of autoimmune thyroid disorders. Even minor disturbances in thyroid function can adversely affect implantation, placentation, and fetal development, increasing the risk of miscarriage, preeclampsia, preterm birth, and fetal growth restriction [19,20]. Subclinical hypothyroidism and the presence of thyroid peroxidase antibodies are particularly associated with unfavorable pregnancy outcomes, even in the absence of pronounced clinical symptoms [11].

Recent studies indicate a close relationship between autoimmune thyroiditis and systemic metabolic disturbances, including insulin resistance, dyslipidemia,

endothelial dysfunction, and chronic inflammation [17]. These changes are considered important pathogenetic mechanisms underlying placental insufficiency and adverse perinatal outcomes. Nutritional factors, especially deficiencies of iodine, selenium, and vitamin D, also play a significant role in the progression of autoimmune processes and metabolic imbalance [10].

Despite the increasing number of studies devoted to thyroid pathology during pregnancy, the issues of early diagnosis and prediction of adverse pregnancy outcomes in women with AIT remain insufficiently investigated. There are still no unified approaches to identifying endocrine and metabolic predictors associated with gestational complications. Therefore, further investigation of the relationship between autoimmune thyroiditis, metabolic disorders, and adverse perinatal outcomes is highly relevant for improving early diagnosis, prevention, and personalized pregnancy management strategies.

Autoimmune thyroiditis is a chronic inflammatory disease of the thyroid gland characterized by lymphocytic infiltration, production of thyroid autoantibodies, and gradual impairment of thyroid function. Among endocrine disorders in women of reproductive age, AIT occupies a leading position and is considered the primary cause of hypothyroidism [1]. Over the past decade, the prevalence of autoimmune thyroid diseases has steadily increased, leading to growing scientific interest in their impact on reproductive health and pregnancy outcomes [5].

Physiological pregnancy is associated with significant alterations in endocrine and immune system activity. Increased demand for thyroid hormones, changes in the hypothalamic–pituitary–thyroid axis, and immunological adaptation during gestation create favorable conditions for the development or progression of thyroid dysfunction [2]. Even subclinical thyroid abnormalities may negatively affect the course of pregnancy and fetal development [3].

Current evidence demonstrates that autoimmune thyroiditis in pregnant women is associated with an increased risk of miscarriage, preterm birth, preeclampsia, placental insufficiency, and fetal growth restriction [19,20]. The pathogenesis of these complications is multifactorial and includes not only hormonal disturbances but also pronounced metabolic abnormalities. Deficiency of thyroid hormones contributes to impaired carbohydrate and lipid metabolism, insulin resistance, dyslipidemia, and endothelial dysfunction, ultimately leading to placental circulation disorders and chronic fetal hypoxia [17].

Nutritional factors are also essential in the development and progression of autoimmune thyroid disease. Deficiencies of iodine, selenium, and vitamin D have been shown to exacerbate autoimmune inflammation, impair thyroid hormone synthesis, and aggravate metabolic disorders [10]. Therefore, correction of micronutrient deficiencies is increasingly considered an important component of comprehensive management in pregnant women with AIT.

In addition to endocrine and metabolic changes, immunological mechanisms play a crucial role in the pathogenesis of pregnancy complications associated with AIT. Proinflammatory cytokines, imbalance of T-helper cell populations, and thyroid autoantibodies may interfere with implantation and placentation processes [18]. Furthermore, thyroid autoimmunity contributes to systemic inflammatory responses and vascular dysfunction, which additionally increase the risk of adverse perinatal outcomes.

Thus, autoimmune thyroiditis should be regarded as a multifactorial disorder exerting systemic effects on maternal health and pregnancy progression. Identification of endocrine and metabolic predictors of adverse pregnancy outcomes is essential for improving diagnostic accuracy, developing personalized management strategies, and optimizing perinatal outcomes in women with autoimmune thyroid disease.

The aim of this study was to evaluate endocrine and metabolic predictors of adverse pregnancy outcomes in women with autoimmune thyroiditis, as well as to assess the impact of thyroid dysfunction, obesity, and micronutrient imbalance on the course of gestation and perinatal outcomes. In addition, the study aimed to improve approaches to early diagnosis, risk stratification, and personalized management of pregnant women with autoimmune thyroid disease.

METHODS

The study was carried out at the multidisciplinary clinic and maternity complex of Samarkand State Medical University and had a prospective comparative clinical design. A total of 120 pregnant women were examined and divided into two groups according to thyroid status and metabolic characteristics. The main group included 60 pregnant women diagnosed with autoimmune thyroiditis, hypothyroidism, and obesity, while the control group consisted of 60 apparently healthy pregnant women without thyroid pathology.

The diagnosis of autoimmune thyroiditis was established on the basis of clinical examination, hormonal profile assessment, detection of thyroid peroxidase antibodies (anti-TPO), and ultrasound examination of the thyroid gland. Inclusion criteria comprised confirmed autoimmune thyroiditis, pregnancy at different gestational ages, and informed

consent to participate in the study. Women with severe endocrine disorders unrelated to thyroid disease, severe somatic or infectious pathology, and those who failed to comply with the study protocol were excluded from the investigation.

All participants underwent comprehensive clinical, laboratory, hormonal, biochemical, and ultrasound examinations. Clinical evaluation included assessment of endocrine-related symptoms such as fatigue, somnolence, emotional lability, dry skin, constipation, hair loss, sleep disturbances, and excessive weight gain. Hormonal investigations included serum thyroid-stimulating hormone (TSH), free thyroxine (fT4), and anti-TPO levels measured by enzyme-linked immunosorbent assay. In addition, serum selenium, vitamin D, calcium, glucose, and lipid profile parameters were determined in all pregnant women.

Ultrasound examination of the thyroid gland and fetal screening were performed at 12–14, 22–24, and 32–34 weeks of gestation. Particular attention was paid to placental condition, fetal growth, and fetal brain development due to the known influence of maternal thyroid dysfunction on neurodevelopmental outcomes.

Pregnant women in the main group received standard therapy combined with micronutrient correction, including selenium, vitamin D, and calcium supplementation, as well as lifestyle modification involving dietary intervention and controlled physical activity. Patients were monitored throughout pregnancy by obstetricians, endocrinologists, and rehabilitation specialists. Pregnancy outcomes assessed during the study included threatened miscarriage, gestational anemia, preeclampsia, placental insufficiency, preterm birth, fetal growth restriction, and neonatal condition evaluated according to Apgar score and anthropometric indicators.

Statistical analysis was performed using standard methods of medical statistics. Quantitative data were expressed as mean ± standard deviation (M±m). The significance of differences between groups was assessed using Student's t-test, and a p-value of less than 0.05 was considered statistically significant.

RESULTS

The analysis of clinical and demographic characteristics demonstrated that the pregnant women included in the study were comparable at baseline. The mean age of women in the main group was 26.8±3.2 years, whereas in the control group it was 27.1±3.5 years, with no statistically significant difference between the groups ($p>0.05$). The majority of participants in both groups were multiparous women of reproductive age.

Assessment of anthropometric parameters revealed significant metabolic disturbances in pregnant women with autoimmune thyroiditis and hypothyroidism. The mean body weight in the main group was 88.4±6.2 kg compared to 79.1±5.9 kg in the control group ($p<0.05$). Body mass index (BMI) was significantly higher in the main group, reaching 32.3±2.1 kg/m² versus 24.8±1.9 kg/m² in healthy pregnant women ($p<0.001$), confirming the presence of obesity and metabolic imbalance among women with thyroid dysfunction.

Clinical symptom analysis showed that manifestations of hypothyroidism were significantly more frequent in the main group. General weakness and fatigue were observed in 73.3% of patients with autoimmune thyroiditis compared to 28.3% in the control group ($p<0.001$). Somnolence and apathy were detected in 66.7% and 21.7% of women, respectively ($p<0.001$). Dry skin was reported in 63.3% of women in the main group versus 18.3% in controls ($p<0.001$), while hair loss occurred in 56.7% and 16.7% of cases, respectively ($p<0.001$). Constipation was identified in 46.7% of women with thyroid dysfunction compared to 13.3% in the control group ($p<0.01$). Increased sensitivity to cold and emotional instability were also significantly more prevalent among women with autoimmune thyroiditis ($p<0.05$).

Laboratory investigations demonstrated characteristic hormonal alterations associated with autoimmune thyroiditis and hypothyroidism. Serum TSH levels in the main group were significantly elevated and reached 4.8±1.2 mIU/L, whereas in the control group the mean TSH level was 2.1±0.8 mIU/L ($p<0.001$). Free thyroxine (fT4) concentrations were lower in women with thyroid pathology, accounting for 10.6±1.8 pmol/L compared to 14.2±2.1 pmol/L in healthy pregnant women ($p<0.001$). Anti-thyroid peroxidase antibody (anti-TPO) levels were markedly increased in the main group (185±42 IU/mL) in comparison with the control group (34±11 IU/mL; $p<0.001$), confirming active autoimmune thyroid inflammation.

Analysis of micronutrient status revealed significant deficiencies in women with autoimmune thyroiditis. Selenium levels in the main group were reduced to 63.2±8.6 µg/L compared to 91.4±7.2 µg/L in the control group ($p<0.001$). Vitamin D deficiency was also pronounced, with serum concentrations of 19.1±4.3 ng/mL in the main group versus 33.6±5.2 ng/mL in healthy pregnant women ($p<0.001$). Calcium levels were significantly lower in women with thyroid dysfunction (2.08±0.12 mmol/L) than in controls (2.29±0.10 mmol/L; $p<0.01$).

Biochemical analysis showed evidence of metabolic abnormalities in the main group. Total cholesterol levels reached 5.6±0.8 mmol/L compared to 4.5±0.6

mmol/L in the control group (p<0.01), while triglyceride concentrations were significantly elevated (2.1±0.4 mmol/L versus 1.4±0.3 mmol/L; p<0.01). Fasting glucose levels were also higher in women with autoimmune thyroiditis and obesity, accounting for 5.8±0.6 mmol/L compared to 4.7±0.5 mmol/L in healthy pregnant women (p<0.05), indicating the presence of insulin resistance and metabolic dysregulation.

Complete blood count analysis demonstrated lower hemoglobin levels in the main group (84.6±8.2 g/L) than in controls (95.2±7.9 g/L; p<0.01), suggesting a higher prevalence of gestational anemia among women with endocrine pathology. Leukocyte counts remained within physiological ranges in both groups and did not differ significantly (p>0.05).

Coagulation profile assessment revealed signs of hypercoagulability in pregnant women with autoimmune thyroiditis. Fibrinogen levels were elevated in the main group (4.5±0.6 g/L) compared with controls (3.8±0.4 g/L; p<0.05), whereas activated partial thromboplastin time (APTT) was slightly shortened (26.4±2.8 s versus 29.1±2.5 s; p<0.05), reflecting increased thrombotic potential and impaired placental circulation.

Evaluation of pregnancy outcomes demonstrated significantly higher rates of obstetric complications in women with autoimmune thyroiditis, hypothyroidism, and obesity. Threatened miscarriage was diagnosed in 36.7% of women in the main group compared to 11.7% in controls (p<0.01). Preeclampsia developed in 21.7% versus 6.7% of pregnant women, respectively (p<0.05). Placental insufficiency was observed in 30.0% of cases in the main group and only 8.3% in healthy women (p<0.01). Preterm birth occurred in 18.3% of women with endocrine pathology compared to 5.0% in the control group (p<0.05), while fetal growth restriction was diagnosed in 16.7% and 3.3% of cases, respectively (p<0.05).

Neonatal outcomes were also significantly worse among infants born to mothers with autoimmune thyroiditis. The mean Apgar score at 1 minute was 6.8±0.7 in the main group compared to 7.9±0.6 in controls (p<0.01). Mean neonatal birth weight was significantly lower in the main group (2860±320 g) than in healthy pregnant women (3340±290 g; p<0.01). Cases of neonatal hypoxia and early adaptation disorders were more frequent among newborns of mothers with thyroid dysfunction.

Overall, the obtained results demonstrate that autoimmune thyroiditis, hypothyroidism, obesity, and associated micronutrient deficiencies are accompanied by significant endocrine and metabolic disturbances, contributing to a substantial increase in adverse obstetric and perinatal outcomes.

DISCUSSION

The findings of the present study confirm that autoimmune thyroiditis combined with hypothyroidism and obesity represents a significant risk factor for adverse obstetric and perinatal outcomes. The observed association between thyroid dysfunction and metabolic disturbances is consistent with contemporary international data demonstrating the systemic nature of autoimmune thyroid disease during pregnancy [1,5,17].

The increased frequency of gestational complications identified in women with autoimmune thyroiditis may be explained by the complex interaction between endocrine, metabolic, and immunological mechanisms. Current evidence suggests that thyroid hormones play a central role in regulating placental development, vascular adaptation, and fetal growth. Therefore, even subclinical thyroid dysfunction can impair placental circulation and contribute to pregnancy complications [3,20]. Similar conclusions were reported by Turunen et al. [19], who demonstrated a significantly increased risk of preterm birth and hypertensive disorders in women with thyroid dysfunction.

An important aspect of the present study is the confirmation of the relationship between autoimmune thyroiditis and metabolic imbalance, including obesity, dyslipidemia, and impaired glucose metabolism. These findings correspond with the results of Scrinic et al. [17], who emphasized that autoimmune thyroid disease should be considered not only as an endocrine disorder but also as a systemic metabolic condition associated with insulin resistance and endothelial dysfunction. Such disturbances may aggravate placental insufficiency and fetal hypoxia through impaired vascular regulation and chronic inflammatory activation.

The high prevalence of micronutrient deficiencies identified in the study also supports current international concepts regarding the role of selenium, vitamin D, and calcium in thyroid autoimmunity and pregnancy outcomes. Previous investigations have demonstrated that selenium deficiency contributes to oxidative stress and increased autoimmune activity within thyroid tissue, while vitamin D deficiency is associated with immune dysregulation and unfavorable obstetric outcomes [10,18]. In this context, micronutrient correction may represent an important component of comprehensive pregnancy management in women with autoimmune thyroiditis.

The present results additionally highlight the importance of thyroid autoantibodies as independent

predictors of adverse pregnancy outcomes. Contemporary studies indicate that elevated anti-TPO levels may negatively affect implantation, placentation, and fetal development even in euthyroid women [11,18]. This supports the concept that autoimmune mechanisms themselves, independent of overt hormonal deficiency, contribute substantially to reproductive complications.

Particular attention should be paid to the combined effect of autoimmune thyroiditis and obesity observed in this study. Obesity is currently recognized as a chronic low-grade inflammatory state capable of amplifying autoimmune and metabolic disturbances. International studies have demonstrated that excessive adipose tissue influences thyroid hormone metabolism, increases leptin-mediated inflammatory responses, and exacerbates insulin resistance, thereby further increasing the risk of gestational complications [5,17]. The coexistence of obesity and hypothyroidism therefore creates a particularly unfavorable metabolic environment during pregnancy.

The obtained findings support modern recommendations emphasizing the need for early screening and individualized management of pregnant women with thyroid dysfunction. According to the American Thyroid Association guidelines and recent European recommendations, timely detection of thyroid abnormalities and adequate correction of endocrine and metabolic disturbances may significantly improve maternal and fetal outcomes [1,2]. The results of the present study further underline the importance of a multidisciplinary approach involving obstetricians, endocrinologists, nutrition specialists, and rehabilitation professionals.

At the same time, several limitations should be considered. The study was conducted in a single clinical center and involved a relatively limited sample size. In addition, long-term neonatal and neurodevelopmental outcomes were not evaluated. Nevertheless, the consistency of the obtained results with current international literature confirms the clinical relevance of the identified endocrine and metabolic predictors.

Thus, autoimmune thyroiditis in pregnancy should be regarded as a multifactorial systemic disorder associated with significant endocrine, metabolic, and immunological alterations contributing to adverse gestational and perinatal outcomes. Early identification of high-risk patients and implementation of personalized management strategies may improve pregnancy outcomes and reduce the incidence of maternal and neonatal complications.

CONCLUSION

Autoimmune thyroiditis in pregnant women is associated with significant endocrine and metabolic disturbances, including elevated thyroid-stimulating hormone levels, decreased free thyroxine concentrations, obesity, dyslipidemia, impaired carbohydrate metabolism, and micronutrient deficiencies. Women with autoimmune thyroiditis and hypothyroidism demonstrated a significantly higher incidence of adverse obstetric complications, including threatened miscarriage, preeclampsia, placental insufficiency, preterm birth, and fetal growth restriction compared with healthy pregnant women. Elevated anti-thyroid peroxidase antibody levels, obesity, insulin resistance, and deficiencies of selenium and vitamin D may be considered important predictors of unfavorable pregnancy and perinatal outcomes in women with autoimmune thyroid disease. The metabolic and endothelial dysfunction associated with autoimmune thyroiditis contribute to impaired placental circulation and chronic fetal hypoxia, negatively affecting fetal growth and neonatal adaptation. Correction of endocrine and micronutrient imbalance, together with individualized pregnancy management and multidisciplinary monitoring, may improve maternal and perinatal outcomes in women with autoimmune thyroiditis. The obtained findings confirm the necessity of early screening for thyroid dysfunction and metabolic abnormalities during pregnancy, particularly in women with obesity and autoimmune thyroid disease, in order to optimize preventive, diagnostic, and therapeutic strategies.

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